Program Schedule from the 40th American Society of Andrology Annual Meeting

18 – 21 April, 2015

Salt Lake City, Utah
ASA 40th Annual Conference
April 18 – 21, 2015

XXIIIrd North American Testis Workshop
April 15 – 18, 2015

ASA Special Symposium
April 18, 2015

ASA Trainee Directed Mini-Symposium
April 18, 2015

ASA 40th Annual Conference
Forty & Forward
“A Lifetime of Male Reproductive Health”
April 18 – 21, 2015
The Little America Hotel
Salt Lake City, Utah

Program Chairs: Edward D. Kim, MD and William Wright, PhD
Location: Grand Ballroom A-B

FRIDAY, APRIL 17, 2015

2:00 p.m. – 6:00 p.m. Registration/Information Desk Open
Location: Grand Ballroom A Foyer

SATURDAY, APRIL 18, 2015

7:00 a.m. – 7:00 p.m. Registration/Information Desk Open
Location: Grand Ballroom A Foyer

4:00 p.m. – 9:30 p.m. Exhibit Hall Open
Location: Grand Ballroom Reception A-C

11:30 a.m. – 1:00 p.m. ASA LABORATORY SCIENCE FORUM LUNCHEON*
Location: Arizona Laboratory Disaster Preparedness
Susan A. Rothmann, PhD, HCLD
Fertility Solutions, Inc.
(Ticket required)
*Not CME Accredited

1:00 p.m. – 5:15 p.m. ASA 2015 Special Symposium
(See pg 27 for full schedule)

1:30 p.m. – 4:30 p.m. ASA Trainee Directed Mini-Symposium*
(See pg 28 for full schedule)
*Not CME Accredited

6:00 p.m. – 6:10 p.m. Welcome and Opening Remarks

SUNDAY, APRIL 19, 2015

6:30 a.m. – 8:00 a.m. Past President’s Breakfast
Location: Snowbasin

7:00 a.m. – 6:00 p.m. Registration/Information Desk Open
Location: Grand Ballroom A Foyer

7:00 a.m. – 4:00 p.m. Exhibit Hall Open
Location: Grand Ballroom Reception A-C

7:00 a.m. – 8:00 a.m. Continental Breakfast
Location: Grand Ballroom Reception A-C

8:00 a.m. – 9:00 a.m. AUA LECTURE
Reproductive Genetics and the Aging Male
Paul J. Turek, MD, FACS, FRSM
The Turek Clinic
(Introduced by: Dolores J. Lamb, PhD, HCLD)

6:00 p.m. – 6:10 p.m. Welcome Reception
Location: Grand Ballroom Reception A-C

1:00 p.m. – 5:15 p.m. ASA 2015 Special Symposium
(See pg 27 for full schedule)

1:30 p.m. – 4:30 p.m. ASA Trainee Directed Mini-Symposium*
(See pg 28 for full schedule)
*Not CME Accredited

6:00 p.m. – 6:10 p.m. Welcome and Opening Remarks

9:00 a.m. – 9:15 a.m. Distinguished Service Award

© 2015 American Society of Andrology and European Academy of Andrology
Andrology, 2015, Supplement, 1
SCHEDULE AT A GLANCE

9:15 a.m. – 10:45 a.m. SYMPOSIUM I – Basic Science – Stem Cells, Niches and Reproductive Function
Moderator: Jon M. Oatley, PhD

Heterogeneity of Spermatogonia and Its Relationship to the Stem Cell Niche – A Review
Makoto Nagano, PhD, DVM
McGill University

Sertoli Cells Constrain Pluripotent iPS Cells to Form Spermatogenic Cells in Vivo
Renee A. Reijo Pera, PhD
Montana State University

MicroRNA Regulation of Spermatogonial Development
Wei Yan, MD, PhD
University of Nevada School of Medicine

10:45 a.m. – 11:00 a.m. Quick Break

11:00 a.m. – 12:30 p.m. Poster Session I
Location: Grand Ballroom C
*Not CME Accredited
(See pg 51 for full schedule)

12:30 p.m. – 2:00 p.m. Lunch (on your own)

12:30 p.m. – 2:00 p.m. Mentoring Luncheon Sponsored by the Diversity and Trainee Affairs Committees*
Finding Your Path in Andrology
(not included in general registration: separate registration required)
Location: Wyoming
Susan A. Rothmann, PhD, HCLD
Fertility Solutions, Inc.
*Not CME Accredited

2:00 p.m. – 3:30 p.m. CONCURRENT SESSIONS

Oral Session I: Basic Science
Location: Grand Ballroom A-B
Moderator: William Wright, PhD
(See pg 30 for full schedule)

Oral Session II: Clinical
Location: Arizona
Moderator: Edward Kim, MD
(See pg 31 for full schedule)

3:30 p.m. – 4:00 p.m. Refreshment Break
Location: Grand Ballroom Reception A-C

4:00 p.m. – 4:45 p.m. LECTURE I
Reproductive Toxicology: From Science to Public Policy
Sally Perreault Darney, PhD
US Environmental Protection Agency
(Introduced by: Douglas T. Carrell, PhD, HCLD)

4:45 p.m. – 5:30 p.m. LECTURE II
Fertility Preservation in the Male: A New Clinical Paradigm
Robert E. Brannigan, MD
Northwestern University Feinberg School of Medicine
(Introduced by: Edward D. Kim, MD)

5:30 p.m. – 6:00 p.m. ASA 40th Anniversary Special Presentation I
“From Bellbottoms to Bluetooth: 40 Years of Clinical Andrology”
Terry T. Turner, PhD
University of Virginia Health System
Paul J. Turek, MD
The Turek Clinic

6:00 p.m. – 8:00 p.m. Trainee Forum & Mixer
(All Trainee Travel Awards will be distributed and celebrated at this event)
Location: Olympus

MONDAY, APRIL 20, 2015

7:00 a.m. – 6:00 p.m. Registration/Information Desk Open
Location: Grand Ballroom A Foyer

7:00 a.m. – 3:30 p.m. Exhibit Hall Open
Location: Grand Ballroom Reception A-C

7:00 a.m. – 8:00 a.m. Continental Breakfast
Location: Grand Ballroom Reception A-C

8:00 a.m. – 9:00 a.m. WOMEN IN ANDROLOGY LECTURE
Father’s Lasting Influence: Paternal Environment and the Health of his Future Generations
Janice L. Bailey, PhD
Department des Sciences Animales, Universite Laval
(Introduced by: Sophie La Salle, PhD)

9:00 a.m. – 9:15 a.m. Matthew P. Hardy
Young Andrologist Award

© 2015 American Society of Andrology and European Academy of Andrology
Andrology, 2015, Supplement, 2
9:15 a.m. – 10:15 a.m. **SYMPOSIUM II – Special Concerns for Older Fathers**
Co-Chairs: Peter Chan, MD
Keith A. Jarvi, MD

Therapeutic Advances in the Treatment of Peyronie’s Disease
Wayne J.G. Hellstrom, MD, FACS
Tulane University School of Medicine

Impact of Drugs and Environmental Exposures on Sperm Production
Cigdem Tanrikut, MD
Massachusetts General Hospital

Novel Oral Hormone Replacement Therapies: The Era of the SERMs?
Andrew R. McCullough, MD
Albany Medical College

10:15 a.m. – 10:30 a.m. Quick Break

10:30 a.m. – 11:15 a.m. **DIVERSITY LECTURE**
Current Trends in the Treatment of Infertility in Men with Spinal Cord Injury
Nancy Brackett, PhD, HCLD
University of Miami Miller School of Medicine
(Introduced by: Maria Christina W. Avellar, PhD)

11:15 a.m. – 12:30 p.m. **Poster Session II**
Location: Grand Ballroom C
*Not CME Accredited
(See pg 58 for full schedule)

12:30 p.m. – 1:45 p.m. Lunch (on your own)

12:30 p.m. – 1:45 p.m. **WOMEN IN ANDROLOGY LUNCHEON AND DISCUSSION***
*"Preparing Female Scientists for Successful Transitions to Leadership: Paths to Leadership”
Speaker: Sally Perreault Damey, PhD
Host & Moderator: Sarah Kimmins, BSc, MSc, PhD
(not included in general registration; ticket required)
Location: Wyoming
*Not CME Accredited

1:45 p.m. – 3:15 p.m. **SYMPOSIUM III – Male Rejuvenation**
Co-Chairs: Mark Sigman, MD
Ajay K. Nangia, MBBS, FACS

What do Patients Want from an Anti-Aging Clinic?
Martin Miner, MD
Alpert School of Medicine, Brown University

Hormonal Replacement for Male Rejuvenation: Is There Scientific Evidence?
Christina Wang, MD
Harbor-UCLA Medical Center & LA Biomedical Res. Ins.

Dangers Associated with Rejuvenation Therapy
Adrian S. Dobs, MD, MHS
Johns Hopkins University School of Medicine

3:15 p.m. – 3:30 p.m. Refreshment Break
Location: Grand Ballroom Reception A-C

3:30 p.m. – 4:15 p.m. **LECTURE III**
Meiosis Alleles and the Genetics of Human Infertility
John Schimenti, PhD
Cornell University
( Introduced by: William Wright, PhD)

4:15 p.m. – 5:00 p.m. **LECTURE IV**
Erectile Dysfunction and Radical Prostatectomy: Where is the Next Breakthrough?
Trinity J. Bivalacqua, MD, PhD
Johns Hopkins Medical (Introduced by: Alan Diekman, PhD)

5:00 p.m. to 5:45 p.m. **EAA LECTURE**
Post-Testicular Sperm DNA Oxidative Damage: Are the Chromosomes at an Equal Risk?
Joël R. Drevet, PhD
University of Blaise Pascal
( Introduced by: Ewa Rajpert-De Meyts, MD, PhD)

5:45 p.m. – 6:15 p.m. ASA 40th Anniversary Special Presentation II*
*"40 Years and Beyond: An Andrologist’s Guide to the Galaxy”
Sophie La Salle, PhD
Midwestern University
*Not CME Accredited

6:15 p.m. ASA Business Meeting
SCHEDULE AT A GLANCE

7:30 p.m. – 11:00 p.m.  Annual Banquet
Location: Natural History
Museum of Utah
Buses depart from hotel lobby
starting at 7:15 p.m.
(not included in registration fee:
ticket required)

TUESDAY, APRIL 21, 2015

7:00 a.m. – 8:00 a.m.  2016 Program Committee Meeting
Location: Casper

7:00 a.m. – 12:00 p.m.  Registration/Information Desk Open
Location: Grand Ballroom A Foyer

7:00 a.m. – 8:00 a.m.  Continental Breakfast
Location: Grand Ballroom Reception A-C

8:00 a.m. – 9:15 a.m.  SYMPOSIUM IV – The Effects of Testosterone on the Heart
Moderator: Barry Zirkin, PhD

Testosterone and the Heart:
Putting the FDA Advisory in Perspective
Shalender Bhasin, MD
Brigham and Women’s Hospital

Potential Therapeutic Role for Testosterone in Cardiac Diastolic Dysfunction
Theodore Abraham, MD, FACC, FASE
Johns Hopkins University
School of Medicine

Genetic Variants of Chromosome Y (chrY) Regulate the Responses of Cardiac Genes to Androgens Via Chromatin-Dependent and Circadian Related Effects
Christian F. Deschepper, MD
University of Montreal

9:15 a.m. – 9:30 a.m.  Refreshment Break
Location: Grand Ballroom Reception A-C

9:30 a.m. – 10:30 a.m.  INTERNATIONAL LECTURE
A Perspective from Downunder: TGBβ Signaling in Testis Development and Spermatogenesis
Kate Loveland, PhD
Monash University and MIMR-PHI Institute of Medical Research, Australia
(Introduced by: TBD)

10:30 a.m. – 12:00 p.m.  SYMPOSIUM V: Novel Male Contraceptive Strategies
Moderators: Bernard Robaire, PhD
David Sokal, MD

Na, K-ATPase 4 Isoform as a Target for Male Contraception
Gustavo Blanco, MD, PhD
The University of Kansas Medical Center

Retinoic Acid Receptor Antagonists for Male Contraception
Debra J. Wolgemuth, PhD
Columbia University Medical Center

Will there be a Role for Male Hormonal Based-Contraception Strategies?
William J. Bremner, MD, PhD
University of Washington

12:00 p.m.  MEETING ADJOURNED

Disclaimer Statement
Statements, opinions and results of studies contained in the program are those of the presenters/authors and do not reflect the policy or position of the ASA nor does the ASA provide any warranty as to their accuracy or reliability.

THANK YOU TO OUR 2015 PROMOTIONAL PARTNER

Platinum Level:
AbbVie
Table of Contents

Schedule at a Glance ................................................................. 1
President’s Welcome ................................................................. 6
Past Presidents ......................................................................... 6
State of Utah Governor Gary Herbert Letter ......................... 7
Salt Lake City Mayor Ralph Becker Proclamation .................. 8
ASA Officers ............................................................................ 9
General Information ................................................................. 10
Special Events ......................................................................... 12
Message from the Program Co-Chairs .................................... 13
ASA Lecturer Award ................................................................. 14
Distinguished Andrologist Award ............................................. 15
Distinguished Service Award .................................................. 16
Matthew P. Hardy Young Andrologist Award ......................... 17
Outstanding Trainee Investigator Award ................................ 18
Thanks to Donors and Sponsors .............................................. 19
Course Objectives & CME Credit Information ......................... 21
Schedule of Events ................................................................. 23
Speaker Abstracts ..................................................................... 33
Poster Session I ....................................................................... 51
Poster Session II ..................................................................... 58
Index of Abstract Authors ....................................................... 65
Abstracts Full Text ................................................................. 67
Committee Listing ................................................................. 124
President’s Welcome

Forty years! The American Society of Andrology is now 40 years old. While 40 often signifies the beginning of middle age, there is no evidence that our society is slowing down. That is why I am excited to welcome you to the 40th Annual Meeting of the ASA, entitled “A Lifetime of Male Reproductive Health,” here at the Little America Hotel in Salt Lake City, Utah, April 18 – 21, 2015.

Our Program Chairs, Dr. Edward Kim (University of Tennessee-Knoxville) and Dr. William Wright (Johns Hopkins Bloomberg School of Public Health), have put together a fantastic lineup of speakers, talks, and topics. Additionally, there promises to be cutting edge research presented by our members, trainees and other scientists from all over the world.

Some of the highlights of our upcoming meeting include:

- Special Symposium: Controversies in Testosterone Therapy
- Emil Steinberger Memorial Lecture: Mechanisms and Environmental Sensitivity
- AUA Lecture: Reproductive Genetics and the Aging Male
- Symposia regarding stem cells, reproductive health and aging
- Lectures featuring world-renowned speakers on reproductive toxicology, fertility preservation and more
- Special talks on diversity, women in andrology and male rejuvenation
- European Andrology Association Lecture: Post-Testicular Sperm DNA Oxidative Damage: Are the Chromosomes at an Equal Risk?
- ASA Awards, Trainee Mixer and, of course, the Annual Banquet
- And much more.

An important function of ASA is engaging students in our endeavors. A Mentoring Luncheon is scheduled on Sunday that will examine what it takes to embark on a scientific career. Our membership committee is working diligently to recruit more student members to ASA so please encourage your students to join.

Be sure to attend the Annual Banquet, which will be held at the Natural History Museum of Utah on Monday night, as well as Saturday’s Welcome Reception at 8:00 p.m.

The ASA is a special society, bringing together basic scientists, translational research and clinicians in a unique environment. Thank you for coming to help us celebrate our 40th birthday (remember, 40 is the new 30). Welcome to Salt Lake City!

Jay I. Sandlow, MD
President, American Society of Andrology

Past Presidents of the American Society of Andrology

<table>
<thead>
<tr>
<th>Years</th>
<th>President</th>
</tr>
</thead>
<tbody>
<tr>
<td>1975-1977</td>
<td>Emil Steinberger*</td>
</tr>
<tr>
<td>1977-1978</td>
<td>Don W. Fawcett*</td>
</tr>
<tr>
<td>1978-1979</td>
<td>C. Alvin Paulsen*</td>
</tr>
<tr>
<td>1979-1980</td>
<td>Nancy J. Alexander</td>
</tr>
<tr>
<td>1980-1981</td>
<td>Philip Troen</td>
</tr>
<tr>
<td>1981-1982</td>
<td>Richard M. Harrison</td>
</tr>
<tr>
<td>1982-1983</td>
<td>Richard J. Sherins</td>
</tr>
<tr>
<td>1983-1984</td>
<td>Andrzej Bartke</td>
</tr>
<tr>
<td>1984-1985</td>
<td>Rudi Ansibacher</td>
</tr>
<tr>
<td>1985-1986</td>
<td>Anna Steinberger</td>
</tr>
<tr>
<td>1986-1987</td>
<td>William D. Odell</td>
</tr>
<tr>
<td>1987-1988</td>
<td>Larry L. Ewing*</td>
</tr>
<tr>
<td>1988-1989</td>
<td>C. Wayne Bardin</td>
</tr>
<tr>
<td>1989-1990</td>
<td>Rupert Amann</td>
</tr>
<tr>
<td>1990-1991</td>
<td>Howard Nankin</td>
</tr>
<tr>
<td>1991-1992</td>
<td>David W. Hamilton</td>
</tr>
<tr>
<td>1992-1993</td>
<td>Ronald S. Swerdloff</td>
</tr>
<tr>
<td>1993-1994</td>
<td>Bernard Robaire</td>
</tr>
<tr>
<td>1994-1995</td>
<td>Glenn R. Cunningham</td>
</tr>
<tr>
<td>1995-1996</td>
<td>Marie-Claire Orgebin-Crist</td>
</tr>
<tr>
<td>1996-1997</td>
<td>Arnold M. Belker</td>
</tr>
<tr>
<td>1997-1998</td>
<td>Terry T. Turner</td>
</tr>
<tr>
<td>1998-1999</td>
<td>Richard V. Clark</td>
</tr>
<tr>
<td>1999-2000</td>
<td>Barry T. Hinton</td>
</tr>
<tr>
<td>2000-2001</td>
<td>J. Lisa Tenover</td>
</tr>
<tr>
<td>2001-2002</td>
<td>Barry R. Zirkin</td>
</tr>
<tr>
<td>2002-2003</td>
<td>Jon L. Pryor</td>
</tr>
<tr>
<td>2003-2004</td>
<td>Gail S. Prins</td>
</tr>
<tr>
<td>2004-2005</td>
<td>William J. Bremner</td>
</tr>
<tr>
<td>2005-2006</td>
<td>Sally Perreault Darney</td>
</tr>
<tr>
<td>2006-2007</td>
<td>Christina Wang</td>
</tr>
<tr>
<td>2007-2008</td>
<td>Terry R. Brown</td>
</tr>
<tr>
<td>2008-2009</td>
<td>Wayne J.G. Hellström</td>
</tr>
<tr>
<td>2009-2010</td>
<td>Dolores J. Lamb</td>
</tr>
<tr>
<td>2010-2011</td>
<td>Paul J. Turek</td>
</tr>
<tr>
<td>2011-2012</td>
<td>Gail A. Cornwall, PhD</td>
</tr>
<tr>
<td>2012-2013</td>
<td>Donna L. Vogel, MD, PhD</td>
</tr>
<tr>
<td>2013-2014</td>
<td>Erwin Goldberg, PhD</td>
</tr>
</tbody>
</table>

*Deceased
WHEREAS, the American Society of Andrology (ASA) is a unique scientific society that brings together basic scientists, translational scientists, physicians and veterinarians to share scientific advances, discuss emerging male reproductive health issues and problems, and effectively communicate the latest science and technology to patients; and

WHEREAS, the ASA will celebrate its 40th anniversary at its annual meeting being held in Salt Lake City, April 18-21, 2015, by honoring its rich history and discussing the endless possibilities of the future; and

WHEREAS, over the last 40 years, scientists and clinicians from the ASA have played key roles in the research and implementation of major advances in Infertility Intervention; Assisted Reproductive Technologies; Contraception; Reproductive Toxicology; Male Sexual Development; Male Sexual Function; Testicular Cancer and Prostate Cancer; and

WHEREAS, Salt Lake City is pleased to welcome the American Society of Andrology, an international leader in the promotion, education and discovery of male reproductive health.

NOW, THEREFORE, I, Ralph Becker, Mayor of Salt Lake City, do hereby proclaim April 18, 2015 as

ANDROLOGY AWARENESS DAY IN SALT LAKE CITY

Dated __________ 5th ________ of ________ March ________, 2015

________________________

MAYOR
April 18, 2015

Dear Members of the American Society of Andrology,

As governor of the great state of Utah, I extend a warm welcome to Salt Lake City. It is our pleasure to host you here as you celebrate your organization’s 40th Anniversary.

I commend your leadership in advancing education and medical research of male reproductive health. In particular, your efforts to disseminate knowledge through scholarship, academic collaboration, and public health promotion help improve men’s health and make a positive difference people’s lives. In addition, your programs to encourage young people to pursue science and medical careers in andrology, including veterinary medicine, through mentoring, scholarships, and student membership are noteworthy. Thank you for your valuable service in Utah and throughout the country.

Utah offers what we call “Life Elevated.” During your stay, I encourage you to take advantage of world-class shopping at The Gateway and City Creek shopping areas and Park City’s historic Main Street, and enjoy diverse offerings at a bevy of fine restaurants, and various sports and arts events, as well our beautiful mountain ski resorts and Olympic venues.

Again, congratulations on the 40th Anniversary of the American Society of Andrology. Best wishes for a successful conference and a memorable visit in Utah.

Sincerely,

Gary R. Herbert
Governor
American Society of Andrology

OFFICERS
President
Jay I. Sandlow, MD

Vice President
Vassilios Papadopoulos, D Pharm, PhD

Secretary
Jacquetta M. Trasler, MD, PhD

Treasurer
Rex A. Hess, MS, PhD

Past President
Erwin Goldberg, PhD

EXECUTIVE COUNCIL MEMBERS
Sylvie Breton, PhD; Nina S. Davis, MD; Alan Diekman, PhD; George L. Gerton, PhD; Mohit Khera, MD; Jeffrey J. Lysiak, PhD; Ajay K. Nangia, MBBS, FACS; Moira K. O’Bryan, BSc, PhD; Darius A. Paduch, MD, PhD; Mark Sigman, MD; Jacques J. Tremblay, PhD; Pablo E. Visconti, PhD

EXECUTIVE COUNCIL TRAINEE REPRESENTATIVES
Mary Samplaski, MD and Luke Simon, PhD

COMMITTEE CHAIRS
Andrology Laboratories
Charles H. Muller, PhD; Seattle, WA

Archives & History Committee
Steven M. Schrader, PhD; Cincinnati, OH

Awards Committee
Barry R. Zirkin, PhD; Baltimore, MD

Basic Science Workshop
Kate Loveland, PhD; Clayton, VIC Australia (2014 Chair)

Basic Science Workshop 2015
Cristian O’Flaherty, PhD; Montreal, QC, Canada (2016 Chair)

Communications and Media Committee
Jacques J. Tremblay, PhD; Quebec City, QC, Canada

Constitution and ByLaws Committee
Jannette Dufour, PhD; Lubbock, TX

Diversity Committee
Maria Christina W. Avellar, PhD; Sao Paulo, Brazil
George L. Gerton, PhD; Philadelphia, PA (Vice Chair)

Endowment Committee
Susan Ann Rothmann, PhD, HCLD; Cleveland, OH

Ethics Committee
Ronald W. Lewis, MD, FACS; Augusta, GA

Finance Committee
Michael A. Palladino, PhD; West Long Branch, NJ

Future Program Committee
Arthur L. Burnett II, MD; Baltimore, MD (Co-Chair)
Robert S. Viger, PhD; Quebec City, QC, Canada (Co-Chair)

Future Meetings Committee
John McCarrey, PhD; San Antonio, TX

Industrial Relations Committee
Mohit Khera, MD; Houston, TX

International Liaison Committee
Patricia S. Cuasniciu, PhD; Buenos Aires, Argentina

Journal Committee
Rex A. Hess, MS, PhD; Urbana, IL

Journal Editors
Douglas T. Carrell, PhD, HCLD; Salt Lake City, UT (Editors-In-Chief)
Ewa Rajpert-De Meyts, MD, PhD; Copenhagen, Denmark (Editors-In-Chief)

Laboratory Science Forum
David S. Karabinus, PhD, HCLD; Manassas, VA

Liaison Committee
Cristian O’Flaherty, PhD; Montreal, QC, Canada

Membership Committee
Alan Diekman, PhD; Little Rock, AR
Sijo J. Parekkattil, MD; Clermont, FL (Co-Chair)

Nominating Committee
Erwin Goldberg, PhD; Evanston, IL

Program Committee
Edward D. Kim, MD; Knoxville, TN (Co-Chair)
William Wright, PhD; Baltimore, MD (Co-Chair)

Public Affairs and Policy Committee
Ajay K. Nangia, MBBS, FACS; Kansas City, KS

Special Symposium
Mohit Khera, MD; Houston, TX (Co-Chair)
Tobias S. Kohler, MD, MPH, FACS; Springfield, IL (Co-Chair)

Testis Workshop
Jacqueta M. Trasler, MD, PhD; Dorval, QC, Canada
Leslie Lynn Heckert, PhD; Kansas City, KS (Vice Chair)

Trainee Affairs
Peter Liu, MBBS, PhD; Torrance, CA (Co-Chair)
Sophie La Salle, PhD; Downers Grove, IL (Co-Chair)

ANDROLOGY EDITORIAL OFFICE
Andrology
Website: http://mc.manuscriptcentral.com/andrology

EXECUTIVE OFFICE
American Society of Andrology
Two Woodfield Lake
1100 E Woodfield Road, Suite 350
Schaumburg, IL 60173
Phone: (847) 619-4909 | Fax: (847) 517-7229
Email: info@andrologysociety.org

NOTICE TO READERS
Every effort has been made to ensure that the information printed here is correct; however, details are subject to change.

© 2015 American Society of Andrology and European Academy of Andrology
Andrology, 2015, Supplement, 9
GENERAL MEETING
INFORMATION

The Winter Olympics made Salt Lake City a prime travel destination in 2002. The revitalization done in preparation for the Games is still very much a part of the area. With its gorgeous setting between the Wasatch Mountains and the Great Salt Lake, Salt Lake City is also a prime destination for travelers interested in outdoor sports. In the winter, skiing is the most popular, but visitors can always enjoy some great hiking, biking and climbing just outside the city.

ATTRACTIONS
Salt Lake City is the headquarters of the Church of Jesus Christ of Latter-day Saints, and many major tourist attractions focus on LDS history. If you're looking for something unique to Salt Lake, stop in and research your family history. One of Salt Lake’s many nicknames is “Genealogy Capitol of the World.” You can take in the city’s historic sites and points of interest on a guided bike tour or carriage ride around downtown Salt Lake. History buffs will want to check out Temple Square which is Salt Lake’s most popular tourist attraction. Geologists might be more interested in the Great Salt Lake.

SHOPPING
From high-end products, to rocks, to wool, to Utah art, and British foods, chocolates, and goodies, Salt Lake City’s shopping has a lot to offer. Salt Lake City and shopping have gone hand in hand for over a century. The first department store in the United States opened for business in 1868. Today the Salt Lake Valley offers plenty of possibilities for terrific shopping excursions, including malls, shopping villages, specialty shops, antiques and collectibles, books and music, factory outlet malls and outdoor shopping and much more.

DINING/NIGHTLIFE
Salt Lake City has a surprisingly diverse assortment of cafes and restaurants. From great American classics to dining options from every corner of the world, you will find exactly what you are craving for breakfast, lunch, or dinner. Eat hearty to keep up your energy – Salt Lake also boasts a vibrant nightlife with nightclubs, sports bars, piano bars, pubs and martini bars.

WEATHER
Salt Lake City weather in the month of April is characterized by rising daily high temperatures, with daily highs increasing from 56°F to 65°F over the course of the month.

OUTDOOR RECREATION
The area around Salt Lake City is breathtaking in its natural beauty, whether you hike and bike through local canyons and national parks, ride through the forests on horseback or float above the world by hot-air balloon. And don’t miss the breathtaking Red Butte Gardens, to gaze out over the Salt Lake Valley or enjoy seasonal floral exhibits. You can also go out into the wilderness with guided fishing and wildlife experiences and river expeditions.

ARTS AND CULTURE
Salt Lake City is home to the Utah Museum of Contemporary Art, which features current artists both local and international, and the Utah Museum of Fine Arts, which offers art from across thousands of years of human history. If you prefer to stay outdoors, check out the Gilgal Sculpture Garden to see the strange and fascinating sculptures of Thomas Battersby Child, Jr. And don’t forget Salt Lake City’s museums, which cover an incredible array of subjects – from the Natural History Museum of Utah to Fort Douglas Military Museum to Classic Cars International. Traveling with family? Don’t miss Discovery Gateway: The Children’s Museum of Utah, a 60,000 square-foot discovery center featuring fun, interactive learning.

Registration/Information Desk Hours are as follows:
Friday, April 17, 2015
2:00 p.m. – 6:00 p.m.
Saturday, April 18, 2015:
2:00 p.m. – 7:00 p.m.
Sunday, April 19, 2015:
7:00 a.m. – 6:00 p.m.
Monday, April 20, 2015:
7:00 a.m. – 6:00 p.m.
Tuesday, April 21, 2015:
7:00 a.m. – 12:00 p.m.

Exhibit Hall Hours are as follows:
Saturday, April 18, 2015:
4:00 p.m. – 9:30 p.m.
Sunday, April 19, 2015:
7:00 a.m. – 4:00 p.m.
Monday, April 20, 2015:
7:00 a.m. – 3:30 p.m.
HOTEL INFORMATION

The American Society of Andrology 2015 Annual Conference will be held at The Little America Hotel where special room rates have been arranged for meeting attendees.

The Little America Hotel
500 S Main St.
Salt Lake City, UT 84101
Main: (801) 596-5700
Fax: (801) 596-5911
Website: www.saltlake.littleamerica.com

Room Rate: $174.00
Hotel Deadline: March 16, 2015
Reservations: (800) 437-5288

ASA has negotiated a discounted rate of $174.00 per night plus tax (currently 12.6%) at the Little America Hotel.

Hotel Deadline
The deadline to receive the ASA group rate is March 16, 2015. ASA encourages you to make your reservation early, as the hotel and discount block may sellout before this date. After this date, reservations will be accepted based on availability and higher rates may apply.

Reservations
Attendees are responsible for making their reservations by calling the hotel at (800) 437-5288. Please note that discounted rates are not available online. Please reference the ASA to receive the discounted rate.

Hotel Deposit and Cancellation Policy
A deposit equal to one night’s stay is required to hold a reservation. These deposits are fully refundable if the hotel is notified 24 hours prior to arrival and a cancellation number is obtained.
SPECIAL EVENTS

Laboratory Science Forum Luncheon
Disaster Preparedness “Surviving Sandy: Lessons in Disaster Planning and Recovery for Labs, Offices and Institutions”
Date: Saturday, April 18, 2015
Time: 11:30 a.m. – 1:00 p.m.
Location: Arizona
Speaker: Susan A. Rothmann, PhD, HCLD
Description: All labs, whether clinical or research oriented, medical practices, and businesses should have plans to face and recover from disasters. Recent high profile events such as Hurricane Sandy, Hurricane Katrina and the 9/11 attacks impacted many people in many locations and challenged day-to-day operations and recovery. But more common perils such as building fires, pandemics and local power outages also threaten operations. In this year’s Laboratory Science Forum presentation, Dr. Susan Rothmann will use Hurricane Sandy’s impact on her lab and manufacturing company in northeast Ohio as a case lesson for preparedness (or the lack of it!) and highlight lessons learned from other disasters experienced by ASA members. Join us for lunch and learn the critical roles that good disaster plans play in recovery and loss prevention. Key elements of disaster plans will be described.
Cost: $35.00 for Attendees (Member/Non-Member). Please sign up for this event on the registration form.

ASA Welcome Reception
Date: Saturday, April 18, 2015
Time: 8:00 p.m. – 9:30 p.m.
Location: Grand Ballroom Reception A-C
Description: Join us for a welcome reception to connect with friends and colleagues. Admission to the reception is included in your ASA meeting registration fee; however, it is not included if you are only attending the Testis Workshop.
Dress: Business casual or casual attire is appropriate
Cost: One ticket included in ASA registration; $25.00 for additional tickets. Please sign up for this event on the registration form.

Mentoring Luncheon Sponsored by the Diversity and Trainee Affairs Committees
“Finding Your Path in Andrology”
Date: Sunday, April 19, 2015
Time: 12:30 p.m. – 2:00 p.m.
Location: Wyoming
Speaker: Susan A. Rothmann, PhD, HCLD
Description: The field of andrology has many paths to career success. Dr. Rothmann will discuss her path from hematology research to clinical lab andrologist to andrology entrepreneur. The presentation will highlight critical self-assessment tools for creating a personal pathway and identity.
Cost: $25.00 for Trainees, $35.00 for Attendees (Member/Non-Member). Please sign up for this event on the registration form.

ASA Trainee Forum and Mixer
Date: Sunday, April 19, 2015
Time: 6:00 p.m. – 8:00 p.m.
Location: Olympus
Description: The ASA Trainee Forum and Mixer provides an opportunity for trainee members to meet other trainees, as well as more established members of the society. This is a relaxed, informal event with appetizers, beer and wine provided. Senior members of the society will be present in this informal forum and discussion group setting to answer your questions about relevant topics such as grant writing, searching for a post-doctor job, alternative PhD career paths, succeeding in the clinic or lab, etc.
Cost: Complimentary; all members of the society are welcome. Please sign up for this event on the registration form.

Women in Andrology Luncheon and Discussion
“Preparing Female Scientists for Successful Transitions to Leadership: Paths to Leadership”
Date: Monday, April 20, 2015
Time: 12:30 p.m. – 1:45 p.m.
Location: Wyoming
Host: Sarah Kimmins, BSc, MSc, PhD
Speaker: Sally Perreault Darney, PhD
Description: Designed for ASA’s female contingent, in this workshop-style luncheon we will be guided by invited speakers as we explore the characteristics of successful leaders, models for leadership and the dimensions of centered leadership.
Suggested readings and resources:
Lean In: Women, Work and the Will to Lead. Sheryl Sandberg and Nell Scovell
Cost: $25.00 for Trainees, $35.00 for Attendees (Member/Non-Member). Please sign up for this event on the registration form.

ASA Annual Banquet
Date: Monday, April 20, 2015
Time: 7:30 p.m. – 11:00 p.m.
Location: Natural History Museum of Utah
Cost: $75.00 for Attendees (Member/Non-Member), $35.00 for Trainees. The Annual Banquet will be held at the Natural History Museum of Utah. The Museum’s signature Canyon and Terrace Room, offering an architecturally dramatic interior and stunning views, perfect for the night’s event. Includes dinner; beer, wine, and soft drinks; and entertainment. Please sign up for this event on the registration form.
Message from the Program Co-Chairs

Friends and colleagues,

Welcome to the 40th Annual Meeting of the American Society for Andrology!

Since 1976, this society has provided a unique forum for basic scientists and clinician-scientists to discuss the most recent findings about the normal functioning of the male reproductive system, and the biological bases for diseases of this system. The program for this 40th meeting continues and expands that tradition. During the next three days, our lecturers will discuss subjects ranging from the genetics and epigenetics of the developing gamete, to clinical care for older fathers and men undergoing chemotherapy, to the translation of basic research to public policy. Additionally, the two poster sessions greatly expand the scientific breadth of this meeting and provide everyone with exciting opportunities for new scientific collaborations.

This meeting would not have happened without the support of the past and present presidents of the ASA, Erv Goldberg and Jay Sandlow and the many colleagues who suggested topics and speakers for this meeting. We are particularly indebted to Steve Schrader and the Archives Committee for their contribution to the 40th anniversary of the ASA content in the program. Finally, we thank WJ Weiser & Associates for their expert handling of the logistics of this meeting.

Finally, we would like to extend a special greeting to those of you who are attending for the first time the annual meeting of the American Society for Andrology. This society is unique not only because it brings basic scientists and clinician-scientists together to discuss a single topic, but also because almost all who attend have a special enthusiasm for their science and that of their colleagues. You and your science are very welcome here and we hope that you will return often to share your insights and enthusiasm about male reproductive biology and how this underpins a man’s health.

Enjoy the meeting and Salt Lake City!

Bill Wright
William Wright, PhD

Edward Kim
Edward D. Kim, MD

PROGRAM COMMITTEE
Edward D. Kim, MD (Co-Chair)
William Wright, PhD (Co-Chair)
John K. Amory, MD, MPH; Seattle, WA
Maria Christina W. Avellar, PhD; Sao Paulo, Brazil
Robert Edward Brannigan, MD; Hinsdale, IL
Patricia S. Cuasnicu, PhD; Buenos Aires, Argentina
Jurrien Dean, MD; Bethesda, MD
Alan Diekman, PhD; Little Rock, AR
George L. Gerton, PhD; Philadelphia, PA
Michael D. Griswold, PhD; Pullman, WA
Mary Ann Handel, PhD; Bar Harbor, ME
Wayne J.G. Hellstrom, MD FACS; New Orleans, LA
Mohit Khera, MD; Houston, TX
Sarah Kimmins, PhD; Ste-Ann-de-Bellevue, QC, Canada
Sophie La Salle, PhD; Downers Grove, IL
Peter Liu, MBBS, PhD; Torrance, CA
Martin M. Matzuk, MD, PhD; Houston, TX
John McCarrey, PhD, BS, MS; San Antonio, TX
Jon Oatley, PhD; Pullman, WA
Sally Perreault Darney, PhD; Cary, NC
Bernard Robaire, PhD; Montreal, QC, Canada
Jay I. Sandlow, MD; Milwaukee, WI
Paul Ray Shin, MD; Washington, DC
Donald J. Tindall, PhD; Rochester, MN
Jacquetta M. Trasler, MD, PhD; Montreal, QC, Canada
Wei Yan, MD, PhD; Reno, NV

Special Symposium
Mohit Khera, MD; Houston, TX (Co-Chair)
Tobias S. Köhler, MD, MPH, FACS; Springfield, IL (Co-Chair)
Emil Steinberger Memorial Lecture Award

Marisa S. Bartolomei received her BS in biochemistry at the University of Maryland and then obtained her PhD from the Johns Hopkins University School of Medicine under the guidance of Dr. Jeffry Corden. She trained as a postdoctoral fellow with Dr. Shirley Tilghman at Princeton University. In 1993, Dr. Bartolomei was appointed as an assistant professor of cell and developmental biology at the University of Pennsylvania Perelman School of Medicine and was promoted to associate professor with tenure in 1999 and professor in 2006. In 2006, Dr. Bartolomei received the Society for Women’s Health Research Medtronic Prize for Contributions to Women’s Health. In 2011, Dr. Bartolomei received the Jane Glick Graduate School Teaching Award for the University of Pennsylvania School of Medicine and a MERIT award. She was elected as a Fellow of the American Association for the Advancement of Science in 2014. Dr. Bartolomei participates extensively in graduate and medical education, having trained numerous pre- and postdoctoral students, clinicians and other health care professionals. She is a member of the Human Molecular Genetics and Molecular and Cellular Biology editorial boards and is an associate editor for PLOS Genetics. Dr. Bartolomei’s research addresses the epigenetic mechanisms of genomic imprinting and X inactivation, as well as the impact of adverse environmental insults on epigenetic gene regulation using the mouse as a model.

Serono Lectureship Recipients

1980  C. Alvin Paulsen
1981  Pierre Soupart
1982  Kevin J. Catt & Maria L. Dufau
1983  J. Michael Bedford
1984  C. Wayne Bardin
1985  David M. De Kretser
1986  Ronald S. Swerdlow
1987  Roger V. Short
1988  Roger Guillemain
1989  Frank S. French
1990  David C. Page
1991  Tony M. Plant
1992  Yves Clermont
1993  Leroy Hood
1994  Michael D. Griswold
1995  Marie-Claire Orgebin-Crist
1996  Norman B. Hecht
1997  Patrick C. Walsh
1998  Jurrien Dean
1999  Neal First
2000  Bert O’Malley
2001  John D. Gearhart
2002  David Botstein
2003  Victor D. Vacquier

ASA Lectureship Recipients

2004  Judith Kimble
2005  David Page
2006  John R. Aitken
2007  Rudolf Jaenisch
2008  Haifan Lin
2009  Blanche Capel

Emil Steinberger Memorial Lecture Recipients

2010  Andrew Sinclair
2011  Leendert Looijenga
2012  William F. Crowley, Jr.
2013  Deborah O’Brien
2014  Rudolf Jaenisch

The Emil Steinberger Memorial Lecture Award is sponsored by the Emil Steinberger Endowment Fund.
Deborah O’Brien is a Professor in the Department of Cell Biology & Physiology and the Department of Pediatrics at the University of North Carolina (UNC) School of Medicine in Chapel Hill. She is a member of the Laboratories for Reproductive Biology, the Curriculum in Genetics and Molecular Biology and the Lineberger Comprehensive Cancer Center at UNC. Dr. O’Brien grew up in Louisville, Kentucky, and completed her BS in Biology at the University of Dayton. She then moved to Boston where she obtained her PhD in Physiology from Harvard (1979), followed by postdoctoral studies in the Laboratory of Human Reproduction and Reproductive Biology at Harvard Medical School. Her graduate and postdoctoral research was supported by individual fellowships from the Danforth Foundation, NSF and NIH. Dr. O’Brien was a Senior Staff Fellow in the Gamete Biology Group, Laboratory of Reproductive and Developmental Toxicology at the NIH National Institute of Environmental Health Sciences, before becoming a UNC Tar Heel in 1989. She teaches both graduate and medical students and includes young scientists from undergraduates through junior faculty in her research program.

Dr. O’Brien investigates molecular and cellular mechanisms that regulate spermatogenesis and sperm function. A major focus of her current research is sperm energy metabolism, particularly the function of glycolytic isozymes with restricted expression in the male germline. Analysis of GAPDH knockout mice provided the first in vivo evidence that glycolysis is essential for sperm motility and male fertility, and laid the foundation for her contraceptive drug discovery project. This translational project uses structure-based drug design to identify small-molecule inhibitors of GAPDH, with the long-term goal of developing a non-hormonal contraceptive that directly blocks sperm function. The development of software tools for the quantitative analysis of alterations in sperm motility patterns has been central to these studies. Dr. O’Brien’s GAPDH research was recognized with a Discovery Fast Track Award from GlaxoSmithKline in 2013. In addition, her research team has made significant contributions towards understanding unexplained male infertility in several gene knockout models. Her current research in this area uses a systems genetics approach to explore causes of male infertility. The Collaborative Cross (CC) is a multinational project producing recombinant inbred mouse lines that have greater genomic diversity and provide improved capabilities for the analysis of complex traits. Through extensive phenotyping and high-density genotyping, these studies investigate male infertility that has contributed to the extinction of more than 75% of the CC lines. The high incidence of male infertility and wide range of phenotypic defects observed, combined with the CC genetic architecture, offer a unique opportunity to identify natural variation associated with male infertility. Dr. O’Brien is grateful for grant support of her research program from NICHD, CONRAD and the Andrew W. Mellon Foundation and for the outstanding contributions of her trainees and collaborators.

Recognition for Dr. O’Brien’s research accomplishments includes invitations to speak at several national and international meetings, including the ASA Emil Steinberger Memorial Lecture Award in 2013 and the Women in Andrology Lecture in 2005. As an active member of ASA, Dr. O’Brien has served on the Executive Council and several committees, chairing the Awards Committee, the Finance Committee and the 2004 Program Committee. She has served on the editorial boards of the Journal of Andrology, Endocrinology and Biology of Reproduction (Associate Editor, 2009-2011), the NIH CMIR Study Section (2003-2007) and other NIH grant review panels as an ad hoc member. Her service to the reproductive biology community also includes participation in the Male Reproduction Research Focus Group of the NIH Specialized Cooperative Centers Program in Reproduction and Infertility Research (Co-Leader, 1998-2003), the Executive Committee of the Triangle Consortium for Reproductive Biology, several committees of the Society for the Study of Reproduction, and the organizing committees for six North American Testis Workshops.

Distinguished Andrologist Award

Deborah O’Brien is a Professor in the Department of Cell Biology & Physiology and the Department of Pediatrics at the University of North Carolina (UNC) School of Medicine in Chapel Hill. She is a member of the Laboratories for Reproductive Biology, the Curriculum in Genetics and Molecular Biology and the Lineberger Comprehensive Cancer Center at UNC. Dr. O’Brien grew up in Louisville, Kentucky, and completed her BS in Biology at the University of Dayton. She then moved to Boston where she obtained her PhD in Physiology from Harvard (1979), followed by postdoctoral studies in the Laboratory of Human Reproduction and Reproductive Biology at Harvard Medical School. Her graduate and postdoctoral research was supported by individual fellowships from the Danforth Foundation, NSF and NIH. Dr. O’Brien was a Senior Staff Fellow in the Gamete Biology Group, Laboratory of Reproductive and Developmental Toxicology at the NIH National Institute of Environmental Health Sciences, before becoming a UNC Tar Heel in 1989. She teaches both graduate and medical students and includes young scientists from undergraduates through junior faculty in her research program.

Dr. O’Brien investigates molecular and cellular mechanisms that regulate spermatogenesis and sperm function. A major focus of her current research is sperm energy metabolism, particularly the function of glycolytic isozymes with restricted expression in the male germline. Analysis of GAPDH knockout mice provided the first in vivo evidence that glycolysis is essential for sperm motility and male fertility, and laid the foundation for her contraceptive drug discovery project. This translational project uses structure-based drug design to identify small-molecule inhibitors of GAPDH, with the long-term goal of developing a non-hormonal contraceptive that directly blocks sperm function. The development of software tools for the quantitative analysis of alterations in sperm motility patterns has been central to these studies. Dr. O’Brien’s GAPDH research was recognized with a Discovery Fast Track Award from GlaxoSmithKline in 2013. In addition, her research team has made significant contributions towards understanding unexplained male infertility in several gene knockout models. Her current research in this area uses a systems genetics approach to explore causes of male infertility. The Collaborative Cross (CC) is a multinational project producing recombinant inbred mouse lines that have greater genomic diversity and provide improved capabilities for the analysis of complex traits. Through extensive phenotyping and high-density genotyping, these studies investigate male infertility that has contributed to the extinction of more than 75% of the CC lines. The high incidence of male infertility and wide range of phenotypic defects observed, combined with the CC genetic architecture, offer a unique opportunity to identify natural variation associated with male infertility. Dr. O’Brien is grateful for grant support of her research program from NICHD, CONRAD and the Andrew W. Mellon Foundation and for the outstanding contributions of her trainees and collaborators.

Recognition for Dr. O’Brien’s research accomplishments includes invitations to speak at several national and international meetings, including the ASA Emil Steinberger Memorial Lecture Award in 2013 and the Women in Andrology Lecture in 2005. As an active member of ASA, Dr. O’Brien has served on the Executive Council and several committees, chairing the Awards Committee, the Finance Committee and the 2004 Program Committee. She has served on the editorial boards of the Journal of Andrology, Endocrinology and Biology of Reproduction (Associate Editor, 2009-2011), the NIH CMIR Study Section (2003-2007) and other NIH grant review panels as an ad hoc member. Her service to the reproductive biology community also includes participation in the Male Reproduction Research Focus Group of the NIH Specialized Cooperative Centers Program in Reproduction and Infertility Research (Co-Leader, 1998-2003), the Executive Committee of the Triangle Consortium for Reproductive Biology, several committees of the Society for the Study of Reproduction, and the organizing committees for six North American Testis Workshops.

Distinguished Andrologists

<table>
<thead>
<tr>
<th>Year</th>
<th>Andrologist</th>
</tr>
</thead>
<tbody>
<tr>
<td>1975</td>
<td>Roy O. Greep &amp; M.C. Chang</td>
</tr>
<tr>
<td>1976</td>
<td>Robert E. Mancini</td>
</tr>
<tr>
<td>1977</td>
<td>Robert S. Hotchkiss</td>
</tr>
<tr>
<td>1978</td>
<td>Thaddeus Mann</td>
</tr>
<tr>
<td>1979</td>
<td>John MacLeod</td>
</tr>
<tr>
<td>1980</td>
<td>Alexander Albert</td>
</tr>
<tr>
<td>1981</td>
<td>Eugenia Rosemberg</td>
</tr>
<tr>
<td>1982</td>
<td>Kristen B.D. Eik-Nes</td>
</tr>
<tr>
<td>1983</td>
<td>Mortimer B. Lipsett</td>
</tr>
<tr>
<td>1984</td>
<td>Robert H. Foote</td>
</tr>
<tr>
<td>1985</td>
<td>Alfred D. Jost</td>
</tr>
<tr>
<td>1986</td>
<td>Emil Steinberger</td>
</tr>
<tr>
<td>1987</td>
<td>Yves W. Clermont</td>
</tr>
<tr>
<td>1988</td>
<td>C. Alvin Paulsen</td>
</tr>
<tr>
<td>1989</td>
<td>Marie-Claire Orgebin-Crist</td>
</tr>
<tr>
<td>1990</td>
<td>Philip Troen</td>
</tr>
<tr>
<td>1991</td>
<td>C. Wayne Bardin</td>
</tr>
<tr>
<td>1992</td>
<td>Anna Steinberger</td>
</tr>
<tr>
<td>1993</td>
<td>Richard J. Sherins</td>
</tr>
<tr>
<td>1994</td>
<td>Rupert P. Amann</td>
</tr>
<tr>
<td>1995</td>
<td>J. Michael Bedford</td>
</tr>
<tr>
<td>1996</td>
<td>Brian P. Setchell</td>
</tr>
<tr>
<td>1997</td>
<td>Ryuzo Yanagimachi</td>
</tr>
<tr>
<td>1998</td>
<td>Richard D. Amelar</td>
</tr>
<tr>
<td>1999</td>
<td>Bayard T. Storey</td>
</tr>
<tr>
<td>2000</td>
<td>Frank S. French</td>
</tr>
<tr>
<td>2001</td>
<td>Geoffrey M. H. Waites</td>
</tr>
<tr>
<td>2002</td>
<td>David M. de Kretser</td>
</tr>
<tr>
<td>2003</td>
<td>Ronald Swerdloff</td>
</tr>
<tr>
<td>2004</td>
<td>Mitch Eddy</td>
</tr>
<tr>
<td>2005</td>
<td>Norman Hecht</td>
</tr>
<tr>
<td>2006</td>
<td>Eberhard (Ebo) Nieschlag</td>
</tr>
<tr>
<td>2007</td>
<td>Bernard Robaire</td>
</tr>
<tr>
<td>2008</td>
<td>William Bremner</td>
</tr>
<tr>
<td>2009</td>
<td>Dolores Lamb</td>
</tr>
<tr>
<td>2010</td>
<td>Barry Zirkin</td>
</tr>
<tr>
<td>2011</td>
<td>Erwin Goldberg</td>
</tr>
<tr>
<td>2012</td>
<td>Christina Wang</td>
</tr>
<tr>
<td>2013</td>
<td>Gail S. Prins</td>
</tr>
</tbody>
</table>

The Distinguished Andrologist Award is sponsored by the Eugenia Rosemberg Endowment Fund

© 2015 American Society of Andrology and European Academy of Andrology  Andrology, 2015, Supplement, 15
Dr. Steven Schrader leads the Reproductive Health Assessment Team for the National Institute for Occupational Safety and Health (NIOSH). NIOSH is one of the Centers of the Centers for Disease Control and Prevention (CDC). Dr. Schrader received his BS (1974), MS (1975), and PhD (1978) from the University of Missouri – Columbia. He completed his Post-Doctoral Research at University of Miami (Florida). He was an assistant professor at Roosevelt University (Chicago) before joining NIOSH in 1983. At NIOSH he established the NIOSH male reproductive health assessment program. His work enabled the NIOSH reproductive health assessment team to conduct numerous occupational field investigations across the US, including Hawaii, and in Canada, China, and Russia. Dr. Schrader’s work on the evaluation of sexual function in bicycle police officers has led to expanded research in this area for male and female bicyclists, and has inspired other aspects of research on the effects of occupational hazards on male sexual function. Numerous improved bicycle saddle designs aimed at alleviating sexual dysfunction have been developed and are now being utilized by cyclists.

Dr. Schrader has been invited to present his research nationally and internationally. The success of his research program has led to collaborative reproductive research with universities, other federal and international agencies. He was asked to speak to the United Nations Commission on Sustainable Development on how endocrine disrupter chemicals can adversely impact reproductive health of men. Dr. Schrader served on the WHO workgroup that prepared and published the WHO Laboratory Manual for the Examination and Processing of Human Semen. He served on the CDC workgroup that prepared the National Public Health Action Plan for the Detection, Prevention and Management of Infertility.

Dr. Schrader has been active in the American Society of Andrology since 1983. He has made over 60 scientific presentations at the ASA meetings. Dr. Schrader has served on the ASA Executive Council and as Secretary. He served on the Program Committee in 1986, 2003, 2004, and 2005. He was elected to the Nominating Committee in 2014 and is on the Endowment Committee. Dr. Schrader’s two biggest passions have been the Andrology Laboratories Committee and the Archives and History Committee. He has chaired the Andrology Laboratories Committee four times and has been a faculty member of the Andrology Laboratory Workshop no fewer than a dozen times. He became Dr. Jean Fourcroy’s photography assistant and since she established the Archives and History Standing Committee in 2001, he has served on that committee. He currently serves as the chair of the Archives and History Committee.

In 2014, Dr. Schrader coordinated a joint meeting of the leadership of both the ASA and CDC to determine common interests and establish mechanisms of interaction between both groups.

Distinguished Service Award

Distinguished Service Award Recipients

1993 C. Alvin Paulsen
1994 Andrzej Bartke
1995 Philip Troen
1996 Marie-Claire Orgebin-Crist
1997 Rupert P. Amann
1998 David W. Hamilton
1999 Bernard Robaire
2000 Gail S. Prins
2001 Terry T. Turner
2002 Arnold M. Belker
2003 J. Lisa Tenover
2004 Barry Hinton
2005 Barry Zirkin
2006 Sally Perreault Darney
2007 Matthew P. Hardy
2008 Erwin Goldberg
2009 Joel L. Marmar
2010 Christina Wang
2011 Terry R. Brown
2012 Rex A. Hess
2013 Susan Rothmann

Distinguished Service Award is sponsored by the American Society of Andrology.
Matthew P. Hardy Young Andrologist Award

Jon M. Oatley, PhD is the director of the Center for Reproductive Biology and an associate professor in the School of Molecular Biosciences at Washington State University. Dr. Oatley obtained his PhD from Washington State University in 2004, was a postdoctoral fellow in the laboratory of Dr. Ralph Brinster at the University of Pennsylvania, and began as an independent investigator in 2007. His research focuses on deciphering the mechanisms that regulate formation of the germline stem cell pool in mammalian testes during development and maintenance of the population in adulthood. Because the actions of the germline stem cell pool provide the foundation for continual spermatogenesis, Dr. Oatley’s research is related directly to understanding fundamental process that underpins male fertility. Dr. Oatley has authored more than 30 papers in top-tier journals in the fields of reproductive and developmental biology including PNAS, the Biology of Reproduction, Development, the Journal of Cell Science, and Genes & Development. As an independent investigator, his research program has been funded by multiple grants from the National Institutes of Health and the US Department of Agriculture. Dr. Oatley’s honors include the Dean’s Award for Outstanding Research from the College of Veterinary Medicine at Washington State University, the Baron Lecturer in Reproductive Biology Award from the University of Florida, and the New Investigator Award from the Society for the Study of Reproduction.

Matthew P. Hardy Young Andrologist Award Recipients

1981 L.J.D. Zaneveld
1982 William B. Neaves
1983 Lonnie D. Russell
1984 Bruce D. Schanbacher
1985 Stephen J. Winters
1986 Ilpo T. Huhtaniemi
1987 Larry Johnson
1988 Barry T. Hinton
1989 Luis Rodriguez/Rigau
1990 Patricia M. Saling
1991 Gary R. Klinefelter
1992 Robert Chapin
1993 Wayne J.G. Hellstrom
1994 Christopher DeJonge
1995 Paul S. Cooke
1996 Gail A. Cornwall
1997 William R. Kelce
1998 Stuart E. Ravnik
1999 Matthew P. Hardy
2000 Jacquetta Trasler
2001 Christopher L.R. Barratt
2002 Joanna E. Ellington
2003 Kate Loveland
2004 Janice Bailey
2005 Janice P. Evans
2006 John K. Amory
2007 Moira K. O’Bryan
2008 Michael A. Palladino
2009 Peter Liu
2010 Humphrey Yao
2011 Wei Yan
2012 Jacques J. Tremblay
2013 Sarah Kimmins

The Matthew P. Hardy Young Andrologist Award is sponsored by the Matthew P. Hardy Endowment Fund
Outstanding Trainee Investigator Award

The Outstanding Trainee Investigator Award is given to the ASA trainee member with the best abstract and research presentation at the annual meeting. The award encourages trainee members to submit and present their best work and contribute to the scientific excellence of the society.

The recipient of the 2015 Outstanding Trainee Investigator Award will be announced during the Annual Business Meeting on Monday, April 20, 2015 at 6:15 p.m.

New Investigator Award Recipients

1983  Thomas T. Tarter
1984  Peter S. Albertson
1985  Randall S. Zane
1986  Mark A. Hadley
1987  Peter Grosser
1988  Stuart E. Ravnik
1989  Tracy L. Rankin
1990  Donna O. Bunch
1991  Robert Viger
1992  John Kirby
1993  Michael A. Palladino
1994  Linda R. Johnson
1995  Mehdi A. Akhondi
1996  Wei Gu, Daniel B. Rudolph
1997  Loren D. Walensky
1998  Dolores D. Mruk
1999  Jacques J. Tremblay
2000  Jeffrey J. Lysiak
2001  Alexander T.H. Wu
2002  Ebtesam Attaya
2003  Mustafa Faruk Usta

Outstanding Trainee Investigator Award Recipients

2004  Darius Paduch
2005  Tara Barton
2006  Liwei Huang
2007  Steve Tardif
2008  Duangporn Jamsai
2009  Catherine Itman
2010  Michael Elliott
2011  Matthew Marcello
2012  Andrew Major
2013  Mary Samplaski
2014  Andrew Midzak
The American Society of Andrology, Inc. gratefully acknowledges these lifetime contributors to the various ASA Endowment or Asset Funds

Gold Level
(Total Contributions greater than or equal to $10,000)

- Douglas T. Carrell, PhD
- Anna Steinberger, PhD
- Bayard T. Storey, PhD
- J. Lisa Tenover, MD, PhD
- Donna L. Vogel, MD, PhD
- Christina Wang, MD

Silver Level
(Total Contributions greater than or equal to $5,000)

- William J. Bremner, MD, PhD
- Erwin Goldberg, PhD
- Rex Hess, MS, PhD
- Ronald W. Lewis, MD, FACS
- Gail S. Prins, PhD
- Susan Ann Rothmann, PhD, HCLD
- Peter N. Schlegel, MD
- Richard J. Sherins, MD
- Women in Andrology

Sustaining
(Total Contributions greater than or equal to $2,000)

- Rupert P. Amann, PhD
- Richard D. Amelar, MD
- Rudi Ansbacher, MD
- Andrzej Bartke, PhD
- Arnold M. Belker, MD
- Glenn R. Cunningham, MD
- Sally Perreault Darney, PhD
- E. Mitch Eddy, PhD
- Frank S. French, MD
- Wayne J.G. Hellstrom, MD FACS
- Barry T. Hinton, PhD
- Dolores J. Lamb, PhD, HCLD
- Joel L. Marmar, MD
- Marvin L. Meistrich, PhD
- Jon Lee Pryor, MD
- Bernard Robaire, PhD
- Barbara M. Sanborn, PhD
- Ronald Swerdloff, MD
- Terry T. Turner, PhD
- Richard Van Clark, MD, PhD

Contributions to the ASA Annual Fund
July 1, 2013 – July 31, 2014

$1000+
- Andrzej Bartke, PhD
- William J. Bremner, MD, PhD
- Douglas T. Carrell, PhD
- Cryogam Colorado - Betsy Cairo, PhD
- Fertility Solutions - Susan Rothmann, PhD, HCLD
- Erwin Goldberg, PhD
- David J. Handelsman, MD, PhD
- Sarah Kimmins, PhD
- Kirk C. Lo, MD, FRCSC
- Marvin L. Meistrich, PhD
- William Neaves, PhD
- Vassiliios Papadopoulos, PhD
- Gail S. Prins, PhD
- Susan Ann Rothmann, PhD, HCLD
- Jay I. Sandlow, MD
- Peter N. Schlegel, MD, FACS
- Richard J. Sherins, MD
- Mark Sigman, MD
- Anna Steinberger, PhD
- J. Lisa Tenover, MD, PhD
- Christina Wang, MD
- Barry R. Zirkin, PhD

$250-$999
- John K. Amory, MD, MPH
- Rudi Ansbacher, MD
- Janice L. Bailey, PhD
- Christopher Burrratt, PhD
- Anna - Marie Bort
- Paul Cooke, PhD
- George L. Gerton, PhD
- Barry T. Hinton, PhD
- Thomas B. Knudsen, PhD
- Ronald W. Lewis, MD, FACS
- Martin M. Matzuk, MD, PhD
- Michael A. Palladino, PhD
- Robin Pillow, BS, CT (ASCP)
- Donna L. Vogel, MD, PhD
Contributions to the ASA Annual Fund

$100-$249
Robert Edward Brannigan, MD
Golden Rule Consulting
F. Kent Hamra, PhD
Mary Ann Handel, PhD
Wylie C. Hembree, MD
Rex A. Hess, MS, PhD
Barry T. Hinton, PhD
Carin V. Hopps, MD
Kate Loveland, PhD
Clinton Mac Donald, PhD
Joel Marmor, MD
Patricia A. Martin-DeLeon, PhD
Adam Millar, MD, MScCH
Patricia L. Morris, PhD, MS
Charles H. Muller, PhD
Darius A. Paduch, MD, PhD
Sally Perreault Darney, PhD
Steven M. Schrader, PhD
Paul Ray Shin, MD
Suresh C. Sikka, PhD, HCLD, CC (ABB)
David C. Sokal, MD
Bayard T. Storey, PhD
Jacques J. Tremblay, PhD
Pablo E. Visconti, PhD
Wei Yan, MD, PhD
Humphrey Yao, PhD

$1-$99
Sunny O. Abarikwu, PhD
Sylvie Breton, PhD
Arthur L. Burnett, II, MD
Anne Marie Downey, BSc
Jorge Hallak, MD, PhD
Matthew Kovak
Sophie La Salle, PhD
Sandra Maria Miraglia
Burak Ozkosem, PhD
Genevieve Plane, BSc
Mary Katherine Samplaski, MD
Luke Simon, PhD
Mayra Miranda Spooner
Hitoshi Takeshima, MD

THANK YOU TO OUR:

2015 ASA Exhibitors
AbbVie
Fertility Technology Resources, Inc.
Imprimis Pharmaceuticals
LifeGlobal/IVFonline.com
Projectes | Serveis R+D SL (PROiSer)
SCSA Diagnostics, Inc
Sigma-Tau Pharmaceuticals, Inc.

2015 ASA Educational Grant Provider
American Urological Association, Inc.

2015 ASA Contributors
The Eunice Kennedy Shriver National Institute of Child Health and Human Development
Handyem, Inc.
International Society of Andrology
The Lalor Foundation
The National Institute of Environmental Health Sciences
Educational Needs & Objectives

40th Annual ASA Meeting
“A Lifetime of Male Reproductive Health”

Educational Needs
Reproductive health starts at birth and continues throughout life. Male fertility can be impacted at multiple stages by numerous factors ranging from genomic imprinting to environmental factors. Increasingly, the role of aging has been recognized as a significant contributor to male reproductive health. New tools, approaches and therapies are becoming available to deal with the regulation of fertility and the improvement of health. The use of these modern approaches requires the integration of physiology, endocrinology, genetics, neurobiology and psychology, along with consideration of lifestyle and environmental exposures. There must be extensive interactions among clinicians and translational scientists in order to both recognize and treat clinical conditions related to male fertility and reproductive health.

The American Society of Andrology 40th Annual Conference will provide a forum for clinicians and basic scientists to exchange ideas and raise new clinically applicable questions that can lead to novel research directions and efficacious therapies. Renowned researchers working in the fields of urology, endocrinology, clinical andrology, genetics, reproductive medicine and reproductive biology will come together to present cutting edge developments in the physiological and molecular foundations of male reproductive function.

Educational Objectives
At the conclusion of the ASA 40th Annual Conference, attendees should be able to:

1. Evaluate the mechanisms of genomic imprinting on male reproductive physiology in relationship to maternal and paternal alleles.
2. Identify the role of aging on specific genetic factors that may impact spermatogenesis and DNA repair pathways.
3. Describe how the stem cell niche regulates the replication and differentiation of spermatogonial stem cells.
4. Identify the role of the somatic sertoli cells in constraining the development of stem cells to the spermatogonial lineage.
5. Describe the role of specific microRNAs in maintenance of the spermatogonial stem cell pool.
6. Describe the science of reproductive toxicology and how to translate benchwork to policy formulation.
7. Recognize appropriate candidates, methodology and utilization of cryopreservation strategies in pediatric and adult cancer patients.
9. Assess the negative impact of drugs and environmental toxins on sperm production and male fertility.
10. Evaluate the potential role of newer oral therapies for the treatment of secondary male hypogonadism.
11. Review the current management of infertility and sperm retrieval techniques in the spinal cord injured male in the era of IVF-ICSI.
12. Describe the perils and pitfalls of the boom in anti-aging therapies.
13. Recognize the effects of single nucleotide polymorphisms on the function and expression of genes required for spermatogenesis.
14. Identify novel and promising approaches to the treatment and prevention of erectile dysfunction after radical prostatectomy.
15. Describe the effect of single nucleotide polymorphisms on the function of genes required for successful spermatogenesis.
16. Identify the effects of endogenous and exogenous testosterone, as well as deficiency, on human cardiac function.
17. Explain the genetic and hormonal basis for male-specific aspects of cardiomyocyte function.
18. Describe the role of the TGF-β signaling in the development and normal function of the testis.
19. Describe recent advances in the targeting of signaling pathways in spermatogenic cells for the purposes of male contraception.
20. Explain recent advances in the development of steroid-based male contraceptives.
21. Identify two genetic abnormalities in sperm DNA that are associated with advanced paternal age (APA).
22. Explain APA associations with miscarriages, preterm birth and fetal death.
23. Describe a chromosomal disorder and a single gene mutation disorder that occur with increased frequency in APA offspring.

ASA Special Symposium
“Controversies in Testosterone Therapy”

Educational Needs
Providers need to be aware of the recent FDA advisory panel regarding testosterone. Specific topics include who should be prescribed testosterone, what truly constitutes hypogonadism, and the risks and benefits of testosterone treatment.

Today the main reason why clinicians do not prescribe testosterone is the fear that it may cause prostate cancer or heart disease. However, there is no compelling data to support this. Many clinicians are unaware of the published data on testosterone and prostate cancer.

Finally, many clinicians are completely unaware of the practices of bodybuilders and testosterone abuse.

Educational Objectives
At the conclusion of the ASA Special Symposium, attendees should be able to:

1. Explain the controversy of the recent FDA panel recommendations.
2. Describe how testosterone affects the heart and overall cardiac function.
3. Identify the cardiovascular and metabolic risks associated with low testosterone and how low testosterone is associated with an increased risk of mortality.
4. Describe the published literature on testosterone and prostate cancer.
5. Identify the cardiovascular and metabolic risks associated estrogen, SHBG levels and the T/E ratio.
6. Describe the effects of testosterone on the prostate and its relative safety in men with prostate cancer.
7. Explain the common practices of bodybuilders as relates to T manipulating hormones and practices.
Accreditation Statement
This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of the University of Oklahoma College of Medicine and the American Society of Andrology. The University of Oklahoma College of Medicine is accredited by the ACCME to provide continuing medical education for physicians.

The University of Oklahoma College of Medicine designates this live activity for a maximum of 21.00 AMA PRA Category 1 Credits™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Conflict Resolution Statement
The University of Oklahoma College of Medicine, Office of Continuing Professional Development has reviewed this activity’s speaker and planner disclosures and resolved all identified conflicts of interest, if applicable.

Equal Opportunity Statement
The University of Oklahoma is an equal opportunity institution. www.ou.edu/eoo

Accommodation Statement
Accommodations on the basis of disability are available by contacting the American Society of Andrology at (847) 619-4909 as soon as possible.

Acknowledgement of Commercial and In-Kind Support
Commercial support is financial, or in-kind, contributions given by a commercial interest, which is used to pay all or part of the costs of a CME activity. A commercial interest is any entity producing, marketing, re-selling or distributing health care goods or services consumed by, or used on, patients.

This activity is made possible in part by an unrestricted, educational grant from the American Urological Association, Inc.

Policy on Faculty, Presenters and Joint Provider Disclosure
It is the policy of the University of Oklahoma College of Medicine that the faculty, presenters and joint provider disclose real or apparent conflicts of interest relating to the topics of this educational activity, and also disclose discussions of unlabeled/unapproved uses of drugs or devices during their presentation(s).

Disclaimer Statement
Statements, opinions and results of studies contained in the program are those of the presenters, authors and joint provider and do not reflect the policy or position of the Board of Regents of the University of Oklahoma (“OU”) nor does OU provide any warranty as to their accuracy or reliability.

Every reasonable effort has been made to faithfully reproduce the presentations and material as submitted. However, no responsibility is assumed by OU for any claims, injury and/or damage to persons or property from any cause, including negligence or otherwise, or from any use or operation of any methods, products, instruments or ideas contained in the material herein.

Mark Your Calendars

ASA 41st Annual Conference
April 2 – April 5, 2016
Astor Crowne Plaza
New Orleans, LA

ASA Special Symposium
April 2, 2016

ASA Basic Science Workshop
April 2, 2016

ASA Andrology Lab Workshop
April 2 – April 3, 2016

ASA Trainee-Directed Mini Symposium
April 2, 2016

Faculty Disclosure Report
The University of Oklahoma College of Medicine and the Irwin H. Brown Office of Continuing Professional Development must ensure balance, independence, objectivity and scientific rigor in all its activities. We have implemented a process where everyone who is in a position to control the content of an education activity has disclosed to us all relevant financial relationships with any commercial interest. In addition, should it be determined that a conflict of interest exists as a result of a financial relationship one may have, this will be resolved prior to the activity. This policy is designed to provide the target audience with an opportunity to review any affiliations between the CME organizers/ presenters and supporting organizations for the purpose of determining the potential presence of bias or influence over educational content. The Disclosure Report may be found at the following link: http://andrologysociety.org/2015Disclosures.pdf
SCHEDULE OF EVENTS

XXIIIrd North American Testis Workshop
“Healthy Sperm – Healthy Children”
April 15 – 18, 2015
Chair: Jacquetta M. Trasler, MD, PhD
Vice-Chair: Leslie L. Heckert, PhD

All sessions located in Grand Ballroom A-B unless otherwise noted
Speakers and times are subject to change

WEDNESDAY, APRIL 15, 2015

6:00 p.m. – 8:30 p.m. Registration/Information Desk Open
Location: Grand Ballroom A Foyer

7:00 p.m. – 7:15 p.m. Welcome
Jacquetta Trasler, MD, PhD
McGill University

7:15 p.m. – 8:15 p.m. Keynote Address
Human Primordial Germ Cells: Intergenerational Epigenetic Gatekeepers
Amander Clark, PhD
UCLA

8:15 p.m. – 9:30 p.m. Testis Workshop Welcome Reception
Location: Grand Ballroom Reception A-B

THURSDAY, APRIL 16, 2015

7:00 a.m. – 6:00 p.m. Registration/Information Desk Open
Location: Grand Ballroom A Foyer

7:15 a.m. – 8:00 a.m. Continental Breakfast

8:00 a.m. – 8:45 a.m. Benchmark Lecture I
Chair: William Wright, PhD, Johns Hopkins University
Therapeutic Promise of Primate Spermatogonial Stem Cells
Stefan Schlatt, PhD
WWU Münster, Germany

SESSION I: MALE FERTILITY ACROSS GENERATIONS
SETTING THE STAGE

8:45 a.m. – 8:50 a.m. Chair and Introduction to Session I
Ralph Meyer, PhD
Utah State University

8:50 a.m. – 9:25 a.m. Identification of a Novel DNA Methylation in C. Elegans and Its Role in Transgenerational Inheritance
Eric Greer, PhD
Children’s Hospital Boston and Harvard Medical School

9:25 a.m. – 10:00 a.m. Paternal Stress Alteration of Sperm miRNAs Reprogram Stored Maternal mRNAs and Offspring Neurodevelopment
Tracy Bale, PhD
University of Pennsylvania

10:00 a.m. – 10:25 a.m. Break

10:25 a.m. – 11:00 a.m. Father’s In Utero and Postnatal Folate Exposures Affect Offspring Health
Amanda MacFarlane, PhD
Health Canada

11:00 a.m. – 11:15 a.m. Short Talk #1
Implications of Lifetime Folate Deficiency and Supplementation on Intergenerational Health
Lundi Ly, BSc
McGill University

11:15 a.m. – 11:30 a.m. Short Talk #2
The RHOX10 Homeobox Transcription Factor Drives the Initial Establishment of Spermatogonial Stem Cells
Hye-Won Song, PhD
University of California

11:30 a.m. – 1:00 p.m. Lunch (on your own)

SESSION II: HEALTHY STEM CELLS, HEALTHY AGING

1:00 p.m. – 1:05 p.m. Chair and Introduction to Session II
Kyle Orwig, PhD
University of Pittsburgh

1:05 p.m. – 1:40 p.m. Sex Determination in the Somatic Gonad and Germline
Mark Van Doren, PhD
Johns Hopkins University

1:40 p.m. – 2:15 p.m. Biological Functions of Pax7+
Spermatogenesis
Diego Castrillon, MD, PhD
University of Texas Southwestern

2:15 p.m. – 2:40 p.m. Break

2:40 p.m. – 3:15 p.m. Aging Effects on the Spermatogenic Cell Epigenome
Christopher Payne, PhD
Northwestern University

3:15 p.m. – 3:50 p.m. Aging and Leydig Cells
Barry Zirkin, PhD
Johns Hopkins University
SCHEDULE OF EVENTS

FRIDAY, APRIL 17, 2015

3:50 p.m. – 6:00 p.m.  Poster Session I
Location: Grand Ballroom C

6:00 p.m. – 8:00 p.m.  Post-Poster Social Event
Location: Idaho
(not included in registration: ticket required)

7:00 a.m. – 6:00 p.m.  Registration/Information Desk Open
Location: Grand Ballroom A Foyer

7:15 a.m. – 8:00 a.m.  Continental Breakfast

8:00 a.m. – 8:45 a.m.  Benchmark Lecture II
Chair: Kate Loveland, PhD, Monash University
Male-Female Signaling By Seminal Fluid: Effects on Metabolic Phenotype of Offspring
Sarah Robertson, PhD
University of Adelaide

SESSION III: REGULATION OF GENE EXPRESSION FROM PROGENITOR CELLS THROUGH MEIOSIS

8:45 a.m. – 8:50 a.m.  Chair and Introduction to Session III
Wei Yan, MD, PhD
University of Nevada – School of Medicine

8:50 a.m. – 9:25 a.m.  Small RNAs Target Active Transposable Elements to Establish the Repressive Chromatin Mark in Germ Cells
Alexei Aravin, PhD
Caltech

9:25 a.m. – 10:00 a.m.  Investigating the Role of Argonaute Proteins in Mammalian Meiosis
Paula Cohen, PhD
Cornell University

10:00 a.m. – 10:25 a.m.  Break

10:25 a.m. – 11:00 a.m.  How Polyadenylation Controls Gene Expression in Testis and Brain
Clinton MacDonald, PhD
Texas Tech University

11:00 a.m. – 11:15 a.m.  Short Talk #3
Evaluating L1 Transgenes Regulated by the Endogenous Mouse L1 Promoter
Wenfeng An
South Dakota State University

11:15 a.m. – 11:30 a.m.  Short Talk #4
Overexpression of ID4 Alters Cell Cycle Progression and Transition from the Stem Cell to Progenitor State in Mouse Spermatogonia
Jon M. Oatley, PhD
Washington State University

11:30 a.m. – 1:00 p.m.  Lunch (on your own)

SESSION IV: DETERMINING AND PERTURBING TESTICULAR FUNCTION

1:00 p.m. – 1:05 p.m.  Chair and Introduction to Session IV
Leslie Heckert, PhD
University of Kansas Medical Center

1:05 p.m. – 1:40 p.m.  Protecting Maturing Sperm from Environmental Toxicants: The Role of the Epididymis
Daniel Cyr, PhD
INRS

1:40 p.m. – 2:15 p.m.  Safeguarding Sperm: Identification of Mutagenic Hazards to Future Generations
Carole Yauk, PhD
Health Canada

2:15 p.m. – 2:30 p.m.  Short Talk #5
Direct Germline Editing in Spermatogonia Eliminates CRISPR/CAS9 Catalyzed Animal Mosaicism
F. Kent Hamra, PhD
University of Texas Southwestern Medical Center

2:30 p.m. – 2:45 p.m.  Short Talk #6
The Role of Peritubular Myoid (PM) Cells in the Regulation of Spermatogonial Stem Cell (SSC) Self-Renewal, Proliferation and Differentiation in the Testis Niche
Liang-Yu Chen
NIEHS

SESSION V: SOMATIC CELLS

3:10 p.m. – 3:15 p.m.  Chair and Introduction to Session V
Katja Teerds, PhD
Wageningen University

3:15 p.m. – 3:50 p.m.  Sertoli Cells: Immune Privilege & Novel Roles in Cell Based Gene Therapy
Jannette Dufour, PhD
Texas Tech University
SCHEDULE OF EVENTS

3:50 p.m. – 4:25 p.m.  NOTCH Signaling in Sertoli Cells  10:25 a.m. – 11:00 a.m.  Genetic Causes of Human Infertility: From X Chromosome High Resolution Array-CGH to Whole Exome Studies
   Marie-Claude Hofmann, PhD
   University of Texas – MD Anderson Cancer Center

4:25 p.m. – 4:40 p.m.  Short Talk #7  11:00 a.m. – 11:15 a.m.  Short Talk #9
   Cholesterol Trafficking for Steroid Biosynthesis in MA-10 Mouse Tumor Leydig Cells
   Sathvika Jagannathan, MSc
   McGill University

4:40 p.m. – 4:55 p.m.  Short Talk #8
   Requirement for Adenosine Deaminase Containing Proteins in Male Germ Cell Development
   Elizabeth Snyder, PhD
   The Jackson Laboratory

5:00 p.m. – 7:00 p.m.  Poster Session II
   Location: Grand Ballroom C

SATURDAY, APRIL 18, 2015

7:00 a.m. – 2:00 p.m.  Registration/Information Desk Open
   Location: Grand Ballroom A Foyer

7:15 a.m. – 8:00 a.m.  Continental Breakfast

8:00 a.m. – 8:45 a.m.  Benchmark Lecture III
   Chair: Mitch Eddy, PhD
   Androgen-Signaling in Lifelong Health and Well Being
   Lee B. Smith, PhD
   MRC Centre for Reproductive Health – Edinburgh

SESSION VI: HUMAN FERTILITY, INFERTILITY AND THE NEXT GENERATION

8:45 a.m. – 8:50 a.m.  Chair and Introduction to Session VI
   Vassilios Papadopoulos, DPharm, PhD
   McGill University, Research Institute

8:50 a.m. – 9:25 a.m.  Endocrine Disruptors, Early Exposures and Sperm Function
   Jorma Toppari, MD, PhD
   University of Turku

9:25 a.m. – 10:00 a.m.  Infertility, Aging, ART and Sperm Epigenetics
   Douglas Carrell, PhD, HCLD
   University of Utah

10:00 a.m. – 10:25 a.m.  Break

© 2015 American Society of Andrology and European Academy of Andrology
Andrology, 2015, Supplement, 25
1:00 p.m. – 2:50 p.m.  T & the FDA Panel: ASA Expert
Panel Debates Five Critical Questions*
Moderator: Ajay K. Nangia, MBBS, FACS
Panelists: James M. Dupree, MD, MPH
Michael Butcher, DO
James A. Kashanian, MD
Alexander W. Pastuszak, MD, PhD
Charles Welliver Jr., MD

1:00 p.m. – 1:10 p.m.  Introduction

1:10 p.m. – 1:25 p.m.  Question 1:
“The whole idea is to try to rein in the inappropriate advertising and use of these drugs.”

What is the evidence that T is being overprescribed? If so, to whom and by whom? Has T advertising from prescription drug companies (not supplements) been inappropriate?
Charles Welliver Jr, MD

1:25 p.m. – 1:40 p.m.  Question 2:
“One of the stickiest problems had been the vagueness of testosterone drug labels, which many doctors have interpreted to include any man with low testosterone.”

The FDA panel has great concerns about the difference between the symptoms of normal aging (lower energy, decreased libido, weak erections) and “true” low testosterone. Is this distinction important and how do you differentiate who should be given a trial of low T? Do you utilize trials of discontinuation?
Alexander W. Pastuszak, MD, PhD

1:40 p.m. – 1:55 p.m.  Question 3:
“Panelists said the label should be limited to men with serious medical conditions, such as pituitary gland problems. It was not clear what share of men that represented, though officials said it was a small minority of users.”

The FDA Panel seeks to minimize use of T, specifically in the most common form of low T (idiopathic) – What is their rationale and does this make sense?
Michael Butcher, DO

1:55 p.m. – 2:10 p.m.  Question 4:
“Many experts began raising alarms, saying that the benefits and longer-term risks of the drugs were unknown.”
Much concern has been brought up about the safety of T for thromboembolic events and prostate cancer – What is the evidence of these risks? Is there any common patient scenario in which you would not give T?
James M. Dupree, MD, MPH

2:10 p.m. – 2:25 p.m.  Question 5:
“The FDA has said that the benefits of testosterone treatments for healthy, aging men are unproven.”

The FDA states there is no evidence to support T is beneficial in “healthy men.” Based on previous statements, it seems men with low T (idiopathic) are being considered healthy. Is there evidence to support positive effects of low T in these “healthy men”? Can you touch on the relationship of testosterone, obesity and compare testosterone to bariatric surgery?
James A. Kashanian, MD

2:25 p.m. – 2:50 p.m.  Closing Remarks/Panel Discussion

2:50 p.m. – 3:00 p.m.  Break

3:00 p.m. – 4:10 p.m.  Realities & Secrets of Anabolic Steroid Abuse

3:00 p.m. – 3:30 p.m.  Structured Interview with Chad Schaive – Prior Pro-level Body Builder

3:30 p.m. – 3:50 p.m.  Anabolic Steroids, Hypogonadism and Beyond
Jason R. Kovac, MD, PhD, FRCS

3:50 p.m. – 4:10 p.m.  Q&A

4:10 p.m. – 4:20 p.m.  Break

4:20 p.m. – 5:15 p.m.  Hormones and the Heart: Improved or Infarcted?

4:20 p.m. – 4:40 p.m.  Testosterone and Cardiovascular Disease
Jesse N. Mills, MD

4:40 p.m. – 5:00 p.m.  Estrogens, the T/E Ratio, SHBG & Cardiovascular Disease – From Population Genetic to Gender Epidemiology
Darius A. Paduch, MD, PhD

5:00 p.m. – 5:15 p.m. Q&A

*All quotes taken from the New York Times article “FDA Panel Backs Limits on Testosterone Drugs,” by Sabrina Tavernise (September 18, 2014). Read the article online at nytimes.com.
SCHEDULE OF EVENTS

ASA Trainee Directed Mini-Symposium*
“Bridging Your Career: Transitioning from Trainee to Mentor”
April 18, 2015
The Little America Hotel
Salt Lake City, Utah
*Not CME Accredited
Program Chairs: Mary K. Samplaski, MD, and Luke Simon, PhD

All sessions will be held in Wyoming unless otherwise noted.

1:30 p.m. – 1:45 p.m. Opening Remarks
Luke Simon, PhD
Jay I. Sandlow, MD, ASA President

1:45 p.m. – 2:15 p.m. Building and Maintaining Successful Collaborations
Moderator: Mary K. Samplaski, MD
Speakers: Dolores J. Lamb, PhD
Kirk C. Lo, MD

2:15 p.m. – 2:30 p.m. Q & A

2:30 p.m. – 3:15 p.m. Panel Discussion: Making the Transition from Trainee to Faculty
Moderators: Mary K. Samplaski, MD
Luke Simon, PhD
Panelists: Mara Roth, MD
Sophie La Salle, PhD
Ajay K. Nangia, MBBS, FACS
Barry T. Hinton, PhD

3:15 p.m. – 3:45 p.m. Break

3:45 p.m. – 4:25 p.m. Grant Workshop
Donna L. Vogel, MD, PhD

NIH Representatives:
Stuart B. Moss, PhD
NICHBD
Thaddeus T. Schug, PhD
NIEHS

An overview of NIH funding mechanisms. Participants will then break into smaller groups overseen by NIH-funded clinicians and basic scientists to discuss various aspects of the grant application process.

4:25 p.m. – 4:30 p.m. Closing Remarks

This career development mini-symposium is being held for trainees, in direct response to requests by trainees.
## SCHEDULE OF EVENTS

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>6:00 p.m. – 6:10 p.m.</td>
<td>Welcome and Opening Remarks</td>
</tr>
<tr>
<td>6:10 p.m. – 6:30 p.m.</td>
<td>Updates from NICHD &amp; NIEHS</td>
</tr>
<tr>
<td>Stuart B. Moss, PhD</td>
<td>National Institutes of Child Health and Human Development</td>
</tr>
<tr>
<td>Thaddeus T. Schug, PhD</td>
<td>National Institute of Environmental Health Sciences</td>
</tr>
<tr>
<td>6:30 p.m. – 6:50 p.m.</td>
<td>Andrology Journal Award</td>
</tr>
<tr>
<td>Andrology Prize Paper for 2014: Maselli J, Hales BF, Robaire B.</td>
<td>“Paternal exposure to testis cancer chemotherapeutics alters sperm fertilizing capacity and affects gene expression in the eight-cell stage rat embryo”</td>
</tr>
<tr>
<td>Awarded to: Bernard Robaire, PhD</td>
<td>McGill University</td>
</tr>
<tr>
<td>(Presented by: Douglas T. Carrell, PhD, HCLD, Editor-in Chief, Andrology)</td>
<td></td>
</tr>
<tr>
<td>6:50 p.m. – 7:45 p.m.</td>
<td>EMIL STEINBERGER MEMORIAL LECTURE</td>
</tr>
<tr>
<td>Genomic Imprinting: Mechanisms and Environmental Sensitivity</td>
<td>Marisa S. Bartolomei, PhD Perelman School of Medicine, University of Pennsylvania</td>
</tr>
<tr>
<td>(Introduced by: Jay I. Sandlow, MD)</td>
<td></td>
</tr>
<tr>
<td>7:45 p.m. – 8:00 p.m.</td>
<td>Distinguished Andrologist Award</td>
</tr>
<tr>
<td>8:00 p.m. – 9:30 p.m.</td>
<td>Welcome Reception</td>
</tr>
<tr>
<td>Location: Grand Ballroom Reception A-C</td>
<td></td>
</tr>
<tr>
<td>11:30 a.m. – 1:00 p.m.</td>
<td>ASA LABORATORY SCIENCE FORUM LUNCHEON*</td>
</tr>
<tr>
<td>Location: Arizona Laboratory Disaster Preparedness</td>
<td>&quot;Surviving Sandy: Lessons in Disaster Planning and Recovery for Labs, Offices and Institutions”</td>
</tr>
<tr>
<td>Speaker: Susan A. Rothmann, PhD, HCLD Fertility Solutions, Inc.</td>
<td></td>
</tr>
<tr>
<td>(not included in registration: ticket required)</td>
<td></td>
</tr>
<tr>
<td>*Not CME Accredited</td>
<td></td>
</tr>
<tr>
<td>1:00 p.m. – 5:15 p.m.</td>
<td>ASA 2015 Special Symposium (See pg 27 for full schedule)</td>
</tr>
<tr>
<td>1:30 p.m. – 4:30 p.m.</td>
<td>ASA Trainee Directed Mini-Symposium* (See pg 28 for full schedule)</td>
</tr>
<tr>
<td>*Not CME Accredited</td>
<td></td>
</tr>
</tbody>
</table>
8:00 a.m. – 9:00 a.m.  **AUA LECTURE**  Reproductive Genetics and the Aging Male  
Paul J. Turek, MD, FACS, FRSM  
The Turek Clinic  
(Introduced by: Dolores J. Lamb, PhD, HCLD)

9:00 a.m. – 9:15 a.m.  Distinguished Service Award

9:15 a.m. – 10:45 a.m.  **SYMPOSIUM I – Basic Science**  
- Stem Cells, Niches and Reproductive Function  
Moderator: Jon M. Oatley, PhD

  Heterogeneity of Spermatogonia and Its Relationship to the Stem Cell Niche – A Review  
Makoto Nagano, PhD, DVM  
McGill University

  Sertoli Cells Constrain Pluripotent iPS Cells to Form Spermatogenic Cells in Vivo  
Renee A. Reijo Pera, PhD  
Montana State University

  MicroRNA Regulation of Spermatogonial Development  
Wei Yan, MD, PhD  
University of Nevada School of Medicine

10:45 a.m. – 11:00 a.m.  Quick Break

11:00 a.m. – 12:30 p.m.  **Poster Session I**  
Location: Grand Ballroom C  
*Not CME Accredited  
(See pg 49 for full schedule)

12:30 p.m. – 2:00 p.m.  Lunch (on your own)

12:30 p.m. – 2:00 p.m.  **Mentoring Luncheon Sponsored by the Diversity and Trainee Affairs Committees**  
Finding Your Path in Andrology (not included in general registration: separate registration required)  
Location: Wyoming  
Susan A. Rothmann, PhD, HCLD  
Fertility Solutions, Inc.  
*Not CME Accredited

12:30 p.m. – 2:00 p.m.  **Editorial Board Luncheon**  
Location: Snowbasin

2:00 p.m. – 3:30 p.m.  **CONCURRENT SESSIONS**  
Oral Session I: Basic Science  
Location: Grand Ballroom A-B  
Moderator: William Wright, PhD

  2:00 PM –#1  
MULTICELLULAR HUMAN TESTICULAR ORGANOID: A NOVEL IN VITRO GERM CELL AND TESTICULAR TOXICITY MODEL  
Speaker: Samuel Pendergraft, MS  
Wake Forest University

  2:15 PM –#2  
CONDITIONAL STEROIDOGENIC CELL-TARGETED DELETION OF THE TRANSLOCATOR PROTEIN (TSPO) UNVEILS ITS CRUCIAL ROLE IN VIABILITY AND HORMONE-DEPENDENT STEROID FORMATION  
Speaker: Andrew Midzak, PhD  
Research Institute of the McGill University Health Centre

  2:30 PM –#3  
EARLY-LIFE EXPOSURE TO AN ENVIRONMENTAL ORGANOCHLORINE MIXTURE REDUCES THE FERTILITY OF MALE RATS AND INDUCES DIFFERENTIAL EXPRESSION OF SPERM PROTEINS ACROSS MULTIPLE GENERATIONS IN A PATERNALLY-MEDIATED MANNER  
Speaker: Nancy Côté, PhD  
Université Laval

  2:45 PM –#4  
MACROPHAGES AND DENDRITIC CELLS COOPERATE TO SURVEY THE EPIDIDYMAL LUMEN  
Speaker: Tegan Smith, PhD  
Massachusetts General Hospital/Harvard Medical School

  3:00 PM –#5  
THE SPLICING FACTOR RBM5 IS REQUIRED FOR SPERMATOGONIA DIFFERENTIATION  
Speaker: Duangporn Jamsai, PhD  
Monash University

  3:15 PM –#6  
MECHANISM OF HYPOGONADISM IN THE TRANSGENIC SICKLE CELL MOUSE  
Speaker: Biljana Musicki, PhD  
Johns Hopkins University
SCHEDULE OF EVENTS

2:00 p.m. – 3:30 p.m.  
CONCURRENT SESSIONS  
Oral Session II: Clinical  
Location: Arizona  
Moderator: Edward Kim, MD

2:00 PM –#7  
THE RISK OF CONGENITAL BIRTH DEFECTS IS NOT ASSOCIATED WITH SEMEN PARAMETERS OR MODE OF CONCEPTION IN OFFSPRING OF MEN VISITING A REPRODUCTIVE CLINIC  
Speaker: Alexander W. Pastuszak, MD, PhD  
Baylor College of Medicine

2:15 PM –#8  
EFFICACY AND PHARMACOKINETICS OF LPCN 1021, A NOVEL ORAL TESTOSTERONE REPLACEMENT THERAPY (TRT), IN OBESE AND NON-OBESE HYPOGONADAL MEN: STUDY OF ANDROGEN REPLACEMENT (SOAR)  
Speaker: Adrian Dobs, MD, MHS  
Johns Hopkins University  
School of Medicine

2:30 PM –#9  
CIGARETTE SMOKING AND THE SPERM EPIGENOME  
Speaker: Timothy Jenkins, PhD  
University of Utah

2:45 PM –#10  
WHOLE-EXOME SEQUENCING IDENTIFIES NOVEL HOMOZYGOUS MUTATION IN NPAS2 IN FAMILY WITH NONOBSTRUCTIVE AZOOSPERMIA  
Speech: Ranjith Ramasamy  
Baylor College of Medicine

3:00 PM –#11  
ENCLOMID AND TOPICAL TESTOSTERONE ELEVATE TESTOSTERONE IN HYPOGONADAL MEN BUT ENCLOMID DOES NOT DECREASE TESTES SIZE  
Speaker: Ronald Wiehle, PhD  
Repros Therapeutics

3:15 PM –#12  
CONCENTRATIONS OF THE RETINOIC ACID SYNTHESIZING ENZYME ALDH1A2 ARE SIGNIFICANTLY REDUCED IN MEN WITH OLIGOZOOSPERMIA  
Speaker: John Amory, MD  
University of Washington

3:30 p.m. – 4:00 p.m.  
Refreshment Break  
Location: Grand Ballroom Reception A-C

4:00 p.m. – 4:45 p.m.  
LECTURE I  
Reproductive Toxicology: From Science to Public Policy  
Sally Perreault Darney, PhD  
US Environmental Protection Agency  
(Introduced by:  
Douglas T. Carrell, PhD, HCLD)

4:45 p.m. – 5:30 p.m.  
LECTURE II  
Fertility Preservation in the Male: A New Clinical Paradigm  
Robert E. Brannigan, MD  
Northwestern University  
Feinberg School of Medicine  
(Introduced by: Edward D. Kim, MD)

5:30 p.m. – 6:00 p.m.  
ASA 40th Anniversary Special Presentation I*  
“From Bellbottoms to Bluetooth: 40 Years of Clinical Andrology”  
Terry T. Turner, PhD  
University of Virginia Health System  
Paul J. Turek, MD  
The Turek Clinic  
*Not CME Accredited

6:00 p.m. – 8:00 p.m.  
Trainee Forum & Mixer  
(All Trainee Travel Awards will be distributed and celebrated at this event)  
Location: Olympus

MONDAY, APRIL 20, 2015

7:00 a.m. – 6:00 p.m.  
Registration/Information Desk Open  
Location: Grand Ballroom A Foyer

7:00 a.m. – 3:30 p.m.  
Exhibit Hall Open  
Location: Grand Ballroom Reception A-C

7:00 a.m. – 8:00 a.m.  
Continental Breakfast  
Location: Grand Ballroom Reception A-C

8:00 a.m. – 9:00 a.m.  
WOMEN IN ANDROLOGY LECTURE  
Father’s Lasting Influence: Paternal Environment and the Health of his Future Generations  
Janice L. Bailey, PhD  
Department des Sciences Animales, Universite Laval  
(Introduced by: Sophie La Salle, PhD)

9:00 a.m. – 9:15 a.m.  
Matthew P. Hardy  
Young Andrologist Award

© 2015 American Society of Andrology and European Academy of Andrology Andrology, 2015, Supplement, 30
# SCHEDULE OF EVENTS

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Location</th>
</tr>
</thead>
</table>
| 9:15 a.m. – 10:15 a.m. | **SYMPOSIUM II – Special Concerns for Older Fathers**  
Co-Chairs: Peter Chan, MD  
Keith A. Jarvi, MD  
Therapeutic Advances in the Treatment of Peyronie’s Disease  
Wayne J.G. Hellstrom, MD, FACS  
Tulane University School of Medicine  
Impact of Drugs and Environmental Exposures on Sperm Production  
Cigdem Tanrikut, MD  
Massachusetts General Hospital  
Novel Oral Hormone Replacement Therapies: The Era of the SERMs?  
Andrew R. McCullough, MD  
Albany Medical College |  |
| 1:45 p.m. – 3:15 p.m. | **SYMPOSIUM III – Male Rejuvenation**  
Co-Chairs: Mark Sigman, MD  
Ajay K. Nangia, MBBS, FACS  
What do Patients Want from an Anti-Aging Clinic?  
Martin Miner, MD  
Alpert School of Medicine, Brown University  
Hormonal Replacement for Male Rejuvenation: Is There Scientific Evidence?  
Christina Wang, MD  
Harbor-UCLA Medical Center & LA Biomedical Res. Ins.  
Dangers Associated with Rejuvenation Therapy  
Adrian S. Dobs, MD, MHS  
Johns Hopkins University School of Medicine |  |
| 10:15 a.m. – 10:30 a.m. | Quick Break  
| 10:30 a.m. – 11:15 a.m. | **DIVERSITY LECTURE**  
Current Trends in the Treatment of Infertility in Men with Spinal Cord Injury  
Nancy Brackett, PhD, HCLD  
University of Miami  
Miller School of Medicine  
(Introduced by: Maria Christina W. Avellar, PhD) | Location: Grand Ballroom Reception A-C  
| 11:15 a.m. – 12:30 p.m. | **Poster Session II***  
Location: Grand Ballroom C  
*Not CME Accredited  
(See pg 57 for full schedule)  
| 12:30 p.m. – 1:45 p.m. | Lunch (on your own)  
| 12:30 p.m. – 1:45 p.m. | **WOMEN IN ANDROLOGY LUNCHEON AND DISCUSSION***  
“Preparing Female Scientists for Successful Transitions to Leadership: Paths to Leadership”  
Speaker: Sally Perreault Darney, PhD  
Host & Moderator: Sarah Kimmins, BSc, MSc, PhD  
(not included in general registration; ticket required)  
Location: Wyoming  
*Not CME Accredited  
| 5:00 p.m. to 5:45 p.m. | **EAA LECTURE**  
Post-Testicular Sperm DNA Oxidative Damage: Are the Chromosomes at an Equal Risk?  
Joël R. Drevet, PhD  
University of Blaise Pascal  
(Introduced by: Ewa Rajpert-De Meyts, MD, PhD) |  |
| 5:45 p.m. – 6:15 p.m. | **ASA 40th Anniversary Special Presentation II***  
“40 Years and Beyond: An Andrologist’s Guide to the Galaxy”  
Sophie La Salle, PhD  
Midwestern University  
*Not CME Accredited |  |

*Not CME Accredited

---

© 2015 American Society of Andrology and European Academy of Andrology

Andrology, 2015, Supplement, 31
SCHEDULE OF EVENTS

6:15 p.m.  ASA Business Meeting

7:30 p.m. – 11:00 p.m.  Annual Banquet
Location: Natural History Museum of Utah
Buses depart from hotel lobby starting at 7:15 p.m.
(not included in registration fee: ticket required)

7:00 a.m. – 8:00 a.m.  2016 Program Committee Meeting
Location: Casper

7:00 a.m. – 12:00 p.m.  Registration/Information Desk Open
Location: Grand Ballroom A Foyer

7:00 a.m. – 8:00 a.m.  Continental Breakfast
Location: Grand Ballroom Reception A-C

8:00 a.m. – 9:15 a.m.  SYMPOSIUM IV – The Effects of Testosterone on the Heart
Moderator: Barry Zirkin, PhD
Testosterone and the Heart: Putting the FDA Advisory in Perspective
Shalender Bhasin, MD
Brigham and Women’s Hospital
Potential Therapeutic Role for Testosterone in Cardiac Diastolic Dysfunction
Theodore Abraham, MD, FACC, FASE
Johns Hopkins University School of Medicine
Genetic Variants of Chromosome Y (chrY) Regulate the Responses of Cardiac Genes to Androgens Via Chromatin-Dependent and Circadian Related Effects
Christian F. Deschepper, MD
University of Montreal

9:15 a.m. – 9:30 a.m.  Refreshment Break
Location: Grand Ballroom Reception A-C

9:30 a.m. – 10:30 a.m.  INTERNATIONAL LECTURE
A Perspective from Downunder: TGBβ Signaling in Testis Development and Spermatogenesis
Kate Loveland, PhD
Monash University and MIMR-PHI Institute of Medical Research, Australia

10:30 a.m. – 12:00 p.m.  SYMPOSIUM V – Novel Male Contraceptive Strategies
Moderators: Bernard Robaire, PhD
David Sokal, MD
Na, K-ATPase 4 Isoform as a Target for Male Contraception
Gustavo Blanco, MD, PhD
The University of Kansas Medical Center
Retention Receptor Antagonists for Male Contraception
Debra J. Wolgemuth, PhD
Columbia University Medical Center
Will there be a Role for Male Hormonal Based-Contraception Strategies?
William J. Bremner, MD, PhD
University of Washington

TUESDAY, APRIL 21, 2015

12:00 p.m.  MEETING ADJOURNED

Disclaimer Statement
Statements, opinions and results of studies contained in the program are those of the presenters/authors and do not reflect the policy or position of the ASA nor does the ASA provide any warranty as to their accuracy or reliability.
SPEAKER ABSTRACTS

SATURDAY, APRIL 18, 2015
6:50 p.m. – 7:45 p.m.

EMIL STEINBERGER MEMORIAL LECTURE
GENOMIC IMPRINTING: MECHANISMS AND ENVIRONMENTAL SENSITIVITY
Marissa S. Bartolomei, PhD
University of Pennsylvania School of Medicine, Philadelphia, PA, USA

Imprinted genes are expressed from a single parental allele and most reside in clusters that are located throughout the mammalian genome. The clusters typically contain an imprinting control region (ICR), which harbors allele-specific methylation and governs the imprinting of the entire domain. Although most imprinted clusters use long non-coding RNAs to regulate imprinted gene expression, a few are regulated by CTCF and allele-specific insulator function. One such cluster harbors the H19 and Igf2 imprinted genes, and is controlled by an ICR that contains multiple CTCF binding sites. Gain of maternal methylation and loss of paternal hypermethylation of the H19/Igf2-ICR are associated with the human growth disorders Beckwith-Wiedemann Syndrome and Silver-Russell Syndrome, respectively. Using gene targeting and genome editing, we have generated ES cells, iPSC lines and mice to study the mechanisms of imprinting for these imprinted loci and to model the epigenetic mutations in human syndromes. We have also developed SNV-FISH to study the dynamics of allele-specific gene expression at the single cell level in cell lines and tissues with loss of imprinting. We have additionally studied imprinting in animal models of Assisted Reproductive Technologies (ART) and endocrine disrupting chemical exposures (EDCs). Both ART and EDCs are associated with increased loss of imprinting of various genes and with DNA methylation aberrations. The effects are especially pronounced in placenta, where regulation of multiple genes and DNA methylation of repetitive elements are perturbed, and where morphological changes are evident.

This work is supported by the NIH (GM051279, HD068157, ES023284, EB019767).

SUNDAY, APRIL 19, 2015
8:00 a.m. – 9:00 a.m.

AUA LECTURE
REPRODUCTIVE GENETICS AND THE AGING MALE
Paul Turek, MD, FACS, FRSM
The Turek Clinic

Objectives: To provide an overview of the known effects of advanced paternal age on sperm genetics and birth defects and disease in offspring


Results: Advanced paternal age (>40 years) is linked to changes in quality control associated with spermatogenesis and meiosis. The consequences of these changes include well-delineated anomalies in sperm chromosomes, both numerical and structural, and increased sperm DNA damage (3%/year) and single gene mutations (10-fold). Associated increases in offspring-related events have also been described, including miscarriage (2-fold) and fetal loss (2-fold). An increase in rare, single gene disorders (relative risk 1.3 to 12) and congenital anomalies (20%) among offspring also exists. Recent research suggests that rates of autism, schizophrenia and other forms of “psychiatric morbidity” increase in offspring (relative risk 1.5 to 5.7) with advanced paternal age, and genetic mechanisms related to sperm quality control in the single gene mutation pathway have been implicated as root causes.

Conclusions: Advanced paternal age is associated with increased genetic risk to offspring. However, the precise age at which risk develops and the magnitude of the risk are poorly defined or may have graduated effects. Currently, there are no screening or diagnostic panels that target disorders associated with advanced paternal age. Concerned couples or care providers should pursue or recommend genetic counseling and prenatal testing regarding specific disorders.

Funding: None

SUNDAY, APRIL 19, 2015
9:15 a.m. – 10:45 a.m.

SYMPOSIUM I – Basic Science – Stem Cells, Niches and Reproductive Function
HETEROGENEITY OF SPERMATOGONIA AND ITS RELATIONSHIP TO THE STEM CELL NICHE – A REVIEW
Makoto Nagano, PhD, DVM
McGill University and The Research Institute of McGill University Health Centre, Montreal, Quebec, Canada

It has been just over 20 years since spermatogonial transplantation was reported. It functionally detects spermatogonial stem cells and is simple in its technical concept. However, this technique also revolutionized our approach to looking at the foundation of spermatogenesis. The heterogeneity in spermatogonia appeared to be established by 1901 while the concept of spermatogonial stem cells emerged by 1885. Since then, a large amount of information has been accumulated and survived over time in the study of spermatogonia and spermatogenesis in general, mainly based on morphological observations. Spermatogonial transplantation, reported in 1994, was novel in part because it freed us from this restriction, cell morphology, and allowed us to ignore it to study spermatogonial stem cells, even though it detects only one type of male germ cells. While the research based on this technique opened new avenues in research of spermatogenesis, it also introduced confusions and conflicts. Here, I intend to discuss what we know about the heterogeneity of spermatogonia and how it could relate to the function of their environment, and potentially, the regulation of stem cell fate.

© 2015 American Society of Andrology and European Academy of Andrology Andrology, 2015, Supplement, 33
mouse line lacking two miRNA clusters (called herein dKO mice), which encode five miRNAs (miR-449a, 449b, 449c, 34b and 34c) that share the same “seed sequence”. These mice display defects in all three phases of spermatogenesis. In particular, both prospermatagonia and spermatogonia display abnormalities in the dKO males, suggesting a critical role of these miRNAs in the control of spermatogonial development.

Methods: dKO mice were generated by crossing the miR-34b/c KO mice with miR-449a/b/c KO mice. Histological and molecular analyses were conducted using testes dissected from dKO and control (WT or single KO) male mice.

Results: ~50% of the dKO males died at P7. Those survived beyond P7 tended to be smaller in body size before week 7, and similar body weight could be achieved after week 8. However, all male dKO mice were sterile. Abnormalities in all three phases of spermatogenesis were observed in adult dKO males. The testicular histology in dKO males was characterized by very thin seminiferous epithelia consisting of almost all types of spermatogenic cells, but much less in number at the age of 10 weeks. Epididymal sperm counts were drastically reduced and the dKO sperm were all deformed. During the initial cycle of spermatogenesis, the number of spermatogenic cells and the thickness of the seminiferous epithelia were comparable between dKO and WT testes. However, the dKO testes displayed much thinner seminiferous epithelia from the second round of spermatogenesis onward. No enhanced germ cell apoptosis was observed in either developing and adult dKO testes, and the number of both spermatocyte and spermatids was drastically reduced, whereas the number of differentiated spermatogonia appeared to be increased in dKO seminiferous tubules compared to controls.

Conclusion: Our data suggest an enhanced spermatogonial differentiation and a reduced meiotic entry when spermatogonia lack the five miRNAs.

*Funding for this study was provided by the NIH (HD060858)
markers not only help identify genes involved in spermatogenesis, but also are being used to elucidate molecular and cellular mechanisms of testicular toxicity. A revolution in toxicity testing is underway, based on high throughput in vitro screening and computational toxicology approaches. It derives from public concern about Endocrine Disrupting Chemicals which, in turn, emerged from reports suggesting that sperm counts may be declining in the Western world, and testicular cancer increasing, potentially due to chemicals in our environment. In this context, basic knowledge about androgen receptor function has been applied to in vitro screens for chemicals that interfere with androgen action and thereby impact male reproductive development. The fungicide vinclozolin provides an illustrative example. Thus, as emphasis shifts from adult to fetal sensitivities, knowledge of how early life exposures may impact life-long fertility and cancer risk is expanding. Coming full circle, evidence for epigenetic re-programming during development is extending concerns to risks of obesity, metabolic syndrome and cardio-vascular health in adult men, with ever broader public policy implications.

SUNDAY, APRIL 19, 2015
4:45 p.m. – 5:30 p.m.

LECTURE II
FERTILITY PRESERVATION IN THE MALE: A NEW CLINICAL PARADIGM
Robert E. Brannigan, MD
Professor, Department of Urology
Northwestern University, Feinberg School of Medicine

Cancer is a highly prevalent condition, as is evident in the fact that a male has an approximately 50% chance of developing cancer during the course of his lifetime. Over the past century, the focus of cancer therapy has predominately been on devising therapeutic regimens to increase patient survival. Over time, however, a paradigm shift has occurred. While the overriding aim of therapy is still survival, oncologic treatment planning has increasingly incorporated strategies to mitigate the co-morbidities that often result from cancer therapy. Primary among these co-morbidities is male factor infertility. In this presentation, I will overview the impact of cancer and cancer therapies on male reproductive health, and I will discuss fertility preservation options for males with cancer. Three unique patient groups will specifically be considered: the prepubertal male, the adolescent male, and the adult male.

MONDAY, APRIL 20, 2015
8:00 a.m. – 9:00 a.m.

WOMEN IN ANDROLOGY LECTURE
FATHER’S LASTING INFLUENCE: PATERNAL ENVIRONMENT AND THE HEALTH OF HIS FUTURE GENERATIONS
Janice L. Bailey, PhD¹, Clotilde Maurice, PhD¹, Serge McGraw, PhD², Romain Lambrot, PhD², Nancy Côté¹, Arnaud Droit, PhD¹, Jacquetta M. Trasler, MD, PhD² and Sarah Kimmins, PhD²
¹ Université Laval, Québec, Canada; ²McGill University, Montreal, Canada

Although chemicals are a part of our daily lives, society is concerned about the impact of environmental contaminants on human health. Our team is particularly interested in Persistent Organic Pollutants (POPs), including PCBs and some insecticides, which bioaccumulate and biomagnify in the food chain. POPs are restricted according to the Stockholm Convention; however, exemptions are made for DDT, which is widely used in malaria-endemic areas. Therefore, POPs remain ubiquitous worldwide and particularly accumulate in the Arctic. We and others have demonstrated that reproductive parameters are compromised in men who are exposed to high levels of POPs, although there is little evidence that fertility is affected. More recently, the “developmental origins of adult disease” model has been proposed to explain how exposure of the developing fetus to environmental stressors while still in the womb predisposes it to dysfunction later in life. Indeed, we have shown that prenatal exposure to a mixture of POPs, designed to mimic that which contaminates the Arctic, induces male reproductive dysfunction and subfertility in the rat. We further hypothesized that prenatal exposure to this environmentally-relevant POPs mixture affects the paternal sperm epigenome and the health of his unexposed future generations. We used the F1 prenatally-exposed sires to produce F2, F3 and F4 generations. Numerous health defects, including male subfertility were observed throughout these three generations. Moreover, >200 genes in the sperm from the F1 prenatally-exposed males were differentially methylated, including those in regions involved in embryo development. Pathologies linked to the altered genes include metabolic, neurological, psychological and cardiovascular disorders, cancers and reproductive dysfunction, many of which are either documented to be related to prenatal exposure to organochlorines or are of concern to Arctic populations. In conclusion, our study indicates that prenatal paternal exposure to environmentally-relevant POPs induces reproductive dysfunction as well as developmental pathologies in his offspring and future generations, possibly due to epimutations in his sperm DNA. Financed by FQRNT & CIHR.
SPEAKER ABSTRACTS

MONDAY, APRIL 20, 2015
9:15 a.m. – 10:15 a.m.

SYMPOSIUM II – Special Concerns for Older Fathers

THERAPEUTIC ADVANCES IN THE TREATMENT OF PEYRONIE’S DISEASE
Wayne J.G. Hellstrom, MD, FACS
Tulane University School of Medicine

Introduction: Peyronie’s disease (PD) is a localized penile collagen disorder of the tunica albuginea of the penis associated with significant physical deformity and psychological impairment. Previously published treatment reports have been limited by small, short-term, uncontrolled trials with varied quality assessments and lack of PD-specific, validated measures of the psychological impact of PD.

Objective: IMPRESS (Investigation for Maximal Peyronie’s Reduction Efficacy and Safety Studies) I and II investigated the clinical efficacy of and safety of collagenase clostridium histolyticum (CCH) (Xiaflex®, Auxilium, Malvern, PA) intraleisonal injections in subjects with PD. Co-primary outcomes in 2 identical phase 3 randomized, double-blind, placebo-controlled studies included % change in the penile curvature and change in PD questionnaire symptom bother score from baseline to 52 weeks.

Materials and Methods: IMPRESS I and II examined CCH intraleisonal injections in 417 and 415 subjects through a maximum of four treatment cycles (2 injections per cycle); each separated by 6 weeks. Men were stratified by baseline penile curvature (30-60 vs. 61-90 degrees) and randomized to CCH or placebo 2:1.

Results: IMPRESS I and II data analysis revealed that PD men treated with CCH showed a mean 34% improvement in penile curve (mean ±SD −17±14.8 degree change per subject) compared to a 18.2% improvement (−9.3 ± 13.6 degree change per subject) for placebo (p<0.001). The mean change in PD bother score was also significantly improved in treated vs. placebo (−2.8 ± 3.8 vs 1.8 ± 3.5, p=0.0037). Three serious adverse effects (corpal rupture) were successfully surgically repaired.

Conclusion: IMPRESS I and II support the clinical efficacy and safety of CCH for the physical and psychological aspects of PD. Clinicians now have an effective FDA-approved intraleisonal product to offer their patients suffering with PD.

MONDAY, APRIL 20, 2015
9:15 a.m. – 10:15 a.m.

SYMPOSIUM II – Special Concerns for Older Fathers

NOVEL ORAL HORMONE REPLACEMENT THERAPIES: THE ERA OF THE SERMS?
Andrew McCullough, MD, Professor of Surgery/Division of Urology
Albany Medical College, Albany, New York

For decades, the only FDA approved treatment for hypogonadism has been T replacement (TREP). Current guidelines for approvals are all based on T restoration to normalize T levels and not symptomatic improvement. Barring major lifestyle changes, men diagnosed with hypogonadism will require treatment for life, not unlike another highly prevalent condition, type II diabetes. Yet, the treatment of type 2 diabetes is not universally insulin replacement but either oral medication to increase insulin sensitivity or insulin secretion. 58% of diabetics are on oral hypoglycemics with only 12% of diabetics on replacement therapy with insulin. Why is the only recommended therapy for hypogonadism, replacement, particularly since 85% of men are secondarily hypogonadal? These are not men with absent gonadotropins but men with inappropriately low gonadotropins for the low levels of T. Is there another possible therapeutic strategy other than replacement? Can we “restore” T production in the aging male by stimulation of the testes? Current exogenous therapies are fraught with the potential of abuse, possible testosterone transfer to other parties, erythrocytosis, induction of infertility by pituitary suppression, gynecomastia from hyper-estrogemism, the morbidity of a lifetime of intramuscular injections or testosterone pellet insertions and the expense of proprietary applications. The purpose of this article is to explore the current status of testosterone oral restorative (TRES) therapies. The reader should be warned that none of the discussed therapies are FDA approved.

CC was originally designed for female infertility. Approved by the FDA in 1967 it has since become an inexpensive generic drug. It is a selective estrogen receptor modulator comprised of a 38%/62% racemic mixture of cis and trans isomers, zuclophenine and enclomiphene, respectively. It has antagonistic effects on the estrogen receptors in the hypothalamus and the pituitary thereby increasing endogenous gonadotropin releasing hormones, LH and FSH. It ability to increase LH in men was recognized as early at 1968. As with all SERMs organ estrogen agonistic effects are also possible. In a study aimed at using CC challenges to diagnose hypogonadotropic hypogonadism, Paulsen demonstrated significant increases in LH, FSH and T in normal older men taking 50 mgs of CC twice a day. Sherins et al were able show the CC was able to block the LH and FSH suppression that occurs with exogenous T and estrogen administration, thus demonstrating that estrogen was the primary inhibitory hormone on GnRH, LH and FSH. Over the ensuing decades, CC was used to increase male fertility with mixed results. Though an increase in T and estrogen level was consistently demonstrated, no consistent effect of seminal parameters or pregnancy rates was observed. A 6 month multicenter international placebo controlled study cast doubts on the efficacy of CC on idiopathic male infertility. It is important to realize that in the international study, the infertile population was eugonadal with the mean baseline T levels of 481ng/dl. Well controlled studies in the hypogonadal infertile male are lacking, despite the high prevalence of secondary hypogonadism in this group of men.

Tenover et al looked at an 8 week trial of CC (50mg BID) in 5 healthy older and 5 young eugonadal men (mean age 73 vs 29; mean baseline T 518 vs 498) and demonstrated that older men both increased LH and FSH and T and E-2. Though levels of T were significantly lower in the older group, the levels achieved in both groups were at least comparable to those achieved with many current day exogenous treatments. Lim observed normalization of testosterone levels in 5 hypogonadal uremic men with uniform increase in libido, sexual potency, and a general sense of well-being using 100 mgs of CC daily for as long as 12 months. The normalization of T continued for 4-5 years and FSH. Over the ensuing decades, CC was used to increase male fertility with mixed results. Though an increase in T and estrogen level was consistently demonstrated, no consistent effect of seminal parameters or pregnancy rates was observed. A 6 month multicenter international placebo controlled study cast doubts on the efficacy of CC on idiopathic male infertility. It is important to realize that in the international study, the infertile population was eugonadal with the mean baseline T levels of 481ng/dl. Well controlled studies in the hypogonadal infertile male are lacking, despite the high prevalence of secondary hypogonadism in this group of men.

Guay el al challenged 21 older men with erectile dysfunction and secondary hypogonadism with 50 mg CC bid for 7 days and normalized their T, demonstrating that at that at least in the short term, the concept of testosterone restoration was possible in older men. He then expanded the concept with an eight week double blind placebo controlled crossover study in older men (mean age 62) with secondary hypogonadism and erectile dysfunction (documented with nocturnal penile tumescence scan (NPT)). Again, normalization of
SPEAKER ABSTRACTS

serum testosterone was seen but no improvement was seen in NPT or sexual function questionnaires in the group as a whole. When the study population was split between younger and older groups (mean age 53 and 66 respectively) in a post hoc analysis, not surprisingly, the differences between the treatment groups with the sexual function questionnaires and NPT testing achieved statistical significance. The older men were more likely to have “end organ” disease refractory to hormonal manipulation. This was the first demonstration that CC could not only normalize T levels in SHGD but result in symptomatic improvement. Guay then began treating men in his practice with SHGD with CC (50 mgs) three times a week. He reported an observational series of 173 men with ED and SHGD treated for 4 months. The diagnosis of ED was based on self-report and not a validated questionnaire and a placebo arm was lacking. The outcome was measured as “responder” to treatment (successful intercourse >75% of the time), partial responder (successful intercourse 50-75% of the time) and non-responder. As in his previous studies, LH, FSH and free testosterone levels increased. Sexual function improved in 75% and did not change in 25%. Age and vascular co-morbidities negatively affected the response rates.

Taylor et al in an observational study compared the biochemical efficacy of CC to exogenous gel treatment (TRT) in 104 men (65 CC vs 39 on TRT). The groups were not strictly identical but demonstrated comparable increases in testosterone with a 182 $ monthly savings in the CC group. PSA levels and HCT did not significantly change in follow up (23 months). Moskovic demonstrated an excellent chemical response in a younger cohort of 29 men (mean age 44) followed for three years on CC 25 mgs every other day. In addition, despite an unusually high percentage of men with altered bone mineral density at baseline (75%) BMD normalized at one year in 25%. No improvement in BMD was observed after the first year. Though estradiol increased significantly no gynecomastia or breast tenderness occurred. No side effects were reported.

The efficacy of CC in relieving the symptoms of hypogonadism is often anecdotally reported as being inferior to exogenous therapy without the support of randomized double blind studies. Katz et al retrospectively looked at symptom relief with CC (25mg every other day) in 86 young (mean age 29) hypogonadal men, most of whom were presenting for infertility (57%) over a 4 year period at a Sloan Kettering andrology practice. The men were followed for a mean of 19 months. Surprisingly the median number of positive baseline responses on the androgen deficiency in aging males (ADAM) questionnaire was 5 that dropped to 2. These “generally very healthy” young men started at a mean T level of 192 ng/dl and increased their T to 485 (despite a target treatment level of 550 ng/dl). The symptoms that showed significant increases included “decreased libido, lack of energy, decreased life enjoyment, sad/grumpy, decreased sports performance”. The lack of a placebo arm weakens the strength of the study. Further support of the efficacy of CC in relieving hypogonadal symptoms comes from a retrospectively gathered observational comparative study from Baylor by Ramasamy. In examining the effect of CC vs replacement therapy on hypogonadal symptoms, no significant differences were seen in between T injections, T gels or CC. T levels were highest with injections (1104 ng/dl) vs CC (504 ng/dl) or the gels (412 ng/dl). The lack of a difference in symptom relief supports the concept that symptom relief may be tied to a threshold level that is achieved with TRES and TREP. Unfortunately pre-treatment quantitative ADAM scores (QADAM) were not reported and the QADAM has not been fully psychometrically validated.

Recently there has been interest in the trans isomer of CC (EC). Distinct differential pharmacokinetics of the two isomers have been demonstrated. Though the Cmax, and Tmax were comparable, the AUC for the isomers was dramatically different after a single dose administration of 50 mgs of CC in women with polycystic ovaries. At 456 hours, ZC was detected in 9/9 patients vs 1/9 for EC. The half-life of EC is 7-8 hrs. EC was evaluated in an early proof of concept randomized, open-label, fixed dose, active-control (7EC and 5 exogeneous gel), two-center phase IIB study in 12 men with secondary hypogonadism treated previously with topical testosterone. After T discontinuation of exogenous T, T levels in both groups averaged 165ng/dl. After treatment T levels increased in both groups to over 540 ng/dl but decreased to baseline after cessation of treatment suggesting that the hypothalamic testicular axis reverts to its pretreatment state and continued therapy is necessitated. Whereas sperm counts were increased in all men on EC at 6 months only 2 of 5 of gel patients increased their sperm concentrations to over 20 million/cc. GTP increased only in the EC arm. In follow up clinical trials, safety and clinical efficacy were comparable to a gel preparation while preserving sperm counts. Sperm counts were decreased in the men treated with gels. Side effects were comparable to CC. The most significant adverse events were hot flushes (10%), visual disturbances headaches, nausea and vomiting. Aside from the hot flushes, all events occurred in less than 5% of the study population. The ease of use, low side effect profile, therapeutic efficacy and preservation of fertility, make EC, if approved, an attractive therapeutic alternative to standard TREP.

Summary
In view of the EMAS studies secondary hypogonadism accounts for over 85% of late onset hypogonadism. Ample evidence exists for a deficiency in GTP stimulation with the older men and the ability of the testes to respond to increased GTP production. We currently have generic medications that accomplish an increase in GTP and normalization of serum testosterone with a favorable side effect profile. Though shown to be efficacious and well tolerated in a number of trials, restorative strategies are not FDA approved and caution must be advised in their off label use. Hopefully future trials will be undertaken to establish the long term efficacy and safety these restorative therapies. Early clinical trials of the compound enclomiphene are encouraging and hopefully will lead to a change in paradigm from TREP to TRES.
DIVERSITY LECTURE
CURRENT TRENDS IN THE TREATMENT OF INFERTILITY IN MEN WITH SPINAL CORD INJURY
Nancy L. Brackett, PhD, HCLD
University of Miami Miller School of Medicine, Miami, FL

Objectives: This presentation will describe causes and treatments for infertility in men with spinal cord injury (SCI).

Methods: Evidence from published medical literature, as well as recent findings from my laboratory, will be presented.

Results: Most men with SCI are infertile due to a combination of erectile dysfunction, ejaculatory dysfunction, and semen abnormalities. Treatments that are effective for erectile dysfunction in the general population are also effective in men with SCI. In anejaculatory patients who wish to father children, semen retrieval is necessary. Penile vibratory stimulation (PVS) is recommended as the first line of treatment. Patients who fail PVS can be referred for electroejaculation. Surgical sperm retrieval should be considered as a last resort when other methods fail. Most men with SCI have a unique semen profile characterized by normal sperm concentration but abnormally low sperm motility. This problem does not seem to be due to lifestyle factors, such as elevated scrotal temperature from sitting in a wheelchair, infrequency of ejaculation, or methods of bladder management. Longitudinal and cross-sectional studies have found no progressive decline in semen quality with the ensuing years post-injury. Endocrinopathies may be present, but are not the sole cause of abnormal semen quality in these men. Evidence suggests that a toxic seminal plasma environment contributes to the problem. For example, the inflammasome may play a role in elevating semen cytokines in these men. Inactivating components of the inflammasome, and/or neutralizing elevated semen cytokines, improves sperm motility in this severely affected group of patients.

Conclusions: Despite sexual dysfunction and semen abnormalities, biologic fatherhood is possible men with SCI. Semen retrieval by PVS or electroejaculation often results in sufficient numbers of total motile sperm to consider intruterine insemination or even intravaginal insemination in couples with SCI male partners. Surgical sperm retrieval combined with in vitro fertilization and intracytoplasmic sperm injection should be considered as a last resort for assisted conception. New therapies for abnormal semen quality in this population are on the horizon.
The definition of rejuvenation is the process of making someone look or feel younger. Aging men may not be hormone deficient and replacement in not indicated. Human growth hormone and androgens including dehydroepiandrosterone (DHEA) and testosterone (T) have been used in the rejuvenation community because these hormones decline with aging in men. Data on recombinant human growth hormone do not show consistent efficacy or evidence to justify its use in older men in the absence of demonstrated low GH levels and a definable congenital or acquired causal mechanism. DHEA is a weak androgen and supplements of DHEA are not useful in producing androgenic effects except as a precursor of T. Recent studies in several countries/continent showed that serum T levels decrease with age in older men over the age 60 to 70 years. The decrease in serum T levels is associated with symptoms of male hormone deficiency in about 2 to 6% men between 40 to 70 years. Co-morbidities such as obesity, metabolic syndrome, diabetes and chronic illness are associated with low T levels. Life style modification for obesity and treatment of the medical conditions may sometimes restore serum T to the adult malerange. There is controversy regarding T replacement in older men because of relative benefits versus risks. The benefits of T substitution shown in small placebo controlled randomized clinical trials include: increased sexual desire/activity, bone mass, lean mass, improved erectile dysfunction, and decreased fat mass. Studies have not conclusively shown that T substitution improves quality of life, mood, vitality or cognition in older men. A larger scale randomized controlled trial using transdermal T in elderly men with unequivocal low T levels (The T Trial) has been completed but awaiting data analyses. The long term effects of T substitution in older men with low T levels on risks of prostate cancer or cardiovascular disease are unknown and controversial. Given the unknown long term adverse effects of T and inconclusive data on subjective improvement in symptoms, there is no justification of administration of T treatment for older men without consistently low T levels and symptoms consistent with a hypogonadal syndrome. In symptomatic men with persistently low T levels despite management of concurrent comorbidities, T substitution to achieve serum T level in the mid adult male range may be used. Under all circumstances analysis/consideration of benefit/risk of intervention is prudent.

Funding in part is from the NY State Stem Cell Program (NYSTEM)
Monday, April 20, 2015
4:15 p.m. – 5:00 p.m.

Lecture IV
Erectile Dysfunction and Radical Prostatectomy: Where is the Next Breakthrough?
Trinity J. Bivalacqua, MD, PhD
Johns Hopkins Hospital

A common treatment of prostate cancer is prostate removal or radical prostatectomy (RP). This cancer operation is associated with high rates of erectile dysfunction (ED). There has been major advances in the treatment of ED with the advent of phosphodiesterase type 5 (PDE5) inhibitors. However, post-RP ED is refractory to oral PDE5 inhibitor therapy. Thus new disease specific therapies are necessary. The CME goals of this lecture are to discuss the evidence for penile rehabilitation using PDE5 inhibitors, discuss novel disease-specific molecular based therapies including pharmacotherapies, small molecular inhibitors, and stem cell based therapies.

Monday, April 20, 2015
5:00 p.m. to 5:45 p.m.

EAA Lecture
Post-Testicular Sperm DNA Oxidative Damage: Are the Chromosomes at an Equal Risk?
Genetics Reproduction & Development laboratory, CNRS UMR6293–INSERM U1103–Clermont Université, France.

When it comes to nuclear integrity, spermatozoa and oocytes are not equal. The oocyte has DNA repair activities throughout its life while the mature spermatozoa is devoid of it. Therefore, immediately post-fertilization one of the most important tasks of the oocyte is to repair sperm nuclear DNA damage prior to initiating S-phase of the first mitotic division. If there are too many sperm DNA lesions, the repair mechanisms activated in the oocyte may be overwhelmed, leading to errors during the ensuing DNA replication. The most frequent sperm DNA alteration in natural as well as in assisted reproduction involves an oxidative attack, leading to the formation of oxidized base adducts such as 8-hydroxy-2’-deoxyguanosine. Via the use of mouse transgenic strains in which a post-testicular oxidative stress of oxidized base adducts such as 8-hydroxy-2’-deoxyguanosine. Via the use of mouse transgenic strains in which a post-testicular oxidative stress of oxidized base adducts such as 8-hydroxy-2’-deoxyguanosine. Via the use of mouse transgenic strains in which a post-testicular oxidative stress of oxidized base adducts such as 8-hydroxy-2’-deoxyguanosine. Via the use of mouse transgenic strains in which a post-testicular oxidative stress of oxidized base adducts such as 8-hydroxy-2’-deoxyguanosine. Via the use of mouse transgenic strains in which a post-testicular oxidative stress of oxidized base adducts such as 8-hydroxy-2’-deoxyguanosine. Via the use of mouse transgenic strains in which a post-testicular oxidative stress of oxidized base adducts such as 8-hydroxy-2’-deoxyguanosine. Via the use of mouse transgenic strains in which a post-testicular oxidative stress of oxidized base adducts such as 8-hydroxy-2’-deoxyguanosine.

Tuesday, April 21, 2015
8:00 a.m. – 9:15 a.m.

Symposium IV – The Effects of Testosterone on the Heart
Testosterone and the Heart: Putting the FDA Advisory in Perspective
Shalender Bhasin, MD
Harvard Medical School
Brigham and Women’s Hospital
Boston, MA 02115

The risk/benefit ratio associated with testosterone therapy may vary with the context of use. In young men with classical hypogonadism due to known diseases of the testis, pituitary and hypothalamus, testosterone improves many symptoms of hypogonadism and is associated with a low frequency of adverse events. In contrast, neither the risks nor the benefits of testosterone therapy have been demonstrated in older men with age-related decline in testosterone concentration or in elderly men with frailty, mobility limitations, or critical illness. A number of pre-clinical and clinical observations support the biological plausibility of a relation between testosterone administration and risk of cardiovascular events. T increases hemoglobin and hematocrit. Testosterone administration reduces plasma HDL cholesterol, induces platelet aggregation, is associated with sodium and water retention. In pre-clinical models, and has been shown to promote smooth muscle proliferation and increased VCAM expression. Testosterone also has been shown to have potentially beneficial effects on the cardiovascular system. Testosterone acts a vasodilator by inhibition of L-type calcium channels, resulting in increased coronary and penile blood flow. Testosterone consistently decreases whole body, subcutaneous and intra-abdominal fat. Testosterone has been reported to reduce vascular reactivity and improve endothelial function. Testosterone has been reported to increase both prothrombotic as well as anti-thrombotic factors. A small number of epidemiologic studies have reported an inverse relationship between testosterone concentrations and common carotid artery intima-media thickness. The relationship of testosterone and coronary artery disease and CV events is inconsistent. A meta-analysis of 11 randomized trials by Araujo et al found that in aggregate, lower testosterone levels were associated with higher risk of all-cause mortality, especially cardiovascular mortality. There are no published or ongoing trials that were specifically designed or powered to determine the effects of testosterone therapy on CV events. Retrospective analyses of data have yielded conflicting results. Some studies have reported an association of testosterone therapy and increased cardiovascular events, while others have not. TOM trial was a placebo-controlled randomized trial of testosterone in older men with mobility limitation. The trial was stopped early due to the increased frequency of cardiovascular-related events in men assigned to testosterone arm than in placebo arm. The divergence in cardiovascular events continued throughout the 6-month intervention duration, and abated after treatment was discontinued. The cardiovascular-events were small in number overall, and variable in their severity and significance. The TOM trial was not designed for cardiovascular events. Accordingly, cardiovascular events were not pre-specified, were not collected in a standardized manner, and cardiovascular events were not adjudicated prospectively. Therefore, the available data from randomized clinical trials are insufficient to establish a causal link between testosterone therapy and cardiovascular events. To more clearly understand the risks of testosterone therapy in older men with low testosterone levels, we need larger randomized trials and prospective mechanisms for tracking of adverse events, particularly cardiovascular events and major cardiovascular events.
Objective: To examine the role of Testosterone (T) deficiency in contributing to cardiac relaxation abnormality (diastolic dysfunction) and if this dysfunction is potentially reversible by T replacement.

Methods and Results: Castrated and sham-operated male rats were randomized to placebo versus T replacement for 6 weeks. After 3 weeks of castration, invasive hemodynamic measurements revealed that rats developed evidence of diastolic dysfunction as evidenced by slower dp/dtmin (rate of relaxation) and longer tau (time constant of relaxation). There was also a non-significant trend towards increase in left ventricular end-diastolic pressure. All these variables were reversed and returned to normal range in the T-treated rats but remained abnormal in the placebo-treated group.

Conclusions: T deficiency contributes to left ventricular diastolic dysfunction while T replacement completely reverses these abnormalities. An ongoing clinical pilot study in hypogonadal men will help determine if clinical T effects on diastolic function are worthy of a larger randomized clinical trial.

In view of evidence showing that low endogenous bioavailable testosterone associates with higher rates of cardiovascular mortality, some have hypothesized that testosterone replacement therapy might have beneficial effects. In contrast to initial expectations, testosterone replacement therapy has been shown to increase the risk of cardiac morbidity. Interpretation of such paradoxical findings would be facilitated by a thorough understanding of the effects of testosterone on the heart, but information on this topic is still limited. In mice, we have compared two mouse strains harboring genetic differences that are restricted to only chrY, i.e. male C57BL/6J mice and their consomic C57.YA counterparts (i.e. the same mouse strain where the original chrY has been replaced by that from the A/J strain). We found that castration affected the expression of more cardiac genes in male C57.YA mice than in C57BL/6J mice. These effects of chrY genetic variants were explained (at least in part) by two phenomena. Firstly, it is known that the activational effects of testosterone in adults depend on the organizational effects exerted by the peak of testosterone that occurs after birth. Measurements of anogenital distances in male pups showed that exposure to testosterone was greater in C57BL/6J than in C57.YA, and perinatal endocrine manipulations showed that these differences contributed to the strain-specific differences in the response of adult cardiac cells to testosterone. Secondly, chrY polymorphisms associated both in newborn and adult hearts with strain-specific differences in genomic regions showing either occupancy with androgen receptors or other marks of chromatin remodeling. The same regions contained some of the genes showing strain-specific differences in their responses to castration, with many of them corresponding to genes having well-known roles in cardiac growth and contractility. These chrY-dependent differences in chromatin remodeling are compatible with the observation that newborn C57BL/6J and C57.YA males show differential expression of Uty, a chrY-encoded histone demethylase that is involved in chromatin remodeling and may thus in turn affect gene expression. Interestingly, a recent human study showed that subjects belonging to chrY haplogroups with differences in cardiovascular risk show differences in expression of that same gene.

Thus, chrY genetic variants may dictate (at least in part) which particular cardiac genes respond to testosterone, and may be responsible for inter-individual differences in the effects of testosterone on the heart. In mice, some of the cardiac genes showing greatest strain-specific differences in their responses to castration belonged to the family of circadian genes. To extend these findings, we profiled the expression of 15 different circadian genes in hearts of C57BL/6J and C57.YA mice at different times of the day. We found that strain-specific differences were found for only 3 circadian genes, i.e. Dbp, Tef and Hif, which are all functionally redundant members of the PARbZip family. Previous studies in mice devoid of all three genes have shown that they collectively regulate left ventricular function. The effects of chrY variants on these three genes were seen at only one particular time point, i.e. 2PM, and were found only in intact (but not castrated) mice. Interestingly, we found that castration decreased the expression of contractility genes in hearts from C57.YA mice at 2 PM, but not at 10 AM, and did not affect the expression of these genes in C57BL/6J mice at either time, thus mirroring the strain-specific differences in circadian gene expression. The data indicate that, downstream of chromatin remodeling, differential regulation of circadian genes may constitute one of the mechanisms via which chrY genetic variants regulate the effects of testosterone on the heart.
INTERNATIONAL LECTURE
A PERSPECTIVE FROM DOWNUNDER: TGB SIGNALING IN TESTIS DEVELOPMENT AND SPERMATOGENESIS
Kate Lakoski Loveland, PhD
School of Clinical Sciences, Monash University and MIMR-PHI
Medical Research Institute, Clayton, Victoria Australia

A precise molecular dialogue between testicular somatic and germ cells is required for normal spermatogenesis. During fetal and postnatal life, this communication influences tightly controlled periods of germ cell reprogramming, proliferation and quiescence, migration and cell fate selection, events relevant to formation of testicular germ cell tumours (TGCTs) which are the most common solid tumour in young men. Transforming growth factor (TGF)-β signaling pathway components exhibit gender-biased production in fetal gonads, with male gonads making activin A and female gonads making its potent inhibitor, follistatin. Through animal model studies, we and others discovered that activin beta A levels determine Sertoli and germ population cell size and maturation pace. Levels of key proteins such as Kit and Dmrt1 correlate with activin levels during development, providing clues to how activin impacts on male fertility. The restriction of activin signalling by the inhibitory inhibin alpha subunit is essential for normal Sertoli cell maturation, and the mechanisms by which Sertoli cells respond to activin alters as they develop. Exposure of juvenile mice to the phthalate DBP upregulates inhibin alpha subunit levels inappropriately, and this may be linked with reduced adult fertility. In humans, activin receptors present in Sertoli and germ cells indicate both are potential targets of activin and TGF- ligands in normal and neoplastic adult testes. Exposure of the TCam-2 model human seminoma cell line to activin A, to the TGF- ligand, BMP4, or to retinoic acid altered transcripts encoding activin receptors and Kit, and also impacted on cell survival or proliferation.

Our recent analyses with testis tissue fragments from testicular cancer patients showed activin A reduced KIT mRNA and protein amounts in seminoma samples, reinforcing the understanding that regulated activin A bioactivity is important for male reproductive health. This talk will offer a framework for understanding how altered structure or function of TGF- superfamily components, including inhibin alpha, NODAL, TGFBR3/betaglycan and BMP7, may be implicated in male infertility and in TGCTs.

SYMPOSIUM V: Novel Male Contraceptive Strategies
NA,K-ATPase 4 ISOFORM AS A TARGET FOR MALE CONTRACEPTION
Gladis Sánchez, MD, Jeff P. McDermott, PhD and Gustavo Blanco, MD, PhD
Department of Molecular and Integrative Physiology. University of Kansas Medical Center. Kansas City, KS 66160

Objectives: Na,K-ATPase comprises a group of plasma membrane enzymes that hydrolyze ATP to exchange cytoplasmic Na+ for extracellular K+. Na,K-ATPase is composed of different molecular forms of a catalytic and a glycosylated subunit. Na,K-ATPase 4 is a testis specific subunit, restricted to male germ cells and the sperm flagellum. We have explored the role of 4 in sperm physiology.
Methods: We used a pharmacological approach, taking advantage of the unique high sensitivity of 4 to the inhibitor ouabain and a genetic approach, deleting or over-expressing 4 in mice.
Results: Selective ouabain inhibition showed a role for 4 in sperm motility and hyperactivation. Knockout of Na,K-ATPase 4 in mice resulted in complete male, but not female infertility. Moreover, sperm from these mice were incapable of fertilizing oocytes in vitro, demonstrating the essential role that 4 plays in male fertility. Deletion of 4 resulted in severe loss of sperm motility and hypermotility. Sperm lacking 4 also exhibited several other defects, including a bend in the sperm flagellum and alterations in intracellular Na+, membrane potential and pH. Maintenance of these cell parameters represents the mechanisms by which 4 supports sperm flagellar beat, sperm capacitation and fertility. In contrast, 4 does not appear to be involved in sperm acrosomal reaction. On the other hand, overexpression of 4 in transgenic mice resulted in activation of total and multiple parameters of sperm motility, further demonstrating the crucial role that 4 plays in sperm flagellar beat.
Conclusion: Our results highlight the specificity of function of Na,K-ATPase 4 in sperm physiology and male fertility. This places Na,K-ATPase 4 as a potential marker for male fertility and an attractive candidate for male contraception.

[NIH grant U01HD080423].
RETINOIC ACID RECEPTOR ANTAGONISTS FOR MALE CONTRACEPTION
Debra J. Wolgemuth, PhD
Columbia University Medical Center

Objectives: A combination of physiological, genetic, and pharmacological experimental approaches has revealed that all trans retinoic acid, a metabolite of vitamin A, and its receptor retinoic acid receptor alpha (RAR) are key players in the regulation of spermatogenesis. Following up on initial reports of ‘testicular toxicity’ in rats resulting from pan-RAR antagonists, we showed that in the mouse model, spermatogenesis could be inhibited by the antagonists, importantly in a reversible manner and without overt side effects. We now extend these observations to assess the lowest doses that can be effective, the length treatment that can be tolerated with restoration of fertility, the molecular targets of antagonist actions, and the possibility of developing RAR-specific antagonists.

Methods: Adult male mice were administered BMS189453/compound 9 or newly synthesized RAR-selective antagonists by oral gavage at various concentrations (mg/kg body weight) for varying lengths of dosing periods as described in our previous studies and expanded in the present study. Inhibition of fertility was assessed by testis weight, presence of sperm in the epididymis, mating studies, extensive morphological analysis of testicular histology, and ability of recovered males to sire offspring.

Results: Treatment with the pan-antagonist BMS189453/compound 9 at 5mg/kg/day for days was shown to inhibit spermatogenesis in a reversible manner. Extension of these regimens to lower doses and longer periods (as low as 1mg/kg/day for as long as 16 weeks) was shown to reversibly disrupt spermatogenesis. In fact, mating studies and extensive morphological analysis of testicular histology, and ability of recovered males to sire offspring.

Results: Treatment with the pan-antagonist BMS189453/compound 9 at 5mg/kg/day for days was shown to inhibit spermatogenesis in a reversible manner. Extension of these regimens to lower doses and longer periods (as low as 1mg/kg/day for as long as 16 weeks) was shown to reversibly disrupt spermatogenesis. In fact, mating studies and extensive morphological analysis of testicular histology, and ability of recovered males to sire offspring.

Conclusions: Our results suggest that spermatogenesis is exquisitely sensitive to disruption of retinoid signaling and that RAR-antagonists may represent new lead molecules in developing non-steroidal male contraceptives.

Funding provided by a grant from the NIH, U01 HD060479
ANABOLIC STEROIDS, HYPOGONADISM AND BEYOND

Characterized by low serum testosterone and a multitude of debilitating symptoms, male hypogonadism is a common condition. Primarily treated with exogenous testosterone supplementation therapy (TST), novel adjuncts are being studied. For example, nandrolone, or deca-durabolin, is a steroid administered in a manner similar to injectable testosterone cypionate. It is highly effective in developing muscle mass and may be useful in hypogonadal men with premature alopecia and joint pain.

A further role for TST lies in the treatment of hypogonadism associated with obesity and its related pathologies (i.e. metabolic syndrome, cardiovascular disease and diabetes mellitus). Indeed a role of testosterone in counteracting obesity is well known. Anavar, or oxandrolone, an orally administered androgen, has been studied in HIV-associated weight loss increasing well-being and muscle mass. Growth hormone has also been found to improve muscle mass and stimulate lipolysis in adipocytes. These agents thus represent novel adjuncts to the treatment of obesity in hypogonadal males.

This presentation will seek to provide a background and rationale for the use of these agents in Men’s Health.

TESTOSTERONE AND CARDIOVASCULAR DISEASE

Objective: Testosterone replacement therapy (TRT) has come under increasing scrutiny over the last few years due to a few recent landmark articles exposing a potential increased hazard of cardiovascular events in men on therapy. However, the literature supporting a positive role for TRT in cardiovascular health dates back over 30 years and includes multiple prospective studies. Two of the most disturbing studies, the ones by Vigen et al in the Journal of the American Medical Association (JAMA), and Finkle et al in PLoS One, were retrospective chart reviews that had an alarming amount of missing data.

Methods: This talk will provide a literature review outlining the data, both pro and con, surrounding testosterone therapy and cardiovascular health. By the end of the talk, the audience should be able to understand the controversy surrounding cardiovascular health and TRT.

Results: The data overwhelmingly paint a supportive role for testosterone replacement and cardiac health. To date, there are over 50 articles that support metabolic improvements in testosterone replaced men. There are 4 articles that call into question the potential role of TRT on the heart. However, these articles have been widely panned by international testosterone experts and formally by the Androgen Study Group, a cohort of multi-disciplinary experts that have petitioned at least JAMA to retract the most damning article. To date, this article has been revised twice to account for statistical irregularities.

Funding: None.
MULTICELLULAR HUMAN TESTICULAR ORGANOID: A NOVEL IN VITRO GERM CELL AND TESTICULAR TOXICITY MODEL

Samuel Pendergraft, MS¹, Hooman Sadri-Ardekani, MD, PhD², Tanya Reid, BS³, Anthony Atala, MD² and Colin Bishop, PhD¹
¹(1) Molecular Medicine and Translational Science Graduate Program, Wake Forest University Health Sciences, Winston-Salem, NC; (2) Wake Forest Institute for Regenerative Medicine, Wake Forest School of Medicine, Winston-Salem, NC; (3) Wake Forest Institute for Regenerative Medicine, Wake Forest School of Medicine, Winston-Salem, NC

Introduction: Mammalian spermatogenesis is regulated through paracrine and endocrine activity, cell signaling, and local control mechanisms. These highly specific signaling interactions are effectively absent upon placing testicular cells into two-dimensional primary culture. The specific changes that occur between key cell types and involved spermatogenesis signaling pathways during primary culture remain to be elucidated. However, current protocols to produce mature germ cells in vitro are inefficient and are limited in supporting post-meiotic cells. In order to address these limitations we have developed a 3-dimensional (3D) testis organoid in vitro by combining stem cell and tissue engineering approaches. This model can be utilized as a means to evaluate gonadotoxic agents, and as a means to address critical deficiencies in our understanding of basic human spermatogenesis. The overall goal of this study is to establish, characterize, and culture a multicellular, 3D, human testis organoid and to assess its functionality and spermatogenic capacity over time.

Methods: Development of our model system consisted of (1) Identification and analysis of specific cellular components necessary for use in our 3D culture method, (2) Establishment of basic design parameters, culture conditions, and (3) Characterization of human testicular organoids using live cell imaging, immunofluorescence, immunohistochemistry, cell type and stage-specific gene expression, and viability assays.

Results: Human Spermatogonial stem cells (SSCs), Sertoli, and Leydig cells were isolated, characterized, and expanded from tissue obtained through the National Disease Research Interchange (Philadelphia, PA, USA). These cell types were integrated successfully into 3D organoids and maintained viability as determined by ATP and Live/Dead assays for over 4 weeks in culture. Gene expression within these multicellular human testis organoids was measured over time for cell and stage-specific parameters, culture conditions, and (3) Characterization of human testicular organoids using live cell imaging, immunofluorescence, immunohistochemistry, cell type and stage-specific gene expression, and viability assays.

Results: Human Spermatogonial stem cells (SSCs), Sertoli, and Leydig cells were isolated, characterized, and expanded from tissue obtained through the National Disease Research Interchange (Philadelphia, PA, USA). These cell types were integrated successfully into 3D organoids and maintained viability as determined by ATP and Live/Dead assays for over 4 weeks in culture. Gene expression within these multicellular human testis organoids was measured over time for cell and stage-specific markers including UCHL1, DAZL, VASA, SYCP3, SPO11, PRM1, ACROSIN, SOX9, GATA4, INSL3, and HSD3B.

Conclusion: Testicular in vitro organoids were successfully generated using isolated human SSC, Sertoli, and Leydig cells and maintained long term. Future directions include optimizing the spermatogenic capacity of the organoids and evaluating their use as a novel testicular toxicity model.

Funding: AFIRM II, Award No. W81XWH–13–2–0052. NIH grant SU42RR006042 and Erret-Fisher Foundation grant GTS 3679.

© 2015 American Society of Andrology and European Academy of Andrology
and form corticosterone. Changes in the mRNA expression of Star and Cyp11a1 steroidogenic genes were observed to be increased in testes and adrenals of these mice, suggestive of adaptive changes. Moreover, expression of steroidogenic signaling receptors were divergent in the tissue of the Tspo cKO mice, with Lhcgr levels increased in testis, whereas adrenal Mc2r levels were unaffected.

**Conclusion:** The results of these genetic engineering experiments provide evidence that, in an in vivo setting, TSPO is required for preimplantation embryo development as well as hormone–stimulated adrenal steroid biosynthesis.

**SUNDAY, APRIL 19, 2015**
2:30 p.m. – 2:45 p.m.

CONCURRENT SESSIONS – Oral Session I – Basic Science
Podium/Poster #3

**EARLY-LIFE EXPOSURE TO AN ENVIRONMENTAL ORGANOCHLORINE MIXTURE REDUCES THE FERTILITY OF MALE RATS AND INDUCES DIFFERENTIAL EXPRESSION OF SPERM PROTEINS ACROSS MULTIPLE GENERATIONS IN A PATERNALLY-MEDIATED MANNER**

Nancy Côté, PhD, Clotilde Maurice, PhD, Florence Roux-Dalvai, MSc, Arnaud Droit, PhD and Janice L. Bailey, PhD
Université Laval

(Submitted By: Nancy Côté, PhD)

**Introduction:** Organochlorines (OC) are a family of persistent hydrocarbon compounds that were used for industrial and agricultural purposes in North America and Europe between 1930 and the mid–1980s. Due to their high lipophilicity and resistance to biodegradation, OC bioaccumulate in fatty tissues, are biomagnified through the food chain and have accumulated in Arctic populations. OC exposure is associated with decreased sperm quality in men and prenatal exposure to an environmentally–relevant OC mixture impairs reproductive development in male rats. We hypothesized that early–life paternal exposure to an environmentally–relevant OC mixture impairs fertility and changes the protein profile of sperm across multiple generations.

**Methods:** We compared sperm proteins from paternally non–exposed and exposed rat lineages to an OC mixture over three generations (F1, F2, F3). We used isobaric tags for relative and absolute quantitation (iTRAQ) labelling and 2D–LC–MS/MS analysis to identify proteins that were differentially expressed. One differently expressed protein per generation was confirmed by immunoblotting.

**Results:** F1 males exposed to OC during early development had decreased sperm motility (P=0.04), lower daily sperm production per testis (P=0.006), and decreased epididymal sperm concentration (P=0.0001). Their F2 OC sons were subfertile (P=0.02) and their F3 OC grandsons had fewer pups per litter (P=0.0001). In generations F1, F2 and F3, respectively 7, 19 and 37 differentially–expressed sperm proteins were identified due to OC exposure of the F1 fathers. Cytochrome C, Superoxide Dismutase 1 (SOD1) and Glutathione Peroxidase 4 (GPX4) were reduced in F1 OC males. In their F2 OC sons, Citrate Synthase, Solute Carrier Family 2 member 3 (SLC2A3) and Calicin were decreased. In F3, IZUMO and Zona Pellucida Binding Protein (ZPBP) were reduced in OC–exposed males. By western–blot, we confirmed that SOD1, Citrate Synthase and ZPBP are significantly reduced in F1, F2 and F3 OC males, respectively.

**Conclusion:** This is the first study to compare sperm protein levels due to paternal toxicant exposure across multiple generations using iTRAQ technology. OC exposure induced a decrease in key proteins implicated in sperm motility and cell death (SOD1 and GPX4) in F1 fathers, a reduction in proteins involved in gamete fusion and sperm head cytoskeleton (Citrate Synthase, SLC2A3 and Calicin) in their F2 sons, and finally, a decrease in proteins playing a role in fertilization (IZUMO and ZPBP) in their F3 grandsons.
Conclusion: 

undifferentiated spermatogonia per tubule. 

that mutant testes contained a significant increase in number of testes. This result was confirmed by PLZF immunostaining showed c−Kit negative, Ki67 positive) in the mutant compared to wild−type increase in number of undifferentiated spermatogonia (PLZF positive, 

Further, FACS analyses of the adult testes showed a significant postnatal day 7, suggesting a failure of spermatogonial commitment. 

The number of germ cells observed in postnatal day 0 and day 3 testes in the Rbm5 mutant testes was normal; however, a significant reduction compared to that in wild type animals was seen at postnatal day 7, suggesting a failure of spermatogonial commitment. Further, FACS analyses of the adult testes showed a significant increase in number of undifferentiated spermatogonia (PLZF positive, c−Kit negative, Ki67 positive) in the mutant compared to wild−type testes. This result was confirmed by PLZF immunostaining showed that mutant testes contained a significant increase in number of undifferentiated spermatogonia per tubule. 

Conclusion: 

Taken together, our findings define for the first time a critical role for RBM5 in spermatogonia differentiation.

INTRODUCTION: Balance of spermatogonial stem and progenitor cell (SSPC) self-renewal and differentiation is essential for the homeostasis of spermatogenesis and the maintenance of male fertility. Regulation of SSPC function requires a complex interplay of intrinsic and extrinsic niche-derived factors. In this study, we identified the splicing factor RBM5 as a novel regulator of spermatogonia differentiation. Male mice carrying an ENU-induced missense mutation (R263P) in the second RNA recognition motif (RRM2) of RBM5 were sterile due to a round spermatid arrest, which ultimately led to azoosperma. We have shown that RBM5 is an essential splicing factor in round spermatids and the R263P mutation resulted in aberrant splicing in several target pre-mRNAs that are required for spermatid differentiation. Within the adult mouse testis, RBM5 localises to the nucleus of somatic and germ cells including spermatogonia, spermatocytes and round spermatids. Further, a stereological analysis revealed that in addition to the spermatid arrest phenotype Rbm5 mutant mice have a decreased conversion of spermatogonia into spermatocytes and significant loss of late spermatocytes. 

METHODS: In order to investigate the loss of spermatocytes, Rmb5 mutant versus wild type testes were stained for MVH as a marker of total germ cell content. 

RESULTS: The number of germ cells observed in postnatal day 0 and day 3 testes in the Rbm5 mutant testes was normal; however, a significant reduction compared to that in wild type animals was seen at postnatal day 7, suggesting a failure of spermatogonial commitment. Further, FACS analyses of the adult testes showed a significant increase in number of undifferentiated spermatogonia (PLZF positive, c−Kit negative, Ki67 positive) in the mutant compared to wild−type testes. This result was confirmed by PLZF immunostaining showed that mutant testes contained a significant increase in number of undifferentiated spermatogonia per tubule. 

CONCLUSION: Taken together, our findings define for the first time a critical role for RBM5 in spermatogonia differentiation.

INTRODUCTION: Hypogonadism is associated with sickle cell disease (SCD), but its underlying mechanism is not known. We investigated the mechanism of testosterone (T) deficiency in a mouse model of human SCD. 

METHODS: 7 month old homozygote SCD (Sickle) mice were used. Age−matched wild type (WT) and heterozygote SCD (Hemi) mice served as controls. Blood was obtained for measurements of T and luteinizing hormone (LH) by radioimmunoassay (RIA). Testes were collected for Leydig cell isolation, measurements of intratesticular T by RIA, and protein expressions of steroidogenic acute regulatory protein (StAR), cholesterol side−chain cleavage enzyme (P450sc, gp91phox subunit of the reactive oxygen species−generating enzyme NADPH oxidase, oxidative stress (4−hydroxy−2−nonenal, 4−HNE), and an antioxidant glutathione peroxidase−1 (GPx1) by Western blot. Leydig cells were treated with LH (0.5 and 10 ng/ml), dibutyryl cAMP (dbcAMP, 1 mM), 22−hydroxycholesterol (22HC, 25 µM), and pregnenolone (P5, 25 µM), and T produced into the media was measured by RIA. 

RESULTS: Plasma T levels were significantly (P<0.05) decreased in Sickle compared to WT and Hemi mice, while intratesticular T levels were significantly (P<0.05) decreased in Sickle compared to WT mice. Serum LH levels were significantly (P<0.05) increased in Sickle and Hemi compared to WT mice. LH−, dbcAMP−, and P5− (but not 22HC) stimulated testosterone production from Leydig cells isolated from Sickle and Hemi mouse testis was significantly (P<0.05) decreased compared to that of WT mice. Protein expression of StAR (but not P450sc) was significantly (P<0.05) reduced in the testis of Sickle and Hemi compared to that of WT mice. Protein expression of gp91phox was significantly (P<0.05) increased in the testis of Sickle compared to that of WT mice, while 4−HNE was significantly (P<0.05) reduced in the testis of Sickle and Hemi compared to that of WT mice. Protein expression of GPx1 did not differ between WT, Hemi, and Sickle mouse testis. 

CONCLUSION: Hypogonadism is present in Sickle mice, mimicking the human condition. The defects in Leydig cell steroidogenic pathway, mainly due to reduced availability of cholesterol for T production, may be related to NADPH oxidase−derived oxidative stress. Mice heterozygous for the human sickle globin exhibit intermediate hypogonadal changes between those of control and Sickle mice.
THE RISK OF CONGENITAL BIRTH DEFECTS IS NOT ASSOCIATED WITH SEMEN PARAMETERS OR MODE OF CONCEPTION IN OFFSPRING OF MEN VISITING A REPRODUCTIVE CLINIC

Michael Eisenberg, MD¹, Alexander W. Pastuszak, MD, PhD², Peter Langois, PhD³, Karen Moffitt³, Dolores J. Lamb, PhD⁴ and Larry I. Lipshultz, MD²

¹Stanford University; ²Baylor College of Medicine; ³Texas Department of State Health Services
(Presented By: Alexander W. Pastuszak, MD, PhD)

Introduction and Objectives: Approximately 15% of couples have fertility problems, with a 50% male factor contribution. While assisted reproductive technologies (ART) have greatly enhanced the ability of couples with fertility difficulties to conceive, evidence suggests an increased risk for congenital defects in children conceived using ART. Both the technique of in vitro fertilization (IVF) as well as infertility itself are possible explanations. We sought to determine if the severity of male factor infertility, as assessed by sperm quality and mode of conception, was associated with birth defect rates.

Methods: Fathers with semen analysis data in the Baylor College of Medicine Semen Database (BCMSD) were linked with offspring in the Texas Birth Defects Registry (TBDFR) using data from 1999–2009. To determine the association between birth defects and semen parameters, we identified the subset of men with complete data. Hierarchical linear modeling was used to determine odds ratios between birth defect rates, semen parameters, and mode of conception before and after adjustment for paternal, maternal, and birth covariates. Semen parameters were stratified based on subfertile cutoffs defined by the WHO 5th edition.

Results: Initial linkage between the BCMSD and TBDFR yielded 6,087 men with linked data. No association between semen parameters and birth defects was observed. As a sensitivity analysis, a subset of 1,382 men who had been evaluated for infertility was identified. After the above correction, 109 infants with and 2,115 infants without birth defects were identified. No statistically significant association was observed between birth defect rates, semen parameters, and mode of conception before or after adjustment for covariates (Table 1). Likewise, mode of conception, including infertility treatment and ART, did not affect birth defect rates.

Conclusion: Birth defect rates do not appear to be associated with semen quality or mode of conception. The current study suggests that the severity of male factor infertility does not impact the rate of congenital anomalies. This information is important when counseling couples concerned about the relationship between impaired semen quality and birth defects.

© 2015 American Society of Andrology and European Academy of Andrology
Andrology, 2015, Supplement, 48

ORAL ABSTRACTS

CONCURRENT SESSIONS – Oral Session II – Clinical

Podium/Poster #7

EFFICACY AND PHARMACOKINETICS OF LPCN 1021, A NOVEL ORAL TESTOSTERONE REPLACEMENT THERAPY (TRT), IN OBESE AND NON-OBESE HYPOGONADAL MEN: STUDY OF ANDROGEN REPLACEMENT (SOAR)

Adrian Dobs, MD, MHS¹, Jed Kaminskiy, MD², Martin Miner, MD³, Anthony Delconte, MD⁴, Nachiappan Chidambaram, PhD⁵, Satish Nachaegiri, MS⁶, Mahesh Patel, PhD⁷, Pavan Yadav, MD⁸ and Christina Wang, MD⁶

¹The Johns Hopkins University School of Medicine and Lipocine; ²University Urology Associates, New York, NY; ³Brown University and the Miriam Hospital, Providence, RI; ⁴Saint Joseph’s University, Philadelphia, PA; ⁵Lipocine, Inc.; ⁶Harbor-UCLA Medical Center and Los Angeles Biomedical Research Institute, Torrance, CA
(Presented By: Adrian Dobs, MD, MHS)

Introduction: TRT is indicated for treating hypogonadal men with low serum testosterone (T) levels and related symptoms. However, T products administered as topical or parenteral formulations are associated with inadvertent T transfer, messy application, poor retention rates, and superphysiologic T levels in some patients. There is a need for T formulations that are more user friendly, limit blood level dose excursions, and avoid T transdermal transfer. LPCN 1021 is a novel oral T undecanoate formulation being assessed in a Phase 3 trial that may avoid some of the undesirable attributes of non–oral T formulations. We sought to determine the effect of BMI on PK values after administration of LPCN 1021.

Methods: SOAR is a randomized, active-controlled, 2-arm, 12-months, open–label, multicenter, dose–titration ongoing trial that included 18–80 years old hypogonadal (T<300ng/dL on 2 separate days) men. Participants were randomized to either oral TU (n=210) or Androgel® 1.62% (n=105). In the oral TU arm, 92 subjects were non-obese (BMI < 30 kg/m2) and 118 subjects were obese (BMI ≥ 30 kg/m2). The dose could be titrated up (e.g. if T Cmax was >1500 ng/dL) at weeks 4 and 8 based on 24 h PK. Efficacy was assessed on week 13 based on serum T Cave,24h collected over 24h for T assayed by LC−MS/MS. Analysis was conducted using the full analysis set (subjects with at least one PK profile, N=193; BMI <30 kg/m2 N=82; BMI ≥ 30 kg/m2 N=111).

Results: LPCN 1021 restored and maintained T levels in the eugonadal range (300–1140 ng/dL) in 89.0% of non-obese hypogonadal men.
SUNDAY, APRIL 19, 2015
2:30 p.m. – 2:45 p.m.

CONCURRENT SESSIONS – Oral Session II – Clinical
Podium/Poster #9
CIGARETTE SMOKING AND THE SPERM EPIGENOME
Timothy Jenkins, PhD, Kenneth Aston, PhD, James Hotaling, MD, MS and Douglas Carrell, PhD
University of Utah
(Presented By: Timothy Jenkins, PhD)

Introduction: Objective: To evaluate the negative impacts of smoking on the sperm epigenome.
Methods: Illumina 450k human methylation array was used to assess sperm DNA methylation patterns across the entire genome in general population subjects attending University of Utah Andrology and IVF Laboratories for an Institutional Review Board approved study. We analyzed regional and single CpG DNA methylation patterns by two different approaches. First, we analyzed the differences in methylation patterns between smokers and age matched individuals who do not smoke. We then analyzed the effects of both length of time smoking and the volume of cigarettes consumed by analyzing the effect of “pack years” on sperm methylation patterns with a pack years value of <10 (n=11) being considered low and >10 (n=7) being considered high.
Results: Our findings indicate that there are some regions of the sperm genome that are consistently affected by cigarette smoke. Two genes displayed significant alterations to their methylation profile in smokers, namely GPCR133 and SDFK1. Additionally, we identified increased methylation variability in smokers across all CpGs probed in our analyses with an average coefficient of variance of 18.67 in our non-smoking group and 26.23 in our smoking group. This difference was significant (p=0.022).
Conclusion: Our data demonstrate that there are alterations that occur to the sperm epigenome as a result of cigarette smoke exposure. Of particular interest in this study are changes seen to general methylation variability in the sperm suggesting that smoke exposure has a destabilizing effect on the sperm epigenome which may affect an individual’s fertility or possibly their ability to produce healthy offspring. More targeted studies are required to fully address this hypothesis and the potential impact these alterations may have on offspring. More targeted studies are required to fully address this hypothesis and the potential impact these alterations may have on offspring.

CONCURRENT SESSIONS – Oral Session II – Clinical
Podium/Poster #10
WHOLE-EXOME SEQUENCING IDENTIFIES NOVEL HOMOZYGOUS MUTATION IN NPAS2 IN FAMILY WITH NONOBLACTIVE AZOOSPERMIA
Ranjith Ramasamy¹, M. Emre Bakircioglu, MD², Cenk Cengiz, BS¹, Ender Karaca, MD¹, Jason Scovell, BS¹, Matthew Bainbridge, PhD¹, James Lupski, PhD¹ and Dolores Lamb, PhD¹
¹Baylor College of Medicine; ²Bahçeci Fulya IVF Center, Istanbul, Turkey
(Presented By: Ranjith Ramasamy)

Introduction: Nonobstructive azoospermia (NOA) is characterized by lack of sperm in the ejaculate due to severe testicular failure. Due to genetic and clinical heterogeneity, the diagnosis is not straightforward. Current clinical practices have focused on karyotype and microdeletions. In the present study, we investigated the genetic cause of NOA in a consanguineous Turkish family through homozygosity mapping followed by targeted exon/whole−exome sequencing to identify genetic variations.
Methods: We designed a whole-exome sequencing (WES)-based approach using an in-house designed capture reagent followed by high-throughput sequencing on the Illumina platform. We sequenced the exomes of two affected siblings. Exome analysis resulted in the identification of 442 variants in the index patients. All variants passing filter criteria were validated with Sanger sequencing to confirm familial segregation and absence in the control population.
Results: A novel non-synonymous mutation in neuronal PAS domain 2 domain (NPAS2) was identified in a consanguineous family from Turkey. This mutation in exon 14 (chr2: 101592000 C>G) of NPAS2 is likely a disease−causing mutation as it segregates with the disease. Family segregation of the variants showed the presence of homozygous mutation in the three brothers with NOA and heterozygous mutation in one brother and one sister who were both fertile. The mutation is not found in the single nucleotide polymorphism (SNP) database, the 1000 Genomes Project, Baylor College of Medicine cohort of 500 Turkish patients (not a founder mutation) or matching 50 fertile controls.
Conclusion: Using WES, we identified a novel homozygous mutation in NPAS2 as a likely disease-causing variant in a Turkish family diagnosed with NOA. Our data reinforce the clinical role of WES in the molecular diagnosis of highly heterogeneous genetic diseases where conventional genetic approaches have previously failed in achieving a proper diagnosis.
SUNDAY, APRIL 19, 2015
3:00 p.m. – 3:15 p.m.

CONCURRENT SESSIONS – Oral Session II – Clinical
Podium/Poster #11
ENCLOMID AND TOPICAL TESTOSTERONE ELEVATE TESTOSTERONE IN HYPOGONADAL MEN BUT ENCLOMID DOES NOT DECREASE TESTES SIZE
Ronald Wiehle, PhD, Gregory Fontenot, PhD, Martin Sandel, BS and Jaye Thompson, PhD
Repros Therapeutics
(Presented By: Ronald Wiehle, PhD)

Introduction: Men with secondary hypogonadism have low normal LH and low testosterone and are often treated with exogenous or topical testosterone.

Objective: Our aim was to evaluate oral enclomiphene citrate or Androxal as an alternative to topical testosterone replacement therapy for men with secondary hypogonadism.

Methods: Two trials (ZA−304 and ZA−305) were randomized, double blind, placebo- and active-control, multi−center phase III studies in 224 men with secondary hypogonadism between 25 and 60 years of age. Men received 12.5mg or 25mg of enclomid as a daily capsule and were provided with a placebo gel. Other men received AndroGel 1.6% and placebo capsules. Other men received placebo capsules and gels.

Results: To be enrolled subjects needed to have two baseline testosterone (T) values below 300ng/dL. The End of Study (EOS) was after 16 weeks of treatment. There was a statistically significant rise in T in men receiving either enclomiphene citrate or topical testosterone into the normal range (see table). Placebo subjects did not change. Encloolid did not decrease sperm counts unlike the topical gel. As we have seen before, enclomiphene citrate increased LH and FSH while men in the topical arm showed decreases (not shown). All men were similar at baseline in testes volume (p = 0.94, ANOVA) by orchidometry. In both studies, men on topical testosterone demonstrated decreases in mean testicular volume (−0.86 cm3) and a significant decrease overall compared to the enclomid (p < 0.05) or placebo (p < 0.05).

Conclusion: Encloomiphene citrate significantly increased total serum testosterone, LH and FSH which suggests that the drug normalized endogenous testosterone production through the hypothalamic–pituitary–testicular axis and supported the natural continuation of sperm number and testes volume.

SUNDAY, APRIL 19, 2015
3:15 p.m. – 3:30 p.m.

CONCURRENT SESSIONS – Oral Session II – Clinical
Podium/Poster #12
CONCENTRATIONS OF THE RETINOIC ACID SYNTHESIZING ENZYME ALDH1A2 ARE SIGNIFICANTLY REDUCED IN MEN WITH OLIGOZOOスポメリア
John Amory, MD, MPH, Margarett Shnorhavorian, MD, MPH, Samuel Arnold, MD, Faith Stelvison, BS, Nina Isoherranen, PhD, Thomas Walsh, MD, MPH and Charles Muller, PhD
University of Washington
(Presented By: John Amory, MD, MPH)

Introduction: Vitamin A, and its active metabolite, retinoic acid, are known to be necessary for spermatogenesis in many species including man. Retinoic acid is synthesized in tissues from Vitamin A by one of three aldehyde dehydrogenases, ALDH1A1, 1A2 or 1A3. We have shown that testicular ALDH1A2 levels are reduced in men with infertility in proportion to germ-cell number on testicular biopsy; however, the relationships between testicular ALDH1A2 and semen parameters, as well as the cellular localization of ALDH1A2 within the testes have not been reported.

Methods: We conducted an observational analysis of testicular ALDH1A2 on human testis samples from 5 men with normal sperm parameters and 5 men with infertility due to oligozoospermia. Testicular tissue was analyzed by immunohistochemistry for ALDH1A2 and ALDH1A2 protein levels were quantified by a LC/MS/MS peptide assay.

Results: Men with oligozoospermia had significantly reduced levels of ALDH1A2 in their testicular tissue compared to men with normozoospermia (p<0.03). Immunohistochemistry revealed that ALDH1A2 was localized primarily in spermatogonia, and absent from Sertoli cells.

Conclusion: The finding that ALDH1A2 co-localizes with early germ cells in the human testis suggests that i) early germ cells are a site of retinoic acid biosynthesis within the seminiferous epithelium, ii) reduced ALDH1A2 may be associated with male infertility, iii) inhibition of ALDH1A2 may be a reasonable strategy for the development of novel male contraceptives.

This work was funded by The Eunice Kennedy Shriver National Institute of Child Health and Human Development supported this work through cooperative agreement U54 HD42454 as part of the Cooperative Contraceptive Research Centers Program.
POSTER SESSION I

Sunday, April 19, 2015
11:00 a.m. – 12:30 p.m.
Location: Grand Ballroom C

Podium/Poster #1 MULTICELLULAR HUMAN TESTICULAR ORGANOID: A NOVEL IN VITRO GERM CELL AND TESTICULAR TOXICITY MODEL
Samuel Pendergraft, MS¹, Hooman Sadri-Ardekani, MD, PhD², Tanya Reid, BS³, Anthony Atala, MD² and Colin Bishop, PhD⁴
¹(1) Molecular Medicine and Translational Science Graduate Program, Wake Forest University Health Sciences, Winston-Salem, NC (2) Wake Forest Institute for Regenerative Medicine, Wake Forest School of Medicine, Winston-Salem, NC; ²(1) Wake Forest Institute for Regenerative Medicine, Wake Forest School of Medicine, Winston-Salem, NC (2) Department of Urology, Wake Forest School of Medicine, Winston-Salem, NC; ³(1) Wake Forest Institute for Regenerative Medicine, Wake Forest School of Medicine, Winston-Salem, NC
(Presented By: Samuel Pendergraft, MS)

Podium/Poster #2 CONDITIONAL STEROIDOGENIC CELL-TARGETED DELETION OF THE TRANSLOCATOR PROTEIN (TSPO) UNVEILS ITS CRUCIAL ROLE IN VIABILITY AND HORMONE-DEPENDENT STEROID FORMATION
Andrew Midzak, PhD¹, Jinjiang Fan, PhD², Enrico Campioli, PhD, PharmD², Martine Culty, PhD² and Vassilios Papadopoulos, PhD, PharmD²
¹Res; ²Research Institute of the McGill University Health Centre
(Presented By: Andrew Midzak, PhD)

Podium/Poster #3 EARLY-LIFE EXPOSURE TO AN ENVIRONMENTAL ORGANOCHLORINE MIXTURE REDUCES THE FERTILITY OF MALE RATS AND INDUCES DIFFERENTIAL EXPRESSION OF SPERM PROTEINS ACROSS MULTIPLE GENERATIONS IN A PATERNALLY-MEDIATED MANNER
Nancy Côté, PhD, Clotilde Maurice, PhD, Florence Roux-Dalvai, Msc, Arnaud Droit, PhD and Janice L. Bailey, PhD
Université Laval
(Presented By: Nancy Côté, PhD)

Podium/Poster #4 MACROPHAGES AND DENDRITIC CELLS COOPERATE TO SURVEY THE EPIDIDYMAL LUMEN
Tegan Smith, PhD, Gabriel Courties, PhD, Claire Barton, BA, Matthias Nahrendorf, MD, PhD and Nicolas Da Silva, PhD
Massachusetts General Hospital and Harvard Medical School
(Presented By: Tegan Smith, PhD)

Podium/Poster #5 THE SPLICING FACTOR RBM5 IS REQUIRED FOR SPERMATOGONIA DIFFERENTIATION
Duangporn Jamsai, PhD, Morgan Oatley, BSc, Anne O’Connor, BSc (Hons), Jo Merriner, BSc, Robin Hobbs, PhD and Moira O’Bryan, PhD
Monash University
(Presented By: Duangporn Jamsai, PhD)

Podium/Poster #6 MECHANISM OF HYPOGONADISM IN THE TRANSGENIC SICKLE CELL MOUSE
Biljana Musicki, PhD, Haolin Chen, PhD, Yuxi Zhang, MD, Terry Brown, PhD, Barry Zirkin, PhD and Arthur Burnett, MD
Johns Hopkins University
(Presented By: Biljana Musicki, PhD)

Podium/Poster #7 THE RISK OF CONGENITAL BIRTH DEFECTS IS NOT ASSOCIATED WITH SEMEN PARAMETERS OR MODE OF CONCEPTION IN OFFSPRING OF MEN VISITING A REPRODUCTIVE CLINIC
Michael Eisenberg, MD¹, Alexander W. Pastuszak, MD, PhD², Peter Langlois, PhD³, Karen Moffitt³, Dolores J. Lamb, PhD² and Larry I. Lipshultz, MD³
¹Stanford University; ²Baylor College of Medicine; ³Texas Department of State Health Services
(Presented By: Alexander W. Pastuszak, MD, PhD)

Podium/Poster #8 EFFICACY AND PHARMACOKINETICS OF LPCN 1021, A NOVEL ORAL TESTOSTERONE REPLACEMENT THERAPY (TRT), IN OBESE AND NON-OBESE HYPOGONADAL MEN: STUDY OF ANDROGEN REPLACEMENT (SOAR)
Adrian Dobs, MD, MHS¹, Jed Kaminski, MD², Martin Miner, MD³, Anthony Delconte, MD⁴, Nachiappan Chidambaram, PhD⁵, Satish Nachaegiri, MS⁶, Mahesh Patel, PhD⁴, Pavan Yadev, MD⁶ and Christina Wang, MD⁶
¹The Johns Hopkins University School of Medicine and Lipocine; ²University Urology Associates, New York, NY; ³Brown University and the Miriam Hospital, Providence, RI; ⁴Saint Joseph’s University, Philadelphia, PA; ⁵Lipocine, Inc.; ⁶Harbor-UCLA Medical Center and Los Angeles Biomedical Research Institute, Torrance, CA
(Presented By: Adrian Dobs, MD, MHS)

Podium/Poster #9 CIGARETTE SMOKING AND THE SPERM EPIGENOME
Timothy Jenkins, PhD, Kenneth Aston, PhD, James Hotaling, MD, MS and Douglas Carrell, PhD
University of Utah
(Presented By: Timothy Jenkins, PhD)

© 2015 American Society of Andrology and European Academy of Andrology Andrology, 2015, Supplement, 51
Podium/Poster #10 WHOLE-EXOME SEQUENCING IDENTIFIES NOVEL HOMOZYGOUS MUTATION IN NPAS2 IN FAMILY WITH NONOBSTRUCTIVE AZOOSPERMIA
Ranjith Ramasamy¹, M. Emre Bakircioglu, MD², Cenk Cengiz, BS³, Ender Karaca, MD¹, Jason Scovell, BS¹, Matthew Bainbridge, PhD¹, James Lupski, PhD⁴ and Dolores Lamb, PhD⁴
¹Baylor College of Medicine; ²Bahceci Fulya IVF Center, Istanbul, Turkey
(Presented By: Ranjith Ramasamy)

Podium/Poster #11 ENCLOMID AND TOPICAL TESTOSTERONE ELEVATE TESTOSTERONE IN HYPOGONADAL MEN BUT ENCLOMID DOES NOT DECREASE TESTES SIZE
Ronald Wiehle, PhD, Gregory Fontenot, PhD, Martin Sandel, BS and Jaye Thompson, PhD
Repros Therapeutics
(Presented By: Ronald Wiehle, PhD)

Podium/Poster #12 CONCENTRATIONS OF THE RETINOIC ACID SYNTHESIZING ENZYME ALDH1A2 ARE SIGNIFICANTLY REDUCED IN MEN WITH OLIGOZOOSPERMIA
John Amory, MD, MPH, Margarett Shnorhavorian, MD, MPH, Samuel Arnold, MD, Faith Stevison, BS, Nina Isoherranen, PhD, Thomas Walsh, MD, MPH and Charles Muller, PhD
University of Washington
(Presented By: John Amory, MD, MPH)

Poster #13 INVESTIGATIONS ON THE EFFECTS OF TYPHA CAPENSIS ON TM3 LEYDIG CELLS
Abdulkarem Ilfergane, MSc, Nicole Haines-Arries, MSc, Leonardo van Zyl, MSc and Ralf Henkel, PhD
University of the Western Cape
(Presented By: Ralf Henkel, PhD)

Poster #14 WHO WERE THE PATIENTS ON TESTOSTERONE THAT HAD MYOCARDIAL INFARCTIONS? THE LOW T EXPERIENCE
Kelly Cook, MPAS, PA-C¹, William Reilly, MD¹ and Robert Tan, MD, MBA²,³
¹Low T Center; ²Opal Medical Clinic; ³Low T Institute
(Presented By: Kelly Cook, MPAS, PA-C)

Poster #15 ANDROGENIC EFFECT OF CINNAMON ZEYLANICUM ON SPERMATOGENESIS
Arash Khaki, PhD
Department of Pathobiology, Tabriz Branch, Islamic Azad University, Tabriz, Iran.
(Presented By: Arash Khaki, PhD)

Poster #16 EFFECTS OF ORGANOPHOSPHATE FLAME RETARDANTS ON LEYDIG CELL FUNCTION
Gauthier Schang, Barbara F. Hales, PhD and Bernard Robaire, PhD
Department of Pharmacology and Therapeutics, McGill University
(Presented By: Gauthier Schang)

Poster #17 FINASTERIDE 1MG/DAILY CONSUMPTION IMPAIRS SPERMATOGENESIS BY HISTOLOGICAL EVALUATION AND SEMEN QUALITY IN MEN IN REPRODUCTIVE AGE
Juliana Pariz, MSc, PhD student¹,² and Jorge Hallak, MD, PhD¹,²
¹Androscience; ²Universidade de São Paulo
(Presented By: Juliana Pariz, MSc, PhD student)

Poster #18 EFFECT OF ALCOHOL CONSUMPTION ON MALE REPRODUCTIVE POTENTIAL
Artemis da Silva, BSc¹,², Juliana Pariz, MSc, PhD student¹,² and Jorge Hallak, MD, PhD¹,²
¹Androscience; ²Universidade de São Paulo
(Presented By: Artemis da Silva, BSc)

Poster #19 YOGA AND MEDITATION - THERAPEUTIC FOR SPERM DNA HEALTH
Shiv Basant Kumar, MSc¹, Bhavna Chawla, MD², Raj Kumar Yadav, MD³, Surabhi Gautam, MSc⁴ and Rima Dada, MD, PhD⁴
¹Laboratory for molecular reproduction and genetics, Department of Anatomy, All India Institute of Medical Sciences, New Delhi, India.; ²Ocular Oncology & Pediatric Ophthalmology Service, Rajendra Prasad Centre for Ophthalmic Sciences; ³Integral Health Clinic, Department of Physiology, All India Institute of Medical Sciences, New Delhi, India; ⁴Laboratory for molecular reproduction and genetics, Department of Anatomy, All India Institute of Medical Sciences, New Delhi, India
(Presented By: Shiv Basant Kumar, MSc)
**POSTER SESSION I**

**Poster #20** GENITOURINARY INFECTION ALTERS SEMEN PARAMETERS AND INCREASES PRESENCE OF ANTI-SPERM ANTIBODIES  
Tábata Martins, BSc student¹,²,³, Juliana Pariz, MSc, PhD student¹,², Rosa Alice Monteiro, Bsc¹,² and Jorge Hallak, MD, PhD¹,²  
¹Androscience; ²Universidade de São Paulo; ³Faculdades Metropolitanas Unidas  
(Presented By: Tábata Martins, BSc student)

**Poster #21** CHARACTERIZATION OF PRIMARY CULTURES OF ADULT HUMAN EPIDIDYMIS EPITHELIAL CELLS  
Shih-Hsing Leir, PhD¹, James Browne, PhD¹, Scott Eggenger, MD² and Ann Harris, PhD¹  
¹Human Molecular Genetics Program, Lurie Children’s Research Center/Northwestern University Feinberg School of Medicine, Chicago, IL; ²Section of Urology, University of Chicago Medical Center, Chicago, IL  
(Presented By: Shih-Hsing Leir, PhD)

**Poster #22** COMPARATIVE ANALYSIS OF EPIDIDYMIS TRANSCRIPTOME IN FERTILE AND SUBFERTILE BULL  
Christine Legare, MSc¹, Ayodélé Akintayo, MSc¹, Patrick Blondin, PhD² and Robert Sullivan, PhD¹  
¹Laval University; ²L’Alliance Boviteq  
(Presented By: Christine Legare, MSc)

**Poster #23** CONTRIBUTION OF PRINCIPAL AND CLEAR CELLS IN THE REGULATION OF LUMINAL PH IN THE MOUSE EPIDIDYMIS  
Yoo-Jin Park, PhD, Bong-Ki Kim, PhD and Sylvie Breton, PhD  
Massachusetts General Hospital  
(Presented By: Yoo-Jin Park, PhD)

**Poster #24** TESTICULAR FLUID REGULATES APICAL BLEBBING IN THE PORCINE EPIDIDYMIS  
Jennifer Hughes and Trish Berger, PhD  
UC Davis  
(Presented By: Jennifer Hughes)

**Poster #25** DIFFERENTIAL PLATING RATIO OF NON-ADHERENT TO ADHERENT CELLS ISOLATED FROM AN AZOOSPERMIC MICRO TESTICULAR TISSUE EXTRACTION (MICROTESE) SAMPLE HAS A PROFOUND EFFECT ON IN VITRO GERM CELL COLONY FORMATION  
Itai Gat¹,², Leila Maghen¹, Ekaterina Shlush¹, Hanna Balakier¹, Andrée Gauthier-Fisher¹, Keith Jarvi³, Kirk C. Lo¹ and Clifford Librach¹,⁴,⁵,⁶  
¹The Create Fertility Centre, 790 Bay Street, Suite 1100, Toronto M5G 1N8, Canada; ²Talpiot Medical Leadership Program, Sheba Medical Center, Ramat Gan, Israel; ³Department of Urology, Mount Sinai Hospital; ⁴Department of Obstetrics and Gynecology; ⁵Department of Physiology, University of Toronto; ⁶Department of Gynecology, Women’s College Hospital, Toronto, Ontario  
(Presented By: Itai Gat)

**Poster #26** REQUIREMENT FOR MOV10L1 RNA HELICASE ACTIVITY IN THE PROCESSING OF PIRNA PRECURSORS  
Qi Fu, Anastassios Vourekas, PhD¹, Ke Zheng, PhD², Erica Goode and P. Jeremy Wang, PhD¹  
¹The University of Pennsylvania; ²Nanjing Medical University School  
(Presented By: Qi Fu)

**Poster #27** SEMEN PARAMETERS, PATIENT CHARACTERISTICS, AND ASSOCIATED SPERM EPIGENETIC PROFILES  
Timothy Jenkins, PhD, Kenneth Aston, PhD, James Hotaling, MD, MS and Douglas Carrell, PhD  
University of Utah  
(Presented By: Timothy Jenkins, PhD)

**Poster #28** AN ASSOCIATION BETWEEN THE GLUCOSE TRANSPORTER GLUT3 AND MALE INFERTILITY  
Alexander W. Pastuszak, MD, PhD, Carolina Jorgez, PhD, Larry I. Lipshultz, MD and Dolores J. Lamb, PhD  
Baylor College of Medicine  
(Presented By: Alexander W. Pastuszak, MD, PhD)

**Poster #29** PATERNAL FACTORS IN EARLY EMBRYONIC DEVELOPMENT  
Manoj Kumar, MSc¹, Dipika Deka, MD², Vatsala Dadhwal, MD² and Rima Dada, PhD¹  
¹Laboratory for Molecular Reproduction and Genetics, Department of Anatomy, All India Institute of Medical Sciences, New Delhi 110 029, India; ²Department of Obstetrics and Gynaecology, All India Institute of Medical Sciences, New Delhi 110 029, India  
(Presented By: Manoj Kumar, MSc)
Poster #30 EXPRESSION OF SELECTED MICRORNAS LOCATED ON THE X CHROMOSOME IN KLINEFELTER SYNDROME
Jennifer Reifsnyder, MD, Anna Mielenik, MS, Peter Schlegel, MD and Darius Paduch, MD, PhD
New York Presbyterian Hospital-Weill Cornell Medical Center
(Presented By: Jennifer Reifsnyder, MD)

Poster #31 LIFETIME FOLATE DEFICIENCY AND SUPPLEMENTATION INDUCES ABERRANT SPERM DNA METHYLATION AND REPRODUCTIVE HEALTH
Lundi Ly, BSc¹, Donovan Chan², Mylene Landry³, Nathalie Behan³, Amanda MacFarlane³ and Jacquetta Trasler³
¹Department of Human Genetics, McGill University, Montreal, QC, Canada; ²Research Institute of the McGill University Health Centre at the Montreal Children’s Hospital; ³Health Canada, Ottawa ON, Canada; ⁴Departments of Human Genetics, Pediatrics, and Pharmacology and Therapeutics, McGill University
(Presented By: Lundi Ly, BSc)

Poster #32 IMPACT OF HIGH DOSE FOLATE SUPPLEMENTATION ON THE HUMAN AND MOUSE SPERM EPIGENOME
Mahmoud Aarabi, MD, PhD¹, Maria C. San Gabriel, PhD²,³, Donovan Chan, PhD², Armand Zini, MD²,³ and Jacquetta Trasler, MD, PhD³
¹Department of Human Genetics, McGill University and Research Institute of the McGill University Health Centre at the Montreal Children’s Hospital, Montreal, QC; ²Division of Urology, Department of Surgery, McGill University; ³Research Institute of the McGill University Health Centre at the Royal Victoria Hospital, Montreal, QC; ⁴Departments of Human Genetics, Pediatrics and Pharmacology & Therapeutics, McGill University and Research Institute of the McGill University Health Centre at the Montreal Children’s Hospital
(Presented By: Mahmoud Aarabi, MD, PhD)

Poster #33 THE IMPACT OF LEUKOCYTOSPERMIA ON CHROMATIN CONDENSATION, STRUCTURE INTEGRITY, DNA FRAGMENTATION AND CORRELATION WITH OTHER SPERM PARAMETERS
Ruben Burnazyan, MD, PhD and Mohamed Hammadeh, Prof
(Presented By: Ruben Burnazyan, MD, PhD)

Poster #34 CAFFEINE AND MELATONIN SUPPLEMENTATION IMPROVES MOTILITY PARAMETERS AND MITOCHONDRIAL ACTIVITY IN POST-THAW SEMINAL SAMPLES: INITIAL REPORT
Juliana Pariz, MSc, PhD student¹,² and Jorge Hallak, MD, PhD¹,²
¹Androscience; ²Universidade de São Paulo
(Presented By: Juliana Pariz, MSc, PhD student)

Poster #35 SPERM GENOME: IMPLICATIONS IN ART FAILURE AND IDIOPATHIC MALE INFERTILITY
Swetasmita Mishra, MSc¹, Rajeev Kumar, MD², Neena Malhotra, MD³ and Rima Dada, MD, PhD⁴
¹PhD Scholar; ²Department of Urology, AIIMS; ³Department of Obs. & Gyn., AIIMS; ⁴Department of Anatomy
(Presented By: Swetasmita Mishra, MSc)

Poster #36 INFERTILITYDB DATABASE: A UNIFIED POINT OF ACCESS TO KNOWLEDGE OF KNOCKOUT MOUSE MODELS OF MALE INFERTILITY
Burak Özkösem, PhD
Arizona State University
(Presented By: Burak Özkösem, PhD)

Poster #37 WHY ME? LIVE EXPERIENCE OF MEN UNDERGOING INFERTILITY TREATMENT
Anshu Baranwal and Aparajita Chattopadhyay, PhD
International Institute for Population Sciences, Mumbai, India
(Presented By: Anshu Baranwal)

Poster #38 PROFILE DIAGNOSIS OF PATIENTS IN A PRIVATE SEMEN BANK
Artemis da Silva, BSc¹,², Juliana Pariz, MSc, PhD student¹,² and Jorge Hallak, MD, PhD¹,²
¹Androscience; ²Universidade de São Paulo
(Presented By: Artemis da Silva, BSc)

Poster #39 WORLD HEALTH ORGANIZATION GUIDELINES AND ITS INFLUENCE IN CONDUCT OF VARICOCELE TREATMENT
Tábata Martins, BSc student¹,²,³, Juliana Pariz, MSc, PhD student¹,² and Jorge Hallak, MD, PhD¹,²
¹Androscience; ²Universidade de São Paulo; ³Faculdades Metropolitanas Unidas
(Presented By: Tábata Martins, BSc student)
Poster #40 FLOW CYTOMETRIC EVALUATION OF DNA CONTENT FOR CLASSIFICATION OF NON-OBSTRUCTIVE AZOOSPERMIA MTESE SAMPLES
Ekaterina Shlush, MD, Sergey I. Moskovtsev, MD, PhD, Melissa Felice, MSc, Andree Gauthier-Fisher, PhD, Hanna Balakier, PhD, Keith Jarvi, Kirk C. Lo and Clifford L. Librach
1CREAte Fertility Centre, Toronto, Canada; 2Department of Obstetrics and Gynecology, University of Toronto, Toronto, Canada; 3Department of Urology, Mount Sinai Hospital; 4Department of Gynecology, Women’s College Hospital, Toronto, Canada
(Presented By: Ekaterina Shlush, MD)

Poster #41 THERAPEUTIC POTENTIAL OF MUCUNA PRURIENS (LINN.) ON ERECTILE DYSFUNCTION DUE TO SCHWANN CELL DAMAGE IN DORSAL NERVE OF PENIS INDUCED BY AGEING
Prakash Seppan, PhD, Ibrahim Muhammed, PhD, Karthik Ganesh Mohanraj, MSc, Ganesh Lakshmanan, MSc, Dinesh Premavathy, MSc, Sakthi Jothi Muthu, MSc and Khayinmi Wungpam Shimray, MSc
University of Madras
(Presented By: Prakash Seppan, PhD)

Poster #42 IMPROVEMENTS IN PATIENT REPORTED SEXUAL FUNCTION AFTER MICROSURGICAL VARICOCELECTOMY
Bobby Najari, MD, Leonard Introna and Darius Paduch, MD, PhD
Weill Cornell Medical College
(Presented By: Bobby Najari, MD)

Poster #43 HIGH PREVALENCE OF ERECTILE AND EJACULATORY DYSFUNCTION IN MEN WITH OPIOID INDUCED ANDROGEN DEFICIENCY
Bobby Najari, MD, Matthew Wosnitzer, MD, Peter Schlegel, MD and Darius Paduch, MD, PhD
1Weill Cornell Medical College; 2Northeast Medical Group - Yale New Haven Health
(Presented By: Bobby Najari, MD)

Poster #44 EFFECT OF AQUEOUS CISSAMPELOS CAPENSIS EXTRACT ON PROSTATE CANCER, LEYDIG AND SERTOLI CELL FUNCTION
Keenau Pearce, MSc, Donavon Hiss, PhD, Frans Weitz, MSc, Uta-Christina, Hipler, PhD, Cornelia Wiegand, PhD and Ralf Henkel, PhD
1University of the Western Cape; 2University of Jena
(Presented By: Ralf Henkel, PhD)

Poster #45 RAPID METHOD FOR THE ISOLATION OF SPERM DNA
Haotian Wu, Matthew de Gannes, Gianna Luchetti and J. Richard Pilsner
Department of Environmental Health Sciences, UMass Amherst
(Presented By: Haotian Wu)

Poster #46 WITHDRAWN

Poster #47 ASSOCIATION BETWEEN PROSTATE-SPECIFIC ANTIGEN AND BIOMARKERS OF SUBCLINICAL SYSTEMIC INFLAMMATION IN MIDDLE-AGE HEALTHY MEN FROM THE GENERAL POPULATION
Saad Elzanaty, MD, PhD, Babak Rezanezad, MD, Ronnie Willenheimer, MD, PhD and Rasmus Borgquist, MD, PhD
(Presented By: Saad Elzanaty, MD, PhD)

Poster #48 DO FAMILY MEMBERS OF INFERTILE MEN HAVE AN INCREASED RISK OF CANCER?
Ross Anderson, MD, MCR, Heidi Hanson, PhD, Mitchell Bassett, MD, Chong Zhang, MS, Angela Presson, PhD, Kenneth Aston, PhD, William Lowrance, MD, MPH, Douglas Carrell, PhD, Ken Smith, PhD and James Hotaling, MD, MS
1University of Utah, Department of Surgery, Division of Urology; 2University of Utah, Department of Family and Preventive Medicine, Population Sciences, Huntsman Cancer Institute; 3University of Utah, Department of Family and Preventive Medicine Chong.Zhang@hsc.utah.edu; 4University of Utah, Department of Family and Preventive Medicine; 5University of Utah, Department of Surgery, Andrology and IVF Laboratories; 6University of Utah, Department of Surgery, Huntsman Cancer Institute; 7University of Utah, Department of Surgery, Director of IVF and Andrology Laboratories; 8University of Utah, Population Sciences, Huntsman Cancer Institute
(Presented By: Ross Anderson, MD, MCR)

Poster #49 EFFECT OF SPERM DNA DAMAGE ON ART OUTCOMES: A SYSTEMATIC REVIEW AND META-ANALYSIS
Luke Simon, PhD, Armand Zini, MD and Douglas Carrell, PhD
1University of Utah; 2St Mary’s Hospital Center
(Presented By: Luke Simon, PhD)
POSTER SESSION I

Poster #50 SPERM CHROMATIN QUALITY ASSESSMENT: OPTIMIZATION OF THE HIGH THROUGHPUT COMET ASSAY
Océane Albert, PhD¹, Robert G. Berger, PhD², Wolfgang Reintsch, PhD³, Barbara F. Hales, PhD¹ and Bernard Robaire, PhD²
¹Department of Pharmacology & Therapeutics, McGill University, Montreal, QC, Canada; ²Departments of Pharmacology & Therapeutics and of Obstetrics & Gynecology, McGill University, Montreal, QC, Canada
(Presented By: Océane Albert, PhD)

Poster #51 ROLE OF SPERM THIOLS' REDOX STATUS IN KEEPING RAT SPERM QUIESCENT IN CAUDA EPIDIDYMIS
Santosh Yadav, PhD, Lokesh Kumar, MSc, Aastha Pandey, MSc, Bhavana Kushwaha, MSc, Jagdamba Maikhuri, PhD and Gopal Gupta, PhD
CSIR-Central Drug Research Institute, Lucknow, UP, India
(Presented By: Santosh Yadav, PhD)

Poster #52 ENERGY METABOLISM OF QUIESCENT SPERM IN CAUDA EPIDIDYMIS OF RAT
Lokesh Kumar, MSc, Santosh Yadav, PhD, Vikas Verma, MSc, Aastha Pandey, MSc, Bhavana Kushwaha, MSc, Vikas Sharma, MSc, Jagdamba Maikhuri, PhD and Gopal Gupta, PhD
CSIR-Central Drug Research Institute, Lucknow, UP, India
(Presented By: Lokesh Kumar, MSc)

Poster #53 CRYOPRESERVATION OF SPERMATOZOA: DO PERMEABLE CRYOPROTECTANTS IMPROVE MOTILE SPERM YIELDS?
Cigdem Tanrikut, MD, Jie Liu, PhD, Diane Wright, PhD, Gloria Lee, MA, Mehmet Toner, PhD and Thomas Toth, MD
Massachusetts General Hospital
(Presented By: Cigdem Tanrikut, MD)

Poster #54 THE IMPACT OF OXIDATIVE STRESS ON CHAPERONE-MEDIATED HUMAN SPERM-EGG INTERACTION
Brett Nixon, Elizabeth Bromfield, BBiotechnology (Hons) and R. John Aitken, BSc, MSc, PhD
The University of Newcastle
(Presented By: Brett Nixon)

Poster #55 LOWER SEMEN QUALITY AS A MARKER FOR INCREASED FAMILIAL MORTALITY
Mitchell Bassett, MD¹, Heidi Hanson, PhD², Ross Anderson, MD, MCR³, Kenneth Aston, PhD⁴, Douglas Carrell, PhD⁵, Ken Smith, PhD⁶ and James Hotaling, MD, MS¹
¹University of Utah, Department of Surgery, Division of Urology; ²University of Utah, Department of Family and Preventive Medicine, Population Sciences, Huntsman Cancer Institute; ³University of Utah, Department of Surgery, Director of IVF and Andrology Laboratories; ⁴University of Utah, Population Sciences, Huntsman Cancer Institute
(Presented By: Mitchell Bassett, MD)

Poster #56 PROTEOMIC PROFILING OF HUMAN SPERMATOZOA PROTEIN IN RECURRENT PREGNANCY LOSS AND ITS CORRELATION TO OXIDATIVE STRESS
Gayatri Mohanty, MPhil¹, Nirlipta Swain, MPhil¹, Luna Samanta, PhD¹ and Sujata Kar, MD²
¹Department of Zoology, Redox Biology Laboratory, Ravenshaw University, Cuttack, Odisha, India; ²Kar Clinic and Hospital, Bhubaneswar, Odisha, India
(Presented By: Gayatri Mohanty, MPhil)

Poster #57 AUTOMATIC SPERM TRACKING AND ANALYSIS OF SWIMMING PATTERN TRANSITIONS
Leonardo Urbano, PhD¹, Puneet Masson, MD², Matthew VerMilyea, PhD² and Moshe Kam, PhD³
¹Drexel University; ²Penn Fertility Care, Hospital of the University of Pennsylvania; ³College of Engineering, New Jersey Institute of Technology
(Presented By: Leonardo Urbano, PhD)

Poster #58 EFFECT OF RESVERATROL ON SPERMATIC PARAMETERS OF ADULT RATS SUBMITTED TO EXPERIMENTAL VARICOCELE INDUCED IN THE PERIPUBERTY
Talita B. Mendes, Master Student¹, André C. Vaz, Master Student², Camila C. Paccola, Doctoral Student², Taiza Stumpp, Doctor² and Sandra M. Miraglia, Doctor³
¹Federal University of Sao Paulo - Unifesp - Brazil; ²Unifesp (Presented By: Talita B. Mendes, Master Student)

Poster #59 EFFECTS OF BETAINES SUPPLEMENTATION ON SPERM FUNCTIONAL PARAMETERS IN HUMANS AND MICE WITH DEFECTS IN CHOLINE METABOLISM
Summer Goodson, PhD¹, Martin Kohlmeier, MD² and Steven Zeisel²
¹UNC Chapel Hill Nutrition Research Institute; ²UNC Chapel Hill Nutrition Research Institute and Department of Nutrition, UNC Chapel Hill
(Presented By: Summer Goodson, PhD)
Poster #60 ORIGIN OF THE STEROIDOGENIC POOL OF CHOLESTEROL USED IN CAMP-INDUCED ACUTE STEROID FORMATION
Sathvika Jagannathan, MSc¹, Seimia Chebbi, BSc¹, Françoise Hulin-Matsuda, PhD², Toshihide Kobayashi, PhD³ and Vassilios Papadopoulos, PhD⁴
¹Research Institute of the McGill University Health Centre and Department of Medicine, McGill University; ²Lipid Biology Laboratory, RIKEN Advanced Science Institute, Wako, Saitama, Japan
(Presented By: Sathvika Jagannathan, MSc)

Poster #61 HENMT1 IS INVOLVED IN THE STABILIZATION OF PACHYTENE PIRNAS, RETROTRANSPOSON SILENCING AND REGULATING THE SPERMIOTGENIC PROGRAM
Shu Ly Lim, PhD¹, Duangporn Jamais, PhD², Hamish S. Scott, PhD³, Anna-Lena Hempfeling, Msc⁴, Martin Bergmann, PhD⁵, David L. Adelson, PhD⁶ and Moira K. O’Bryan, PhD⁷
¹Monash University; ²Department of Anatomy and Developmental Biology, Monash University, Vic, Australia; ³School of Molecular and Biomedical Science, University of Adelaide, SA, Australia 3. Department of Molecular Pathology and; ⁴ACRF Cancer Genomics Facility, Centre for Cancer Biology, SA pathology, Australia; ⁵Institute of Veterinary Anatomy, Histology and Embryology, Justus Liebig University Giessen; ⁶School of Molecular and Biomedical Science, University of Adelaide, SA, Australia
(Presented By: Shu Ly Lim, PhD)

Poster #62 ACETAMINOPHEN VERSUS IBUPROFEN: EFFECTS ON NEONATAL TESTICULAR GONOCYTE DEVELOPMENT
Gurpreet Manku, PhD¹, Philippos Papadopoulos² and Martine Culty, PhD¹
¹The Research Institute of the McGill University Health Centre, and the Departments of Pharmacology & Therapeutics, and Medicine, McGill University, Montreal, Quebec, Canada; ²Research Institute of the McGill University Health Centre, Montreal, Quebec, Canada
(Presented By: Gurpreet Manku, PhD)

Poster #63 NOVEL ACTION OF FOLLICLE STIMULATING HORMONE (FSH) ON MOUSE TESTICULAR STEM CELLS
Hiren Patel, MSc and Deepa Bhartiya, PhD
Stem Cell Biology Department, National Institute for Research in Reproductive Health, Jehangir Merwanji Street, Parel, Mumbai 400 012, INDIA
(Presented By: Hiren Patel, MSc)

Poster #64 IMPORTANCE OF SOMATIC NICHE IN REGULATING TESTICULAR STEM CELLS DIFFERENTIATION INTO SPERM
Sandhya Anand, MSc, Kalpana Sriraman, PhD, Hiren Patel, MSc, Smita Bhutda, MSc and Deepa Bhartiya, PhD
Stem Cell Biology Department, National Institute for Research in Reproductive Health, Jehangir Merwanji Street, Parel, Mumbai 400 012, INDIA.
(Presented By: Sandhya Anand, MSc)

Poster #65 GHRELIN-INDUCED ATTENUATION OF TESTICULAR DAMAGE IN MOUSE CRYPTORCHID TESTES
Enrica Bianchi, PhD¹, Mark Sigman, MD, PhD², Kim Boekelheide, MD, PhD³ and Kathleen Hwang, MD, PhD²
¹Division of Urology, Brown University; ²Division of Urology, Brown University.; ³Department of Pathology and Laboratory Medicine, Brown University.
(Presented By: Enrica Bianchi, PhD)

Poster #66 LATE EFFECT OF NICOTINE ON THE SEMINIFEROUS EPITHELium OF THE OFFSPRING FROM RAT DAMS TREATED THROUGHOUT PREGNANCY AND LACTATION
Camila Paccola, doctoral student, Flavia Neves, doctoral student and Sandra Miraglia, Doctor
Federal University of Sao Paulo
(Presented By: Camila Paccola, doctoral student)

Poster #67 REQUIREMENT FOR ADENOSINE DEAMINASE CONTAINING PROTEINS IN MALE GERM CELL DEVELOPMENT
Elizabeth Snyder, PhD, Anuj Srivastava, PhD and Robert Braun, PhD
The Jackson Laboratory
(Presented By: Elizabeth Snyder, PhD)

Poster #68 VITAMIN B12-INDUCED SPERMATOGENIAL MITOTIC ACTIVITY IN THE TESTES OF CIMETIDINE-TREATED RATS
Flavia Luciana Beltrame, PhD¹, Estela Sasso-Cerri, PhD² and Paulo Sérgio Cerri, PhD²
¹Department of Morphology and Genetics. Federal University of São Paulo - UNIFESP; ²Department of Morphology. São Paulo State University - UNESP
(Presented By: Flavia Luciana Beltrame, PhD)
Poster #69 MEF2 AND COUP-TFII COOPERATE TO REGULATE AKR1C14 GENE EXPRESSION IN MOUSE MA-10 LEYDIG CELLS
Mickael Di-Luoffo, MSc, Catherine Brousseau, MSc, Raifish E. Mendoza-Villarroel, PhD and Jacques J. Tremblay, PhD
CRCHUQ-Universite Laval
(Presented By: Mickael Di-Luoffo, MSc)

Poster #70 CURCUMIN TARGETS RAT TESTICULAR 11 -HYDROXYSteroid Dehydrogenase 1 TO ANTAGONIZE AGAINST STRESS-INDUCED INHIBITION OF TESTOSTERONE
Xiaoheng Li, MS, Qiqi Zhu, MS, Xiudi Wang, MD, Shuyan Cao, MS, Ying Wu, MS, Haifang Ge, BS, Linxi Li, PhD, Kaimin Yuan, MD, Han Lin, MD, Hong-yu Zhou, PhD, Qingquan Lian, MD and Ren-shan Ge, MD
The Second Affiliated Hospital, Wenzhou Medical University
(Presented By: Xiaoheng Li, MS)

Poster #71 HUMAN CHORIONIC GONADOTROPIN SUPPLEMENTAL DOSING OPTIMIZATION FOR THE MAINTENANCE OF MALE FERTILITY WHILE ON LONG TERM TESTOSTERONE REPLACEMENT OVER 4 YEARS
George Toth, MD
TGH, OV AMC
(Presented By: George Toth, MD)

Poster #72 HOW LONG SHOULD HYPOGONADAL SUBJECTS BE TREATED? INTERMISSION AND RESUMPTION OF LONG-TERM TESTOSTERONE REPLACEMENT THERAPY (TRT) AND EFFECTS ON HORMONAL AND ANTHROPOMETRIC PARAMETERS IN HYPOGONADAL ELDERLY MEN
Farid Saad, DVM, PhD¹, Aksam Yassin, MD, PhD², Yousef Al Mehmadi, MD, PhD³, Gheorghe Doros, PhD⁴ and Abdulmaged Traish, PhD⁴
¹Global Medical Affairs Andrology, Bayer Pharma AG, Berlin, Germany; ²Institute of Urology and Andrology; ³Boston University School of Public Health; ⁴Boston University School of Medicine
(Presented By: Farid Saad, DVM, PhD)

Poster #73 INTERMISSION AND RESUMPTION OF LONG-TERM TESTOSTERONE REPLACEMENT THERAPY (TRT) AND EFFECTS ON METABOLIC PARAMETERS IN HYPOGONADAL ELDERLY MEN
Farid Saad, DVM, PhD¹, Aksam Yassin, MD, PhD², Yousef Al Mehmadi, MD, PhD³, Gheorghe Doros, PhD⁴ and Abdulmaged Traish, PhD⁴
¹Global Medical Affairs Andrology, Bayer Pharma AG, Berlin, Germany; ²Institute of Urology and Andrology; ³Boston University School of Public Health; ⁴Boston University School of Medicine
(Presented By: Farid Saad, DVM, PhD)

Poster #74 KNOCKOUT OF THE TRANSCRIPTION FACTOR NRF2: EFFECTS ON TESTOSTERONE PRODUCTION BY AGING MOUSE LEYDIG CELLS
Haolin Chen, PhD¹, Shiyiing Jin, PhD¹, Jingjing Guo, PhD², Shyam Biswal, PhD³, Renshan Ge, MD⁴ and Barry Zirkin, PhD⁴
¹Department of Biochemistry and Molecular Biology, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland 21205; ²The Second Affiliated Hospital, Wenzhou Medical University, Wenzhou, Zhejiang, China; ³Department of Environmental Health Sciences, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland 21205
(Presented By: Haolin Chen, PhD)

Poster #75 THE MITOCHONDRIAL PEPTIDE ANALOGUE HNG PROTECTS AGAINST CYCLOPHOSPHAMIDE-INDUCED DECREASE IN SPERM OUTPUT AND NEUTROPENIA
Yan-He Lue, MD¹, Ronald Swerdlow, MD¹, Junxiang Wan, PhD², Vince Atienza, BS³, Brian Stone, BS³, Sima Baravarian, PhD³, Yue Jia, MD⁴, Pinchas Cohen, MD² and Christina Wang, MD¹
¹LABioMed at Harbor-UCLA; ²USC Davis School of Gerontology
(Presented By: Yan-He Lue, MD)

Poster #76 PRO-ANDROGENIC EFFECTS OF LOW DOSE DEHP ARE ANTAGONIZED BY GENISTEIN IN YOUNG ANIMALS EXPOSED IN-UTERO
Steven Jones, MSc¹, Annie Boisvert, MSc¹, Sade Francois, BSc¹, Liandong Zhang, MD³ and Martine Culty, PhD¹
¹McGill University; ²Xi’an Jiaotong University
(Presented By: Steven Jones, MSc)

© 2015 American Society of Andrology and European Academy of Andrology
Andrology, 2015, Supplement, 58
Poster #77 EFFECTS OF IN UTERO EXPOSURE TO DIISONONYL PHTHALATE ON RAT FETAL LEYDIG CELL FUNCTION AND AGGREGATION
Tiao Bu, MD, Linxi Li, PhD, Yiyan Wang, MD, Yuanyuan Hu, MD, Gaolong Zhang, MD, Yuanyuan Shan, MD, Zhichuan Chen, MD, Danyan Zhu, MD, Renai Xu, MD, Junwei Li, MD, Guoxin Hu, PhD, Qingquan Lian, MD, and Ren-Shan Ge, MD
The 2nd Affiliated Hospital & Research Academy of Reproductive Biomedicine, Wenzhou Medical University
(Presented By: Tiao Bu, MD)

Poster #78 EFFECTS OF IN UTERO MIXED EXPOSURE TO DIETHYL AND DIETHYLHEXYL PHTHALATES ON RAT FETAL LEYDIG CELL GENE EXPRESSIONS AND FUNCTIONS
Guoxin Hu, Junwei Li, MD¹, Yaoyao Dong, MSC¹, Dongxin Chen, MSc¹, Wenwen Yao, MSc¹, Ermin Gu, MSc¹, Yuanyuan Shan, MSc¹, Yuanyuan Hu, MSc¹, Yiyan Wang, MSc¹, Qing-quan Lian, MD² and Ren-shan Ge, MD³
¹Wenzhou Medical University; ²Department of Anestheiology, the 2nd Affiliated Hospital, Wenzhou Medical University; ³Institute of Reproductive Biomedicine, Wenzhou Medical University
(Presented By: Guoxin Hu)

Poster #79 MOLECULAR ALTERATIONS IN SPERM ARE SENSITIVE INDICATORS OF TESTICULAR DYSFUNCTION
Linnea Anderson, MSc¹, Edward Dere, PhD² and Kim Boekelheide, MD, PhD¹
¹Brown University; ²Rhode Island Hospital
(Presented By: Linnea Anderson, MSc)

Poster #80 EFFECTS OF IN UTERO EXPOSURE OF DICYCLOHEXYL PHTHALATE ON FETAL LEYDIG CELLS
Huina Su, Yuanyuan Shan, MD, Yuanyuan Hu, MD, Yiyan Wang, MD, Yaoyao Dong, MD, Dongxin Chen, MD, Qiqi Zhu, MD, Linxi Li, MD, Junwei Li, MD, Guoxin Hu, MD, Qingquan Lian, MD and Ren-Shan Ge, MD
The 2nd Affiliated Hospital & Research Academy of Reproductive Biomedicine, Wenzhou Medical University
(Presented By: Huina Su)

Poster #81 EFFECTS OF DIBUTYL AND MONO-BUTYL PHTHALATES ON RAT IMMATURE LEYDIG CELL STEROIDOGENESIS IN VITRO
Yunfei Xu, MD, Guanghui Hu, MD¹, Baiping Mao, MD², Xiaolong Wu, MD², Binghuan Chi, MD², Senlin Li, MD², Yanfang Bai, MD², Huang Wang, MD², Hongguo Guan, MD² and Ren-shan Ge, MD³
¹The Affiliated 10th People’s Hospital of Tongji University; ²Research Academy of Reproductive Biomedicine, Wenzhou Medical University
(Presented By: Yunfei Xu, MD)

Poster #82 WALNUTS ADDED TO A WESTERN DIET ARE ASSOCIATED WITH DECREASED DNA STRAND BREAKAGE IN SPERM
Lin Xun, MS, Catherine Carpenter, PhD, Yewande Sanusi, BS, Susanne Henning, PhD and Wendie Robbins, PhD
University of California Los Angeles
(Presented By: Lin Xun, MS)

Poster #83 OPEN CHROMATIN MAPPING IDENTIFIES TRANSCRIPTIONAL NETWORKS REGULATING HUMAN EPIDIDYMIS EPITHELIAL FUNCTION
James Browne, PhD¹, Rui Yang, BSc¹, Lingyun Song, PhD², Greg Crawford, PhD², Shih-Hsing Leir, PhD¹ and Ann Harris, PhD¹
¹Human Molecular Genetics Program, Lurie Children’s Research Center, Chicago, IL, USA, Department of Pediatrics, Northwestern University Feinberg School of Medicine, Chicago, IL, USA; ²Department of Pediatrics, Division of Medical Genetics, Duke University Medical School, Durham, NC, USA, Center for Genomic and Computational Biology, Duke University Medical School, Durham, NC, USA
(Presented By: James Browne, PhD)

Poster #84 A SUSCEPTIBILITY LOCUS, RS7099208, IS ASSOCIATED WITH NON-OBSTRUCTIVE AZOOSPERMIA VIA REDUCTION IN THE EXPRESSION OF FAM160B1
Yan Zhang, Mingxi Liu, Associate Professor¹, Xuejiang Guo, Associate Professor¹ and Jiahao Sha, Professor²
¹Teacher; ²Tutor
(Presented By: Yan Zhang)

Poster #85 REGULATION OF THE PROLIFERATION AND DIFFERENTIATION OF RAT STEM AND PROGENITOR LEYDIG CELLS BY ACTIVIN
Linxi Li, PhD, Renai Xu, MD, Shiwen Liu, MD, Yiyan Wang, MSc, Yuanyuan Shan, MSc, Yuanyuan Hu, MSc, Yaoyao Dong, MSc, Qiqi Zhu, MSc, Xiaoheng Li, MSc, Jingjing Guo, MD, Haolin Chen and Ren-Shan Ge, MD
The Second Affiliated Hospital, Wenzhou Medical University
(Presented By: Linxi Li, PhD)
POSTER SESSION II

Poster #86 CHROMOSOMAL TRANSLOCATIONS AND MALE INFERTILITY
Mohamed Arafa, MD, Haitham El Bardisi, MD, Sami ElSaid, MD, Ahmad Majzoub, MD and Ahmad AlMalki, MD
Urology Department, HMC, Qatar
(Presented By: Mohamed Arafa, MD)

Poster #87 MITOCHONDRIAL DNA EPIGENETICS: CPG AND NON-CPG CYTOSINE METHYLATION IN THE SPERM MITOCHONDRIAL GENOME
Monis B. Shamsi, PhD, Timothy G. Jenkins, PhD, KI Aston, PhD and Douglas T. Carrell, PhD
Andrology and IVF Laboratories, Department of Surgery, University of Utah School of Medicine, Salt Lake City, Utah, United States of America.
(Presented By: Monis B. Shamsi, PhD)

Poster #88 SPATA22 LOCALIZES TO MEIOTIC RECOMBINATION NODULES AND IS REQUIRED FOR FERTILITY IN THE MOUSE
Vinita Daniel, Zachary Ferguson, Patrick Davis, Chelsea Schonert, Emily Hays and Sophie La Salle, PhD
Midwestern University
(Presented By: Vinita Daniel)

Poster #89 SEMEN CRYOPRESERVATION IN MEN WITH CANCER; THE USAGE RATE AND OUTCOME OF ASSISTED REPRODUCTIVE TECHNOLOGY IN 898 PATIENTS
Iris Muller, MD¹, Ralph J.A. Oude Ophuis, PhD², Frank J.M. Broekmans, MD, PhD² and Tycho M.T.W. Lock, MD, FEBU³
¹Department of Urology, University Medical Centre Utrecht, Utrecht, The Netherlands; ²Department of Reproductive Medicine and Gynaecology, University Medical Centre Utrecht, Utrecht, The Netherlands; ³Department of Urology, University Medical Centre Utrecht, Utrecht, The Netherlands and Department of Urology, Central Military Hospital, Utrecht, the Netherlands
(Presented By: Tycho M.T.W. Lock, MD, FEBU)

Poster #90 OUTCOME OF MICROSURGICAL TESTICULAR SPERM EXTRACTION IN FAMILIAL IDIOPATHIC NON-OBSTUCTIVE AZOOSPERMIA
Haitham El Bardisi, MD, Mohamed Arafa, MD, Sami AlSaid, MD, Abdulla AlAnsari, MD, Ahmad Majzoub, MD, Ahmad AlMalki, MD and Iyad AlRobi, MD
Urology Department, HMC, Qatar
(Presented By: Haitham El Bardisi, MD)

Poster #91 ICSI OUTCOME IN KLINEFELTER’S SYNDROME: QATAR EXPERIENCE
Ahmad Majzoub, MD, Mohamed Arafa, MD, Sami ElSaid, MD and Haitham El Bardisi, MD
Urology Department, HMC, Qatar
(Presented By: Ahmad Majzoub, MD)

Poster #92 SPERM RETRIEVAL SHOULD BE PERFORMED AT THE TIME OF TUMOR RESECTION IN MEN WITH CONGENITAL ADRENAL HYPERPLASIA AND BILATERAL TESTICULAR ADRENAL REST TUMORS
Parviz Kavoussi, MD, Roxanne Summers-Colquitt, MS, TS, Kate Odenwald, MSN, RN, ACNP-BC, Thomas Pool, PhD and Shahryar Kavoussi, MD, MPH
Austin Fertility & Reproductive Medicine
(Presented By: Parviz Kavoussi, MD)

Poster #93 WHY WE ESTABLISHED THE MALE CONTRACEPTION INITIATIVE
David Sokal, MD and Aaron Hamlin, MEd, MPH, JD
Male Contraception Initiative
(Presented By: David Sokal, MD)

Poster #94 RAPID SELECTION OF MOTILE SPERM WITH HIGH DNA INTEGRITY USING MICROFLUIDICS
Krista Zeidan, MSc¹, Maria C. San Gabriel, MSc, PhD¹, Reza Nosrati, PhD candidate², Lise Eamer, MSc², Marion Vollmer, PhD², David Sinton, PhD, P Eng² and Armand Zini, MD¹
¹McGill University; ²Toronto University
(Presented By: Maria C. San Gabriel, MSc, PhD)

Poster #95 COMPARATIVE STUDY OF MICROFLUIDIC DEVICE (MFD) AND DENSITY GRADIENT CENTRIFUGATION (DGC) IN SELECTING SPERM WITH HIGH DNA INTEGRITY
Maria C. San Gabriel, MSc, PhD¹, Krista Zeidan, MSc¹, Khalid Alrabeelah, MD¹, Reza Nosrati, PhD candidate², Lise Eamer, MSc², Marion Vollmer, PhD², David Sinton, PhD, PEng² and Armand Zini, MD¹
¹McGill University; ²Toronto University
(Presented By: Maria C. San Gabriel, MSc, PhD)
Poster #96 PROTEOMIC PATHWAYS OF OXIDATIVE STRESS IN THE HUMAN SEMINAL PLASMA
Paula Intasqui, MSc¹, Mariana Camargo, MSc¹, Mariana P. Antoniassi, BSc¹, Karina H. M. Cardozo, PhD², Valdemir M. Carvalho, PhD² and Ricardo P. Bertolla, DVM, PhD¹
¹Department of Surgery, Division of Urology, Sao Paulo Federal University; ²Fleury Group
(Presented By: Paula Intasqui, MSc)

Poster #97 TIME FOR PUBLIC HEALTH ACTION ON INFERTILITY: UPDATES FROM THE CENTERS FOR DISEASE CONTROL AND PREVENTION
Steven Schrader, PhD¹, Lee Warner, PhD, MPH³, Richard Wang, MD³ and Hubert Vesper, PhD³
¹CDC/NIOSH; ²CDC/NCCDHP; ³CDC/NCEH
(Presented By: Steven Schrader, PhD)

Poster #98 CRYOPRESERVATION OF SPERMATOZOA: OPTIMIZATION OF MOTILITY WITH A NONPERMEABLE CRYOPROTECTANT
Jie Liu, PhD, Cigdem Tanrikut, MD, Diane Wright, PhD, Gloria Lee, Mehmet Toner, PhD and Thomas Toth, MD
Massachusetts General Hospital and Harvard Medical School, Boston, MA
(Presented By: Cigdem Tanrikut, MD)

Poster #99 NON-MOTILE SPERM CELL SEPARATION USING A SPIRAL CHANNEL
Jiyoung Son, MS¹, Raheel Samuel, PhD², Kristin Murphy, PhD², Douglas Carrell, PhD², Bruce Gale, PhD³ and James Hotaling, MD³
¹Electrical and Computer Engineering of University of Utah; ²Urology Division, Department of Surgery, University of Utah School of Medicine; ³Mechanical Engineering of University of Utah
(Presented By: Jiyoung Son, MS)

Poster #100 QUANTITATIVE EVALUATION OF EXPRESSION OF THE CATSFER CHANNEL IN HUMAN SPERM AND RELATION WITH FUNCTIONAL PARAMETERS
Lara Tamburrino, Sara Marchiani, Cami Marta, Forti Gianni, Muratori Monica and Elisabetta Baldi
Dept. of Biomedical, Experimental and Clinical Sciences, University of Florence, Italy
(Presented By: Elisabetta Baldi)

Poster #101 WITHDRAWN

Poster #102 THE GENERAL METHOD OF PLACING THE RESERVOIR IN INFLATABLE PENILE PROSTHESIS OPERATION
Chen Bin, MD, Zhan Junxin, Chen Chaoyue, Huang Fengjin and Zhu Xihong
(Presented By: Chen Bin, MD)

Poster #103 FAILURE TO ATTAIN STRETCHED PENILE LENGTH AFTER INTRACAVERNOSAL INJECTION OF A VASODILATOR AGENT IS PREDICTIVE OF VENO-OCCCLUSIVE DYSFUNCTION ON PENILE DUPLEX DOPPLER ULTRASONOGRAPHY
Faysal A. Yafi, MD, FRCS, Ian R. McCaslin, MD, Russell P. Libby, MD, Premsant Sangkum, MD, Suresh Sikka, PhD and Wayne J.G. Hellstrom, MD, FACS
Tulane University School of Medicine
(Presented By: Faysal A. Yafi, MD, FRCS)

Poster #104 THE HISTORY OF PENILE ENHANCEMENT - TO CUT A SHORT STORY LONG
Paul Cleaveland, MBChB¹, Zubeir Ali, MBChB² and Ian Pearce, MBChB³
¹Royal Preston Hospital; ²South Manchester Teaching Hospitals NHS Trust; ³Central Manchester Teaching Hospitals
(Presented By: Paul Cleaveland, MBChB)

Poster #105 THE EFFECT OF AN AQUEOUS TYPHA CAPENSIS EXTRACT ON THE AGEING MALE REPRODUCTIVE SYSTEM
Nicole Haines-Arries, MSc, Abdulkarem Ilfergane, MSc and Ralf Henkel, PhD
University of the Western Cape
(Presented By: Ralf Henkel, PhD)

Poster #106 ASSOCIATION BETWEEN ERECTILE FUNCTION AND SUBCLINICAL ATHEROSCLEROSIS: A STUDY BASED ON MIDDLE-AGE HEALTHY MEN FROM THE GENERAL POPULATION
Babak Rezanezhad, Rasmus Borgquist, MD, PhD, Ronnie Willenheimer, MD, PhD and Saad Elzanaty, MD, PhD
(Presented By: Babak Rezanezhad)

Poster #107 PENILE HEMODYNAMIC IN PATIENTS WITH HIGH RISK OF CARDIOVASCULAR DISEASES
Evgeny Efremov, Professor¹, Yaroslav Melnik² and Stepan Krasnyak
¹Head of the Department of Andrology and Human Reproduction; ²Scientist, Department of Andrology and Human Reproduction
(Presented By: Stepan Krasnyak)
© 2015 American Society of Andrology and European Academy of Andrology
Andrology, 2015, Supplement, 61
Poster #108 ORAL TREATMENT WITH A COMBINATION OF 4 NUTRACEUTICALS (GINGER, L-CITRULLINE, MUIRA PUAMA AND PAULINIA CUPANA) THAT UPREGULATE THE NO-CGMP PATHWAY CAN DELAY THE ONSET OF AGING ASSOCIATED ERECTILE DYSFUNCTION
Su M. Hlaing, BS, Andre Chan, BS, Jorge N. Artaza, MS, PhD and Monica G. Ferrini, PhD¹,²
¹Department of Internal Medicine, Charles R. Drew University of Medicine & Science, Los Angeles, CA 90059; ²Department of Health and Life Science, College of Science and Health, Charles R. Drew University of Medicine & Science, Los Angeles, CA 90059
(Presented By: Monica G. Ferrini, PhD)

Poster #109 THE SECONDARY HYPOGONADISM POPULATION THAT CAN BE TREATED WITH ENCLOMIPHENE CITRATE AND RESULTS
Ronald Wiehle, PhD, Gregory Fontenot, PhD and Jaye Thompson, PhD
Repros Therapeutics
(Presented By: Ronald Wiehle, PhD)

Poster #110 3-ADRENERGIC RECEPTORS ARE INVOLVED IN REGULATING NITRIC OXIDE SIGNALING AND NEUROGENIC FORCE OF CONTRACTION IN CORPUS Cavernosum OBTAINED FROM PATIENTS WITH ERECTILE DYSFUNCTION
Serap Gur, MD¹, Faysal Yafi, MD², Suresh Sikka, MD³, Philip Kadowitz, MD³ and Wayne Hellstrom, MD³
¹Ankara University; ²Tulane University School of Medicine
(Presented By: Faysal Yafi, MD)

Poster #111 EARLY EXPERIENCE WITH MICROSURGICAL SPERMATIC CORD DENERVATION FOR CHRONIC ORCHALGIA IN A CANADIAN CENTRE
Darby Cassidy, MD
University Hospital of Northern British Columbia
(Presented By: Darby Cassidy, MD)

Poster #112 WITHDRAWN

Poster #113 PROSTATORRHEA REVISTED
Ahmad Motawi, MSc, FECSM, Hussein Ghanem, MD, FECSM, Mohammad Abbas, MD and Ashraf Zeidan, MD, FECSM
Faculty of Medicine, Cairo University
(Presented By: Ahmad Motawi, MSc, FECS)

Poster #114 TRANSCRIPTIONAL REGULATION OF HUMAN SPERM-ASSOCIATED ANTIGEN 16 BY S-SOX5
Ling Zhang, PhD¹, Junpin Liu, MD¹, Wei Li, MD², Jerome Strauss III, MD, PhD² and Zhijing Zhang³
¹Wuhan University of Science & Technology; ²Virginia Commonwealth University; ³Virginia Commonwealth Univ/OB/Gyn
(Presented By: Zhijing Zhang)

Poster #115 MULTIDRUG RESISTANT BACTERIAL ISOLATES CAUSING NOSOCOMIAL URINARY TRACT INFECTION IN A TERTIARY CARE HOSPITAL, NEPAL
Manoj Sah, Master of Science in Clinical Microbiology¹ and Shyam Mishra, MScClinical Microbiology²
¹Kathmandu University, Kantipur Dental College, Kathmandu, NEPAL; ²TU, Nepal
(Presented By: Manoj Sah, Master of Science in Clinical Microbiology)

Poster #116 CRISP3 IS PRO-TUMORIGENIC IN THE PROSTATE
Moira O’Bryan, PhD¹, Marianna Volpert, BSc (hons), PhD², Duangporn Jamsai, BSc, PhilD², Gail Risbridger, BSc (hons), PhilD² and Luc Furic, BSc (hons), PhilD²
¹Monash University; ²The Department of Anatomy and Developmental Biology, Monash University
(Presented By: Moira O’Bryan, PhD)

Poster #117 WITHDRAWN

Poster #118 HISTOLOGICAL PATTERN WITH PREDICTIVE PROGNOSTIC VALUE OF IMPROVED FERTILITY IN PATIENTS UNDERGOING MICROSURGICAL VARICOCELECTOMY
Jorge Hallak, MD, PhD¹,², Robertson Dutra, BSc, MSc student³ and Juliana Pariz, MSc, PhD student¹,²
¹Androscience; ²Universidade de São Paulo
(Presented By: Jorge Hallak, MD, PhD)

Poster #119 PROTEOMIC PROFILING OF DETERGENT RESISTANT MEMBRANES (LIPID RAFTS) OF PROSTASOMES AND THEIR REVESICULATION
Louise Dubois, Göran Ronquist, Bo Ek, Gunnar Ronquist and Anders Larsson
(Submitted By: Göran Ronquist)

© 2015 American Society of Andrology and European Academy of Andrology Andrology, 2015, Supplement, 62
**POSTER SESSION II**

**Poster #120 SEMEN QUALITY AND TESTICULAR CANCER: RESULTS FROM THE UTAH POPULATION DATABASE**
Heidi Hanson, PhD¹, Ross Anderson, MD, MCR², Chong Zhang, MS³, Angela Presson, PhD⁴, Kenneth Aston, PhD⁵, Douglas Carrell, PhD⁶, Ken Smith, PhD⁷, and James Hotaling, MD, MS⁸
¹University of Utah; ²Department of Surgery, Division of Urology, University of Utah; ³Department of Family and Preventive Medicine, University of Utah; ⁴Department of Internal Medicine, University of Utah; ⁵University of Utah, Department of Surgery, Andrology and IVF Laboratories; ⁶University of Utah, Department of Surgery, Director of IVF and Andrology Laboratories; ⁷Department of Family and Consumer Studies, University of Utah; ⁸Population Sciences, Huntsman Cancer Institute
(Presented By: Heidi Hanson, PhD)

**Poster #121 IMPACT OF GALECTIN-3 SINGLE NUCLEOTIDE POLYMORPHISM (SNP) ON INCREASED ODDS OF PROSTATE CANCER (PCA) AND ON PROTEOLYSIS BY PROSTATE SPECIFIC ANTIGEN (PSA)**
Matthew Kovak, MS¹, David Schoen, BS¹, Horace Spencer, MS², Sarika Saraswati, PhD³ and Alan Diekman, PhD¹
¹Department of Biochemistry and Molecular Biology, College of Medicine, University of Arkansas for Medical Sciences; ²Department of Biostatistics, College of Public Health, University of Arkansas for Medical Sciences; ³Department of Pathology, Microbiology, and Immunology, College of Medicine, Vanderbilt University
(Presented By: Matthew Kovak, MS)

**Poster #122 ULTRASOUND FOR PALPABLE SCROTAL MASSES: WHAT ARE WE FINDING?**
Marah Hehemann, MD¹, James Kashanian, MD², Christopher Morrison, MD³, Daniel Mazur, MD⁴, Valary Raup, MS⁴, Brian Trinh, MS³, Mohammed Said, MS², Andrew Choi, MS³ and Robert E. Brannigan, MD²
¹Loyola University Health Systems; ²Northwestern University
(Presented By: Marah Hehemann, MD)

**Poster #123 VARICOCELE IS ASSOCIATED WITH INDICATORS OF INFLAMMATORY ACTIVITY WHICH DECREASE AFTER VARICOCELECTOMY**
Mariana Camargo, MSc¹, Emad Ibrahim, MD², Paula Intasqui, MSc¹, Teodore Aballa, MSc², Charles Lynne, MD³, Ricardo Bertolla, MVD, PhD and Nancy Brackett, PhD²
¹Human Reproduction Section, Division of Urology, Sao Paulo Federal University; ²The Miami Project to Cure Paralysis, University of Miami; ³Department of Urology, University of Miami Miller School of Medicine
(Presented By: Mariana Camargo, MSc)

**Poster #124 ACTION OF RESVERATROL ON THE REPRODUCTIVE PARAMETERS OF LATE PUBERTAL RATS TREATED WITH ANTI-CANCER AGENTS (BEP PROTOCOL MODIFIED), FROM PERIPUBERTY: PART II**
Flávia Macedo de Oliveira Neves, Doctoral student, Camila Cicconi Paccola, Doctoral student, Vanessa Vendramini, PhD and Sandra Maria Miraglia, PhD
Federal University of Sao Paulo - Brazil
(Presented By: Flávia Macedo de Oliveira Neves, Doctoral student)

**Poster #125 RAMAN MAPPING SHOWS UVB CAUSES SPERM DNA FRAGMENTATION BUT THE ASSOCIATED MITOCHONDRIAL DYSFUNCTION DOES NOT**
Con Mallidis, PhD, Victoria Sanchez, PhD, Joachim Wistuba, PhD, Michael Zitzmann, MD, Sabine Kliesch, MD and Stefan Schlatt
CeRA
(Presented By: Stefan Schlatt)

**Poster #126 FLUORESCENCE IN-SITU HYBRIDIZATION DETECTS INCREASED SPERM ANEUPLOIDY IN MEN WITH RECURRENT PREGNANCY LOSS**
Ranjith Ramasamy, Jason Scovell, BA, Jason Kovac, MD, Peter Cook, BA and Dolores Lamb, PhD
Baylor College of Medicine
(Presented By: Ranjith Ramasamy)

**Poster #127 STUDY OF RNA BIOMARKERS OF NORMAL SPERMIOGENESIS IN NORMAL SEMEN AND SPERM VIA TRANSCRIPTOME ANALYSIS**
Alexander Yatsenko, MD, PhD, Archana Kishore, PhD, Andrew Georgiadis, Randy Beadling, Etta Volk, Joseph Sanfilippo, Thomas Jaffe, James Lyons-Weiler and Tamanna Sultana
MWRI
(Presented By: Alexander Yatsenko, MD, PhD)
POSTER SESSION II

Poster #128 THE RELATIONSHIP BETWEEN SOME SEMEN QUALITY MEASUREMENTS, SCROTAL CIRCUMFERENCE, BODY WEIGHT AND FERTILITY OF AWASSI RAMS
Basim J. Awda¹, Luma W. Abdul Latif², Abdul Jabbar AL-Khazraji¹, Hussein O. Kready¹ and Mahaba R. Ali²
¹Department of Medical and Molecular Biotechnology, College of Biotechnology, Al-Nahrain University; ²Department of Applied Biotechnology, College of Sciences, Al-Nahrain University, Baghdad, Iraq; ³Ministry of Science and Technology, Baghdad, Iraq
(Presented By: Basim J. Awda)

Poster #129 THE RELATIONSHIP BETWEEN SOME BLOOD BIOCHEMICAL PROPERTIES, SCROTAL CIRCUMFERENCE, BODY WEIGHT AND FERTILITY OF AWASSI RAMS
Basim J. Awda¹, Mahaba R. Ali², Hussein O. Kready¹, Abdul Jabbar AL-Khazraji³ and Luma W. Abdul Latif²
¹Department of Medical and Molecular Biotechnology, College of Biotechnology, Al-Nahrain University; ²Department of Applied Biotechnology, College of Sciences, Al-Nahrain University, Baghdad, Iraq; ³Ministry of Sciences and Technology, Baghdad, Iraq
(Presented By: Basim J. Awda)

Poster #130 SYSTEMATIC ANALYSIS OF THE PHOSPHOPROTEOME AND KINASE-SUBSTRATE NETWORKS IN THE MOUSE TESTIS
Lin Qi, Yueshuai Guo, PhD, Tao Zhou, PhD, Mingxi Liu, PhD and Xuejiang Guo, PhD
State Key Laboratory of Reproductive Medicine, Department of Histology and Embryology, Nanjing Medical University
(Presented By: Lin Qi)

Poster #131 THE EFFECT OF PULSATILE TREATMENT OF FSH AND TESTOSTERONE ON DIFFERENTIAL GENE EXPRESSION IN RAT SERTOLI CELLS DURING POSTNATAL TESTICULAR MATURATION
Indrashis Bhattacharya, PhD¹, Mukkesh Gautam, PhD², Bhaloshankar Pradhan, PhD³ and Subeer Majumdar, PhD⁴
¹HNB Garhwal University, Srinagar, India; ²The Ken & Ruth Davee Department of Neurology, Northwestern University, Chicago, USA; ³Division of Cellular Endocrinology, National Institute of Immunology, New Delhi, India
(Presented By: Indrashis Bhattacharya, PhD)

Poster #132 HISTONE H4K20 DEMETHYLASE REGULATES SPERMATOGENESIS
Charlie Degui Chen
(Presented By: Charlie Degui Chen)

Poster #133 WITHDRAWN

Poster #134 NR4A1 EXPRESSION IS REGULATED BY THE CALCIUM SIGNALING PATHWAY THROUGH DISTINCT AP1/CREB AND MEF2 ELEMENTS IN LEYDIG CELLS
Nicholas Robert, Houssein Salem Abdou, PhD and Jacques J. Tremblay, PhD
CHUQ Research Centre - Laval University
(Presented By: Nicholas Robert)

Poster #135 INTRAFLAGELLAR TRANSPORTER PROTEIN IFT20 IS ESSENTIAL FOR SPERMIOGENESIS IN MICE
James Foster¹, Zhengang Zhang, MD, PhD², Wei Li, MD³, Yong Zhang, MD, PhD⁴, Honglei Li, MD⁴, Ling Zhang, MD, PhD⁵, Maria Teves, PhD⁵, Gregory Pazour, PhD⁵, Rex Hess, PhD⁵, Jerome Strauss III, MD, PhD⁶ and Zhibing Zhang, MD, PhD⁷
¹Randolph-Macon College; ²Huazhong University of Science and Technology; ³Virginia Commonwealth University; ⁴Huazhong University of Science & Technology; ⁵Wuhan University of Science & Technology; ⁶University of Massachusetts; ⁷University of Illinois
(Presented By: James Foster)

Poster #136 ANABOLIC STEROIDS AND HYPOGONADISM IN ADVANCED CANCER: TO TREAT OR NOT TO TREAT
Domenico Fuoco, PharmD, PhD¹, Robert D. Kilgour, PhD, FACSM² and Antonio L. Vigano, MD, MSc³
¹Supportive and Palliative Care Service, McGill University Health Centre, McGill Nutrition and Performance Laboratory, ²Department of Exercise Science, Concordia University, Montreal, Canada
(Presented By: Domenico Fuoco, PharmD, PhD)
# INDEX OF ABSTRACT AUTHORS

| A | Aarabi, M. | Poster #32 |
|   | Albert, O. | Poster #50 |
|   | Amory, J.  | Abstract #12 |
|   | Anand, S.  | Poster #64 |
|   | Anderson, L. | Poster #79 |
|   | Anderson, R. | Poster #48 |
|   | Arafa, M.  | Poster #86 |
|   | Awda, B.   | Poster #128, 129 |

| B | Baldi, E. | Poster #100 |
|   | Baranwal, A. | Poster #37 |
|   | Bassett, M. | Poster #55 |
|   | Beltrame, F. | Poster #68 |
|   | Bhattacharya, I. | Poster #131 |
|   | Bianchi, E. | Poster #65 |
|   | Bin, C. | Poster #102 |
|   | Browne, J. | Poster #83 |
|   | Bu, Tiao. | Poster #77 |
|   | Burnazyan, R. | Poster #33 |

| C | Camargo, M. | Poster #123 |
|   | Cassidy, D. | Poster #111 |
|   | Chen, C. | Poster #132 |
|   | Chen, H. | Poster #74 |
|   | Cleaveland, P. | Poster #104 |
|   | Cook, K. | Poster #14 |
|   | Côté, N. | Abstract #3 |

| D | da Silva, A. | Poster #18, 38 |
|   | Daniel, V. | Poster #88 |
|   | Di-Luoffo, M. | Poster #69 |
|   | Dobs, A. | Abstract #8 |

| E | El Bardisi, H. | Poster #90 |
|   | Elzanaty, S. | Poster #47 |

| F | Ferrini, M. | Poster #108 |
|   | Foster, J. | Poster #135 |
|   | Fu, Q. | Poster #26 |
|   | Fuoco, D. | Poster #136 |

| G | Gat, I. | Poster #25 |
|   | Goodson, S. | Poster #59 |

| H | Hallak, J. | Poster #118 |
|   | Hanson, H | Poster #120 |
|   | Hehemann, M. | Poster #122 |
|   | Henkel, R. | Poster #13, 44, 105 |
|   | Hu, G. | Poster #78 |
|   | Hughes, J. | Poster #24 |

| I | Intasqui, P. | Poster #96 |

| J | Jagannathan, S. | Poster #60 |
|   | Jamsai, D. | Abstract #5 |
|   | Jenkins, T. | Abstract #9, Poster #27 |
|   | Jones, S. | Poster #76 |

| K | Kavoussi, P. | Poster #92 |
|   | Khaki, A. | Poster #15 |
|   | Kovak, M. | Poster #121 |
|   | Krasnyak, S. | Poster #107 |
|   | Kumar, L. | Poster #52 |
|   | Kumar, M. | Poster #29 |
|   | Kumar, S. | Poster #19 |

| L | Legare, C. | Poster #22 |
|   | Leir, S. | Poster #21 |
|   | Li, L. | Poster #85 |
|   | Li, X. | Poster #70 |
|   | Lim, S. | Poster #61 |
|   | Lock, T. | Poster #89 |
|   | Lue, Y. | Poster #75 |
|   | Ly, L. | Poster #31 |

| M | Macedo de Oliveira Neves, F. | Poster #124 |
|   | Majzoub, A. | Poster #91 |
|   | Manku, G. | Poster #62 |
|   | Martins, T. | Poster #39 |
|   | Mendes, T. | Poster #58 |
|   | Midzak, A. | Abstract #2 |
|   | Mishra, S. | Poster #35 |
|   | Mohanty, G. | Poster #56 |
|   | Motawi, A. | Poster #113 |
|   | Musicki, B. | Abstract #6 |

| N | Najari, B. | Poster #42, 43 |
|   | Nixon, B. | Poster #54 |
## INDEX OF ABSTRACT AUTHORS

<table>
<thead>
<tr>
<th>O</th>
<th></th>
<th>X</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>O'Bryan,M.</td>
<td>Poster #116</td>
<td>Xu, Y.</td>
<td>Poster #81</td>
</tr>
<tr>
<td>Özkösem,B.</td>
<td>Poster #36</td>
<td>Xun, L.</td>
<td>Poster #82</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>P</th>
<th></th>
<th>Y</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Paccola,C.</td>
<td>Poster #66</td>
<td>Yadav, S.</td>
<td>Poster #51</td>
</tr>
<tr>
<td>Pariz,J.</td>
<td>Poster #17, 34</td>
<td>Yafi, F.</td>
<td>Poster #103</td>
</tr>
<tr>
<td>Park,Y.</td>
<td>Poster #23</td>
<td>Yafi, F.</td>
<td>Poster #110</td>
</tr>
<tr>
<td>Pastuszak,A.</td>
<td>Abstract #7, Poster #28</td>
<td>Yatsenko,A.</td>
<td>Poster #127</td>
</tr>
<tr>
<td>Patel,H.</td>
<td>Poster #63</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pendergraft,S.</td>
<td>Abstract #1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Q</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Qi,L.</td>
<td>Poster #130</td>
<td>Zhang,Y.</td>
<td>Poster #84</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Zhang,Z.</td>
<td>Poster #114</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>R</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Ramasamy,R.</td>
<td>Abstract #10, Poster #126</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reifsnyder,J.</td>
<td>Poster #30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rezanezhad,B.</td>
<td>Poster #106</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Robert,N.</td>
<td>Poster #134</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ronquist,G.</td>
<td>Poster #119</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>S</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Saad,F.</td>
<td>Poster #72, 73</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sah,M.</td>
<td>Poster #115</td>
<td></td>
<td></td>
</tr>
<tr>
<td>San Gabriel,M.</td>
<td>Poster #94, 95</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schang,G.</td>
<td>Poster #16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schlatt,S.</td>
<td>Poster #125</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schrader,S.</td>
<td>Poster #97</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Seppan,P.</td>
<td>Poster #41</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shamsi,M.</td>
<td>Poster #87</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shlush,E.</td>
<td>Poster #40</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simon,L.</td>
<td>Poster #49</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smith,T.</td>
<td>Abstract #4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Snyder,E.</td>
<td>Poster #67</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sokal,D.</td>
<td>Poster #93</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Son,J.</td>
<td>Poster #99</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Su,H.</td>
<td>Poster #80</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>T</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Tábata Martins,T.</td>
<td>Poster #20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tanrikut,C.</td>
<td>Poster #53, 98</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Toth,G</td>
<td>Poster #71</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>U</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Urbano,L.</td>
<td>Poster #57</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>W</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Wiehle,R.</td>
<td>Abstract #11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wiehle,R.</td>
<td>Poster #109</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wu,H.</td>
<td>Poster #45</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
long term. Future directions include optimizing the spermatogenic process using isolated human SSC, Sertoli, and Leydig cells and maintained viability as determined by ATP and Live/Dead assays. These cell types were integrated successfully into 3D organoids through the National Disease Research Interchange (Philadelphia, PA, USA). Testicular in vitro organoids were successfully generated for over 4 weeks in culture. Gene expression within these multicellular organoids was measured over time for cell and stage-specific markers including UCHL1, DAZL, VASA, SYCP3, SPO11, NR5A1, and LHCGR. Human spermatogonial stem cells (SSCs), Sertoli, and Leydig cells were isolated, characterized, and expanded from tissue obtained through the National Disease Research Interchange (Philadelphia, PA, USA). These cell types were integrated successfully into 3D organoids and maintained viability as determined by ATP and Live/Dead assays for over 4 weeks in culture. Gene expression within these multicellular human testis organoids was measured over time for cell and stage-specific markers including UCHL1, DAZL, VASA, SYCP3, SPO11, PRM1, ACROSIN, SOX9, GATA4, INSL3, and HSD3B. Identification and analysis of specific cellular components necessary for use in our 3D culture method, (2) Establishment of basic design parameters, culture conditions, and (3) Characterization of human testicular organoids using live cell imaging, immunofluorescence, immunohistochemistry, cell type and stage-specific gene expression, and viability assays.

**Results:** Human spermatogonial stem cells (SSCs), Sertoli, and Leydig cells were isolated, characterized, and expanded from tissue obtained through the National Disease Research Interchange (Philadelphia, PA, USA). These cell types were integrated successfully into 3D organoids and maintained viability as determined by ATP and Live/Dead assays for over 4 weeks in culture. Gene expression within these multicellular human testis organoids was measured over time for cell and stage-specific markers including UCHL1, DAZL, VASA, SYCP3, SPO11, PRM1, ACROSIN, SOX9, GATA4, INSL3, and HSD3B. These confounding findings led us to establish steroidogenic cell-specific Tspo KO mice, generated by crossing Nr5a1−Cre mice with Tspo−floxed mice. Sertoli/Leydig cell−targeting Amhr2−Cre mice were crossed with Tspo−floxed mice to obtain F1 Amhr2−driven Tspo KO mice (Tspo II/I, Amhr2−Cre /−). An unexpected Mendelian ratio of 4.4% KO mice, instead of 25%, was observed. To confirm this finding, dpc 12.5 embryos were genotyped, the age at which Amhr2−Cre is gonadally expressed. The same 4% ratio of Tspo KO was observed, suggesting preimplantation selection. Tspo expression profile analysis across several microarray datasets, were obtained from the omic embryo, showed that Tspo expression increases after the morula stage. Amhr2 levels, however, briefly spike at the two and eight cell stages, suggesting that Tspo gene modification occurred very early in development, supporting the observed abnormal Mendelian ratio. These confounding findings led us to establish steroidogenic cell-specific Tspo KO mice, generated by crossing Nr5a1−Cre mice with Tspo−floxed mice.

**Results:** The expected Mendelian ratio, Nr5a1−driven Tspo KO mice exhibited reduced Tspo expression in their gonads and adrenals, though no significant changes in gonadal or adrenal morphology were observed. Interestingly, basal steroid production by the gonads and adrenals was unchanged in Tspo KO mice. However, although the response of these genetically modified animals to hCG treatment resembled that of their wild−type littermates, the Tspo KO mice lost their ability to respond to ACTH and form corticosterone. Changes in the mRNA expression of Star and Cyp11a1 steroidogenic genes were observed to be increased in testes and adrenals of these mice, suggestive of adaptive changes. Moreover, expression of steroidogenic signaling receptors were divergent in the tissue of the Tspo KO mice, with Lhcg levels increased in testis, whereas adrenal Mc2r levels were unaffected.

**Conclusion:** The results of these genetic engineering experiments provide evidence that, in an in vivo setting, Tspo is required for preimplantation embryo development as well as hormone−stimulated adrenal steroid biosynthesis.
Conclusion: Reduced in F1, F2 and F3 OC males, respectively, we confirmed that SOD1, Citrate Synthase and ZPBP are significantly reduced in OC−exposed males. By western−blot, sons, Citrate Synthase, Solute Carrier Family 2 member 3 (SLC2A3) and Glutathione Peroxidase 4 (GPX4) were reduced in F1 OC males. In their F2 OC grandsons had fewer pups per litter (P<0.0001). Their F2 OC sons were subfertile (P=0.02) and their F3 sons, and finally, a decrease in proteins playing a role in fertilization head cytoskeleton (Citrate Synthase, SLC2A3 and Calicin) in their F2 fathers, a reduction in proteins involved in gamete fusion and sperm motility and cell death (SOD1 and GPX4) in F1 fathers, a reduction in proteins involved in spermatogenesis and fertilization (IZUMO and ZPBP) in their F3 grandsons.

Methods: We compared sperm proteins from paternally non−exposed and exposed rat lineages to an OC mixture over three generations (F1, F2, F3). We used isobaric tags for relative and absolute quantitation (iTRAQ) labelling and 2D−LC−MS/MS analysis to identify proteins that were differentially expressed. One differently expressed protein per generation was confirmed by immunoblotting.

Results: F1 males exposed to OC during early development had decreased sperm motility (P=0.04), lower daily sperm production per testis (P=0.006), and decreased epididymal sperm concentration (P=0.0001). Their F2 OC sons were subfertile (P=0.02) and their F3 OC grandsons had fewer pups per litter (P=0.0001). In generations F1, F2 and F3, respectively 7, 19 and 37 differentially−expressed sperm proteins were identified due to OC exposure of the F1 fathers. Cytochrome C, Superoxide Dismutase 1 (SOD1) and Glutathione Peroxidase 4 (GPX4) were reduced in F1 OC males. In their F2 OC sons, Citrate Synthase, Solute Carrier Family 2 member 3 (SLC2A3) and Calicin were decreased. In F3, IZUMO and Zona Pellucida Binding Protein (ZPBP) were reduced in OC−exposed males. By western−blot, we confirmed that SOD1, Citrate Synthase and ZPBP are significantly reduced in F1, F2 and F3 OC males, respectively.

Conclusion: This is the first study to compare sperm protein levels due to paternal toxicant exposure across multiple generations using iTRAQ technology. OC exposure induced a decrease in key proteins implicated in sperm motility and cell death (SOD1 and GPX4) in F1 fathers, a reduction in proteins involved in gamete fusion and sperm head cytoskeleton (Citrate Synthase, SLC2A3 and Calicin) in their F2 sons, and finally, a decrease in proteins playing a role in fertilization (IZUMO and ZPBP) in their F3 grandsons.
**5 (Oral/Poster)**

**THE SPLICING FACTOR RBM5 IS REQUIRED FOR SPERMATOGENONIA DIFFERENTIATION**

Duangporn Jamsai, PhD, Morgan Oatley, BSc, Anne O’Connor, BSc (Hons), Jo Merriner, BSc, Robin Hobbs, PhD and Moira O’Bryan, PhD

Monash University

(Presented By: Duangporn Jamsai, PhD)

**Introduction:** Balance of spermatogonial stem and progenitor cell (SSPC) self-renewal and differentiation is essential for the homeostasis of spermatogenesis and the maintenance of male fertility. Regulation of SSPC function requires a complex interplay of intrinsic and extrinsic niche-derived factors. In this study, we identified the splicing factor RBM5 as a novel regulator of spermatogonia differentiation. Male mice carrying an ENU-induced missense mutation (R263P) in the second RNA recognition motif (RRM2) of RBM5 were sterile due to a round spermatid arrest, which ultimately led to azoosperma. We have shown that RBM5 is an essential splicing factor in round spermatids and the R263P mutation resulted in aberrant splicing in several target pre-mRNAs that are required for spermatid differentiation. Within the adult mouse testis, RBM5 localises to the nucleus of somatic and germ cells including spermatogonia, spermatocytes and round spermatids. Further, a stereological analysis revealed that in addition to the spermatid arrest phenotype Rbm5 mutant mice have a decreased conversion of spermatogonia into spermatocytes and significant loss of late spermatocytes.

**Methods:** In order to investigate the loss of spermatocytes, Rmb5 mutant versus wild type testes were stained for MVH as a marker of total germ cell content.

**Results:** The number of germ cells observed in postnatal day 0 and day 3 testes in the Rbm5 mutant testes was normal; however, a significant reduction compared to that in wild type animals was seen at postnatal day 7, suggesting a failure of spermatogonial commitment. Further, FACS analyses of the adult testes showed a significant increase in number of undifferentiated spermatogonia (PLZF positive, c−Kit negative, Ki67 positive) in the mutant compared to wild−type testes. This result was confirmed by PLZF immunostaining showed that mutant testes contained a significant increase in number of undifferentiated spermatogonia per tubule.

**Conclusion:** Taken together, our findings define for the first time a critical role for RBM5 in spermatogonia differentiation.

---

**6 (Oral/Poster)**

**MECHANISM OF HYPOGONADISM IN THE TRANSGENIC SICKLE CELL MOUSE**

Biljana Musicki, PhD, Haolin Chen, PhD, Yuxi Zhang, MD, Terry Brown, PhD, Barry Zirkin, PhD and Arthur Burnett, MD

Johns Hopkins University

(Presented By: Biljana Musicki, PhD)

**Introduction:** Hypogonadism is associated with sickle cell disease (SCD), but its underlying mechanism is not known. We investigated the mechanism of testosterone (T) deficiency in a mouse model of human SCD.

**Methods:** 7 month old homozygote SCD (Sickle) mice were used. Age-matched wild type (WT) and heterozygote SCD (Hemi) mice served as controls. Blood was obtained for measurements of T and luteinizing hormone (LH) by radioimmunoassay (RIA). Testes were collected for Leydig cell isolation, measurements of intratesticular T by RIA, and protein expressions of steroidogenic acute regulatory protein (StAR), cholesterol side-chain cleavage enzyme (P450scc), gp91phox subunit of the reactive oxygen species-generating enzyme NADPH oxidase, oxidative stress (4–hydroxy−2–nonenal, 4–HNE), and an antioxidant glutathione peroxidase−1 (GPx1) by Western blot. Leydig cells were treated with LH (0.5 and 10 ng/ml), dibutyryl cAMP (dbcAMP, 1 mM), 22−hydroxycholesterol (22HC, 25 µM), and pregnenolone (P5, 25 µM), and T produced into the media was measured by RIA.

**Results:** Plasma T levels were significantly (P<0.05) decreased in Sickle compared to WT and Hemi mice, while intratesticular T levels were significantly (P<0.05) decreased in Sickle compared to WT mice. Serum LH levels were significantly (P<0.05) increased in Sickle and Hemi compared to WT mice. LH−, dbcAMP−, and P5− (but not 22HC) stimulated testosterone production from Leydig cells isolated from Sickle and Hemi mouse testis was significantly (P<0.05) decreased compared to that of WT mice. Protein expression of StAR (but not P450scc) was significantly (P<0.05) reduced in the testis of Sickle and Hemi compared to that of WT mice. Protein expression of gp91phox was significantly (P<0.05) increased in the testis of Sickle compared to that of WT mice; while 4−HNE was significantly (P<0.05) decreased compared to that of WT mice. Protein expression of GPx1 did not differ between WT, Hemi, and Sickle mouse testis.

**Conclusion:** Hypogonadism is present in Sickle mice, mimicking the human condition. The defects in Leydig cell steroidogenic pathway, mainly due to reduced availability of cholesterol for T production, may be related to NADPH oxidase−derived oxidative stress. Mice heterozygous for the human sickle globin exhibit intermediate hypogonadal changes between those of control and Sickle mice.
Introduction and Objectives: Approximately 15% of couples have fertility problems, with a 50% male factor contribution. While assisted reproductive technologies (ART) have greatly enhanced the ability of couples with fertility difficulties to conceive, evidence suggests an increased risk for congenital defects in children conceived using ART. Both the technique of in vitro fertilization (IVF) as well as infertility itself are possible explanations. We sought to determine if the severity of male factor infertility, as assessed by sperm quality and mode of conception, was associated with birth defect rates.

Methods: Fathers with semen analysis data in the Baylor College of Medicine Semen Database (BCMSD) were linked with offspring in the Texas Birth Defects Registry (TBDFR) using data from 1999–2009. To determine the association between birth defects and semen parameters, we identified the subset of men with complete semen parameters. Hierarchical linear modeling was used to determine odds ratios between birth defect rates, semen parameters, and mode of conception before and after adjustment for paternal, maternal, and birth covariates. Semen parameters were stratified based on subfertile cutoffs defined by the WHO 5th edition.

Results: Initial linkage between the BCMSD and TBDFR yielded 6,087 men with linked data. No association between semen parameters and birth defects was observed. As a sensitivity analysis, a subset of 1,382 men who had been evaluated for infertility was identified. No statistically significant association was observed between birth defect rates and semen parameters, before or after adjustment for covariates (Table 1). Likewise, mode of conception, including infertility treatment and ART, did not affect birth defect rates.

Conclusion: Birth defect rates do not appear to be associated with semen quality or mode of conception. The current study suggests that the severity of male factor infertility does not impact the rate of congenital anomalies. This information is important when counseling couples concerned about the relationship between impaired semen quality and birth defects.

# 8 (Oral/Poster)

**Efficacy and Pharmacokinetics of LPCN 1021, A Novel Oral Testosterone Replacement Therapy (TRT), in Obese and Non-Obese Hypogonadal Men: Study of Androgen Replacement (SOAR)**

Adrian Dobs, MD, MHS¹, Jed Kaminetsky, MD², Martin Miner, MD³, Anthony Delconte, MD⁴, Nachiappan Chidambaram, PhD⁵, Satish Nachaegiri, MS⁶, Mahesh Patel, PhD⁷, Pavan Yadav, MD², and Christina Wang, MD⁶

¹The Johns Hopkins University School of Medicine and Lipocine; ²University Urology Associates, New York, NY; ³Brown University and the Miriam Hospital, Providence, RI; ⁴Saint Joseph’s University, Philadelphia, PA; ⁵Lipocine, Inc.; ⁶Harbor-UCLA Medical Center and Los Angeles Biomedical Research Institute, Torrance, CA

**Introduction:** TRT is indicated for treating hypogonadal men with low serum testosterone (T) levels and related symptoms. However, T products administered as topical or parenteral formulations are associated with inadvertent T transfer, messy application, poor retention rates, and superphysiologic T levels in some patients. There is a need for T formulations that are more user friendly, limit blood level dose excursions, and avoid T transdermal transfer. LPCN 1021 is a novel oral T undecanoate formulation being assessed in a Phase 3 trial that may avoid some of the undesirable attributes of non-oral T formulations. We sought to determine the effect of BMI on PK values after administration of LPCN 1021.

**Methods:** SOAR is a randomized, active-controlled, 2-arm, 12-months, open-label, multicenter, dose-titration ongoing trial that included 18–80 years old hypogonadal (T<300ng/dL on 2 separate days) men. Participants were randomized to either oral TU (n=210) or Androgel® 1.62% (n=105). In the oral TU arm, 92 subjects were non-obese (BMI < 30 kg/m2) and 118 subjects were obese (BMI ≥ 30 kg/m2). The dose could be titrated up (e.g. if T Cave, 24h <300 ng/dL) or down (e.g. if T Cmax was >1500 ng/dL) at weeks 4 and 8 based on 24 h PK. Efficacy was assessed on week 13 based on serum T Cave, 24h collected over 24 h for T assayed by LC−MS/MS. Analysis was conducted using the full analysis set (subjects with at least one PK profile, N=193; BMI <30 kg/m2 N=82; BMI ≥ 30 kg/m2 N=111).

---

Table 1: Adjusted association of semen parameters with birth defects in offspring, Texas 1999–2009

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Category</th>
<th>Odds Ratio, Adjusted for ART (95% CI)</th>
<th>Odds Ratio, Adjusted for Father Characteristics (95% CI)</th>
<th>Odds Ratio, Adjusted for Mother Characteristics (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concentration</td>
<td>≤ 15 → ≥ 15</td>
<td>1.07 (0.87–1.34)</td>
<td>1.06 (0.79–1.42)</td>
<td>1.05 (0.84–1.33)</td>
</tr>
<tr>
<td>Motility</td>
<td>≤ 40 → ≤ 45</td>
<td>1.18 (0.97–1.45)</td>
<td>1.01 (0.79–1.29)</td>
<td>1.02 (0.80–1.31)</td>
</tr>
<tr>
<td>Volume</td>
<td>≤ 15 → ≤ 25</td>
<td>1.08 (0.86–1.35)</td>
<td>1.06 (0.83–1.35)</td>
<td>1.03 (0.81–1.27)</td>
</tr>
<tr>
<td>Total Sperm Count</td>
<td>≤ 39 → ≤ 39</td>
<td>1.36 (0.86–1.52)</td>
<td>0.98 (0.63–1.50)</td>
<td>0.90 (0.52–1.45)</td>
</tr>
<tr>
<td>Total Motile Count</td>
<td>≤ 9 → ≤ 5</td>
<td>1.17 (0.97–1.40)</td>
<td>1.14 (0.93–1.37)</td>
<td>1.10 (0.93–1.37)</td>
</tr>
</tbody>
</table>

1. Father’s age, height, education, race/ethnicity; mother’s age, height, education, race/ethnicity; father’s birth year, place of the pregnancy
2. Father’s age, height, education, race/ethnicity; child’s birth year, place of the pregnancy
3. Mother’s age, height, education, race/ethnicity; father’s birth year, place of the pregnancy
4. 95% confidence interval

---

© 2015 American Society of Andrology and European Academy of Andrology

Andrology, 2015, Supplement, 70
Results: LPCN 1021 restored and maintained T levels in the eugonadal range (300–1140 ng/dL) in 89.0% of non-obese hypogonadal men (lower bound 95% CI = 80.3%) and 86.5% of obese hypogonadal men (lower bound 95% CI = 78.8%). Mean T Cave, 24h value was 498±200 ng/dL and 467±194 ng/dL, mean T Cmax value was 1288±557 ng/dL and 1224±625 ng/dL for non-obese and obese men, respectively. No significant differences were observed between obese and non-obese hypogonadal men in terms of percent of subjects restored in the eugonadal range, mean T Cave, 24h and mean T Cmax (p>0.1) suggesting LPCN 1021 is effective in treating both non-obese and obese hypogonadal men.

Conclusion: LPCN 1021 is an orally administered TRT product with acceptable serum T levels for both non-obese and obese hypogonadal men. LPCN 1021 may improve patient adherence as a generally safe, effective, and convenient option compared to presently used T products.

9 (Oral/Poster)
CIGARETTE SMOKING AND THE SPERM EPIGENOME
Timothy Jenkins, PhD, Kenneth Aston, PhD, James Hotaling, MD, MS and Douglas Carrell, PhD
University of Utah
(Presented By: Timothy Jenkins, PhD)

Introduction: Objective: To evaluate the negative impacts of smoking on the sperm epigenome.

Methods: Illumina 450k human methylation array was used to assess sperm DNA methylation patterns across the entire genome in general population subjects attending University of Utah Andrology and IVF Laboratories for an Institutional Review Board approved study. We analyzed regional and single CpG DNA methylation patterns by two different approaches. First, we analyzed the differences in methylation patterns between smokers and age matched individuals who do not smoke. We then analyzed the effects of both length of time smoking and the volume of cigarettes consumed by analyzing the effect of “pack years” on sperm methylation patterns with a pack years value of <10 (n=11) being considered low and >10 (n=7) being considered high.

Results: Our findings indicate that there are some regions of the sperm genome that are consistently affected by cigarette smoke. Two genes displayed significant alterations to their methylation profile in smokers, namely GPCR133 and SDK1. Additionally, we identified increased methylation variability in smokers across all CpGs probed in our analyses with an average coefficient of variance of 18.67 in our analyses with an average coefficient of variance of 18.67 in our population subjects. Furthermore, we identified changes in methylation variability in smokers across all CpGs probed in our analyses with an average coefficient of variance of 18.67 in our population subjects. Additionally, we identified increased methylation variability in smokers across all CpGs probed in our analyses with an average coefficient of variance of 18.67 in our population subjects. Of particular interest in this study are changes seen to general fertility, fertilization capacity, embryogenesis, and offspring.

Conclusion: LPCN 1021 was significant (p=0.022).

Results: Our findings indicate that there are some regions of the sperm genome that are consistently affected by cigarette smoke. Two genes displayed significant alterations to their methylation profile in smokers, namely GPCR133 and SDK1. Additionally, we identified increased methylation variability in smokers across all CpGs probed in our analyses with an average coefficient of variance of 18.67 in our population subjects.

Conclusion: LPCN 1021 was significant (p=0.022).

10 (Oral/Poster)
WHOLE-EXOME SEQUENCING IDENTIFIES NOVEL HOMOZYGOUS MUTATION IN NPAS2 IN FAMILY WITH NONOBSTRUCTIVE AZOOSPERMIA
Ranjith Ramasamy¹, M. Emre Bakircioglu, MD², Cenk Cengiz, BS¹, Ender Karaca, MD¹, Jason Scovell, BS¹, Matthew Bainbridge, PhD¹, James Lupski, PhD¹ and Dolores Lamb, PhD¹
¹Baylor College of Medicine; ²Bahçeci Fulya IVF Center, Istanbul, Turkey
(Presented By: Ranjith Ramasamy)

Introduction: Nonobstructive azoospermia (NOA) is characterized by lack of sperm in the ejaculate due to severe testicular failure. Due to genetic and clinical heterogeneity, the diagnosis is not straightforward. Current clinical practices have focused on karyotype and microdeletions. In the present study, we investigated the genetic cause of NOA in a consanguineous Turkish family through homozygosity mapping followed by targeted exon/whole–exome sequencing to identify genetic variations.

Methods: We designed a whole-exome sequencing (WES)-based approach using an in-house designed capture reagent followed by high-throughput sequencing on the Illumina platform. We sequenced the exomes of two affected siblings. Exome analysis resulted in the identification of 442 variants in the index patients. All variants passing filter criteria were validated with Sanger sequencing to confirm familial segregation and absence in the control population.

Results: A novel non-synonymous mutation in neuronal PAS 2 domain (NPAS2) was identified in a consanguineous family from Turkey. This mutation in exon 14 (chr2: 101592000 C>G) of NPAS2 is likely a disease-causing mutation as it segregates with the disease. Family segregation of the variants showed the presence of homozygous mutation in the three brothers with NOA and heterozygous mutation in one brother and one sister who were both fertile. The mutation is not found in the single nucleotide polymorphism (SNP) database, the 1000 Genomes Project, Baylor College of Medicine cohort of 500 Turkish patients (not a founder mutation) or matching 50 fertile controls.

Conclusion: Using WES, we identified a novel homozygous mutation in NPAS2 as a likely disease-causing variant in a Turkish family diagnosed with NOA. Our data reinforce the clinical role of WES in the molecular diagnosis of highly heterogeneous genetic diseases where conventional genetic approaches have previously failed in achieving a proper diagnosis.

11 (Oral/Poster)
ENCLOMID AND TOPICAL TESTOSTERONE ELEVATE TESTOSTERONE IN HYPOGONADAL MEN BUT ENCLOMID DOES NOT DECREASE TESTES SIZE
Ronald Wiehle, PhD, Gregory Fontenot, PhD, Martin Sandel, BS and Jaye Thompson, PhD
Repros Therapeutics
(Presented By: Ronald Wiehle, PhD)

Introduction: Men with secondary hypogonadism have low normal LH and low testosterone and are often treated with exogenous or topical testosterone.

Objective: Our aim was to evaluate oral enclomiphene citrate or Androxal as an alternative to topical testosterone replacement therapy for men with secondary hypogonadism.

Methods: Two trials (ZA−304 and ZA−305) were randomized, double
blind, placebo- and active-control, multi−center phase III studies in 224 men with secondary hypogonadism between 25 and 60 years of age. Men received 12.5mg or 25mg of enclomiphene as a daily capsule and were provided with a placebo gel. Other men received AndroGel 1.6% and placebo capsules. Other men received placebo capsules and gels.

Results: To be enrolled subjects needed to have two baseline testosterone (T) values below 300ng/dL. The End of Study (EOS) was after 16 weeks of treatment. There was a statistically significant rise in T in men receiving either enclomiphene citrate or topical testosterone into the normal range (see table). Placebo subjects did not change. Encolomiphene did not decrease sperm counts unlike the topical gel. As we have seen before, enclomiphene citrate increased LH and FSH while men in the topical arm showed decreases (not shown). All men were similar at baseline in testes volume (p = 0.94, ANOVA) by orchidometry. In both studies, men on topical testosterone demonstrated decreases in mean testicular volume (−0.86 cm3) and a significant decrease overall compared to the enclomiphene (p < 0.05) or placebo (p < 0.05).

Conclusion: Encolomiphene citrate significantly increased total serum testosterone, LH and FSH which suggests that the drug normalized endogenous testosterone production through the hypothalamic−pituitary−testicular axis and supported the natural continuation of sperm number and testes volume.

12 (Oral/Poster)
CONCENTRATIONS OF THE RETINOIC ACID SYNTHESIZING ENZYME ALDH1A2 ARE SIGNIFICANTLY REDUCED IN MEN WITH OLIGOZOOSPERMIA
John Amory, MD, MPH, Margarett Shnorhavorian, MD, MPH, Samuel Arnold, MD, Faith Stevison, BS, Nina Isoherranen, PhD, Thomas Walsh, MD, MPH and Charles Muller, PhD
University of Washington
(Presented By: John Amory, MD, MPH)

Introduction: Vitamin A, and its active metabolite, retinoic acid, are known to be necessary for spermatogenesis in many species including man. Retinoic acid is synthesized in tissues from Vitamin A by one of three aldehyde dehydrogenases, ALDH1A1, 1A2 or 1A3. We have shown that testicular ALDH1A2 levels are reduced in men with infertility in proportion to germ-cell number on testicular biopsy; however, the relationships between testicular ALDH1A2 and semen parameters, as well as the cellular localization of ALDH1A2 within the testes have not been reported.

Methods: We conducted an observational analysis of testicular ALDH1A2 on human testis samples from 5 men with normal sperm parameters and 5 men with infertility due to oligozoospermia. Testicular tissue was analyzed by immunohistochemistry for ALDH1A2 and ALDH1A2 protein levels were quantified by a LC/MS/MS peptide assay.

Results: Men with oligozoospermia had significantly reduced levels of ALDH1A2 in their testicular tissue compared to men with normozoospermia (p<0.03). Immunohistochemistry revealed that ALDH1A2 was localized primarily in spermatogonia, and absent from Sertoli cells.

Conclusion: The finding that ALDH1A2 co-localizes with early germ cells in the human testis suggests that i) early germ cells are a site of retinoic acid biosynthesis within the seminiferous epithelium, ii) reduced ALDH1A2 may be associated with male infertility, and iii) inhibition of ALDH1A2 may be a reasonable strategy for the development of novel male contraceptives.

This work was funded by The Eunice Kennedy Shriver National Institute of Child Health and Human Development supported this work through cooperative agreement U54 HD42454 as part of the Cooperative Contraceptive Research Centers Program.

13
INVESTIGATIONS ON THE EFFECTS OF TYPHA CAPENSIS ON TM3 LEYDIG CELLS
Abdulkarem Ilfergane, MSc, Nicole Haines-Arries, MSc, Leonardo van Zyl, MSc and Ralf Henkel, PhD
University of the Western Cape
(Presented By: Ralf Henkel, PhD)

Introduction: Typha capensis (bulrush) is one of South Africa’s indigenous medicinal plants used to treat male fertility problems. Anecdotal data claim that T. capensis has beneficial effects on male reproductive functions and aging male symptoms. The aim of the study was to investigate these effects of T. capensis and to identify active fractions in an in vitro system using TM3-Leydig cells in respect to the induction of testosterone production.

Methods: Rhizomes of the plant were harvested in the four seasons (spring, summer, autumn and winter), extracted with water and fractionated using HPLC. TM3 Leydig cells were then cultured in DMEM medium and incubated with the extract under standard conditions at different concentrations (0.01, 0.02, 0.1, 1, 10, 100 µg/ml) for 24 and 96 hours, respectively. Viability (MTT test), cell morphology, early apoptotic events by means of Annexin V-Cy3 binding, DNA fragmentation by means of the TUNEL assay, and testosterone production (ELISA) were tested. HPLC fingerprinting was carried out.

Results: At concentrations less than 10 µg/ml, the extracts showed no effect on cell viability. At higher concentrations, viability increased, indicating to cellular stress. Testosterone production of TM3 cells increased significantly after exposure to concentrations of T. capensis higher than 0.1 µg/ml. Exposure at low concentrations (0.01, 0.02, 0.1, 1, µg/ml) for 24 – 96 hours showed no increase in early apoptosis and DNA damage when compared to the control. Higher concentrations (10, 100µg/ml) revealed an increase in the percentage of cells with signs of early apoptosis and DNA damage. HPLC data showed that the most effective fraction was the F1 fraction from the summer harvest.

Conclusion: Typha capensis enhanced the production of testosterone and might be useful to treat male infertility and aging male problems. Results further reveal that the F1 fraction from the summer harvest had highest biological activity.
14 WHO WERE THE PATIENTS ON TESTOSTERONE THAT HAD MYOCARDIAL INFARCTIONS? THE LOW T EXPERIENCE
Kelly Cook, MPAS, PA-C¹, William Reilly, MD¹ and Robert Tan, MD, MBA²,³
¹Low T Center; ²Opal Medical Clinic; ³Low T Institute
(Presented By: Kelly Cook, MPAS, PA-C)

Introduction: Controversies abound on whether testosterone causes myocardial infarctions (MI). Some studies show an association of testosterone therapy with MI, while others show a protective or neutral effect. The association of MI with testosterone treatment seems to be linked to age or underlying medical conditions.

Objectives: In general, the Low T Centers, treat younger, relatively healthier men who are hypogonadal with injectable testosterone. While our rates of MI in our treatment group was very low, we performed case finding and root cause analysis of these cases of MI in our practice.

Methods: After IRB approval, cases of MI were identified by ICD-9 coding, using the electronic medical record. Conference calls were held with centers to ensure that each patient was asked specifically for MI and that coding was accurate. 40 Centers were examined. Interviews were also performed on patients & families of patients with MI, and cardiac risks factors were identified. The data was entered into a spreadsheet and descriptive as well as comparative statistics performed.

Results: 39,937 charts were reviewed and about 19,968 patients received testosterone treatment. Of these, there were 9 cases of new MI and 46 patients with pre-existing MI. Of the 9 patients, all had risk factors except one. Our MI rates at 45 per 100,000 are very low in comparison to managed care (Kaiser Permanente) rates, which were 208 per 100,000. Of those who were on testosterone and had MI, 44% were smokers or had hypertension (HTN), 22% had Diabetes (DM). In comparison the prevalence of smoking was 3.5%, HTN 15%, DM was 4% in the overall testosterone treated group. When chi square was applied for differences between the 2 groups (smoking, HTN, DM), p= 0.001.

Conclusion: Our study showed that testosterone therapy is not causal of MI. If carefully monitored, testosterone treatment in a younger population was safe and established risk factors such as smoking, hypertension and diabetes are associated with higher rates of MI in our testosterone treated patients.

15 ANDROGENIC EFFECT OF CINNAMON ZEYLANICUM ON SPERMATOGENESIS
Arash Khaki, PhD
Department of Pathobiology, Tabriz Branch, Islamic Azad University, Tabriz, Iran.
(Presented By: Arash Khaki, PhD)

Introduction: in nowadays herbal medicines in modern countries come to help for diseases treatment, herbal are known a sources of antioxidant and minerals.Objectives: To study the effect of Cinnamon zeylanicum on spermatogenesis in rats.

Methods: in this experimental study, Wistar male rats (n=20) were divided into two groups, a control group (n=10);g−1 and a Cinnamon zeylanicum group(n=10);g−2 that received 75mg/kg/day cinnamon by gavage for 28 days; however, the control group just received an equal volume of distilled water daily. Animals were kept in a standard condition. On day 28, 5 ml blood sample of each rat was taken from tail area to measure testosterone, SOD (superoxide dismutase), CAT (catalase), GPX (glutathione peroxidase), and MDA (malondialdehyde) levels. Testes were collected and were then prepared for sperm analysis by the WHO method.

Results: Sperm parameters, total serum testosterone, SOD, CAT, and GPX levels were significantly increased in the group−2 group in comparison to the group−1 (P<0.05). Besides, group−2 showed a significant decreased in the level of plasma MDA (P<0.05) in comparison to the group−1. There were no significant differences between the groups in testis weight (P>0.05).

Conclusion: Since in our study, 75mg/kg/day Cinnamon has significantly increased the sperm population, motility and viability, it seems using it in mammalian has beneficial potential on spermatogenesis.

16 EFFECTS OF ORGANOPHOSPHATE FLAME RETARDANTS ON LEYDIG CELL FUNCTION
Gauthier Schang, Barbara F. Hales, PhD and Bernard Robaire, PhD
Department of Pharmacology and Therapeutics, McGill University (Presented By: Gauthier Schang)

Introduction: Brominated flame retardants are compounds used to prevent the initiation and propagation of fires. However, it was demonstrated that their efficacy has been overestimated and, more importantly, that they interfere with the hormonal balance of the body. Some of these flame retardants, such as BDE−47, disrupt the regulation of testosterone production by Leydig cells. As an alternative, new chemicals, the organophosphate flame retardants (OPFRs), are being used as “safer” replacements. The objective of this study was to characterize the effects of some common OPFRs, e.g. isopropylated phenyl phosphate, 2−ethylhexyl diphenyl phosphate and triphenyl phosphate, on male reproductive health. We hypothesized that the newer compounds will not affect Leydig cell function.

Methods: To test this hypothesis, we used a commonly used Leydig cell model, the MA−10 cell line, to investigate potential toxic effects on steroidogenesis. MA−10 cells were treated with concentrations of OPFRs ranging from 0.1 to 100 μM for 48h; we then assessed the effects on mitochondrial activity, cell count, superoxide production and steroidogenesis. As a reference, cells were also treated with BDE−47.
ABSTRACTS

Results: Our results showed that all OPFRs inhibited mitochondrial activity to a greater extent (−95% at 100 µM) than BDE-47 (−75% inhibition at 100 µM). All of the OPFRs except triphenyl phosphate reduced total cell numbers by 20% or more at 10 µM, while BDE-47 and triphenyl phosphate had close to no effect at this concentration. Cytotoxicity at 10 µM was correlated with an increase in superoxide production, suggesting that oxidative stress is a factor leading to the observed cell death. OPFRs increased basal steroid production by at least 1.5-fold (reaching up to 3-fold), while inhibiting the ability of cells to respond to external stimuli such as LH by up to 4.4-fold.

Conclusion: These results suggest that none of the OPFRs tested is safer than BDE-47 in this cellular model: all affected mitochondrial activity, cell survivalability and redox status. A significant increase in basal steroid production could have drastic effects on organs such as the prostate, while the decrease in responsiveness to stimuli could lead to long-term consequences on reproductive health, as well as on other tissues such as the brain or muscles. These studies were supported by CIHR and REDIH.

17 FINASTERIDE 1MG/DAILY CONSUMPTION IMPAIRS SPERMATOGENESIS BY HISTOLOGICAL EVALUATION AND SEMEN QUALITY IN MEN IN REPRODUCTIVE AGE
Juliana Pariz, MSc, PhD student¹,² and Jorge Hallak, MD, PhD¹,²
¹Androscience; ²Universidade de São Paulo
(Presented By: Juliana Pariz, MSc, PhD student)

Introduction: Finasteride, an oral type 2.5α-reductase inhibitor, is used in 1 mg/daily doses for the treatment of male pattern hair loss. Its consumption affects the conversion of testosterone to dihydrotestosterone (DHT), which is a more potent androgen, impairing the male reproductive system. Objective: to study the effect of finasteride 1mg/daily consumption on the spermatogenesis and seminal quality.

Methods: We studied 23 male subjects (mean 33 y.o.) who came for an initial andrological evaluation and who self-reported use of finasteride 1mg for more than one year. These subjects were paired and compared, by Paired-Samples T Test (p adopted <0.05), with fertile (pre-vasectomy candidates with no risk factors for sperm/testicular dysfunction) and infertile (for over a year) patients with same age and varicocele grade. In addition, we included six testicular biopsies with spermatogenesis assessment. The study was approved in Ethics Committee (n°12331). We conducted ANOVA test of the means and adopted p <0.05.

Results: The mean of Finasteride consumption was 72.22 months. Finasteride users had significantly decreased in total sperm count (p=0.026 and 0.014) and total motile sperm count (p=0.053 and 0.036) when compared with infertile and fertile group, respectively. Furthermore, morphology by strict (p=0.001) and WHO (p=0.001) criteria and testicular volume (p<0.001) decreases in Finasteride users when compared with fertile men. Creatine-kinase activity which is a marker of sperm immaturity was increased in Finasteride users (p<0.001). In spermatogenesis analysis, four showed spermatogenesis altered and round spermatids; predominant Johnsen score was 7. We conducted T Test paired and adopted and p <0.05.

Conclusion: Our results demonstrate that Finasteride consumption affects negatively the spermatogenesis and semen quality and may be contraindicated to young men that are willing to father their own offspring. We do not yet know the long-term effects on male reproductive health and recovery rate after discontinuation, but this study suggest that Finasteride is of concern for the proportion and widespread prescription by dermatologists and others health professionals unaware of its potential reproductive effects.

18 EFFECT OF ALCOHOL CONSUMPTION ON MALE REPRODUCTIVE POTENTIAL
Artemis da Silva, BSc¹,², Juliana Pariz, MSc, PhD student¹,² and Jorge Hallak, MD, PhD¹,²
¹Androscience; ²Universidade de São Paulo
(Presented By: Artemis da Silva, BSc)

Introduction: Alcohol is a psychoactive substance that may create dependence and affects the overall health of man by different mechanisms, which can be fatal in excessive chronic use. The possible association between alcohol consumption and reduced male fertility has been the subject of several studies and still remains unclear. Objectives: to demonstrate the effects of alcohol consumption in fertile men of reproductive age, evaluating semen parameters and hormonal profile.

Methods: For this study, were included data of semen analysis, hormone profile and testicular volume of pre-vasectomy candidates with no risk factors for sperm/testicular dysfunction from Clinical Hospital of Urology Department, Universidade de São Paulo, Brazil. We excluded patients with infertile, azoospermic, presence of varicocele or any clinical or surgical history that cause sperm changes. The study was approved by Ethics Committee (12331/14). We conducted T-Test for independent samples and adopted p <0.05.

Results: Subjects who reported not being drinkers constituted the control group (n=86), mean age of the patients 34.7 ± 5.43. Who declared themselves consumers was included in alcohol group (n=18), mean age 37.35 ±6.55. Statistical differences were seen in following seminal parameters: pH (7.65 vs. 7.97; p <0.07), motility grade A (8.59 vs. 4.61%; p=0.003), strict criteria (6.46 vs 4.11%; p=0.01) and WHO (21.44 vs. 15.22%; p=0.004) normal morphology and total number of round cells (14.75 vs. 5.66 million; p <0.001). In hormonal parameters, there was an increase of 17-OH progesterone in alcohol consumptions (1.05 vs. 1.54 ng/mL; p<0.011).

Conclusion: In view of results, we suggest that alcohol intake affects adversely the production of 17-OH progesterone and spermatogenesis, resulting in reduced mobile and morphological quality of sperm. Thus, the intake of alcohol appears to be associated with reduced male reproductive potential.
YOGA AND MEDITATION - THERAPEUTIC FOR SPERM DNA HEALTH
Shiv Basant Kumar, MSc¹, Bhavna Chawla, MD², Raj Kumar Yadav, MD³, Surabhi Gautam, MSc⁴ and Rima Dada, MD, PhD⁵
¹Laboratory for molecular reproduction and genetics, Department of Anatomy, All India Institute of Medical Sciences, New Delhi, India; ²Ocular Oncology & Pediatric Ophthalmology Service, Rajendra Prasad Centre for Ophthalmic Sciences; ³Integral Health Clinic, Department of Physiology, All India Institute of Medical Sciences, New Delhi, India; ⁴Laboratory for molecular reproduction and genetics, Department of Anatomy, All India Institute of Medical Sciences, New Delhi, India
(Presented By: Shiv Basant Kumar, MSc)

Introduction: Life style habits adopted by father before the conception may lead to the increase in seminal free radical level and culminate in seminal oxidative stress. Oxidative stress damages sperm nuclear and mitochondrial DNA. Complementary and Alternative Medical therapies such as yoga/meditation are being increasingly used as adjuncts to modern medicine. Therefore, we analyzed the effects of yoga and meditation on sperm DNA integrity in fathers of children with Retinoblastoma (Rb) after interventions (3 and 6 months).

Methods: A total of 26 men (father of child with non-familial Rb) were recruited in this study. Semen samples were collected at base line (day 0), 3 months and after 6 months of yoga practice. Reactive Oxygen Species (ROS), DNA Fragmentation Index (DFI) and 8-hydroxy-2’-deoxyguanosine (8-OHdG) estimation was done at each interval.

Results: Seminal mean ROS levels were reduced after 3 months [p=0.081] and after 6 months [p<0.001] compared to base level (day 0). There was reduction in mean DFI levels [p=0.059] at 3 months and after 6 months DFI significantly reduced [p<0.01] compared to base level (Fig 1). We also observed reduction in levels of 8-OHdG after 3 months [p<0.05] and after follow up of 6 months [p<0.01] with respect to the base level.

Conclusion: The results of this study highlight that the yoga/meditation may significantly lower the DFI, 8-OHdG and ROS levels and thus are therapeutic for maintaining/restoring sperm DNA integrity. To the best of our knowledge, this is the first study to report a reduction in DFI mutagenic load following adoption of yoga and meditation. Recently United Nation’s proposal to celebrate International Yoga Day (21st June) might be an encouraging step and to reduce childhood morbidity.

Genitourinary Infection Alters Semen Parameters and Increases Presence of Anti-Sperm Antibodies
Tâbata Martins, BSc student¹,²,³, Juliana Pariz, MSc, PhD student¹,², Rosa Alice Monteiro, BSc¹,³ and Jorge Hallak, MD, PhD²
¹Androscience; ²Universidade de São Paulo; ³Faculdades Metropolitanas Unidas
(Presented By: Tâbata Martins, BSc student)

Introduction: Pro-inflammatory cytokines produced from bacterial infections induces changes in permeability of blood–luminal barrier (testis/epidydimal/prostate) and may alter the male reproductive potential. Objective: to evaluate the effect of genitourinary infection in semen parameters and presence of anti–sperm antibodies (ASA).

Methods: This retrospective study included 172 infertile men (22 – 56 years-old) of Andrology Clinic between 2006 and 2014 who underwent semen analysis, ASA test and microbiological evaluation of male genitourinary system. Patients who had bacterial infection were classified as infection group and the absence of infection composed the control group. The means of seminal parameters and ASA were compared between groups using the T test for independent samples and was adopted p<0.05 for statistical significance.

Results: Sixty-eight patients were included in infection group and 104 in control group. 59% of patients had infection caused by Staphylococcus spp, 30 % by Enterococcus spp and 11% by Escherichia coli. Reduction in total number of progressive sperm (48.18 million/ejaculate vs 23.38 million/ejaculate; p=0.003), total motility (39.62% vs 23.71%; p<0.001), progressive motility (61.50% vs 50.04%; p<0.001) and motility grade B (35.45% vs 21.06%; p<0.001) and increase in motility grade C (22.04% vs 26.34%, p = 0.011) and grade D (38.34% vs 49.96%, p <0.001) were observed. Increase in percentage of ASA was observed, with 12.31% in control group to 20.34% in infected group (p<0.001)

Conclusion: Our results suggest that the presence of infection in the genitourinary system can interfere with the blood–luminal barrier, resulting in increased presence of testicular ASA, which can affect the quality of sperm motility and male reproductive potential.

CHARACTERIZATION OF PRIMARY CULTURES OF ADULT HUMAN EPIDIDYMIS EPITHELIAL CELLS
Shih-Hsing Leir, PhD¹, James Browne, PhD¹, Scott Eggener, MD² and Ann Harris, PhD²
¹Human Molecular Genetics Program, Lurie Children’s Research Center/Northwestern University Feinberg School of Medicine, Chicago, IL; ²Section of Urology, University of Chicago Medical Center, Chicago, IL
(Presented By: Shih-Hsing Leir, PhD)

Introduction: This study aimed to establish cultures of epithelial cells from all regions of the human epididymis, to provide enough materials for molecular approaches to epididymis function.

Methods: Human epididymis tissue was obtained from nine patients undergoing orchectomy for a clinical diagnosis of testicular cancer. The three different anatomical regions: caput, corpus and cauda, were separated, and the tissues of each segment were digested with collagenase type I and seeded onto collagen I–coated cell culture plasticware. The cells were grown in CMRL 1066 medium and maintained in a humid 5% CO2 incubator at 33°C.
Results: Cultures of caput, corpus and cauda epithelial cells were passaged up to 8 times and maintained differentiation markers. They were also cryopreserved and recovered successfully. Androgen receptor, clusterin and CRISP1 were expressed in cultured cells as shown by immunofluorescence, western blot and quantitative reverse–transcription PCR (qRT–PCR). The distribution of other epididymis markers alone different regions was also investigated by qRT–PCR. Cultures developed transepithelial resistance (TER) when cells were grown on filter inserts, which was androgen responsive in the caput but androgen insensitive in the corpus and cauda where unstimulated TER values were much higher.

Conclusion: The results demonstrate a robust in vitro culture system for differentiated epithelial cell types in the caput, corpus and cauda of the human epididymis. These cells will be a valuable resource for studying biological mechanisms relevant to epididymis in health and disease, which has a pivotal role in male fertility.

22 COMPARATIVE ANALYSIS OF EPIDIDYMIS TRANSCRIPTOME IN FERTILE AND SUBFERTILE BULL
Christine Legare, MSc¹, Ayodélé Akintayo, MSc¹, Patrick Blondin, PhD² and Robert Sullivan, PhD³
¹Laval University; ²L’Alliance Boviteq
(Presented By: Christine Legare, MSc)

Introduction: The epididymis is a single long convoluted tubule that connects the testis to the vas deferens and is responsible for sperm maturation and storage. Gene expression is highly segmented along this organ resulting in the formation of luminal microenvironments that sequentially modify maturing spermatozoa. In this study, we compare the transcriptome signature in the epididymal segments of fertile and subfertile bulls in order to highlight putative subfertility explanations.

Methods: Epididymis from 6 Holstein bulls with documented fertility were used. According to their ‘fertility solution’ (SOL), as calculated by the Canadian dairy network, bulls were divided into 2 groups: high fertility (HF) (SOL>3.0; n=3), and medium–low fertility (−2.8>SOL>−4.9; n=3), SOL=0 being the average. Microarray analysis was performed on GeneChip Bovine Genome Array (Affymetrix®). Hierarchical clustering and Principal Component Analysis revealed an excellent separation between caput, corpus and cauda segments. Among the 23000 bovine qualifiers spotted on the chip, 14725 transcripts were differentially expressed in caput, corpus and cauda region, respectively. To compare gene expression between fertile and subfertile groups, transcripts with a differential expression of at least a 1.5−fold change and a P−value of less than 0.01 were clustered in relation to their intensity profiles.

Results: When comparing fertile vs subfertile transcriptome, 23, 24 and 29 transcripts were differentially expressed in caput, corpus and cauda respectively. Genes with differential expression were grouped according to Gene Ontology annotation. A majority of these genes were associated with cell communication, metabolic and development process. Of the differently expressed genes, nine (including AKAP4, SMCP, SPATA3, TCP11, ODF1, CTCFL, SPATA18, ADAM28, SORD and FAM161A) were found to exert function related to reproduction activity and 5 genes (including DEAD, CYST11, DEFB119, DEFB124 and MX1) were found to be associated to the defense response.

Conclusion: Dysregulation of these two epididymal functions can jeopardise sperm ability to reach and fertilise the oocyte. As fertility can be quantified in bulls used for artificial insemination, this species is a unique model to understand male fertility/subfertility in man.

23 CONTRIBUTION OF PRINCIPAL AND CLEAR CELLS IN THE REGULATION OF LUMINAL PH IN THE MOUSE EPIDIDYMIS
Yoo-Jin Park, PhD, Bong-Ki Kim, PhD and Sylvie Breton, PhD
Massachusetts General Hospital
(Presented By: Yoo-Jin Park, PhD)

Introduction: While spermatozoa undergo epididymal maturation, they remain quiescent thanks to the establishment of a low luminal pH. In the cauda epididymidis (Cd), clear cells (CCs) secrete protons via the proton–pumping ATPase (V−ATPase) to acidify the lumen. However, upon activation principal cells (PCs) can secrete HCO3−, a process that is mediated by CFTR and would contribute to increasing luminal pH. We examined here the relative contribution of CCs and PCs in the regulation of the overall acidic luminal pH.

Methods: The lumen of the Cd was perfused with an acidic (pH 5.5), control (pH 6.6) and alkaline (pH 7.8) phosphate buffer solution. The perfusate was then collected via an incision made at the epididymal/vas deferens junction, and its pH was measured immediately using high sensitivity pH strips (0.2 unit increment).

Results: While the pH of the control solution remained constant at 6.6 after its passage through the Cd lumen, the pH of the acidic perfusate progressively increased from 5.5 to 5.70 ± 0.20 after 10 min and 6.23 ± 0.03 after 20 min. Addition of cpt−cAMP induced a faster recovery, the pH reaching 6.1 ± 0.06 (versus 5.70 ± 0.20 without cAMP) after 10 min, and the CFTR inhibitor (CFTRinh172) abolished recovery (pH 5.5 ± 0.00 after 20 min). Alternatively, the pH of the alkaline perfusate rapidly decreased from 7.8 to 6.4 at 10 min and then remained constant after 20 min. cAMP or CFTRinh172 had no significant effect on this response. V−ATPase labeling of fixed cryostat sections showed “activated” CCs with numerous and long V−ATPase−labeled microplicae when perfused at pH 7.8, and “resting” CCs with very few V−ATPase−labeled microplicae at pH 5.5.

Conclusion: Our results suggest: 1) CFTR−dependent bicarbonate secretion by PCs when the Cd is perfused at acidic pH (pH 5.5); 2) V−ATPase−dependent proton secretion by CCs when the Cd is perfused at alkaline pH (7.8). Both processes would contribute to the re−establishment of luminal pH towards its control value. Our study, therefore, indicates the participation of both CCs and PCs in acid/base transport in the Cd epididymis, and shows that in addition to CCs, PCs can also respond to variations in luminal pH.

Funding: This work was supported by NIH grant HD040793 (to SB) and by the Lalor Foundation (to JYP)
24 TESTICULAR FLUID REGULATES APICAL BLEBBING IN THE PORCINE EPIDIDYMIS
Jennifer Hughes and Trish Berger, PhD
UC Davis
(Presented By: Jennifer Hughes)

Introduction: The epididymis functions to mature spermatozoa. Apical blebbing of the epithelium produces vesicles, termed epididymosomes, which transfer proteins important for fertilizing capacity to maturing spermatozoa. Our understanding of the mechanism by which apical blebs are produced is limited. Prior work from our laboratory indicates that apical blebbing is a mature phenotype not regulated by androgens or estrogens within the epididymis. Reduction of the testicular luminal flow down regulates the appearance of apical blebbing after effertent duct ligation.

Methods: To confirm that luminal content drives apical blebbing we ligated the left caput epididymis at two sites and removed the intervening epididymal tubule during early peri-pubertal development (12 weeks.) Tissues were collected from both epididymides and the corpus morphological appearance of apical blebbing was assessed four weeks later, at 16 weeks of age, a developmental stage when blebbing is easily detectable. The non–manipulated epididymis served as an internal animal control.

Conclusion: Initial findings further support regulation of apical blebbing by a testicular luminal factor.

Funding: This work was supported by the Austin Eugene Lyons Fellowship, W.K. Kellogg Endowment, Henry A. Jastro and Peter J. Shields Research Fellowship, Humphries Fellowship, and W2171 Multistate Research Project.

25 DIFFERENTIAL PLATING RATIO OF NON-ADHERENT TO ADHERENT CELLS ISOLATED FROM AN AZOOSPERMIC MICRO TESTICULAR TISSUE EXTRACTION (MICROTESE) SAMPLE HAS A PROFOUND EFFECT ON IN VITRO GERM CELL COLONY FORMATION
Itai Gat1,2, Leila Maghen3, Ekaterina Shlush1, Hanna Balakier1, Andrée Gauthier-Fisher1, Keith Jarvi1, Kirk C. Lo3 and Clifford Librach1,4,5,6 *Equal contribution
1The Create Fertility Centre, 790 Bay Street, Suite 1100, Toronto M5G 1N8, Canada; 2Talpiot Medical Leadership Program, Sheba Medical Center, Ramat Gan, Israel; 3 Department of Urology, Mount Sinai Hospital; 4 Department of Obstetrics and Gynecology; 5 Department of Physiology, University of Toronto; 6Department of Gynecology, Women’s College Hospital, Toronto, Ontario
(Presented By: Itai Gat)

Introduction: Somatic cell overgrowth limits spermatogonial stem cell (SSC) propagation ex-vivo. We evaluated the effect of differential plating (DP) ratios of non-adherent (NAd) to adherent (Ad) cells isolated from azoospermic microTESE tissue to determine the effect of this on in vitro germ cell colony formation.

Methods: Excess tissue from a hypospermic human testicular sample after microTESE was obtained. After enzymatic digestion and overnight incubation, GFR1+ve and GFR1–ve cell subpopulations were enriched by magnetic activated cell sorting and cultured on 12 well laminin–coated dishes in 3 groups: GFR1+ve with density of 7.5K cells per cm2; GFR1–ve with density of 7.5K; GFR 1–ve with density of 15K (P0). After 10 days, repetitive DP was conducted and passaged (P1) using pre–determined NAd-to-Ad cell ratios. Number and characteristics of germ cell–like colonies were assessed.

Results: 3 patterns were seen at P0: GFR 1+ve cultures had small irregular NAd germ-like cells, together with a low Ad cell concentration followed by cell death without passaging to P1. GFR 1–ve at 7.5K density included 5 colonies associated with somatic cells. GFR 1–ve at 15K density resulted in mostly somatic cells without germ cell–like colony formation. During repetitive DP dramatically different NAd-to-Ad ratios were observed between GFR 1–ve 7.5K and 15K plating densities. After passage to P1, Ad cell density was reduced to 2.5K per cm2 while passing all NAd cells from both GFR 1–ve culture conditions using NAd-to-Ad ratios of 15:1 and 4:1 (figure 1). After 10 days of P1, 200 colonies were observed in the 15:1 culture while none were observed in the 4:1.

Conclusion: Low (GFR1a+ve) or high (GFR1a–ve, 15K) somatic-like Ad cell concentration ratios affected colony formation. We hypothesize that this is due to a lack or over–dominance of somatic cells in culture, respectively. GFR1–ve 7.5K condition demonstrated intermediate somatic cell numbers and enabled colony formation at P0. We show for the first time that repetitive DP and NAd-to-Ad cell ratio can have a profound effect on germ cell colony formation. These results are being repeated with additional samples, with concomitant assessment of miRNA and protein expression.

26 REQUIREMENT FOR MOV10L1 RNA HELICASE ACTIVITY IN THE PROCESSING OF PIRNA PRECURSORS
Qi Fu, Anastassios Vousurekas, PhD1, Ke Zheng, PhD2, Erica Goode and P. Jeremy Wang, PhD1
1The University of Pennsylvania; 2Nanjing Medical University School
(Presented By: Qi Fu)

Introduction: PIWI–interacting RNAs (piRNAs) are a class of small non–coding RNAs highly expressed in the germlines of many species from C. elegans to mammalian species. They most notably protect the integrity of the germline genome through transcriptional and post–transcriptional silencing of active transposable elements (TEs) during germ cell development. piRNA biogenesis is tightly coupled to TE silencing. In mammals, the RNA transcripts of active TEs are targeted into the piRNA processing pathway as piRNA precursors for degradation and biogenesis of primary piRNAs. Primary piRNAs then enter the ping–pong amplification loop to generate secondary piRNAs with complementary sequences. Finally, secondary piRNAs are believed to guide their PIWI proteins to transcriptionally silence active TEs in the nucleus. However, the mechanisms underlying piRNA biogenesis remain unclear.

Methods: Moloney Leukemia Virus 10–like 1 (MOV10L1) is a testes–specific RNA helicase required for piRNA biogenesis. Mov10l1–deficient males are viable but infertile, due to meiotic arrest. Disruption of Mov10l1 leads to the accumulation of piRNA precursors.
Results: Our CLIP–seq results reveal that MOV10L1 directly associates with piRNA precursors. The majority of MOV10L1–bound RNAs map to piRNA hotspots, but do not represent mature piRNA sequences. MOV10L1 binds to RNA near regions with high secondary structure potential. Because RNA helicases recognize and resolve secondary structures, we hypothesize that MOV10L1 processes piRNA precursors through its RNA helicase activity. I designed two Mov10i1 knock−in mouse models containing conserved point mutations in the ATP binding and ATP hydrolysis sites of the MOV10L1 RNA helicase domain. Male Mov10i1 homozygous knock−in mice exhibit meiotic arrest, mislocalization of piRNA pathway proteins, a derepression of the LINE1 TE, and a lack of piRNAs associated with MILI.

Conclusion: In conclusion, MOV10L1 RNA helicase activity is required for piRNA biogenesis. In the future, I plan to determine if MOV10L1 RNA helicase activity is required for the processing of piRNA precursors by measuring the levels of piRNA precursors in Mov10i1 knock−in mice. Our previous and current studies demonstrate that MOV10L1 is a master regulator of piRNA biogenesis in mammals. As an essential germ cell−specific gene, mutations in human Mov10i1 are expected to cause male infertility. Thus, MOV10L1 may be a molecular target for male contraception.

Results: Our findings suggest very a subtle association between BMI (obese vs. normal) and sperm methylation patterns, with a total of 4 genomic regions that are significantly differentially methylated between the two categories. Similarly, only 1 genomic region showed an association between total sperm count and DNA methylation. In contrast, we have identified relatively strong sperm epigenetic associations with progressive motility where 85 genomic regions are significantly differentially methylated between samples with normal and low motility. Interestingly, these alterations were frequently found at imprinted loci and regions important for spermatogenesis. Similarly, paternal age is strongly associated with sperm epigenetic alterations, with 131 genomic regions that are significantly altered with age.

Conclusion: Our data demonstrate that there are some associations between sperm epigenetic profiles and general semen parameters and patient characteristics. The associations identified with aging are in agreement with previous work from our lab and others. Of particular interest in this study are the unanticipated associations identified between sperm motility and DNA methylation patterns. While the etiology of these alterations is unclear, they may be an indication of more general problems during spermatogenesis. Interestingly, the loci where these alterations are found in low motility samples comport with this hypothesis. Further, targeted studies are required to fully address these findings and the potential impact these alterations may have on general fertility, fertilization capacity, embryogenesis, and offspring health.

27 SEMEN PARAMETERS, PATIENT CHARACTERISTICS, AND ASSOCIATED SPERM EPIGENETIC PROFILES

Timothy Jenkins, PhD, Kenneth Aston, PhD, James Hotaling, MD, MS and Douglas Carrell, PhD
University of Utah
(Presented By: Timothy Jenkins, PhD)

Introduction: Objective: To evaluate sperm epigenetic changes associated with patient age and BMI at the time of collection as well as general semen parameters including, sperm motility and total count.

Methods: Illumina 450k human methylation array was used to assess sperm DNA methylation patterns across the entire genome in patients attending the University of Utah Andrology and IVF Laboratories for a routine semen analysis. We analyzed regional and single CpG DNA methylation patterns to identify any associations with BMI (normal, n=23; vs. obese, n=17) and age (<25 years of age, n=20; vs. >40 years of age, n=17) as well as total sperm count (normal, n=58; vs. low, n=6) and progressive motility (normal, n=44; vs. low, n=20).

Results: Our findings suggest a subtle association between BMI (obese vs. normal) and sperm methylation patterns, with a total of 4 genomic regions that are significantly differentially methylated between the two categories. Similarly, only 1 genomic region showed an association between total sperm count and DNA methylation. In contrast, we have identified relatively strong sperm epigenetic associations with progressive motility where 85 genomic regions are significantly differentially methylated between samples with normal and low motility. Interestingly, these alterations were frequently found at imprinted loci and regions important for spermatogenesis. Similarly, paternal age is strongly associated with sperm epigenetic alterations, with 131 genomic regions that are significantly altered with age.

Conclusion: In conclusion, MOV10L1 RNA helicase activity is required for piRNA biogenesis. In the future, I plan to determine if MOV10L1 RNA helicase activity is required for the processing of piRNA precursors by measuring the levels of piRNA precursors in Mov10i1 knock−in mice. Our previous and current studies demonstrate that MOV10L1 is a master regulator of piRNA biogenesis in mammals. As an essential germ cell−specific gene, mutations in human Mov10i1 are expected to cause male infertility. Thus, MOV10L1 may be a molecular target for male contraception.

28 AN ASSOCIATION BETWEEN THE GLUCOSE TRANSPORTER GLUT3 AND MALE INFERTILITY

Alexander W. Pastuszak, MD, PhD, Carolina Jorgez, PhD, Larry I. Lipshultz, MD and Dolores J. Lamb, PhD
Baylor College of Medicine
(Presented By: Alexander W. Pastuszak, MD, PhD)

Introduction: Approximately 15% of couples have fertility problems, with a 50% male factor contribution. In many of these men, a genetic cause is suspected. While numerous known genetic alterations cause male infertility, many other genetic etiologies likely exist. Glucose transporters (GLUTs) may be involved in sperm motility, though their role in this process is unclear and no genetic studies exist supporting a role for GLUTs in fertility. Here, we present data associating GLUT3 with male infertility.

Methods: Genomic DNA from 22 men with nonobstructive azoospermia (NOA) and normal Y−chromosome microdeletion and karyotype assays, as well as 4 fertile controls, was used for array comparative genomic hybridization (aCGH) to assess copy number variations (CNVs). Candidate fertility genes were selected based on 1) the frequency of CNVs in the gene, 2) the magnitude of the gain / loss, and 3) evidence supporting a role in male fertility. CNVs were validated using qPCR and candidate genes were sequenced. Immunohistochemical staining of testis sections used a rabbit polyclonal antibody against GLUT3 and standard protocols.
**ABSTRACTS**

**30**

**EXPRESSION OF SELECTED MICRORNAS LOCATED ON THE X CHROMOSOME IN KLINEFELTER SYNDROME**

Jennifer Reifsnyder, MD, Anna Mielnik, MS, Peter Schlegel, MD and Darius Paduch, MD, PhD
New York Presbyterian Hospital-Weill Cornell Medical Center
(Presented By: Jennifer Reifsnyder, MD)

**Introduction:** Epigenetic regulation of microRNA (miR) expression is a controversial, poorly understood area. MicroRNAs are short RNAs that are often differentially expressed in disease states. Many of the miRs expressed in the testis are located on the X chromosome. As one of the X chromosomes in Klinefelter syndrome (KS) patients undergoes epigenetic inactivation, we hypothesized that expression of X chromosome specific miRs in patients with KS and those with normal karyotype would be similar.

**Methods:** Total RNA was extracted from testicular tissue biopsied in five patients with confirmed Klinefelter syndrome (47,XXY karyotype) and 13 patients with confirmed normal karyotype (46,XY) and azoospermia. We performed miR profiling using real time quantitative polymerase chain reaction (RT–PCR). We compared expression of six miRs located on the X chromosome, and compared expression levels based on karyotype.

**Results:** Of the six miRs mapping to the X chromosome, only two (miR–508–5p and miR–509–3p) were differentially expressed between 47,XXY patients and 46,XY patients (miR–508–5p: 2.05 fold change, p = 0.03; miR–509–3p: 4.27 fold change, p = 0.01). Expression of both miR–508–5p and miR–509–3p was lower in KS patients relative to 46,XY patients. The other four miRs tested (miR–506, miR–508–3p, miR–509–3–5p, and miR–514a) demonstrated no significant difference in fold change in expression between normal and KS karyotypes.

**Conclusion:** We show that several miRs studied on the X chromosome undergo epigenetic regulation similar that of mRNA. However, miR–508–5p and miR–509–3p (members of the miR–506 gene family) seem to escape canonical principles of X chromosome inactivation as demonstrated by their lower expression. These findings suggest that the duplicate X chromosome in KS patients is not generating extraneous expression of miRs, and indirectly show that the duplicate X chromosome is inactive. Further studies are needed to elucidate possible molecular mechanisms of inactivation, as well as to further describe regulation of miR expression in male infertility.

**29**

**PATERNAL FACTORS IN EARLY EMBRYONIC DEVELOPMENT**

Manoj Kumar, MSc¹, Dipika Deka, MD², Vatsala Dadhwal, MD² and Rima Dada, PhD¹
¹Laboratory for Molecular Reproduction and Genetics, Department of Anatomy, All India Institute of Medical Sciences, New Delhi 110 029, India; ²Department of Obstetrics and Gynaecology, All India Institute of Medical Sciences, New Delhi 110 029, India
(Presented By: Manoj Kumar, MSc)

**Introduction:** Recurrent miscarriage (RM) or consecutive pregnancy loss before 20th week of gestation occurs in 1–5% women. RM is usually was seen as a mother’s problem but the developing knowledge shows the role of paternal contribution for the fetal loss. However it is still difficult to diagnose male partners who contribute to pregnancy loss with classical semen analysis. And there is need to establish other molecular diagnostic markers apart from DNA fragmentation index (DFI) which help in the best diagnosis of RM. Our objective is to study the role of sperm gene expression profile in idiopathic RM patients.

**Methods:** Total RNA was isolated from 24 male partners of RM couples and 24 male partners of healthy couples who have fathered healthy child and was reverse transcribed to cDNA. cDNA was amplified and quantified by qPCR and gene expression analysis was performed for TOMM7, RBM9 (RBFox2), RPS6, RPL10A, EIF5A, AKAP4, STAT4, Sox3, and FOXG1 genes.

**Results:** Sperm gene expression of TOMM7, RBM9, RPL10A and AKAP4 were up regulated around one fold, the genes FOXG1, SOX3 and STAT4 were up regulated more than one fold as compared to EIF5A and RPS6 in the male partners of iRM couples compared to the controls.

**Conclusion:** In this study we observed increase in the gene expression of genes which are important for normal fetal development. Future studies can help elucidating their functional importance and how they regulate the fetal development and their over expression leads to embryonic lethality and recurrent miscarriage.
ABSTRACTS

31 LIFETIME FOLATE DEFICIENCY AND SUPPLEMENTATION INDUCES ABERRANT SPERM DNA METHYLATION AND REPRODUCTIVE HEALTH

Lundi Ly, BSc¹, Donovan Chan¹, Mylene Landry¹, Nathalie Behan³, Amanda MacFarlane³ and Jacquetta Trasler⁴
¹Department of Human Genetics, McGill University, Montreal, QC, Canada; ²Research Institute of the McGill University Health Centre at the Montreal Children’s Hospital; ³Health Canada, Ottawa ON, Canada; ⁴Departments of Human Genetics, Pediatrics, and Pharmacology and Therapeutics, McGill University
(Presented By: Lundi Ly, BSc)

Introduction: Epigenetic modifications such as DNA methylation have an essential role in developmental programs. Recent evidence shows that embryos are highly sensitive to signals from the gametes and the environment. Furthermore, disruptions in gamete epigenetic reprogramming which occur primarily in prenatal development, are further associated with adult disease and transgenerational effects. The fetal period is the key to DNA methylation pattern acquisition in developing male germ cells and adequate supply of methyl donors is required. The folate cycle is involved in the production of methyl groups necessary for methylation reactions. Previous studies showed that either postnatal folate deficiency (FD) or supplementation (FS) groups necessary for methylation reactions. The main objective of this study was to determine if lifetime FS or FD induce an aberrant epigenetic landscape in germ cells detrimental to offspring health.

Methods: Female mice (F0; n=15) were placed on one of four amino acid controlled diets: a basal diet (FCD; 2mg folate/kg diet), a 20-fold folate supplemented diet (20FS), a 10-fold folate supplemented diet (10FS) or a 7-fold deficient diet (7FD). F0 females were mated to produce F1 litters whose germ cells were exposed to the folate diets at all stages of development. F1 males were weaned onto their respective prenatal diets. F2 and F3 litters, unexposed to the folate treatments, were subsequently generated. Tissues and organs of interest were collected, and genome-wide DNA methylation analysis by reduced representation bisulfite sequencing (RRBS) was performed.

Results: Despite no apparent health effects in the F1 males, F2 litters derived from 7FD and 20FS exposed sperm were significantly smaller than FCD F2 litters at weaning. Preliminary analysis of RRBS results from F1 sperm (n = 5) demonstrated that perinatal exposure to 7FD, 10FS, and 20FS diets resulted in 153, 132 and 114 differentially methylated (DM) loci, respectively. Affected regions included intergenic, intron, exon, promoter, 5’ and 3’ UTR sequences. Ingenuity Pathway Analysis of associated genes from DM loci implicated various affected pathways such as those involved in embryo development and cell cycle regulation.

Conclusion: These results suggest that lifetime FD and FS can impact sperm development and offspring health. DNA methylation changes in the sperm following these lifetime exposures offer a potential mechanism of action. (Supported by CIHR and CEEHRC).

32 IMPACT OF HIGH DOSE FOLATE SUPPLEMENTATION ON THE HUMAN AND MOUSE SPERM EPIGENOME

Mahmoud Aarabi, MD, PhD¹, Maria C. San Gabriel, PhD²,³, Donovan Chan, PhD⁴, Armand Zini, MD, PhD³, and Jacquetta Trasler, MD, PhD⁵
¹Department of Human Genetics, McGill University and Research Institute of the McGill University Health Centre at the Montreal Children’s Hospital, Montreal, QC; ²Division of Urology, Department of Surgery, McGill University; ³Research Institute of the McGill University Health Centre at the Royal Victoria Hospital, Montreal, QC; ⁴Research Institute of the McGill University Health Centre at the Montreal Children’s Hospital, Montreal, QC; ⁵Departments of Human Genetics, Pediatrics and Pharmacology & Therapeutics, McGill University and Research Institute of the McGill University Health Centre at the Montreal Children’s Hospital
(Presented By: Mahmoud Aarabi, MD, PhD)

Introduction: Supplementation with high doses of folic acid is widely used in clinics to improve the sperm parameters of infertile men. While dietary folate is a major source of methyl groups for epigenetic processes such as DNA methylation, little is known about the impact of high dose folate on the sperm epigenome and whether alterations can be transmitted to the offspring.

Methods: To address the epigenetic consequences of excess folate supplementation, semen and blood samples were collected from 30 men with idiopathic infertility who received 5mg/day of folic acid for 6 months at the McGill University Reproductive Centre and the Clinique OVO, Montreal, Quebec. Folate and hormone levels, semen parameters and the sperm epigenome were investigated before and after treatment. Germ line–specific differentially methylated regions of the imprinted genes H19, DLK1/GTL2, SNRPN, KCNQ1OT1, PLAGL1 and MEST were screened in sperm by pyrosequencing. A next generation sequencing–based method, reduced representation bisulfite sequencing (RRBS), was utilized to study over 3 million DNA methylation sites across the sperm epigenome. RRBS was also used to study the sperm epigenome in Balb/C mice (n=7) treated with high dose (20-fold control) or control folate diets for 12 months.

Results: Blood folate levels increased significantly following the supplementation period (P<0.0001). Sperm parameters and blood homocysteine, vitamin B12 and hormones remained unchanged. Neither infertility nor excess folate affected the methylation levels of imprinted loci. Interestingly, preliminary analysis of RRBS revealed slight but significant loss of methylation across genic and intergenic regions of sperm DNA in both human and mouse although some specific sites demonstrated gain of methylation. Ingenuity Pathway Analysis of differentially methylated sites suggested changes in methylation of genes involved in pathways related to cancer and developmental disorders.

Conclusion: Six month of folate supplementation in infertile men increases blood folate levels while sperm parameters and DNA methylation at imprinted loci remain unchanged. Unexpected loss of methylation across the sperm epigenome suggests the involvement of other factors such as folate metabolic pathways. We are now performing in-depth analysis as well as validation of the RRBS findings. Supported by Canadian Institutes of Health Research (CIHR).
33 THE IMPACT OF LEUKOCYTOSPERMIA ON CHROMATIN CONDENSATION, STRUCTURE INTEGRITY, DNA FRAGMENTATION AND CORRELATION WITH OTHER SPERM PARAMETERS
Ruben Burnazyan, MD, PhD and Mohamed Hammadeh, Prof
(Presented By: Ruben Burnazyan, MD, PhD)

Introduction: Infertility is a worldwide problem, affecting up to 8% of married couples and in some countries much more (WHO 2010). Male factors account for 20% – 50% of cases of infertility and in 25% of cases, the etiology of male infertility is unknown. (Jung, Seo 2014). In some patients infertility is presented on the background of normal conventional semen parameters: concentration, motility, morphology. In some cases the only disturbance, which been documented in semen was leukocytospermia. Infections/inflammations of the man genitourinary tract account rather high value −for approximately 9% of cases of male infertility and are associated with elevated seminal white blood cells (WBC)–leukocyte counts (Weidner et al.2013). DNA in sperm cells is packed heterogeneously. Peripheral portion of it (15%) is packed with histones and its inner core has a highly compact crystalline structure bound to protamines (Montellier et al.2013). So disturbances in nuclear condensation or changes in histone (H2B) to protamine ratio could lead to male infertility. And it is very advisible to evaluate sperm quality by investigating such parameters as DNA damage, abnormal nuclear packaging and nuclear decondensation in patients with leukocytospermia.

Methods: Semen was analyzed according WHO guidelines ,WBC (leukocytes) in semen were estimated by peroxidase method. Chromatin condensation assessment was performed, using chromomycin (CMA3) staining method (Bianchi et al.1993). Assesment of chromatin structure integrity was performed by modified Sperm Chromatin Structure Assay (mSCSA) after staining of smears with acridine orange. DNA fragmentation of spermatozoa was assessed using the TUNEL assay.

Results: The obtained results showed statistically significant correlation between MDA and WBC (p<0.001) and “round cells” (p=0.0084). Besides, a significantly positive correlation was found also between chromatin condensation (CMA3) of spermatozoa and sperm concentration (p=0.002), total and progressive motility (p=0.039), morphology (p=0.027) and vitality (p=0.019). DNA strand breaks (TUNEL) correlates not significantly, negatively with motility (p=0.600), vitality (p=0.467), and membrane integrity (p=0.105), but not with morphology and density.

Conclusion: Correlation between MDA and leukocytes as well as “round cells” points to an association of these cells and the induction of lipid peroxidation in sperm cells and may explain the decrease of the fertilizing potential of spermatozoa in infertile patients.

34 CAFFEINE AND MELATONIN SUPPLEMENTATION IMPROVES MOTILITY PARAMETERS AND MITOCHONDRIAL ACTIVITY IN POST-THAW SEMINAL SAMPLES: INITIAL REPORT
Juliana Pariz, MSc, PhD student¹,² and Jorge Hallak, MD, PhD¹,²
¹Androscience; ²Universidade de São Paulo
(Presented By: Juliana Pariz, MSc, PhD student)

Introduction: Although semen cryopreservation in an effective method, able to fertilize an oocyte and generate a healthy child, the damage it can impair the structural and functional integrity of spermatozoa. Our objective is to evaluate the effects of caffeine (CAF), a stimulant, and melatonin (MEL), an antioxidant, in motility and mitochondrial activity post−thaw semen samples.

Methods: Were selected seven semen samples of patients with infertility. As inclusion criteria, we consider only samples with total motility≥50%. After collection by masturbation, the samples were analyzed according to WHO criteria, processed and cryopreserved in liquid nitrogen with Test Yolk Buffer (1:1). Each sample was divided into four aliquots: Post-thaw (without supplementation), CAF (incubation for 15 minutes with CAF 2 mM after thawing), MEL (MEL 2 mM before cryopreservation) and CAF+MEL (MEL 2mM before cryopreservation and incubated for 15 min with CAF 2mM after thawing) groups. Were performed sperm motility analysis and mitochondrial activity by 3,3´−diaminobenzidine (DAB) method in all samples. We conducted ANOVA test of the means adopted and p <0.05.

Results: The cryopreservation method decreased seminal volume, total progressive motile sperm number, total motile sperm number, total sperm number and sperm concentration parameters of CAF, MEL and CAF+MEL groups when compared with fresh semen (p<0.001). There was a significant improvement of non−progressive motility, DAB I and DAB III parameters of CAF+MEL group when compared to other study groups, resembling the values of fresh semen.

Conclusion: In this initial study, we suggest that supplementation with caffeine and melatonin in cryopreserved semen samples improves motility parameters and mitochondrial activity and may contribute to future implementation in routine semen cryopreservation and assisted human reproduction procedures.
MD³ and Rima Dada, MD, PhD⁴
Swetasmita Mishra, MSc¹, Rajeev Kumar, MD², Neena Malhotra,
¹PhD Scholar; ²Department of Urology, AIIMS; ³Department of Obs.
& Gyn., AIIMS; ⁴Department of Anatomy
(Presented By: Swetasmita Mishra, MSc)

Introduction: Sperm DNA integrity is important for accurate transmission of genetic information to the offspring. There are different molecular factors that explain the origin and impact of sperm DNA damage. Telomeres are highly conserved hexameric repeats part of sperm DNA, which confer chromosome stability & maintain genomic integrity. Telomerase a reverse transcriptase maintain telomere length. As telomeres are Guanine rich repeats, they are highly prone to oxidative damage. Sperm transcript & DNA repair enzymes have a role in DNA integrity. So, this study was planned to evaluate seminal oxidative stress, sperm DNA damage, sperm telomere length & expression of DNA repair genes in infertile men.

Methods: The study included 112 infertile men and 53 controls. Reactive oxygen species estimation was done by chemiluminescence method. The average telomere length from the sperm DNA was measured using a quantitative Real Time PCR. 8−Hydroxy−2−deoxy−Guanosine level was assessed by Cayman’s ELISA kits. DFI was assessed by Sperm Chromatin Structure Assay (SCSA). Microarray of sperm transcript was done & genes selected were validated by real time PCR.

Results: The mean ROS was significantly elevated in cases (66.61±28.32 RLU/sec/million sperm) compared to controls (14.04±10.67 RLU/sec/million sperm). The 8−OHdG level in patients were 30.92±3.27 pg/ml and in controls 14.29±2.24 pg/ml. The mean DNA Fragmentation Index (DFI %) in patient was 36.11 ± 13.69 and in controls 24.17 ± 8.7. The mean telomere length was significantly lower in patient group (ROS>35) as compared to patient group (ROS<22) but it significantly increased in the patient group (ROS=22−35) as compared to patient group (ROS<22). 1077 genes were dysregulated from which 282 were up regulated &790 were down regulated.

Conclusion: In this study we found that in infertile patients oxidative stress leads to sperm DNA damage and telomere shortening. Elevated ROS levels lead to telomere shortening but seminal ROS to a particular level (ROS=22−35 RLU/sec/million sperm) are protective in maintaining telomere length. As an important pathway in the DNA damage repair network, genes of repair mechanisms also play a critical role in the maintenance of genome integrity.

36 INFERTILITYDB DATABASE: A UNIFIED POINT OF ACCESS TO KNOWLEDGE OF KNOCKOUT MOUSE MODELS OF MALE INFERTILITY
Burak Özkösem, PhD
Arizona State University
(Presented By: Burak Özkösem, PhD)

Introduction: The infertilityDB web portal (http://www.infertilitydb.org) is a brand−new and highly curated database dedicated to supporting reproductive biology research using the laboratory mouse model, a premier animal model for the study of genetic and genomic systems relevant to human biology and disease. This manually curated database provides the reproductive biology research community with a unified point of access to mutant mice and rich collection of related emerging and existing mouse phenotype data related to male infertility phenotype. Although several mouse databases have been established, no database has focused on infertility phenotypes. InfertilityDB has two subsections; male infertility and female infertility. International Mouse Phenotyping Consortium (IMPC) and the Mouse Genome Informatics (MGI) worldwide follow rigorous highly structured and standardized protocols for the experimentation, collection and dissemination of data, infertilityDB query into these databases to filter male and female infertility phenotypes.

Conclusion: Currently, there are 909 male infertility strains in infertilityDB, and only 525 strains of those were to be annotated from IMPC database and the rest from MGI database, indicating that queries in mega databases might not be cross talking efficiently. Inefficient cross talk between different mouse databases might be overcome via specific human disease phenom portals. Annotation with biomedical ontologies allows basic scientists and clinicians to easily find mouse strains with phenotypic traits relevant to their reproductive biology research. Data integration with other resources will provide insights into mammalian gene function and human reproductive health. As phenotype data become available for every gene in the mouse, the infertilityDB web portal will become an invaluable tool for reproductive biology researchers studying the genetic, epigenetic contributions of genes to human diseases.
Methods: We conducted a cross-sectional study at two tertiary care hospitals & fertility clinics in Mumbai, India and interviewed 100 male patients of both primary and secondary infertility. The study was approved by ethics committee of the hospitals. In-depth interviews were conducted and verbatim were transcribed. Thematic analysis was done to identify the most expressive and elaborative themes of the data and identified three major areas under which themes were clustered: 1) Individual level, 2) Couple relationship, 3) Financial impact.

Results: Knowing and accepting the infertility status was the toughest thing for men. Many of the respondents suggested creating awareness regarding infertility and its treatment among people. Some of them also suggested for managing separate male infertility section with a male doctor. The study also showed decreased sexual satisfaction and stress during sexual activity in few men while trying for the conception. In addition to these findings, men undergoing IUI/IVF with donor sperms expressed the fear of not having their biological child. One of the major concerns was exorbitant cost of treatments.

Conclusion: The study suggests that clinics/hospitals should provide proper information to men regarding treatment protocol & budget before starting the infertility treatment. It is necessary to provide counselling services at every stage of treatment to satisfy the queries and to control the anxiety of men who are undergoing infertility treatment.

---

ABSTRACTS

38 PROFILE DIAGNOSIS OF PATIENTS IN A PRIVATE SEMEN BANK
Artemis da Silva, BSc1,2, Juliana Pariz, MSc, PhD student1,2 and Jorge Hallak, MD, PhD1,2
1Androscience; 2Universidade de São Paulo
(Presented By: Artemis da Silva, BSc)

Introduction: Semen cryopreservation as fertility preservation method has been used in various situations, especially in cases where the individual has or will have progressive loss of fertility. Within a sperm bank is important to determine the profile of patients, so that the conduct of the healthcare team is more specialized. Objective: To determine the patients profile of a private semen bank and to compare seminal parameters of patients with different diagnoses.

Methods: Were included 132 samples of men aged 16 to 69, between 2000 and 2014, submitted to cryopreservation process. Collected samples were from ejaculate, parenchyma and epididymis fragments, and patients who did not sign the Informed Consent were excluded. Samples were classified into two groups: patients with cancer diagnoses (I) and patients who sought the clinic due to some andrological/urological situation (II). The means were compared between groups using T test for independent samples and adopted p<0.05.

Results: Group I consisted of 60 subjects with a mean age of 31.19 y.o. (±9.84). The main diagnostics in group I was testicular tumors (33%). Seventy-two patients, with 40.65 y.o. (±10.45) were included in group II. The main diagnostics were oligozoospermia (29.2%), vasectomy (22.2%) and azoospermia (18.1%). We observed that groups I and II have different profiles in pre-cryopreservation parameters, respectively: pH (7.80 vs. 9.8; p=0.056), total progressive motile sperm count (53.71 vs. 17.68; p<0.0019), total motile sperm count (104.91 vs. 32.53; p<0.009), total sperm count (160.90 vs. 63.15; p=0.033), sperm concentration (30.42 vs. 70.79; p <0.017), total motility (43.34 vs. 53.58; p<0.049), thus group II showed lower sperm quality when compared with group I. In post-thaw analysis, we observed statistical difference in motility grade B (10.40 vs. 5.97; p <0.042) between the groups.

Conclusion: Neoplasms, combined with immunosuppressive therapies and andrological/urological conditions associated with habits and lifestyle can reduce the male fertile potential. Semen quality after cryopreservation was similar, except motility grade B, suggesting that, regardless diagnosis of patient, cryopreservation seems to be effective. Thus, in an overview, we can conclude that fertility preservation option can be applied in various diagnostic and needs to be widely disseminated to the lay population and especially for the medical population specialized in oncology and other medical professionals.

39 WORLD HEALTH ORGANIZATION GUIDELINES AND ITS INFLUENCE IN CONDUCT OF VARICOCELE TREATMENT
Tábata Martins, BSc student1,2,3, Juliana Pariz, MSc, PhD student1,2 and Jorge Hallak, MD, PhD1,2
1Androscience; 2Universidade de São Paulo; 3Faculdades Metropolitanas Unidas
(Presented By: Tábata Martins, BSc student)

Introduction: Varicocele affects about 20% of the general population, and up to 40% of infertile men or sub-fertile. Surgical correction of varicocele, or varicocelectomy, is widely performed procedure in the treatment of male infertility, with significant improvement in motility and sperm morphology. The results of semen analysis are adopted as the main indicator for varicocelectomy. Objective: To verify the influence of reference values changes for semen analysis established by the World Health Organization (WHO) in conduct of varicocele treatment.

Methods: This retrospective study included infertile men (23–65 y.o.) of Andrology Clinic between the years 2000 and 2014, diagnosed with some degree of varicocele who underwent semen analysis according to the criteria of the World Health Organization (WHO 1999/2010). Patients with varicocele were included in the study group (n=77) and without varicocele composed the control group (n=30). The means of seminal parameters were compared between groups using the T test for independent samples and adopted p<0.05.

Results: When compared with control group, presence of varicocele had detrimental effects on sperm concentration (61.63 vs. 189.74 millions/ml; p<0.001), total sperm count (196.39 vs. 457.91 million/ejaculate; p<0.001), total motile sperm count (118.41 vs. 284.77 millions/ejaculate; p<0.001), total progressive motile sperm count and up to 40% of infertile men or sub-fertile. Surgical correction of varicocele, or varicocelectomy, is widely performed procedure in the treatment of male infertility, with significant improvement in motility and sperm morphology. The results of semen analysis are adopted as the main indicator for varicocelectomy. Objective: To verify the influence of reference values changes for semen analysis established by the World Health Organization (WHO) in conduct of varicocele treatment.

Methods: This retrospective study included infertile men (23–65 y.o.) of Andrology Clinic between the years 2000 and 2014, diagnosed with some degree of varicocele who underwent semen analysis according to the criteria of the World Health Organization (WHO 1999/2010). Patients with varicocele were included in the study group (n=77) and without varicocele composed the control group (n=30). The means of seminal parameters were compared between groups using the T test for independent samples and adopted p<0.05.

Results: When compared with control group, presence of varicocele had detrimental effects on sperm concentration (61.63 vs. 189.74 millions/ml; p<0.001), total sperm count (196.39 vs. 457.91 million/ejaculate; p<0.001), total motile sperm count (118.41 vs. 284.77 millions/ejaculate; p<0.001), total progressive motile sperm count
(47.49 vs. 124.85 millions/ejaculate; p<0.001), increase in non-progressive sperm (25.93 vs. 20.96%; p=0.044) and activity of enzyme Creatine Kinase (0.50 vs. 0.14 U/10^8; p=0.041). In addition, the differences of seminal analysis diagnosis in according WHO guidelines was illustrate in table 1.

**Conclusion:** New reference values published by WHO in 2010 are being questioned by the medical community. It is well established in the literature that varicocele is a factor of male infertility and the varicocelectomy should be indicated in cases of seminal changes. This procedure has a direct injury front changes the values of reference of the WHO, whereas patients who were referred for surgery in 1999 values, does not currently perform varicocelectomy.

### Table 1. Seminal analysis diagnosis frequency in according to 1999 and 2010 World Health Organization guidelines

<table>
<thead>
<tr>
<th>WHO</th>
<th>1999</th>
<th>2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normozoospermia</td>
<td>-</td>
<td>14.9%</td>
</tr>
<tr>
<td>Oligozoospermia</td>
<td>1.7%</td>
<td>5.8%</td>
</tr>
<tr>
<td>Asthenozoospermia</td>
<td>2.5%</td>
<td>21.5%</td>
</tr>
<tr>
<td>Teratozoospermia</td>
<td>17.4%</td>
<td>7.4%</td>
</tr>
<tr>
<td>Oligoasthenozoospermia</td>
<td>0.8%</td>
<td>8.2%</td>
</tr>
<tr>
<td>Oligoteratozoospermia</td>
<td>9.1%</td>
<td>9.1%</td>
</tr>
<tr>
<td>Asthenoteratozoospermia</td>
<td>42.1%</td>
<td>20.7%</td>
</tr>
<tr>
<td>Oligoasthenoteratozoospermia</td>
<td>28.1%</td>
<td>12.4%</td>
</tr>
</tbody>
</table>

**Results:** Flow cytometric analysis of normozoospermic and mTESE samples showed high frequencies of cells displaying a DNA content profile corresponding to diploid cells, which include somatic cells, spermatogonia as well as secondary spermatocytes. Two additional cell populations could be identified: a low percentage of cells showing DNA content corresponding to tetraploid cells (4N) which include primary spermatocytes and up to 15% haploid cells (1N) in mTESE tissue indicative of cells that have completed second meiosis (spermatids). High frequencies of haploid cells were detected in a significant proportion of samples where the embryologists failed to retrieve spermatozoa.

**Conclusion:** Flow cytometric analysis of DNA content can provide timely spermatogenesis status assessment and NOA diagnosis in mTESE cases. The detection of haploid cells in mTESE samples where the embryologists failed to retrieve spermatozoa suggests that a flow cytometry approach could improve the efficiency and success of finding gametes for ICSI. We plan to sort the haploid cells using PI or novel viable cell sorting markers and evaluate morphology and differentiation status.

### 41 THERAPEUTIC POTENTIAL OF MUCUNA PRURIENS (LINN.) ON ERECTILE DYSFUNCTION DUE TO SCHWANN CELL DAMAGE IN DORSAL NERVE OF PENIS INDUCED BY AGEING

Prakash Seppan, PhD, Ibrahim Muhammed, PhD, Karthik Ganesh Mohanraj, MSc, Ganesh Lakshmanan, MSc, Dinesh Premavathy, MSc, Sakti Jothi Muthu, MSc and Khayinmi Wungpam Shimray, MSc

**University of Madras**

(Presented By: Prakash Seppan, PhD)

**Introduction:** Erectile dysfunction (ED) can lead to poor quality of life in elderly population. One of the important factors behind ED is the loss of integrity in dorsal nerve of penis (DNP), affecting towards achieving and maintaining erection. Mucuna pruriens (M. pruriens), a leguminous plant identified for its properties like aphrodisiac and improving fertility, in Indian traditional medicine. Bioavailability and natural source of essential bioactive compounds in the seed of MP has been the motivating force for the design of this study. Objective: To analyze the therapeutic efficacy of M. pruriens on the structural and functional alterations of DNP in ageing in relation to penile erection, using Wistar albino rat

**Methods:** Grouping: Young (3 months), Aged (24−28 months), Aged+ M. pruriens and Young+ M. pruriens (ethanolic extract of the seed at dose of 200 mg/kg b.w for 60 days). Rats were subjected to hypo−thalamo−hypophysial−gonodal axis, nerve conduction velocity (NCV) and penile reflex. DNP processed for electron (EM) & light microscopic studies, nNOS and NADPH diaphorase. Osmium tetroxide stained slides were used for histometric analysis.
Results: Aged rats showed significant disturbance in hypo-thalamo-hypophysial-gonodal axis, degenerative changes in DNP includes demyelination, reduced diameter and number of myelinated fibres and in EM study, vacuolation and indentation of the myelin sheath and Schwann cells degeneration were seen. nNOS and the cofactor (NADPH diaphorase) were reduced along with low levels of antioxidants. NCV was slow in aged rats and concomitant poor penile reflex. These pathological changes were remarkably reduced or recovered in M.pruriens treated aged rats. No pathology was seen in Young+M.pruriens.

Conclusion: Schwann cells degeneration plays crucial role in ED in ageing (reflexogenic erections) and its involvement in nitricergic/neuroparaxial degenerations. Significant reduction or recovery in DNP after M.pruriens treatment indicates the therapeutic potential of extract related with increased antioxidants level or reduced oxidative stress and possible remyelination by androgenic potential, indicative of neural androgen receptor as a promising therapeutic target for myelin repair.

---

42

IMPROVEMENTS IN PATIENT REPORTED SEXUAL FUNCTION AFTER MICROSURGICAL VARICOCELECTOMY

Bobby Najari, MD, Leonard Introna and Darius Paduch, MD, PhD
Weill Cornell Medical College
(Presented By: Bobby Najari, MD)

Introduction: Varicocelectomy improves semen analysis parameters and serum testosterone. Men presenting with infertility and or low testosterone often report erectile dysfunction as well, however limited data exists about effects of varicocelectomy on sexual function. We hypothesized that varicocelectomy improves both serum testosterone and sexual function, as assessed by the Male Sexual Health Questionnaire (MSHQ).

Methods: A retrospective chart review of patients who have undergone varicocelectomy and had both pre- and post-operative MSHQ was performed. The MSHQ is a clinically validated questionnaire that assesses erectile function, ejaculatory function, and sexual satisfaction, with higher scores indicating better function. Clinical parameters pre and post–varicocelectomy were compared with paired t−test. All repairs were performed using microsurgical subinguinal approach with operating microscope by same surgeon (DAP).

Results: Twenty−five patients met study criteria. Twelve patients (50%) presented for infertility, and the remaining 13 had symptomatic varicocele associated with hypogonadism. Average post−surgical follow up was 18.8 ±10.6 months. Baseline characteristics are presented in Table 1. Significant improvements in the total MSHQ score (4.0 ±8.4, p=0.041), the MSHQ erectile function (1.5 ±2.8, p=0.012), and the MSHQ ejaculatory function (1.9 ±3.9, p=0.033) domains were seen. Eleven (44%) men saw improvement in their erectile function and 14 (56%) saw improvement in ejaculatory function. The improvement in serum testosterone was also significant (177.5 ±226.9, 0.009). Eleven (44%) men saw improvement in their erectile function and 14 (56%) saw improvement in ejaculatory function. The improvement in serum testosterone was also significant.

Conclusion: Microsurgical repair of varicocele not only improves testosterone, but also improves patient reported erectile and ejaculatory function. Patients can confidently be counseled that varicocelectomy has the potential to improve sexual function along with serum testosterone.

43

HIGH PREVALENCE OF ERECTILE AND EJACULATORY DYSFUNCTION IN MEN WITH OPIOID INDUCED ANDROGEN DEFICIENCY

Bobby Najari, MD¹, Matthew Wosnitzer, MD², Peter Schlegel, MD¹ and Darius Paduch, MD, PhD¹
¹Weill Cornell Medical College; ²Northeast Medical Group - Yale New Haven Health
(Presented By: Bobby Najari, MD)

Introduction: Chronic use of opioids suppresses GnRH secretion, which can result in hypogonadotropic hypogonadism in many men with chronic pain. While the high prevalence of low testosterone has been described in this population, literature on patient reported outcomes of erectile and ejaculatory dysfunction is lacking.

Methods: Sixteen men with chronic opioid use seeking treatment for symptoms of hypogonadism were enrolled in this study. All men had been using opioids for >6 months of chronic pain of non−malignant etiology. Men were assessed for hypogonadism with the Androgen Deficiency in the Aging Male (ADAM) questionnaire and a serum testosterone measured twice before 11AM. Subjects also filled out validated questionnaires for erectile and ejaculatory dysfunction: the Sexual Health Inventory for Men (SHIM) and Male Sexual Health Questionnaire Short Form for Ejaculatory Dysfunction (MSHQ−EjD).
Results: The mean ±SD age of the men was 53.6 ±8.2 years. Sixteen (100%) of the men had a positive ADAM questionnaire, with an average of 8.3 ±1.7 positive responses out the ten questions. Thirteen men (81%) had two serum AM testosterone <300 ng/dL, with an average of 191.0 ±76.9 ng/dL. The luteinizing hormone for the hypogonadal patients was 2.55 ±1.64 IU/mL, all consistent with hypogonadotropic hypogonadism. The average SHIM score was 14.3 ±6.8, with only 4/13 (31%) having no or mild erectile function. The mean MSHQ–EjD score was 6.4 ±3.5 (possible range 1–15, higher is better), with an average MSHQ bother score of 2.7 ±1.8 (on Likert scale 0–5, higher is more bother). Eight (50%) of men experienced ejaculatory dysfunction at least half time, and nine (56%) men were at least moderately bothered by their symptoms. While the MSHQ bother score did correlate inversely with the SHIM (r=−0.61, p=0.026), some two (13%) men experienced ejaculatory dysfunction despite preserved erectile function.

Conclusion: Opioid induced androgen deficiency is common in men with symptoms of hypogonadism using chronic opioids. Erectile dysfunction and ejaculatory dysfunction are commonly noted in these men. However, querying men for erectile dysfunction alone may miss significant ejaculatory dysfunction in this population.

44 EFFECT OF AQUEOUS CISSAMELOS CAPENSIS EXTRACT ON PROSTATE CANCER, LEYDIG AND SERTOLI CELL FUNCTION
Keenau Pearce, MSc¹, Donavon Hiss, PhD², Frans Weitz, MSc¹, Uta-Christina, Hipler PhD², Cornelia Wiegand, PhD² and Ralf Henkel, PhD¹
¹University of the Western Cape; ²University of Jena
(Presented By: Ralf Henkel, PhD)

Introduction: In Africa, 80% of the population depends on traditional remedies for their primary health care. Cissampelos capensis is a widely used medicinal plant in South Africa that is a rich source of different alkaloids. Traditionally, this plant is used to treat diabetes, menstrual cramps, pain and different types of cancer. Since no scientifically documented information concerning the efficacy of C. capensis on normal testicular function or its use as an anti-cancer agent are available, this study aimed to investigate these aspects using the TM3 Leydig and TM4 Sertoli cell lines, and the prostate cancer cell line LNCaP.

Methods: TM3 Leydig cells, TM4 Sertoli cells and LNCaP prostate cancer cells were cultured under standard conditions in a mixture of 50% DMEM and 50% Ham’s F–12 medium supplemented with 2.5% FBS and 5% Horse serum, and RPMI–1640 medium, respectively, and were exposed to concentrations ranging from 0.001–1000µg/ml of an aqueous extract of C. capensis over 24 and 96 hours, after which the XTT assay was performed to. LNCaP cells were cultured without and with 1000 nM testosterone. The effect on testosterone production in Leydig cells was determined with standard ELISA technique.

Results: Cell viability showed a significant change in TM3 cells at 1000µg/ml over 24–hours, while changes were found at concentrations higher than 100µg/ml after 96–hours. TM4 cells showed a significant change in cell viability at 1000µg/ml over 24–hours, along with changes at concentrations greater than 10µg/ml over 96–hours. Over both 24 and 96–hour incubations, C. capensis produced no biologically significant change in testosterone production in Leydig cells and when used in the presence of testosterone, increased the effectiveness of the extract.

Conclusion: C. capensis produces no observable negative effects towards Leydig and Sertoli cell function and shows no potential for an androgen replacement therapy. However, it might have the potential to prevent the formation of prostate cancer or slowing the progression of prostate cancer. The latter feature might be possible in conjunction with other therapy options as this plant might cause a decrease in the therapeutic concentrations to be used.

45 RAPID METHOD FOR THE ISOLATION OF SPERM DNA
Haotian Wu, Matthew de Gannes, Gianna Luchetti and J. Richard Pilsner
Department of Environmental Health Sciences, UMass Amherst
(Presented By: Haotian Wu)

Introduction: There is a growing interest in elucidating the role of sperm epigenetics and genetics on reproductive success and the trajectory of health outcomes over the lifecourse. However, the condensed nucleus of sperm is resistant to lysis by buffers from commercially available column-based DNA purification kits due to the formation of disulfide bridges between protamines. Our objective was to develop a rapid method for extracting high quality DNA from human sperm for downstream DNA methylation and genetic analyses.

Methods: Sperm from semen samples provided by three human volunteers were isolated and homogenized in the presence of a commercially-available guanidine thiocyanate lysis buffer supplemented with different reducing agents. After homogenization, sperm DNA were extracted using silica-based column kits. DNA methylation analyses of imprinted loci were assessed using the MassARRAY platform (Sequenom).

Results: Our method resulted in yields > 90% of high quality DNA using three different commercially available spin kits. DNA yields did not differ between immediate extraction (2.84 ± 0.04 pg/cell) and after four weeks of homogenate storage at 4°C (2.91 ± 0.13 pg/cell). DNA methylation analyses revealed similar methylation levels at baseline and 4 weeks of storage for the imprinted loci: SNURF (3.5% ± 0.7% and 2.6% ± 1%), PEG10 (3.7% ± 1.8% and 6.9% ± 3.2%), and H19 (94.1% ± 0.1% and 92.2% ± 1.9%).

Conclusion: Our room temperature homogenization protocol resulted in > 90% yield of high quality sperm DNA extracted by user-preferred silica-based spin columns. Our homogenization method produces stable nucleic acids to allow for optional storage of homogenate for future DNA extraction. This method is also amendable for sperm DNA extraction of other mammalian species and RNA extraction using a previously published protocol. Together, our improved method has important implications for research in clinical settings where sample processing constraints likely exist.

46 – WITHDRAWN
ASSOCIATION BETWEEN PROSTATE–SPECIFIC ANTIGEN AND BIOMARKERS OF SUBCLINICAL SYSTEMIC INFLAMMATION IN MIDDLE–AGE HEALTHY MEN FROM THE GENERAL POPULATION

Saad Elzanaty, MD, PhD, Babak Rezanezhad, MD, Ronnie Willenheimer, MD, PhD and Rasmus Borgquist, MD, PhD
(Presented By: Saad Elzanaty, MD, PhD)

Introduction: To determine the association between PSA and biomarkers of subclinical systemic inflammation based on data from 119 middle-age healthy men from the general population.

Methods: Serum levels of PSA and biomarkers of systemic inflammation (CRP and fibrinogen) were measured. Demographic data were also collected. Subjects were divided into two groups according to PSA levels: < 2 µg/L and ≥ 2 µg/L.

Results: The mean (SD) age of men was 55±4.0 years. We found a positive significant correlation between PSA and fibrinogen (r = 0.20, p = 0.04), and between CRP and fibrinogen (r = 0.60, p = <0.001). On the other hand, no significant correlation between PSA and CRP was found. Men with PSA values ≥ 2 µg/L had a significant higher levels of fibrinogen as compared to those with PSA < 2 µg/L (2.9 g/L vs. 2.0 g/L, p = 0.01). In a multivariate regression analysis model adjusted for age, BMI, marital status, smoking, snuff, and alcohol intake with serum levels of PSA as dependent variable, serum level of fibrinogen predicted higher PSA-values (odds ratio = 3.30, 95 % CI = 1.05−10.20, p = 0.04).

Conclusion: The present results indicate that biomarkers of subclinical systemic inflammation are associated with elevated levels of PSA among healthy men from the general population. Further investigations are warranted in order to elucidate how this information could be applied in the daily clinical practice.

DO FAMILY MEMBERS OF INFERTILE MEN HAVE AN INCREASED RISK OF CANCER?

Ross Anderson, MD, MCR¹, Heidi Hanson, PhD², Mitchell Bassett, MD¹, Chong Zhang, MS³, Angela Presson, PhD¹, Kenneth Aston, PhD³, William Lowrance, MD, MPH⁴, Douglas Carrell, PhD⁵, Ken Smith, PhD⁶ and James Hotaling, MD, MS⁷
¹University of Utah; ²St Mary’s Hospital Center; ³University of Utah, Department of Family and Preventive Medicine, Huntsman Cancer Institute; ⁴University of Utah, Department of Family and Preventive Medicine; ⁵University of Utah, Department of Family and Preventive Medicine; ⁶University of Utah, Department of Surgery, Andrology and IVF Laboratories; ⁷University of Utah, Department of Surgery, Huntsman Cancer Institute; ⁸University of Utah, Department of Surgery, Director of IVF and Andrology Laboratories; ⁹University of Utah, Population Sciences, Huntsman Cancer Institute
(Presented By: Ross Anderson, MD, MCR)

Introduction: Male factor infertility is associated with an increased risk of genitourinary cancers. We sought to investigate if this risk of specific cancers extends beyond the men to their first-degree relatives. We hypothesized that family members of men with reduced sperm quality would have an increased risk of site-specific cancers.

Methods: We linked the University of Utah and Intermountain Healthcare semen analysis database with the Utah Population Database (UPDB), a multi-generational epidemiological database, which provides demographic, pedigree and medical information on over 7 million individuals. State death certificate data and the Utah and Idaho Cancer Registries identified cancer diagnoses. We stratified our semen analysis cohort by sperm count: azoospermia, cryptozoospermia (<0.5m/mL), oligozoospermia (<20m/mL), normozoospermia (>20m/mL), and hyperzoospermia (>100m/mL). First–degree relatives comprised siblings or parents, and only those family members with complete UPDB information were included. Cox models were run separately by gender, stratified by birth year, and adjusted for familial clustering.

Results: 24,732 men with 63,433 first–degree relatives underwent semen analysis between 1996 and 2014. The top 5 cancers diagnosed in the relatives of men undergoing semen analyses were: prostate (761), breast (683), melanoma (452), thyroid (184), and cervical (150). For female relatives of azoospermic men, there is a two-fold increase in thyroid cancer (HR=2.07, p=0.023), and test for trend showed a significant inverse relationship between thyroid cancer risk and sperm quality (HR=0.80, p=0.005). There is suggestive evidence that relatives of azoospermic men have a decreased risk of melanoma (HR=0.35, p=0.07). There was no significant difference in the risk of site–specific cancers we investigated in the family members of men with low sperm counts. We also considered the risk of cancer for siblings and parents separately, and the results do not substantively change.

Conclusion: This cohort of men with semen analyses linked with generations of population health data is the largest US study of its kind. We found that lower sperm quality is associated with higher rates of thyroid cancer in first–degree female relatives and possibly lower rates of melanoma. Sperm quality is not associated with increased risk of prostate or the other site–specific cancers we investigated, at least in first–degree relatives.

EFFECT OF SPERM DNA DAMAGE ON ART OUTCOMES: A SYSTEMATIC REVIEW AND META–ANALYSIS

Luke Simon, PhD¹, Armand Zini, MD² and Douglas Carrell, PhD¹
¹University of Utah; ²St Mary’s Hospital Center
(Presented By: Luke Simon, PhD)

Introduction: Sperm DNA damage is prevalent amongst infertile men and is known to influence natural reproduction. However, the impact of sperm DNA damage on assisted reproduction (AR) outcomes remains controversial. The purpose of this study is to further evaluate the relationship between sperm DNA damage and ART outcomes by systematic review and meta–analysis.

Methods: We conducted a systematic review and meta–analysis of studies on sperm DNA damage (assessed by SCSA, TUNEL, SCD or Comet assay) and fertilization rate, embryo quality and clinical pregnancy after IVF and/or ICSI treatment.
RESULTS: We identified all relevant papers published until April 2014 from MEDLINE, EMBASE, and PUBMED database searches for the systematic review. Two–by–two tables were constructed and odds ratios (ORs) were derived from 56 estimates of clinical pregnancy. These studies measured DNA damage (by one of 4 assays: 23 SCSA, 18 TUNEL, 8 SCD and 7 Comet) and included a total of 8,068 treatment cycles (3,734 IVF, 2,282 ICSI and 2,052 mixed IVF+ICSI). The combined OR of 1.68 (95% CI, 1.49–1.89; p<0.0001) indicates that sperm DNA damage is predictive of clinical pregnancy following IVF and/or ICSI. Moreover, the combined OR estimates of IVF (16 estimates, OR =1.65; 95%CI, 1.34–2.04; p<0.0001), ICSI (24 estimates, OR = 1.31; 95% CI, 1.08–1.59; P=0.0068) and mixed IVF+ICSI studies (16 estimates, OR = 2.37; 95% CI, 1.89–2.97; p<0.0001) were also highly significant. Our systematic review demonstrated that sperm DNA damage has an adverse impact on fertilization rate and embryo quality in 38% and 36% of the evaluable studies, respectively.

CONCLUSION: This systematic review and meta–analysis is the first to demonstrate that sperm DNA damage is predictive of clinical pregnancy following IVF and/or ICSI. The data are strong enough to justify the clinical application of sperm DNA testing in the context of IVF and ICSI. These data also provide a rationale for conducting further research aimed at evaluating the underlying mechanism(s) responsible for the effect of sperm DNA damage on IVF and ICSI pregnancy outcomes.

50 SPERM CHROMATIN QUALITY ASSESSMENT: OPTIMIZATION OF THE HIGH THROUGHPUT COMET ASSAY
Océane Albert, PhD¹, Robert G. Berger, PhD¹, Wolfgang Reintsch, PhD¹, Barbara F. Hales, PhD¹ and Bernard Robaire, PhD²
¹Department of Pharmacology & Therapeutics, McGill University, Montreal, QC, Canada; ²Departments of Pharmacology & Therapeutics and of Obstetrics & Gynecology, McGill University, Montreal, QC, Canada
(Presented By: Océane Albert, PhD)

INTRODUCTION: Various agents, including physical or chemotherapeutic agents, irradiation, or xenobiotics, can put human sperm DNA integrity at risk, echoing the growing concern about male fertility. To date, the standard semen parameters used to assess fertility, as described by the World Health Organization, do not include any information about the quality of sperm nuclear material. However, a number of studies show that there is sperm DNA damage in men with apparently normal standard semen parameters, and that this damage can imperil the outcome of pregnancy. The COMET assay (single cell gel electrophoresis) involves the collection of data on sperm DNA damage at the level of the single cell, allowing the use of samples from severe oligospermic patients. However, this particularity makes comet scoring a low throughput procedure that renders large cohort analyses tedious. Our objective is to develop a standardized high throughput COMET assay for human sperm that will increase both its accuracy and efficiency.

METHODS: The assay we have developed includes (i) automated mixing and distribution of sperm and low melting point agarose on a 96–well plate by the Janus® workstation, to ensure evenness across the plate and avoid artificial DNA damage trends; (ii) optimized cell lysis and DNA decondensation treatment parameters for human sperm; (iii) optimal horizontal electrophoresis conditions; (iv) automated detection of SYBR gold stained comets by the Operetta® high content imaging system; and (v) automated scoring of comets by the Columbus™ image data analysis system that comprises assessment of typical comet criteria (% DNA in the tail, tail length and tail extent moment) and that compares to the broadly used Komet™ software.

RESULTS: This standardized high throughput COMET assay offers many advantages compared to the classical 2–well COMET, including higher accuracy and evenness due to automation of sensitive steps, a decrease of up to 90% in overall experimental time, and a 144 fold increase in sample analysis power.

CONCLUSION: Hence, this assay constitutes a more efficient option to assess sperm chromatin quality, and paves the way to using this assay to screen large cohorts.


51 ROLE OF SPERM THIOLS’ REDOX STATUS IN KEEPING RAT SPERM QUIESCENT IN CAUDA EPIDIDYMIS
Santosh Yadav, PhD, Lokesh Kumar, MSc, Aastha Pandey, MSc, Bhavana Kushwaha, MSc, Jagdamba Maikhuri, PhD and Gopal Gupta, PhD
CSIR-Central Drug Research Institute, Lucknow, UP, India
(Presented By: Santosh Yadav, PhD)

INTRODUCTION: The sperm require energy-intensive motility to reach the female gamete for delivering the male genome. This energy is conserved by keeping the sperm quiescent in cauda epididymis before ejaculation. A variety of mechanisms have been proposed to explain the activation of mammalian sperm motility at ejaculation, however the molecular mechanisms controlling this process remain an enigma. Cauda sperm produce H2O2 and we have made an attempt to study the redox regulation of sperm motility in conjunction with other factors.

METHODS: Quiescent and motile sperm were collected from Sprague Dawley rat cauda epididymis and experimented in vitro. Care was taken to prevent motility initiation of quiescent sperm on isolation from epididymis.

RESULTS: The quantitative estimation of free thiols showed that motile rat sperm present about 2-fold free thiols than quiescent sperm. Caudal sperm failed to initiate motility in presence of 0.1% sulfhydryl–alkylating N-ethylmaleimide (NEM), and when applied vaginally before mating 50 mg NEM prevented pregnancy in rabbits. Motile sperm quickly lost motility when placed in 0.1% H2O2, while quiescent sperm did not initiate any motility in 3% H2O2. Caudal sperm remained immotile at pH 4.0, and between pH 4 and 6.5 the motility ranged from zero to control level. Caudal sperm could initiate appreciable motility in a gel of viscosity equal to caudal semen (82 cP).

CONCLUSION: Besides low pH and caudal fluid viscosity, redox status of thiols plays a crucial role in rat sperm quiescence and motility initiation.
52
ENERGY METABOLISM OF QUIESCENT SPERM IN CAUDA EPIDIDYMIS OF RAT
Lokesh Kumar, MSc, Santosh Yadav, PhD, Vikas Verma, MSc, Aastha Pandey, MSc, Bhavna Kushwaha, MSc, Vikas Sharma, MSc, Jagdamba Maikhuri, PhD and Gopal Gupta, PhD
CSIR-Central Drug Research Institute, Lucknow, UP, India
(Submitted By: Lokesh Kumar, MSc)

Introduction: Mature mammalian spermatozoa are held quiescent in the cauda epididymis to conserve energy. While the energy metabolism of motile sperm has been studied well, little is known about the energy metabolism of quiescent sperm, especially the changes associated with motility initiation. We hypothesize that during the quiescent state, sperm may have a different mode of energy generation as the energy requirement is very low, in comparison to motile sperm.

Methods: Motile and quiescent rat sperm were isolated from rat cauda epididymis. Care was taken to prevent any motility activation in quiescent sperm sample. All studies were conducted in vitro.

Results: Motility initiation of caudal sperm in rat was associated with 1.5 to 2 fold increase in activities of the rate limiting enzymes of glycolysis along with an increased expression of HIF−1. Motility activation also increased expression of HSP70 and phosphorylation of MAPK/ERK in sperm. Active pAMPK was associated chiefly with quiescent sperm and was mostly dephosphorylated in the motile rat sperm.

Conclusion: Quiescent sperm are at a low energy level with high AMP activity indicating high AMP:ATP ratio, which may drive sperm to use oxidative metabolism for ATP generation. A rapid drop in redox potential of sperm thiols on motility initiation (unpublished observations) coincides with the activation of MAPK−ERK pathway, activating (by phosphorylation) a number of enzymes including those of energy metabolism. The high energy demand of motile sperm creates hypoxic condition which increases HIF−1 and HSP−70 expression and apparently shifts energy metabolism towards glycolysis.

53
CRYOPRESERVATION OF SPERMATOZOA: DO PERMEABLE CRYOPROTECTANTS IMPROVE MOTILE SPERM YIELDS?
Cigdem Tanrikut, MD, Jie Liu, PhD, Diane Wright, PhD, Gloria Lee, MA, Mehmet Toner, PhD and Thomas Toth, MD
Massachusetts General Hospital
(Submitted By: Cigdem Tanrikut, MD)

Introduction: Preserving sperm while maintaining adequate post−thaw motility remains a challenge in patients with severe male factor infertility. This study sought to assess whether: 1) a permeable cryoprotectant yields better results than the non−permeable cryoprotectant, trehalose, and 2) the combination of trehalose and a permeable cryoprotectant improves post thaw sperm motility.

Methods: Motile sperm were isolated from fresh ejaculates of 10 healthy men using a density gradient. Two to three repeats per sample per treatment were applied. In part 1, 7 different freezing media were compared, made up of human tubal fluid (HTF), 5% human serum albumin (HSA) and one of the following: 5% 1,2−propanediol (PrOH), 5% glycerol, 5% dimethy sulfoxide (DMSO), 10% PrOH, 10% glycerol, 10% DMSO, or 0.25M trehalose. Aliquots of sperm were mixed 1:1 with freezing medium then loaded into a 200 µm silica capillary. The capillary was incubated in liquid nitrogen (LN2) vapor for 5 minutes then lowered into LN2 and stored. To thaw, each capillary was quickly immersed in a room temperature water bath. Capillary contents were expelled into a drop of 12 µl HTF with 5% HSA on a glass slide, then covered by a coverslip and sperm motility was examined.

In part 2, 10 different media were compared. Baseline medium was HTF supplemented with 5% HSA and 0.25M trehalose, and the others were baseline with: 2.5% PrOH, 2.5% glycerol, 2.5% DMSO, 5% PrOH, 5% glycerol, 5% DMSO, 10% PrOH, 10% glycerol, or 10% DMSO. The same vitrification was performed. One−way ANOVA was used to compare group means. Differences were considered significant at P < 0.05.

Results: For the 7 freezing media in part 1, recovered sperm motility (post thaw motility/pre−freeze motility × 100%) was 36.7%, 42.8%, 43.3%, 22.2%, 43.8%, 46.2%, and 63.6%, respectively. Samples containing 0.25M trehalose achieved the greatest recovered motility. For the 10 media in part 2, recovered sperm motility was 70.3%, 58.7%, 73.5%, 74.7%, 49.2%, 64.2%, 66.0%, 33.3%, 64.8%, and 65.3%, respectively. The media composed of 0.25M trehalose, 0.25M trehalose with 2.5% glycerol, and 0.25M trehalose with 2.5% DMSO had the highest rates of recovered motility without significant differences among them.

Conclusions: PrOH, glycerol, or DMSO alone was not as effective as 0.25M trehalose in preserving sperm motility. Adding 2.5% glycerol or DMSO to a medium containing 0.25M trehalose did not significantly improve sperm motility.

54
THE IMPACT OF OXIDATIVE STRESS ON CHAPERONE−MEDIATED HUMAN SPERM−EGG INTERACTION
Brett Nixon, Elizabeth Bromfield, BBiotechnology (Hons) and R. John Aitken, BSc, MSc, PhD
The University of Newcastle
(Submitted By: Brett Nixon)

Introduction: An inability to bind to the zona pellucida (ZP) is commonly encountered in the defective spermatozoa generated by male infertility patients; however, the underlying mechanisms remain unresolved. Recent studies have revealed that ZP−binding is mediated by molecular chaperones, particularly HSPA2, that facilitate the formation of multimeric zona pellucida (ZP)−receptor complexes on the surface of mammalian spermatozoa during capacitation. Given the well−established link between oxidative stress and male−factor infertility, we sought to determine whether such stress might impair sperm function by dysregulating the expression of ZP receptor complexes on the sperm surface.

Methods: For the purpose of this study, low levels of oxidative stress were induced in populations of human spermatozoa by treatment with 4−hydroxynonenal (4HNE) or hydrogen peroxide (H2O2).
55 LOWER SEMEN QUALITY AS A MARKER FOR INCREASED FAMILIAL MORTALITY
Mitchell Bassett, MD¹, Heidi Hanson, PhD², Ross Anderson, MD, MCR³, Kenneth Aston, PhD¹, Douglas Carrell, PhD³, Ken Smith, PhD³ and James Hotaling, MD²
¹University of Utah, Department of Surgery, Division of Urology; ²University of Utah, Department of Family and Preventive Medicine, Population Sciences, Huntsman Cancer Institute; ³University of Utah, Department of Surgery, Director of IVF and Andrology Laboratories; ²University of Utah, Population Sciences, Huntsman Cancer Institute
(Presented By: Mitchell Bassett, MD)

Introduction: Poor semen quality has been linked to increased mortality and disease burden in the infertile male. In order to determine if this association extends to relatives, we investigated the relationship between semen quality and mortality in first-degree relatives of men with poor sperm quality.

Methods: We identified 24,732 men with semen analyses between 1996–2014 at the University of Utah Health Sciences Center or Intermountain Healthcare linked to the Utah Population Database (UPDB). The UPDB is a comprehensive genealogical and epidemiological database, containing over 7 million individuals dating back to the 19th century. Men were grouped as azoospermic, cryptozoospermic (<0.5m/mL), oligozoospermic (<20m/mL), normozoospermic (20m/mL) or hyperzoospermic (>100m/mL). All first-degree relatives of these men with complete information were assigned an exposure group based on the semen quality of the male relative. Cox models were used to test for mortality of relatives by semen quality of tested men. All models were gender-specific and stratified by birth year and adjusted for familial clustering of observations.

Results: Male first degree relatives of azoospermic men have a 25% increase (HR=1.25, p=0.01) in mortality compared to relatives of normozoospermic men (control group). In addition, relatives of hyperzoospermic men have lower mortality (HR=0.91, p=0.02). A test for trend showed that there is an inverse relationship between mortality and sperm concentration levels (HR=0.93, p=0.0001). First-degree male relatives of azoospermic and oligozoospermic men have elevated rates of cardiovascular related mortality (HR=1.52, p=0.02; HR=1.38, p=0.005, respectively). First degree female relatives of azoospermic and oligozoospermic men have elevated rates of mortality caused by congenital malformation (HR=2.4, p=0.07; HR=2.0, p=0.02, respectively).

Conclusion: We find evidence of increased mortality for first degree relatives of men with poor sperm quality, however more research is necessary to understand the familial nature of this association and if it extends to 2nd and 3rd degree relatives.
57 AUTOMATIC SPERM TRACKING AND ANALYSIS OF SWIMMING PATTERN TRANSITIONS
Leonardo Urbano, PhD1, Puneet Masson, MD2, Matthew VerMilyea, PhD2 and Moshe Kam, PhD3
1Drexel University; 2Penn Fertility Care, Hospital of the University of Pennsylvania; 3College of Engineering, New Jersey Institute of Technology
(Presented By: Leonardo Urbano, PhD)

Introduction: Our objective is to develop a fully automated sperm tracking algorithm for analyzing the transitions between sperm swimming patterns over time and with minimal operator intervention. Understanding how and why individual sperm swimming patterns change over time is of significant interest to researchers studying sperm motility and to medical practitioners evaluating male infertility. A single sperm may transition between a number of different progressive and non-progressive swimming patterns, including linear, meandering, circular, and hyperactivated, and may stop swimming and restart again. Analysis of swimming transitions is difficult using today’s computer-assisted semen analysis (CASA) instruments, which require significant user intervention to track sperm swimming in close proximity, or whose paths apparently collide. Similar problems have been addressed by modern target tracking algorithms originally developed for radar and video processing, and their methods can be used for sperm tracking and analysis.

Methods: Videos of 10 washed sperm samples were recorded and digitized at 200x magnification at 15 frames per second. A custom-made MATLAB program was developed to automatically detect sperm in recorded video frames and perform multi-sperm tracking. A joint probabilistic data association (JPDA) filter was used to de-conflict sperm tracks during apparent cell-to-cell collisions.

Results: Sperm motility parameters, including curvilinear velocity (VCL), straight-line velocity (VSL), linearity (LIN), average velocity (VAP), straightness (STR), wobble (WOB), mean angular displacement (MAD), and amplitude of lateral head displacement (ALH) were calculated for each sperm tracked. These parameters changed abruptly at the onset of swimming transitions. For example, VCL and ALH typically decreased in sperm transitioning from linear to non-progressive swimming.

Conclusion: The JPDA algorithm was effective at tracking simultaneously hundreds of sperm through apparent collisions while calculating a host of sperm motility parameters, enabling analysis of transitions between sperm swimming patterns. The biological and clinical significance of these transitions merit further study.

58 EFFECT OF RESVERATROL ON SPERMIC parameters OF ADULT RATS SUBMITTED TO EXPERIMENTAL VARICOCELE INDUCED IN THE PERIPUBERTY
Talita B. Mendes, Master Student1, André C. Vaz, Master Student2, Camila C. Paccola, Doctoral Student2, Taiza Stumpf, Doctor2 and Sandra M. Miraglia, Doctor2
1Federal University of Sao Paulo - Unifesp - Brazil; 2Unifesp
(Presented By: Talita B. Mendes, Master Student)

Introduction: Varicocele is the most common cause of male infertility. It happens primarily in the adolescence and has a progressive harmful effect on fertility. In addition, oxidative stress is the main factor responsible for these damages. Resveratrol, a natural fitoalexin, has several beneficial effects on the human body, including antioxidant and antiapoptotic properties. Objectives: To investigate the protective action of resveratrol against the reproductive damage caused by surgically induced varicocele.

Methods: Seventy–two periubertal Wistar male rats (41dpp) were distributed into 4 groups: Sham–Control (S); Varicocele (V); Resveratrol (R) and Varicocele treated with Resveratrol (VR).

Varicocele was induced in V and VR animals at 41 days postpartum (dpp), through the partial ligation of the left renal vein; for this goal, a 2–0 cotton thread and a catheter with diameter similar to an epidural catheter were utilized. The rats from S group were submitted to the similar surgical procedure, excepting the partial renal vein ligation. The groups R and VR received 300mg/kg/day of resveratrol by gavage, in the morning until the age of 100dpp (euthanasia).

Spermatic parameters (morphology, mitochondrial activity, acrosome integrity and motility), testicular biometry and oxidative stress were investigated in these rats at 100dpp.

Results: There was a reduction of testicular major axis in the group V when compared with the S, R and VR groups; the testicular volume was reduced in the V group in comparison to the S and R groups but not in comparison to the VR group. The frequency of morphologically abnormal sperm was higher in the V and VR groups than in S and R groups.

The frequency of sperm showing 100% of mitochondrial activity and showing normal acrosome integrity was lower in the V group than in VR, S and R groups. Sperm motility was also reduced in the V group when compared to the other groups. Defects of acrosomal integrity and of mitochondrial activity and morphological abnormalities occurred in sperm collected from the right (contralateral side) and left epididymides (varicocele side). The testicular levels of malondialdehyde were higher in V and VR groups but no alteration in oxidative stress levels was observed between V and VR groups.

Conclusion: The preliminary results suggest that daily resveratrol administration to rats with induced–varicocele from periubertcy improves the sperm quality in adulthood. Complementary analyzes are being performed.

59 EFFECTS OF BETAINE SUPPLEMENTATION ON SPERM FUNCTIONAL PARAMETERS IN HUMANS AND MICE WITH DEFECTS IN CHOLINE METABOLISM
Summer Goodson, PhD1, Martin Kohlmeier, MD2 and Steven Zeisel3
1UNC Chapel Hill Nutrition Research Institute; 2UNC Chapel Hill Nutrition Research Institute and Department of Nutrition, UNC Chapel Hill
(Presented By: Summer Goodson, PhD)

Introduction: An estimated 15% of couples experience reproductive issues and in approximately half of these the problem is attributed to male infertility. Genetic factors, including single nucleotide polymorphisms (SNPs) and alterations in genes that disrupt metabolism, may be responsible for some cases of idiopathic male infertility. Males carrying two minor alleles of the common rs12676 SNP, located in the gene encoding for the mitochondrial enzyme choline dehydrogenase (CHDH), have low sperm ATP concentrations, abnormal mitochondrial function and altered sperm motility. Male Chdh−null mice display a similar phenotype: infertility due to defects in sperm motility, low sperm ATP concentrations and dysmorphic sperm mitochondria. Administration of dietary betaine (N,N,N−trimethylglycine) during spermatogenesis partially restores sperm
ABSTRACTS

60 ORIGIN OF THE STEROIDOGENIC POOL OF CHOLESTEROL USED IN CAMP-INDUCED ACUTE STEROID FORMATION

Sathvika Jagannathan, MSc¹, Seimia Chebbi, BSc¹, Francoise Hullin-Matsuda, PhD¹, Toshihide Kobayashi, PhD¹ and Vassilios Papadopoulos, PhD¹
¹Research Institute of the McGill University Health Centre and Department of Medicine, McGill University; ²Lipid Biology Laboratory, RIKEN Advanced Science Institute, Wako, Saitama, Japan
(Presented By: Sathvika Jagannathan, MSc)

Introduction: The hormone-sensitive and rate-limiting step in steroid biosynthesis is the movement of cholesterol from intracellular sources to the inner mitochondrial membrane (IMM) where it is converted to pregnenolone by the cytochrome P450 side chain cleavage enzyme (CYP11A1). Despite the numerous studies carried out to analyze cholesterol trafficking in steroidogenesis, the exact source of cholesterol as well as the mechanism by which it is transported to IMM remains to be elucidated.

Methods: D4 is the fourth domain of perfringolysin O protein, which has the ability to bind with high affinity cholesterol–enriched membranes, i.e. containing cholesterol greater than 30 mol% of total lipid. A fluorescent mCherry–tagged D4 was used to visualize cholesterol trafficking in hormone-responsive MA–10 mouse tumor Leydig cells.

Results: Confocal imaging microscopy showed that in D4–mCherry–transfected MA–10 cells, fluorescence localizes at the plasma membrane, but upon 30–45 minutes treatment with the cAMP analog dibutyryl–cAMP (dbcAMP) a significant reduction in plasma membrane labeling was observed. Functional inhibitors of the steroidogenic acute regulatory protein (STAR), translocator protein (TSPO), voltage dependant anion channel (VDAC) and CYP11A1, proteins involved in cholesterol import into mitochondria and cholesterol metabolism to steroids, blocked steroid formation, and slowed down the movement of D4–mCherry from the plasma membrane. Treatment with the substrate 22R–hydroxycholesterol, which results in maximal steroid formation, also slowed down the D4–mCherry movement, suggesting that elevated steroid formation acts as a feedback mechanism to control plasma membrane cholesterol release. D4–mCherry also localized at the late endosomes upon dbcAMP stimulation suggesting a route for the cholesterol from plasma membrane to mitochondria.

Conclusion: These data suggest that the bulk of the steroidogenic pool of cholesterol, mobilized by cAMP for acute steroidogenesis, likely originates from the plasma membrane.
Conclusion: In summary, our data suggests an important role for HENMT1 in regulating pachytene piRNA stability, post-natal TEs repression and the translational regulation of haploid germ cell mRNAs.

ACETAMINOPHEN VERSUS IBUPROFEN: EFFECTS ON NEONATAL TESTICULAR GONOCYTE DEVELOPMENT
Gurpreet Manku, PhD¹, Philippos Papadopoulos² and Martine Cully, PhD³
¹The Research Institute of the McGill University Health Centre, and the Departments of Pharmacology & Therapeutics, and Medicine, McGill University, Montreal, Quebec, Canada; ²Research Institute of the McGill University Health Centre, Montreal, Quebec, Canada

(Presented By: Gurpreet Manku, PhD)

Introduction: Newborn baby fever is often treated with acetaminophen (AC) (Tylenol®) or ibuprofen (IB) (Motrin®). Both drugs inhibit cyclooxygenases (COXs), enzymes responsible for producing prostaglandins, thromboxanes, and leukotrienes. COXs are involved in platelet aggregation, fever, and inflammation, processes that can be decreased by COX inhibitors.

There are two types of COX enzymes, COX1 and COX2. Although COX2 is not commonly known for a role in male reproductive biology, it has been reported to play a role in the steroidalogenic function of Leydig cells. However, the possible role of COX2 in germ cells is not yet known.

Here, we report that COX2 is abundantly expressed in postnatal day (PND) 3 rat gonocytes, the precursor cells to spermatogonial stem cells which provide a life-long source for sperm production. PND3 gonocytes undergo proliferation, migration followed by differentiation, while abnormal cells are removed by apoptosis. Interestingly, COX2 expression was downregulated in PND8 spermatogonia, indicating a possible role in gonocyte development.

Considering the presence of COX2 in neonatal germ cells, our objective was to determine whether gonocyte proliferation or differentiation could be altered upon exposure to either AC or IB. This is an important question to address as improper gonocyte development has been suggested to lead to testicular tumor formation.

Methods: Isolated PND3 gonocytes were treated with either AC or IB alongside PDGF–BB and 17 estradiol (PE; proliferation) or Retinoic Acid (RA; differentiation).

Results: Although neither drug had any effect on cell survival (trypan blue exclusion analysis), we found that IB stimulated gonocyte proliferation to levels similar to those seen with PE treatment (determined by Proliferating Cell Nuclear Antigen (PCNA) immunohistochemistry analysis). Furthermore, IB reduced the effect of RA on mRNA expression of the differentiation marker Stra8 (Stimulated by RA 8) (quantitative PCR), indicating a negative effect of this COX inhibitor on differentiation, that was not seen using AC.

Conclusion: These data suggest that COX2 activity plays a dual role in gonocytes, being positively involved in gonocyte differentiation, while preventing proliferation. It will be interesting to identify which COX2 products are mediating these effects. Taken together, our data suggests that anti-pyretic medications such as IB could disrupt neonatal gonocyte development, which could potentially lead to the formation of testicular germ cell tumors.
**IMPORTANCE OF SOMATIC NICHE IN REGULATING TESTICULAR STEM CELLS DIFFERENTIATION INTO SPERM**

Sandhya Anand, MSc, Kalpana Sriraman, PhD, Hiren Patel, MSc, Smita Bhutda, MSc and Deepa Bhartiya, PhD

Stem Cell Biology Department, National Institute for Research in Reproductive Health, Jeeangir Merwanji Street, Parel, Mumbai 400 012, INDIA.

(Presented By: Sandhya Anand, MSc)

**Introduction:** We have undertaken studies on busulphan treated mice testes to address fertility issues of cancer survivors. Very small embryonic-like stem cells (VSELs, <8µm, Lin−/CD45−/SCA−1+) exist as a sub-population amongst spermatogonial stem cells (SCs) in adult mice testes and survive busulphan treatment (BT) because of their quiescent nature (0.03±0.002% in normal versus 0.05±0.005% BT by flow cytometry). Spermatogenesis is suppressed in chemoablated testes, possibly due to compromised somatic niche which is crucial for normal proliferation and differentiation of stem cells. Transplantation of healthy niche cells including Sertoli cells (SC) and mesenchymal cells through inter-tubular route restored spermatogenesis from surviving stem cells. Present study aimed to understand the role played by transplanted SC and mesenchymal cells to restore spermatogenesis, in-depth analysis of niche in BT testis and in vitro stem cells-niche interaction to result in spermatogenesis.

**Methods:** SC and mesenchymal cells from GFP mouse were injected in testis of wild type BT mouse and studied on 1, 7, 14, 30 and 60 days post transplantation. To evaluate the effect of BT on niche, SC from normal and BT testis were subjected to microarray studies. In addition, cells from BT testis were cultured for three weeks in SC conditioned medium with 10% FBS and 0.5 IU FSH.

**Results:** Transplanted GFP cells showed formation of neo-tubule like structures in the interstitium. Adjacent germ cells depleted native tubules showed gradual resumption of spermatogenesis from VSELs which survived chemotherapy. Microarray analysis showed up-regulation of 1835 genes and down-regulation of 1768 genes after BT. Several signaling pathways including Wnt pathway (implicated in SC function) were affected. Up-regulation of Wnt4 and beta catenin was observed. During in vitro culture, SC from BT testis attached and provided support to the surviving stem cells which underwent proliferation, clonal expansion and differentiation into sperm within 3 weeks. Various stages of spermiogenesis were observed correlating with an increase in transcript levels of Pcna, Sca−1, Gfra, Prohibitin, Scp3 and Protamine.

**Conclusions:** Crucial role played by the somatic niche by secreting various factors in a paracrine manner to affect stem cells proliferation and differentiation is highlighted. Potential of VSELs to differentiate into sperm (unlike ES cells) in presence of a supportive niche is also demonstrated.

---

**GHRELIN-INDUCED ATTENUATION OF TESTICULAR DAMAGE IN MOUSE CRYPTORCHID TESTES**

Enrica Bianchi, PhD¹, Mark Sigman, MD, PhD¹, Kim Boekelheide, MD, PhD² and Kathleen Hung, MD, PhD¹

¹Division of Urology, Brown University; ²Department of Pathology and Laboratory Medicine, Brown University.

(Presented By: Enrica Bianchi, PhD)

**Introduction:** Cryptorchidism or undescended testis (UDT) is a common congenital abnormality that is associated with increased risks for developing male infertility and even testicular cancer. It is also associated with germ cell loss and impaired spermatogenesis. Previous studies provided evidence of Ghrelin and its receptor expression in rat testis, demonstrating an involvement of this molecule in the direct control of gonadal function. We hypothesized that ghrelin, a 28 amino acid peptide predominantly found in the stomach, may play an important role in the attenuation of testicular damage induced by surgical cryptorchidism in mice.

**Methods:** C57BL/6 mice were subjected to creation of surgical unilateral cryptorchidism and were randomly separated into two groups: treatment group (ghrelin) and control group (saline). Mice received intraperitoneal injections of Ghrelin (0.16 mg/Kg) or saline twice a day for 20 days post-surgery. The animals were then sacrificed at 21 days after surgery and their testes were collected. Cryptorchid testes were embedded in glycol methacrylate for histological and immunohistochemical analysis. The following histological endpoints were used to assess testicular damage: testis weight, seminiferous tubule diameter, percentage of seminiferous tubules with spermatids and with giant cells.

**Results:** Our results suggest that ghrelin treatment exhibits a protective role in testicular damage. Testicular weights and seminiferous tubules diameters were significantly decreased in control mice compared to the ghrelin–treated animals. In addition, histological evaluation demonstrated that ghrelin significantly reduced formation of giant cells and preserved the spermatogenesis in the cryptorchid testes, and subsequent conservation of testicular architecture.

**Conclusion:** These findings indicate that ghrelin attenuates testicular damage induced by elevated abdominal temperatures in cryptorchid mice. In addition, ghrelin therapy may be useful as a suppressor of testicular damage induced by hyperthermia and future investigations will focus on the underlying mechanisms by which ghrelin mitigates the initiation of testicular damage.
LATE EFFECT OF NICOTINE ON THE SEMINIFEROUS EPITHELIUM OF THE OFFSPRING FROM RAT DAMS TREATED THROUGHOUT PREGNANCY AND LACTATION
Camila Paccola, doctoral student, Flavia Neves, doctoral student and Sandra Miraglia, Doctor
Federal University of Sao Paulo
(Presented By: Camila Paccola, doctoral student)

Introduction: Nicotine is largely consumed worldwide through cigarette. It reaches maternal milk, is able to cross the placental membrane, induces apoptosis in different cell types and alters spermatogenesis. Objective: To investigate whether nicotine administration to pregnant and lactating rats, in a similar dose to human consumption (one packet of cigarettes/day), provokes in the offspring a late testicular damage involving apoptosis of both Sertoli and germ cells as well as functional changes in the Sertoli cell and/or in its cytoskeleton.

Methods: Fifteen rats received nicotine (2mg/Kg/day) throughout pregnancy and lactation via subcutaneous osmotic minipumps (N group). Other 15 pregnant rats had minipumps implanted but without nicotine (Sham group) and 15 pregnant rats did not receive minipumps (Control group). The male offspring was distributed in subgroups according to the euthanasia age (30, 60 and 90dpp). Plasmatic levels of FSH and LH were measured by Luminex™ xMAP methodology. The tests were processed for histopathological study and for evaluation of the frequency of the stages of the seminiferous epithelium cycle. The immunolabeling of apoptotic cells (TUNEL, Fas and FasL) and of transferrin, vimentin and β−catenin was performed in the seminiferous epithelium. The numerical density of TUNEL+ cells and the volume densities of Fas, FasL, transferrin, vimentin and β−catenin immunolabeling were obtained using an image analysis system. Expressions of vimentin and β−catenin proteins were investigated considering the stages of the seminiferous epithelium cycle.

Results: FSH and LH plasmatic levels were significantly increased in the N group, in adulthood. Nicotine did not induce changes in the apoptotic cell number nor Fas and FasL expression, but provoked pronounced seminiferous epithelium disorganization and large sloughing of germ cells. Alterations of the frequency of some stages of the seminiferous epithelium cycle of the N group were observed in the puberty and adulthood. Although the transferrin expression in the seminiferous epithelium did not change, vimentin expression was reduced in adult rats of the N group, especially in the early stages of the cycle.

Conclusion: Nicotine exposure during intrauterine and lactation phases provokes early and accentuated germ cell loss and alters the organization of the seminiferous epithelium cycle, the Sertoli cell vimentin expression and the plasmatic levels of pituitary gonadotropins in adulthood.

ABSTRACTS

REQUIREMENT FOR ADENOSINE DEAMINASE CONTAINING PROTEINS IN MALE GERM CELL DEVELOPMENT
Elizabeth Snyder, PhD, Anuj Srivastava, PhD and Robert Braun, PhD
The Jackson Laboratory
(Presented By: Elizabeth Snyder, PhD)

Introduction: Adenosine deaminase, RNA−specific (ADAR) proteins are the only known drivers of adenosine to inosine (A-to-I) RNA editing. Murine ADARs (encoded for by Adar, Adarb1, and Adarb2) contain two conserved domains: an adenosine deaminase (AD) domain, which catalyzes A to I conversion, and one or more double−stranded RNA binding motifs (dsRBM). While expression of Adarb1 and Adarb2 is confined to neural tissue, Adar is observed in a wider range of tissues, including the testis. In addition, the testis expresses two closely related AD domain−containing proteins, Adad1 and Adad2. Both carry amino acid substitutions in critical regions of the AD domain, suggesting they do not have catalytic activity, although this has not been formally proven. Both ADADs contain dsRBMs similar to those found in ADARs, implying they may bind a similar set of targets. Expression profiling in isolated testicular cell types, throughout testis development, and in germ cell ablated mutant models demonstrated both Adad1 and 2 are expressed exclusively in the meiotic and post−meiotic germ cell populations while Adar is expressed in germ and somatic cells.

Methods: The extent of RNA editing in the testis was determined by applying a computational pipeline to high throughput RNA sequence data of isolated testicular cell types. This analysis demonstrated A to I editing in both the germ line and soma, with a much higher number discovered in Sertoli cells as compared to germ cells. To address the functional role of RNA editing in the testis and the specific requirement of AD−domain containing proteins in male germ cell development, we generated germ cell and Sertoli cell−specific knockout models of Adar, as well as CRISPR−induced mutant models of Adad1 and Adad2, respectively.

Results: Despite the occurrence of editing in both cell types, germ cell or Sertoli cell ablation of Adar had no appreciable impact on germ cell development. In contrast, mutation of either Adad1 or 2 resulted in male−specific sterility.

Conclusion: Tolerance for germ cell ADAR loss demonstrates ADAR−mediated editing is not essential for male fertility. However, the absolute requirement of both Adad1 and Adad2 for male fertility confirms a fundamental role of AD−domain containing proteins in germ cell development. Whether ADADs catalyze or regulate RNA−editing events in the germ line or have evolved essential functions outside of RNA editing is unknown. Current studies are aimed at distinguishing between these disparate hypotheses.

© 2015 American Society of Andrology and European Academy of Andrology Andrology, 2015, Supplement, 95
**68**

**VITAMIN B12–INDUCED SPERMATOGONIAL MITOTIC ACTIVITY IN THE TESTES OF CIMETIDINE–TREATED RATS**

Flavia Luciana Beltrame, PhD¹, Estela Sasso-Cerri, PhD² and Paulo Sérgio Cerri, PhD²

¹Department of Morphology and Genetics, Federal University of São Paulo - UNIFESP; ²Department of Morphology, São Paulo State University - UNESP

(Presented By: Flavia Luciana Beltrame, PhD)

**Introduction:** Cimetidine, an antiulcer drug, exerts an antagonist effect on histamin H₂–receptors. In rodents, this drug has caused significant disorders in male reproductive tract, including structural changes in the seminiferous tubules. Vitamin B12 plays an important role in DNA synthesis and cell division; supplementation of cimetidine–treated rats with vitamin B12 has demonstrated to recover the seminiferous epithelium. In this study, we investigated the effect of vitamin B12 on the mitotic and meiotic activities of spermatogenesis in cimetidine–treated rats.

**Methods:** Adult rats were distributed into four groups (n=5): Cimetidine (CMTG), cimetidine/vitamin B12 (CMT/B12G), vitamin B12 (C12G) and control (CG). CMTG received cimetidine (100mg/kg bw) for 50 days. CMT/B12G received cimetidine+3µg vitamin B12G and control (CG). CMTG received cimetidine (100mg/kg bw) for 50 days. CMT/B12G received cimetidine+3µg vitamin B12. B12G and CG received vitamin and saline, respectively. Sperm concentration was obtained and the testes were fixed and embedded in paraffin or historesin for detection of: a) cell death by TUNEL, b) cellular proliferation by PCNA immunohistochemistry; c) quantitative analyses of spermatogonia (A; In/B) and spermatocytes in tubules at stages I–VI, VII–VIII and IX–XIV. Data were statistically analyzed by one way ANOVA followed by Tukey test (p ≤ 0.05).

**Results:** Cimetidine caused a significant reduction in sperm concentration, which increased in the vitamin supplemented animals of CMTG/B12. In CMTG, spermatogonia and spermatocytes showed apoptotic nuclear features and were TUNEL–positive. Moreover, a significant reduction in the number of spermatogonia (A and/or In/B) and spermatocytes was observed at all stages analyzed. In contrast, a significant increase in the number of In/B spermatogonia and a high incidence of PCNA–positive spermatogonia and spermatocytes was found in the tubules at stages I–VI of CMTG/B12, in comparison to CMTG. Although the number of spermatocytes and sperm concentration increased in CMTG/B12, it was not recovered at normal levels. Differences between CG and B12G were not found.

**Conclusion:** The results show that cimetidine treatment reduces the number of spermatogonia and spermatocytes. However, the vitamin B12–induced epithelial recovery is due to the potential effect of this vitamin on A4 and In/B spermatogonia of the cimetidine–damaged testes. Although vitaminB12 was able to recover spermatogonia number, the following spermatogenic processes (meiosis and spermiogenesis) could not be completely restored by this vitamin.

**Funding:** Grant support: Fapesp 2012/23845–3; 2013/25322–0; CNPq.

---

**Monday, April 20, 2015**

11:15 a.m. – 12:30 p.m.

**Poster Session II**

*Not CME Accredited*

Location: Grand Ballroom C

**69**

**MEF2 AND COUP–TFII COOPERATE TO REGULATE AKR1C14 GENE EXPRESSION IN MOUSE MA–10 LEYDIG CELLS**

Mickael Di-Luoffo, MSc, Catherine Brousseau, MSc, Raifish E. Mendoza-Villarroel, PhD and Jacques J. Tremblay, PhD

CRCHUQ-Universite Laval

(Presented By: Mickael Di-Luoffo, MSc)

**Introduction:** Dihydrotestosterone (DHT) is a potent androgen and its bioavailability must be tightly regulated. In mouse Leydig cells, the Akr1c14 gene codes for the 3α−hydroxysteroid dehydrogenase (3αHSD) enzyme which catalyzes the interconversion of DHT and 5α−androstane−3α,17β−dield (3α−dil) via its dual oxidative and reductive activities, thus allowing a balance between DHT synthesis and elimination. Despite its importance, nothing is currently known regarding the regulation of Akr1c14 expression in Leydig cells. Recently, the transcription factors MEF2 and COUP–TFII were identified in the mouse testis, including in Leydig cells. MEF2 and COUP–TFII are important regulators of organogenesis, cell differentiation and development. In the testis, MEF2 and COUP–TFII are present in Leydig cells throughout fetal and adult life where they were found to regulate the expression of genes involved in steroidogenesis. Analysis of the transcriptome of MEF2− or COUP–TFII−deficient (siRNA knockdown) MA−10 Leydig cells revealed a significant decrease in Akr1c14 expression. The aim of the present study was to determine the role and mechanism of action of MEF2 and COUP–TFII in Akr1c14 expression in Leydig cells.

**Methods:** By qPCR, we confirmed that Akr1c14 mRNA levels were decreased by ~55% in MEF2− and in COUP–TFII−deficient MA−10 Leydig cells. Conversely, overexpression of MEF2 in MA−10 cells led to a 2.2 fold increase in endogenous Akr1c14 mRNA levels. In silico analysis of the Akr1c14 promoter revealed the presence of two superimposed MEF2 binding sites at −1246 bp and a COUP–TFII binding site at −1211 bp. Recruitment of MEF2 and COUP–TFII to this region of the Akr1c14 promoter was confirmed by ChIP while DNA precipitation assays showed their binding to the respective elements. In functional promoter studies, MEF2 and COUP–TFII are present in Leydig cells throughout fetal and adult life where they were found to regulate the expression of genes involved in steroidogenesis. Analysis of the transcriptome of MEF2− or COUP–TFII−deficient (siRNA knockdown) MA−10 Leydig cells revealed a significant decrease in Akr1c14 expression. The aim of the present study was to determine the role and mechanism of action of MEF2 and COUP–TFII in Akr1c14 expression in Leydig cells.

**Methods:** By qPCR, we confirmed that Akr1c14 mRNA levels were decreased by ~55% in MEF2− and in COUP–TFII−deficient MA−10 Leydig cells. Conversely, overexpression of MEF2 in MA−10 cells led to a 2.2 fold increase in endogenous Akr1c14 mRNA levels. In silico analysis of the Akr1c14 promoter revealed the presence of two superimposed MEF2 binding sites at −1246 bp and a COUP–TFII binding site at −1211 bp. Recruitment of MEF2 and COUP–TFII to this region of the Akr1c14 promoter was confirmed by ChIP while DNA precipitation assays showed their binding to the respective elements. In functional promoter studies, MEF2 and COUP–TFII were found to cooperate to activate the Akr1c14 promoter. Deletion or mutation of the MEF2 and COUP–TFII sites abolished this cooperation.

**Conclusion:** In conclusion, our results identify a novel cooperation between MEF2 and COUP–TFII in the expression of the Akr1c14 gene involved in regulating DHT levels. Supported by CIHR.
ABSTRACTS

70 CURCUMIN TARGETS RAT TESTICULAR 11−HYDROXYSTEROID DEHYDROGENASE 1 TO ANTAGONIZE AGAINST STRESS−INDUCED INHIBITION OF TESTOSTERONE
Xiaoheng Li, MS, Qi Qi Zhu, MS, Xiudi Wang, MD, Shuyan Cao, MS, Ying Wu, MS, Haifang Ge, BS, Linxi Li, PhD, Kaimin Yuan, MD, Han Lin, MD, Hong-yu Zhou, PhD, Qingquan Lian, MD and Renshan Ge, MD
The Second Affiliated Hospital, Wenzhou Medical University
(Presented By: Xiaoheng Li, MS)

Introduction: It has been demonstrated that stress induces male sexual dysfunction and infertility via excessive active glucocorticoid (corticosterone, CORT, in the rat). In adult Leydig cells, 11−hydroxysteroid dehydrogenase 1 (11−HSD1) alternates between oxidative inactivation of CORT and reductive regeneration of its metabolite 11−dehydrocorticosterone (11DHC). Curcumin is a natural product.

Methods: The effects of curcumin on rat 11−HSD1 in the intact adult Leydig cells and human 11−HSD1 in the intact transfected human HSD11B1 gene were examined in vitro by adding radiolabeled substrate and separating substrate and product in the thin−layer chromatograph and detecting the signal in the radiometer. The adult male rats were randomly divided into eight groups with 10 rats of each group: 1) no stress (vehicle); 2) no stress (curcumin 50 mg/kg); 3) no stress (curcumin 100 mg/kg); 4) no stress (curcumin 200 mg/kg) and 5−8) stress with the treatment of different doses of curcumin (one gavage before immobilization). Then rats were subjected to immobilization stress (stress group) or the no−stress setting.

Results: It was found that curcumin stimulated 11−HSD1 oxidase with the EC50 values of 2.82 μM for rat adult Leydig cells and 2.11 μM for CHOP cells transfected with human HSD11B1 gene. Curcumin also inhibited 11−HSD1 reductase with IC50 value of 5.71 μM for rat Leydig cells and 4.18 μM for human one. Acute immobilization stress (3h) caused significantly suppression of serum testosterone level (0.62 ± 0.13 ng/ml, Mean ± SEM, n = 10) when compared to control (1.72 ± 0.35 ng/ml). Gavage of curcumin (50 mg/kg) did not recover the loss of testosterone. However, gavage of 100 or 200 mg/kg curcumin significantly antagonized the reduction of serum testosterone. Gavage of curcumin did not change the circulating level of CORT levels. However, curcumin significantly reduced the testicular CORT levels.

Conclusion: In conclusion, curcumin dually modulates the testicular 11−HSD1, reducing testicular CORT levels thus against stress−induced suppression of testosterone biosynthesis.

71 HUMAN CHORIONIC GONADOTROPIN SUPPLAMENTAL DOSING OPTIMIZATION FOR THE MAINTENANCE OF MALE FERTILITY WHILE ON LONG TERM TESTOSTERONE REPLACEMENT OVER 4 YEARS.
George Toth, MD
TGH, OVAMC
(Presented By: George Toth, MD)

Introduction: Human Chorionic Gonadotropin (hCG) is a polypeptide hormone released by the placenta to maintain the corpus luteum during pregnancy. The alpha sub-unit is molecularly identical to the pituitary gonadotropins Leutenizing Hormone (LH) and Follicle Stimulating Hormone (FSH). hCG is FDA approved for the treatment of Cryptorchism in men and to induce ovulation in assisted reproduction technologies for women. Off label use has been reported for maintaining male fertility and spermatogenesis during and post long term androgen treatment. hCG is available as purified peptide injections manufactured from pregnant women’s urine known as Novarel & Pregnyl or as a recombinant polypeptide called Ovidrel.

Aim: To study hCG treatment & its optimum dosing relationship to Inhibin−B as a surrogate marker of male Sertoli function & fertility while on testosterone replacement therapy.

Methods: A 46 year old otherwise healthy male previously diagnosed with Idiopathic Adult Onset Mixed Hypogonadism was prescribed Testosterone Cypionate for a period of four years and supplemented with low dose Ovidrel 10ug daily. Serial labs were obtained every 4–6 months prior to injections using LabCorp’s national assays.

Results: The results are presented in Figure 1, depicting the relationship between Inhibin−B and hCG serum concentrations. The graph shows a nonlinear relationship with a peak at approximately 10 mIU/mL of hCG which corresponds to the upper limit of normal for male LH & FSH. Levels exceeding >10 mIU/mL showed diminished Inhibin−B concentrations corresponding to decreased effectiveness. Also, levels below <8 mIU/mL seemed to be ineffective in stimulating Inhibin−B.

Conclusion: This observational study, demonstrated the optimal hCG peak serum concentration of 10 mIU/mL seems to maximally stimulate male Sertoli cells as measured by serum Inhibin−B levels. Also, levels above and below this peak showed decreasing effectiveness which may be a consequence of under or overstimulation and subsequent receptor downregulation. By optimizing low dose daily hCG injections as an adjunct treatment added to chronic long term testosterone treatment, male Sertoli function & fertility can be maintained for over four years.

© 2015 American Society of Andrology and European Academy of Andrology
Andrology, 2015, Supplement, 97
Introduction:
Little is known about optimal duration of TRT, and whether its withdrawal would lead to loss of effects and recurrence of symptoms.

Methods: In an ongoing registry study, 262 hypogonadal men (mean age 59 years) received testosterone undecanoate (TU) 1000 mg injections in 12-week intervals for a maximum of 11 years representing 2088.5 patient-years. After having been on TRT for a mean duration of 66 months, TRT was temporarily interrupted for a mean of 17 months in 147 patients (Group I; I): in 140 men due to cost reimbursement issues, and in 7 men diagnosed with prostate cancer. All men resumed TRT thereafter for a mean period of 14 months. 115 men were treated continuously (Group C; C). To compare on−treatment to off−treatment periods, three periods of equal duration were defined: pre−intermission (on TRT), during intermission (off TRT) and post intermission (on TRT after resumption of TRT). For comparison, the same periods were analysed for those patients who continued TRT throughout.

Results:
Hormonal and anthropometric parameters were measured at every other visit.

Results:

Methods: Optimal duration of TRT is unknown.

Results: Glycemic control:
I: Fasting glucose was 104.14 pre, increased to 116.74 during and dropped to 89.20 mg/dl post TRT interruption. C: fasting glucose decreased progressively from 92.65 to 88.34 and 80.20 mg/dl.
I: HbA1c was 5.94 pre, rose to 6.71 during and decreased to 5.97% post intermission. C: HbA1c decreased continuously from 5.77 to 5.70 and 5.58%.

Lipid pattern (mg/dl):
I: Total cholesterol (TC) was 223.71 pre, increased to 284.20 during and dropped to 200.86 post. C: TC decreased progressively from 197.33 to 185.97 and 173.74.
I: LDL was 131.06 pre, increased to 162.99 during and dropped to 116.15 post intermission. C: LDL decreased progressively from 119.56 to 110.81 and 101.66.
I: HDL was 50.71 pre, decreased to 38.17 during and rose to 57.51 post intermission. B: HDL increased continuously from 54.44 to 55.45 and 58.42.

Blood pressure:
I: Systolic blood pressure (SBP; mmHg) was 125 pre, increased to 137 during and dropped to 121 post TRT interruption. C: SBP decreased from 119 to 117 and 116.
I: Diastolic blood pressure (DBP; mmHg) was 77 pre and remained stable at 77 during and 74 post TRT interruption. C: DBP decreased from 75 to 73 and 72.

Conclusions: Interruption of TRT resulted in worsening of symptoms. Hypogonadism may require lifelong TRT.
KNOCKOUT OF THE TRANSCRIPTION FACTOR NRF2: EFFECTS ON TESTOSTERONE PRODUCTION BY AGING MOUSE LEYDIG CELLS

Haolin Chen, PhD¹, Shiyong Jin, PhD¹, Jingjing Guo, PhD², Shyam Biswal, PhD², Renshan Ge, MD³ and Barry Zirkin, PhD¹

¹Department of Biochemistry and Molecular Biology, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland 21205; ²The Second Affiliated Hospital, Wenzhou Medical University, Wenzhou, Zhejiang, China; ³Department of Environmental Health Sciences, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland 21205

(Presented By: Haolin Chen, PhD)

Introduction: In previous studies, increases in reactive oxygen species (ROS) and decreases in antioxidant defense molecules were shown to be associated with age-related reductions in Leydig cell testosterone formation. It remains unclear whether redox imbalance is the cause of the reduced steroidogenesis that characterizes aging. A number of previous studies have examined the effects on cell function of the acute suppression of individual antioxidant molecules. However, aging is associated with the altered expression of numerous antioxidant molecules, and therefore with the long-term exposure of cells to an altered redox environment. The transcription factor nuclear factor-erythroid2-related factor 1 (Nrf2) is a master regulator of phase 2 antioxidant genes. Therefore its knockout affects the expression of a number of antioxidant molecules, reminiscent of aging. In the current study, we investigated the long-term effect of knocking out Nrf2 on mouse Leydig cell testosterone production.

Methods: Nrf2−deficient C57BL/6 mice were generated. Young (3 month−old), middle aged (8 month−old) and aged (24 month−old) wild−type and knockout mice were used in these studies.

Results: In wild−type C57BL/6 mice, serum testosterone levels and Leydig cell testosterone formation remained unchanged through middle age (8 months), but then were reduced significantly by old age (21−24 months). In contrast, serum testosterone levels were reduced significantly in the Nrf2 knockout (Nrf2−/−) mice as early as middle age, as was Leydig cell testosterone production. Both serum testosterone level and Leydig cell testosterone production were reduced in aged wild−type mice, but significantly more so in the aged Nrf2−/− mice. Reduced Leydig cell steroidogenesis in the knockout mice was associated with increased expression of protein nitrotyrosine residues, a marker of reactive oxygen species (ROS), and by reduced antioxidant levels.

Conclusion: These results strongly suggest that, over time, increases in oxidative stress resulting from Nrf2 knockout contribute to, or cause, the reduced testosterone production that characterizes aging Leydig cells.

THE MITOCHONDRIAL PEPTIDE ANALOGUE HNG PROTECTS AGAINST CYCLOPHOSPHAMIDE−INDUCED DECREASE IN SPERM OUTPUT AND NEUTROPTENIA

Yan-He Lue, MD¹, Ronald Swerdloff, MD¹, Junxiang Wan, PhD², Vince Atienza, BS¹, Brian Stone, BS¹, Sima Baravarian, PhD¹, Yue Jia, MD¹, Pinchas Cohen, MD² and Christina Wang, MD¹

¹LABioMed at Harbor-UCLA; ²USC Davis School of Gerontology

(Presented By: Yan-He Lue, MD)

Introduction: Onco−infertility and neutropenia are the most common adverse events in cancer patients after chemotherapy. We have previously demonstrated that HNG, a potent Humanin analogue, protected male germ cells from apoptosis after a single dose of cyclophosphamide (CP) treatment. The objective of this study was to investigate whether HNG has protective effect on sperm output and peripheral blood cells after multiple doses of CP in mice.

Methods: Thirty adult male mice (C57BL/6J) were randomized into 4 groups: 1) 5 as control; 2) 5 received daily subcutaneously injection of HNG (10mg/kg); 3) 10 were given 6 doses of CP (150mg/kg) intraperitoneally at 5−day intervals; 4) 10 received both HNG and CP. All mice were killed at 28 days. Blood was collected for complete blood cell count using an automated cell counter. Plasma HNG and IGF−1 levels were measured by ELISAs. The cauda epididymal sperm count was performed using hemocytometer.

Results: Plasma HNG levels increased significantly (p<0.001) in HNG treated (80.8±7.8ng/ml), and HNG+CP treated (64.7±1.8ng/ml) mice compared to control (1.3±0.1ng/ml), and CP treated mice (1.7±0.1ng/ml). Compared to control (413.7±44.9ng/ml), plasma IGF−1 levels were significantly (p<0.001) suppressed by HNG (347.2±20.1ng/ml), CP (182.4±10.5ng/ml), and further suppressed by CP+HNG treatment (148.8±8.1ng/ml). Epididymal sperm counts were significantly elevated by HNG (1.7±0.2x10⁶/mg, p=0.04), and significantly suppressed by CP (0.5±0.1x10⁶/mg, p<0.001) as compared to control (1.2±0.2x10⁶/mg). HNG+CP significantly increased sperm count (0.8±0.1x10⁶/mg, p=0.02) as compared to CP. HNG alone had no effect on total white cell count (WBC:2.3±0.6x10⁶/ml), granulocytes (GRA:0.5±0.2x10⁶/ml), monocytes (MON:0.1±0.03x10⁶/ml), and lymphocytes (LYM:1.7±0.4x10⁶/ml) compared to control (WBC:2.4±0.3; GRA:0.2±0.1; MON:0.1±0.02; LYM:2.1±0.4x10⁶/ml). CP treatment significantly (p<0.001) decreased the number of leukocytes (WBC:0.3±0.02; GRA:0.2±0.02; MON:0.01±0.01; LYM:0.07±0.01x10⁶/ml) compared to control. Addition of HNG to CP significantly (p<0.05) rescued the CP induced neutropenia (WBC:0.6±0.04; GRA:0.4±0.03; MON:0.05±0.01; LYM:0.1±0.01x10⁶/ml) as compared to CP.

Conclusion: We conclude that HNG prevents not only CP−induced suppression of sperm output but also CP−induced suppression of granulocytes, monocytes and lymphocytes. Our findings suggest that HNG is a promising adjuvant to chemotherapy by reducing chemotherapy−induced neutropenia and preventing onco−infertility.
**ABSTRACTS**

### PRO-ANDROGENIC EFFECTS OF LOW DOSE DEHP ARE ANTAGONIZED BY GENISTEIN IN YOUNG ANIMALS EXPOSED IN-UTERO

**Steven Jones, MSc¹, Annie Boisvert, MSc¹, Sade Francois, BSc¹, Liandong Zhang, MD² and Martine Culty, PhD¹**  
¹McGill University; ²Xi’an Jiaotong University  
(Presented By: Steven Jones, MSc)

**Introduction:** Early life exposure to environmental endocrine disruptors (EDs) is believed to predispose males to reproductive abnormalities. Although males are exposed to countless combinations of environmental chemicals from the time of conception to adulthood, relatively few studies have attempted to evaluate the effects of ED mixtures at relevant doses. Previous work in our laboratory demonstrated the ability of in utero exposure to a mixture of the phytoestrogen, Genistein (GEN), and plasticizer, DEHP, to induce long term alterations that are substantially different from individual exposures.

**Methods:** In this follow-up study, we examined F1 postnatal-day (PND) 3 and 6 male offspring exposed in-utero from gestational day 14 to parturition with either control corn oil, 10mg/kg GEN, DEHP or combined GEN and DEHP to gain insight into the early molecular events driving long term alterations.

**Results:** Interestingly, DEHP had a stimulatory effect on the mRNA and protein expression of the steroidogenic enzyme, HSD3B1, uniquely in PND3 animals. The pro-androgenic effect of MEHP, the principal bioactive metabolite, was further investigated in PND3 testis organ cultures: 10 μM MEHP stimulated basal testosterone production, an effect that was attenuated by co-treatment with GEN (10 μM). In PND3 DEHP treated animals, concomitant mRNA increases of proliferation (Pcna), Sertoli cell (Wt-1, Nestin) and early germ cell (Hsp90a, Plzf, Foxo1) markers were observed. Lastly, a correlated increase in redox (Nqo1, Sod2, Sod3, Txr, Gst and Cat) and xenobiotic transporter (Abcb1b, Abcg2) gene expression was observed in PND3 DEHP treated animals, while attenuated when combined with GEN, suggesting the involvement of cellular stress in short-term DEHP mediated bi-phasic effects and a possible protective effect of GEN.

**Conclusion:** In contrast to previous reports of androgen suppression by DEHP used at elevated doses, lower dose gestational DEHP and in-vitro MEHP treatment had a stimulatory effect on androgen related processes, somatic and germ cell markers. We propose a potential mechanism by which GEN, through antioxidant action, normalizes the effects of ROS induced up-regulation of androgen related processes in DEHP treated animals. This notion that EDs do not follow classical dose-response effects and involve different mechanisms of toxicity from perinatal ages to adulthood highlights the importance of assessing impacts across a range of doses during appropriate windows of exposure.

### EFFECTS OF IN UTERO EXPOSURE TO DIISONONYL PHTHALATE ON RAT FETAL LEYDIG CELL FUNCTION AND AGGREGATION

**Tiao Bu, MD, Linxi Li, PhD, Yiyian Wang, MD, Yuanyuan Hu, MD, Gaolong Zhang, MD, Yuanyuan Shan, MD, Zhichuan Chen, MD, Danyan Zhu, MD, Renai Xu, MD, Junwei Li, MD, Guoxin Hu, PhD, Qingquan Lian, MD and Ren-Shan Ge, MD**  
The 2nd Affiliated Hospital & Research Academy of Reproductive Biomedicine, Wenzhou Medical University  
(Presented By: Tiao Bu, MD)

**Introduction:** Diisononyl phthalate (DINP) is a synthetic material that has been widely used as a substitute for other plasticizers prohibited due to reproductive toxicity in consumer products. Some phthalates have been associated with testicular dysgenesis syndrome in male fetus when female pregnant dams were exposed to them. The present study investigated effects of DINP on fetal Leydig cell function and testis development.

**Methods:** Female pregnant Sprague Dawley rats received control vehicle (corn oil) or DINP (10, 100, 500, and 1000 mg/kg) by oral gavage from gestational day (GD) 12 to GD 21. At GD 21.5, testicular testosterone production, fetal Leydig cell numbers and distribution, testicular gene and protein expression levels were examined.

**Results:** DINP showed dose-dependent increase of fetal Leydig cell aggregation with the low observed adverse-effect level (LOAEL) of 10 mg/kg and multinucleated gonocyte with LOAEL of 100 mg/kg. At 10 mg/kg, DINP also significantly increased fetal Leydig cell cell size, but inhibited insulin-like 3 and 3β-hydroxysteroid dehydrogenase gene expression and protein levels. DINP inhibited testicular testosterone levels at 1000 mg/kg.

**Conclusion:** The results indicate that in utero exposure to DINP affects the expression levels of some fetal Leydig cell steroidogenic genes, gonocyte multinucleation and Leydig cell aggregation.

### EFFECTS OF IN UTERO MIXED EXPOSURE TO DIETHYL AND DIETHYLHEXYL PHTHALATES ON RAT FETAL LEYDIG CELL GENE EXPRESSIONS AND FUNCTIONS

**Guoxin Hu, Junwei Li, MD¹, Yaoyao Dong, MSc¹, Dongxin Chen, MSc¹, Wenwen Yao, MSc¹, Ermin Gu, MSc¹, Yuanyuan Shan, MSc¹, Yuanyuan Hu, MSc¹, Yiyang Wang, MSc¹, Qing-quan Lian, MD² and Ren-shan Ge, MD³**  
¹Wenzhou Medical University; ²Department of Anestheiology, the 2nd Affiliated Hospital, Wenzhou Medical University; ³Institute of Reproductive Biomedicine, Wenzhou Medical University  
(Presented By: Guoxin Hu)

**Introduction:** Phthalate diesters are chemicals to which humans are ubiquitously exposed. Humans expose simultaneously to the mixtures of multiple phthalates, especially diethyl phthalate (DEP) and di-(2-ethylhexyl) phthalate (DEHP). However, the cumulative effects on fetal Leydig cell aggregation and gene expression levels have not been well understood. The objective of the present study was to investigate cumulative effects of the mixed exposure to DEP and DEHP on fetal Leydig cell aggregation and gene expressions.
Methods: Pregnant female Sprague Dawley rats received control vehicle (corn oil) or DEP (10, 100, 500, and 1000 mg/kg) or DEHP (10, 100, 500, and 1000 mg/kg) or DEP+DEHP (10, 100, 500, and 1000 mg/kg) by oral gavage from gestational day (GD) 12 to GD21. At GD 21.5, testicular testosterone levels, fetal Leydig cell numbers and aggregation, Leydig cell related gene expression levels, and their protein expression levels were examined.

Results: DEP and DEHP showed synergistic effect in the induction of fetal Leydig cell aggregation with the low observed adverse-effect level (LOAEL) of 10 mg/kg. DEP and DEHP significantly decreased fetal Leydig cell size starting at 10 mg/kg, and inhibited Cyp11a1, Cyp17a1, Hsd17b3, and Ins13 expression levels dose-dependently. At the highest dose, DEP and DEHP inhibited testicular testosterone levels at 1000 mg/kg.

Conclusion: These data demonstrate that individual phthalates with a similar mechanism of action can elicit cumulative, dose additive effects on the expression levels of some fetal Leydig cell steroidogenic genes, and Leydig cell aggregation when administered as a mixture.

Funding: This work was in part supported by NSFC 81373032 to G.X.H, by Health Bureau of Zhejiang Province (11–CX29 and 2013ZDA017) to R.S.G and Special Project of Science and Technology Department of Zhejiang Province (2012C13016–1) to Q.Q.L.

79 MOLECULAR ALTERATIONS IN SPERM ARE SENSITIVE INDICATORS OF TESTICULAR DYSFUNCTION
Linnea Anderson, MSc¹, Edward Dere, PhD² and Kim Boekelheide, MD, PhD²
¹Brown University; ²Rhode Island Hospital
(Presented By: Linnea Anderson, MSc)

Introduction: Traditional endpoints used to measure male reproductive toxicity in humans, including semen and hormone analysis, are insensitive and unreliable; those used to monitor toxicity in animal studies, while sensitive, are not easily translatable to humans. It is therefore necessary to develop sensitive and reliable molecular biomarkers of testicular injury that can be used to both monitor human reproductive function and compare animal studies with human exposures.

Methods: We approached this problem by exposing male rats to model testicular toxicants to identify sperm molecular alterations, as these can be compared to highly sensitive histopathological assessments of testicular function. Adult male rats were exposed to cyclophosphamide (CPP) for 12 weeks (1.4, 3.4, or 5.1 mg/kg/day p.o.) or 12 weeks plus a recovery period of 12 weeks (5.1 mg/kg/day p.o.) as a model of germ cell toxicity. Standard reproductive endpoints were examined; in particular, germ cell apoptosis and spermatid head retention were quantified as sensitive markers of damage. mRNA from cauda epididymidal sperm was analyzed for toxicant-induced alterations using a genome–wide microarray, then significant and robust alterations were further examined using qRT–PCR arrays and standard qPCR. Sperm DNA was analyzed for alterations in methylation using reduced representation bisulfate sequencing.

Results: We observed that CPP produced dose–dependent testicular injury that resolved after a 12–week recovery period. The levels of injury correlated with specific changes in transcript abundance and specific changes in DNA methylation, indicating a utility for these mRNAs as translatable biomarkers for male reproductive dysfunction.

Conclusion: These alterations will be examined in additional exposure settings, as well as both fertile and subfertile men to continue to validate the relevance of these alterations.

80 EFFECTS OF IN UTERO EXPOSURE OF DICYCLOHEXYL PHthalate ON FETAL LEyDIG CELLS
Huina Su, Yaoyuan Wang, MD, Yuanyuan Hu, MD, Yiyan Wang, MD, Yaoyao Dong, MD, Dongxin Chen, MD, Qiqi Zhu, MD, Linxi Li, MD, Junwei Li, MD, Guoxin Hu, MD, Qingquan Lian, MD and Ren-Shan Ge, MD
The 2nd Affiliated Hospital & Research Academy of Reproductive Biomedicine, Wenzhou Medical University
(Presented By: Huina Su)

Introduction: Dicyclohexyl phthalate (DCHP) is one of phthalate plasticizers. The present study investigated effects of DCHP on fetal Leydig cell distribution and function as well as testis development.

Methods: Female pregnant Sprague Dawley dams orally received vehicle (corn oil, control) or DCHP (10, 100, 500, and 1000 mg/kg) from gestational day (GD) 12 to GD 21. At GD 21.5 (postnatal day 1), testicular testosterone production, fetal Leydig cell numbers and distribution, testicular gene and protein expression levels were examined.

Results: DCHP showed dose–dependent increase of incidence of multinucleated gonocytes with the low observed adverse–effect level (LOAEL) of 10 mg/kg. DCHP also dose–dependently increased fetal Leydig cell aggregation but decreased fetal Leydig cell size, cytoplasmic and nuclear size with LOAEL of 10 mg/kg. DCHP reduced the expression levels of steroidogenesis–related genes (including Lhgr, Star, Cyp11a1, Hsd3b1, Cyp17a1, and Hsd17b3) and testis–descent related gene Insl3 as well as protein levels of 3β–hydroxy–steroid dehydrogenase 1 (HSD3B1) and insulin–like 3 (INSL3). DCHP significantly inhibited testicular testosterone levels at doses of 500 and 1000 mg/kg.

Conclusion: The results indicate that in utero exposure to DCHP affects the expression levels of some fetal Leydig cell steroidogenic genes, gonocyte multinucleation and Leydig cell aggregation.
Introduction: Phthalate esters such as di-\(n\)-butyl phthalate (DBP) are found in cosmetics and in flexible plastics distributed by the food, construction, and medical products industries. It has been suggested that DBP is metabolized into mono-\(n\)-butyl phthalate (MBP) to activate its toxicity. Immature Leydig cells have steroidogenic capacity during the pubertal development and produce mainly the weak androgen \(5\iota \beta\text{-androstane-3\iota \beta,17\beta\text{-diol}}\) (D1OL) because they have all testosterone biosynthetic enzymes (\text{CYP11A1}, \text{HSD3B1}, \text{CYP17A1} and \text{HSD17B3}) and metabolizing enzymes (\text{SRD5A1} and \text{ARK1C14}).

Methods: We compared the potencies of DBP and MBP in inhibition of steroidogenesis by rat immature Leydig cells. Rat immature Leydig cells (ILCs) were isolated from pre-pubertal male rats (35–day-old). ILCs were cultured with 50 nM–50 \(\mu\text{M} \) DBP or MBP for 24 hrs.

Results: We found that only the highest concentration (50 \(\mu\text{M} \)) of DBP inhibited androgen production. However, MBP at 50 nM had the inhibitory effects on androgen production. Quantitative PCR revealed that at this lowest concentrations, MBP inhibited Scarb1, Cyp11a1 and Hsd3b1 expression levels. However, DBP only at the highest concentration (50 \(\mu\text{M} \)) inhibited Hsd3b1, Hsd17b3 as well as Ark1c14 expression levels. 50 \(\mu\text{M} \) DBP inhibited the enzymatic activities of HSD3B1, HSD17B3 and ARK1C14, and 50 \(\mu\text{M} \) MBP inhibited HSD3B1 activity.

Conclusion: In conclusion, DBP is metabolized into the more potent metabolite MBP, which mainly inhibits androgen biosynthesis by suppressing the expression of Scarb1, Cyp11a1 and Hsd3b1.

82 WALNUTS ADDED TO A WESTERN DIET ARE ASSOCIATED WITH DECREASED DNA STRAND BREAKAGE IN SPERM
Lin Xun, MS, Catherine Carpenter, PhD, Yewande Sanusi, BS, Susanne Henning, PhD and Wendie Robbins, PhD
University of California Los Angeles
(Presented By: Lin Xun, MS)

Introduction: The importance of diet to human male reproductive success has become increasingly apparent. Because sperm DNA damage is a strong predictor of reproductive outcomes, we investigated influences of dietary fatty acids (FAs) on sperm DNA integrity. The purpose of the research was to describe relationships between blood and seminal plasma fatty acids (FAs) and sperm DNA strand breakage in men consuming a Western diet and to determine if walnuts as a source of dietary alpha-linolenic acid (ALA) and other nutrients might have a beneficial effect on sperm DNA integrity.

Methods: This work was nested within a three month dietary RCT investigating efficacy of 75 gm walnuts per day to improve conventional sperm parameters (count, motility, morphology) in 117 healthy young men eating a Western diet. For the current work, measures of body weight, BMI, FAs (gas chromatography, FAs reported as a percent of total FA) and sperm DNA strand breakage (comet assay, reported as moment and %tail DNA) were explored in 105 participants from the parent study (walnut intervention group=54, controls=51).

Results: At baseline, intervention and control groups were similar on age, race, education, weight, BMI, sperm DNA strand breakage, FAs in serum and seminal fluid. Cross-sectional baseline data showed trends toward positive correlation between sperm DNA damage and saturated FAs and negative correlation with polyunsaturated FAs reaching statistical significance only for seminal plasma palmitic and arachidonic acids after correction for multiple comparisons. The intervention group showed a statistically significant increase in blood serum ALA (p<0.0001) and seminal fluid ALA (p<0.04) and decrease in sperm DNA strand breaks (moment p<0.02, %DNA tail p<0.04) after three months eating walnuts compared to the control group who had no significant change.

Conclusions: In a group of men eating a Western diet, addition of walnuts was associated with a decrease in sperm DNA strand breakage compared to a control group. This research suggests that dietary interventions may be beneficial for sperm DNA integrity. It is not clear that the magnitude of change found in this work would improve reproductive success. However, findings point to the importance of continued research into diet and male reproductive health.

Funding: This work was funded by the University of California, Los Angeles, Center for Occupational and Environmental Health and the California Walnut Commission.

83 OPEN CHROMATIN MAPPING IDENTIFIES TRANSCRIPTIONAL NETWORKS REGULATING HUMAN EPIDIDYMIS EPITHELIAL FUNCTION
James Browne, PhD¹, Rui Yang, BS², Lingyun Song, PhD², Greg Crawford, PhD², Shih-Hsing Leir, PhD¹ and Ann Harris, PhD¹
¹Human Molecular Genetics Program, Lurie Children’s Research Center, Chicago, IL, USA,
²Department of Pediatrics, Northwestern University Feinberg School of Medicine, Chicago, IL, USA;
³Department of Pediatrics, Division of Medical Genetics, Duke University Medical School, Durham, NC, USA. Center for Genomic and Computational Biology, Duke University Medical School, Durham, NC, USA
(Presented By: James Browne, PhD)

Introduction: The epithelium lining the epididymis in the male reproductive tract maintains a luminal environment that promotes sperm cell maturation. This process is dependent on the coordinated expression of many genes that encode proteins with a role in epithelial transport. We previously generated genome-wide maps of open chromatin in primary human epididymis epithelial (HEE) cells to identify potential regulatory elements controlling coordinated gene expression in the epididymis epithelium. Subsequent in silico analysis identified transcription factor–binding sites (TFBS) that were over-represented in the HEE open chromatin, including the motif for paired box 2 (PAX2). PAX2 is a critical transcriptional regulator of urogenital tract development, which has been well studied in the kidney but is unexplored in the epididymis.
Methods: Due to the limited lifespan of primary HEE cells in culture, we investigated the role of PAX2 in an immortalized HEE cell line (REP). First, REP cells were evaluated by DNase I digestion followed by high-throughput sequencing and the PAX2-binding motif was again identified as an over-represented TFBS within intergenic open chromatin, though on fewer chromosomes than in the primary HEE cells. To identify PAX2-target genes in REP cells, RNA-seq analysis was performed after siRNA-mediated depletion of PAX2 and compared with that with a non-targeting siRNA.

Results: In response to PAX2-repression, 3135 transcripts were differentially expressed (1333 up-regulated and 1802 down-regulated). Novel PAX2 targets included multiple genes encoding proteins with predicted functions in the epididymis epithelium.

84 A SUSCEPTIBILITY LOCUS, RS7099208, IS ASSOCIATED WITH NON-OBSTRUCTIVE AZOOSPERMIA VIA REDUCTION IN THE EXPRESSION OF FAM160B1
Yan Zhang, Mingxi Liu, Associate Professor¹, Xuejiang Guo, Associate Professor¹ and Jiahao Sha, Professor²
¹Teacher; ²Totur
(Presented By: Yan Zhang)

Introduction: Non-obstructive azoospermia (NOA) is a severe defect in male reproductive health that occurs in 1% of adult men. In a previous study, we identified three risk loci associated with NOA. One, rs7099208, is located within the last intron of FAM160B1 at 10q25.3.

Objectives: This study was undertaken to investigate the biological roles of rs7099208 in spermatogenesis and the potential as targets for NOA.

Methods: We analysed expression Quantitative Trait Loci (eQTL) of FAM160B1, ABLIM1 and TRUB1, the three genes surrounding rs7099208. With immunohistochemistry FAM160B1 expression showed significant weakening trend in NOA testes. And morpholinos were constructed significantly to inhibited FAM160B1 expression at two levels of the mRNA and protein in GC2 cell line.

Results: The expression level of FAM160B1 was reduced for the homozygous alternate genotype (GG) of rs7099208, but not for the homozygous reference or heterozygous genotypes. The expression levels of ABLIM1 or TRUB1 were unaffected by the rs7099208 genotype. And we show that FAM160B1 is predominantly expressed in human testes, where it is found in spermatocytes and round spermatids. We examined testes from 17 patients with NOA and found that expression of FAM160B1 is significantly reduced, or undetectable, in NOA patients, but not in OA cases or normal men. Then we determined that FAM160B1 is expressed in germ cells in mouse testes. Using a mouse germ cell line (GC2) as a model, knockdown of FAM160B1 resulted in a dramatic reduction in cell number, reduced cell viability, and ultimately cell death.

Conclusion: We conclude that rs7099208 is associated with NOA via a reduction in the expression of FAM160B1.

85 REGULATION OF THE PROLIFERATION AND DIFFERENTIATION OF RAT STEM AND PROGENITOR LEYDIG CELLS BY ACTIVIN
Linxi Li, PhD, Renai Xu, MD, Shiwen Liu, MD, Yiyan Wang, MSc, Yuanyuan Shan, MSc, Yuanyuan Hu, MSc, Yaoyao Dong, MSc, Qi Qi Zhu, MSc, Xiaoheng Li, MSc, Jingjing Guo, MD, Haolin Chen and Ren-Shan Ge, MD
The Second Affiliated Hospital, Wenzhou Medical University
(Presented By: Linxi Li, PhD)

Introduction: Stem Leydig cells (SLCs) have been demonstrated to differentiate into adult Leydig cells (ALCs) via intermediate stage of progenitor (PLCs) and immature (ILCs) Leydig cells. However, the exact regulatory mechanisms are unclear. We hypothesized that the proliferation and differentiation of SLCs or PLCs depended upon locally produced factors.

Methods: Microarray analysis revealed that the expression levels of activin type I receptor (Acvrl1) were SLC > PLC > ILC = ALC and those of activin A receptor type II–like 1 (Acvrl11) were SLC > PLC = ILC = ALC. This indicates that that their ligand activin might play important role in stem and progenitor proliferation and differentiation. PLCs were incubated with 10 or 100 ng/ml activin in the absence (basal) or presence (LH–stimulated) of 1 ng/ml LH for 24 hrs.

Results: Activin concentrated–dependently increased the 3H−thymidine incorporation into PLCs by 136% and 203% when cells were treated with activin alone. LH also significantly increased the 3H−thymidine incorporation into PLCs by 268%. However, activin significantly reduced LH–stimulated effects when activin was combined with LH. Activin significantly inhibited the basal testosterone production to 61.77% and 63.08% of control value. At 10 and 100 mg/ml, it also significantly inhibited LH–stimulated testosterone production to 52.36% and 45.34% of control value, respectively.

Methods: We also applied a unique in vitro culture system in which SLCs proliferated on the surface of a cultured seminiferous tubule during one week of culture, and their progeny subsequently differentiated to androgen–forming PLCs during the following 2–4 weeks. ALC–free seminiferous tubules from adult rat testes were cultured with 10 ng/ml activin for three days, and EDU incorporation was used to visualize the proliferative SLCs.

Results: Activin significantly stimulated EDU incorporation by 500% when compared to control. When 10 ng/ml activin were incubated with the seminiferous tubules in the presence of Leydig cell–differentiating medium which contain 10 ng/ml LH plus insulin–transferrin–selenium. Activin inhibited the differentiation of SLCs into PLCs, and this effect was antagonized by the treatment of activin receptor antagonist 100 nM SB431542.

Conclusion: In conclusion, activin primarily stimulates the proliferation of SLCs and PLCs, but inhibits the differentiation of them into Leydig cell lineage in rat testis.
Introduction: Abnormalities of autosomal chromosomes can affect spermatogenesis even in the presence of intact Y chromosome. There are scarce reports in the literature describing the effect of chromosomal translocations on male infertility. The aim of the present study was to record the effect of reciprocal translocations; whether Robertsonian or non-Robertsonian on male infertility.

Methods: The medical records of infertile male patients with chromosomal translocations were reviewed. The patients were classified into 2 groups; group “A” included patients with Robertsonian translocations and group “B” included patients with non-Robertsonian translocations. Semen parameters, hormonal assays and testicular histopathology were reviewed and compared between both groups.

Results: The study included 13 patients with chromosomal translocation, 6 patients in group “A” (Robertsonian translocation) and 7 patients in group “B” (Reciprocal translocation). In general all 13 cases of translocations showed abnormal semen parameters. In Group “A”, 3 patients had Azoospermia and 3 patients had oligoasthenoteratozoospermia. ICSI was scheduled for 4 patients. Sperm were retrieved from 3 patients only without successful pregnancy. In group “B”, 4 patients had Azoospermia and 3 patients had oligoasthenoteratozoospermia. ICSI was scheduled for 5 patients. In all, sperm could be retrieved however without successful pregnancy.

Conclusion: Reciprocal translocations of chromosomes negatively affects spermatogenesis. Chromosomal translocations as a whole has poor prognosis for pregnancy by ICSI.

87 MITOCHONDRIAL DNA EPIGENETICS: CPG AND NON–CPG CYTOSINE METHYLATION IN THE SPERM MITOCHONDRIAL GENOME
Monis B. Shamsi, PhD, Timothy G. Jenkins, PhD, K.I. Aston, PhD and Douglas T. Carrell, PhD
Andrology and IVF Laboratories, Department of Surgery, University of Utah School of Medicine, Salt Lake City, Utah, United States of America.
(Presented By: Monis B. Shamsi, PhD)

Introduction: Recent advances in DNA methylation studies suggest that mitochondrial DNA (mtDNA) may be subjected to epigenetic modifications, and related to or causative of disease development, though the process is poorly understood. It is clear that epigenetic modifications of mtDNA that affect expression of respiratory chain complex subunits may impact energy production and thus cell function. In the sperm however, these potentially important epigenetic marks have not yet been described, which prompted the current investigation.

Methods: Targeted sequencing of bisulphite−converted sperm mtDNA using MiSeq was performed on sperm from normozoospermic (n=5) and asthenozoospermic (n=5) men. Differential methylation analysis was performed to identify regions with methylation differences between the two groups.

Results: A very low magnitude of sperm mtDNA methylation at CpG and non–CpG cytosines was observed in both the study and control groups. Though, globally the difference in methylation was statistically non significant between both groups, we did observe some regions that displayed modest but statistically significant alterations. In protein coding genes, significant differences in methylation at CpGs of CytB gene and non–CpG cytosines of ATPase8, ND4L, ND4, ND6 genes were identified. Non–CpG cytosines of 12S rRNA were significantly hypo−methylated in asthenozoospermic men. Of the 22 tRNAs coded by mtDNA, significant differences between both groups were observed at CpGs of 1 tRNA gene and at non–CpG cytosines of 7 tRNA genes. In the D−loop, non–CpG cytosines were significantly hypermethylated in asthenozoospermic men, and in regulatory regions of the D−loop, significant methylation differences were observed in CpGs at the H−strand origin and non−CpG cytosines of the L−strand promoter region, transcription factor binding sites and at termination associated sequence.

Conclusion: These findings confirm that the level of sperm mtDNA methylation is well below the level reported for nuclear DNA of sperm or other human cell types. The physiological, functional and gene regulatory consequences of the methylation alterations in mtDNA regions, between asthenozoospermic and normozoospermic men are yet to be established. Further study is needed to understand changes in mtDNA methylation patterns, both global and gene specific, and the associated affects on sperm function.

88 SPATA22 LOCALIZES TO MEIOTIC RECOMBINATION NODULES AND IS REQUIRED FOR FERTILITY IN THE MOUSE
Vinita Daniel, Zachary Ferguson, Patrick Davis, Chelsea Schonert, Emily Hays and Sophie La Salle, PhD
Midwestern University
(Presented By: Vinita Daniel)

Introduction: Identifying the cues governing progression of germ cells through meiosis is critical to understand the mechanisms involved in formation of healthy gametes. We previously characterized the mouse ENU-induced repro42 mutation which results in a nonsense codon in spermatogenesis associated 22 (Spata22). Mutant repro42 males and females are infertile due to meiotic arrest at the late zygotene stage, suggesting that SPATA22 plays an essential function during prophase I of meiosis. We set forth to confirm the requirement for Spata22 during gametogenesis by describing a novel allele of this gene.

Methods: Histological and cytological analyses were used to characterize mice carrying the targeted gene trap allele Spata22Gt.
**ABSTRACTS**

**Results:** Similarly to repro42 mutant mice, adult Spata22Gt/Gt males and females are infertile but otherwise healthy. Adult males present with smaller testes devoid of spermatids and spermatozoa. Lack of SPATA22 protein in Spata22Gt/Gt testes was corroborated by immunoblotting. Analysis of surface–spread chromatin confirms that formation of the synaptonemal complex (SC), synopsis and DNA double strand break repair are all impaired in Spata22Gt/Gt spermatocytes as we previously observed in mutant repro42 spermatocytes. A complementation test between Spata22Gt/+ and heterozygous repro42 mice provided genetic evidence that the repro42 phenotype is indeed caused by the mutation identified in Spata22. SPATA22 was previously localized to foci in the nucleus of spermatocytes, but spatiotemporal dynamics were not examined. Analysis of surface–spread chromatin reveals that there are few SPATA22 foci at leptonema but these become prominent along forming SC axes as spermatocytes progress through zygonema. The number of foci decreases upon entry into pachynema, and SPATA22 is present on all chromosomal axes, while persistence of foci following the appearance of histone H1t implies that SPATA22 is still present at mid–pachynema.

**Conclusions:** This study characterizes a novel allele useful to study the function of Spata22 while providing genetic evidence of the origin of the repro42 mutation. Additionally, these results further support a role for SPATA22 during meiotic prophase, most likely during processing and/or resolution of DNA double strand breaks during meiotic recombination.

**SEMEN CRYOPRESERVATION IN MEN WITH CANCER; THE USAGE RATE AND OUTCOME OF ASSISTED REPRODUCTIVE TECHNOLOGY IN 898 PATIENTS**

Iris Muller, MD1, Ralph J.A. Oude Ophuis, PhD2, Frank J.M. Broekmans, MD, PhD2 and Tycho M.T.W. Lock, MD, FEBU3

1Department of Urology, University Medical Centre Utrecht, Utrecht, The Netherlands; 2Department of Reproductive Medicine and Gynaecology, University Medical Centre Utrecht, Utrecht, The Netherlands; 3Department of Urology, University Medical Centre Utrecht, Utrecht, The Netherlands and Department of Urology, Central Military Hospital, Utrecht, the Netherlands

(Presented By: Tycho M.T.W. Lock, MD, FEBU)

**Introduction:** Nowadays, an increasing number of patients survive cancer due to improved treatment techniques. An undesired side effect of these treatments is potential sub– or infertility. Timely cryopreservation of semen is the only way to ensure fertility. Earlier studies showed high success rates of assisted reproductive technology (ART) with cryopreserved semen. The objective of this study was to determine how often cryopreserved semen from cancer patients is used and the success rate of ART in this group in achieving parenthood.

**Method:** All oncological patients who banked their semen before 1983 and 2013, before undergoing treatment, were included in the study. The semen was obtained by masturbation and analysed according to World Health Organization (WHO) guidelines. The semen was frozen in a Planer Kryo560–16 freezer (Planer, United Kingdom) at a rate of 0.5 oC / minute to +5oC, followed by 10 oC / minute to ~80 oC, and finally stored in liquid nitrogen. Patients characteristics and information about the ART were collected from the patient’s medical records in the hospital’s central electronic registration system and the fertility clinic’s specific data management system.

**Results:** 898 patients cryobanked their semen. 96 patients used their cryopreserved semen for ART (10.7%). The clinical pregnancy rate for intra–uterine insemination (IUI), in vitro fertilisation (IVF), intracytoplasmic sperm injection (ICSI) and cryo embryo transfer (ET) were 14%, 37%, 38% and 18%, respectively. A total of 77% of the couples achieved parenthood.

**Conclusion:** Although the success rates of ART are impressive, the usage rate of cryopreserved semen in cancer patients is still low. Health professionals should continue to encourage cancer patients to cryopreserve semen before cancer treatment. Furthermore cancer patients should be advised to return to the fertility clinic if they desire children.

**OUTCOME OF MICROSURGICAL TESTICULAR SPERM EXTRACTION IN FAMILIAL IDIOPATHIC NON–OBSTRUCTIVE AZOOSPERMIA**

Haitham El Bardisi, MD, Mohamed Arafa, MD, Sami AlSaid, MD, Abdulla AlAnsari, MD, Ahmad Majzoub, MD, Ahmad AlMalki, MD and Iyad AlRobi, MD

Urology Department, HMC, Qatar

(Presented By: Haitham El Bardisi, MD)

**Introduction:** Objective: To study the sperm retrieval rate by microsurgical testicular sperm extraction (Micro–TESE) in familial idiopathic non–obstructive azoospermia (NOA).

**Methods:** Study design: This is a cohort retrospective study. The study included 115 patients with idiopathic NOA who underwent micro–TESE over the past 5 years. Medical records of these patients were reviewed. Patients were then divided into two groups; Group “A” with familial idiopathic NOA and Group “B” with non–familial idiopathic NOA. Clinical data as well as data of micro–TESE were recorded.

Main outcome measure(s): Testicular sperm retrieval rate in both groups.

**Results:** Group “A” included the members of seven families, each family contains two brothers (total=14 patients). Group “B” consisted of 101 patients. There was no statistically significant difference in the patients’ demographics between the two groups. Also there was no difference between both groups as regards testicular size, FSH, LH, testosterone and prolactin. In group “A” sperm retrieved rate was 14.29% (2/14 patients) compared to 43.56% in group “B” (44/101 patients) (p= <0.05). The two patients in group “A” with successful sperm retrieval belonged to one family. The histopathological diagnosis was the same in the brothers in each family.

**Conclusion:** The testicular sperm retrieval rate in familial idiopathic NOA is significantly lower than in non–familial idiopathic NOA.
91
ICSI OUTCOME IN KLINEFELTER’S SYNDROME: QATAR EXPERIENCE
Ahmad Majzoub, MD, Mohamed Arafa, MD, Sami ElSaied, MD and Haitham El Bardisi, MD
Urology Department, HMC, Qatar
(Presented By: Ahmad Majzoub, MD)

Introduction: Klinefelter syndrome (KF) is the most common chromosomal disorder associated with male hypogonadism and infertility. Parenthood can be achieved in men with KF by intracytoplasmic sperm injection (ICSI) using testicular sperm. Aim: To evaluate surgical sperm retrieval rate (SSR) in KF patients in Qatar and to investigate methods to improve SSR in this group of patients.

Methods: This is a retrospective study where all the medical records of KF patients who underwent SSR for ICSI, in our center in the past 14 years, were reviewed.

Results: 41 patients were included. 23 underwent conventional testicular sperm extraction (TESE) and 18 underwent microsurgical TESE (Micro−TESE). SSR was significantly higher in the Micro−TESE group than TESE group (33.3% versus 0% respectively). In the Micro−TESE group 14 patients received hormonal stimulation prior to Micro−TESE and 4 patients did not receive. SSR was 42.9% versus 0% in both groups respectively. Within the 14 patients who received hormonal stimulation 8 patients received aromatase inhibitors while the other 6 received other hormonal stimulation. SSR was 62.5% versus 16.7% in both groups respectively.

Conclusion: SSR in KF patients is significantly more when using hormonal stimulation by aromatase inhibitors followed by microsurgical testicular sperm extraction.

92
SPERM RETRIEVAL SHOULD BE PERFORMED AT THE TIME OF TUMOR RESECTION IN MEN WITH CONGENITAL ADRENAL HYPERPLASIA AND BILATERAL TESTICULAR ADRENAL REST TUMORS
Parviz Kavoussi, MD, Roxanne Summers-Colquitt, MS, TS, Kate Odenwald, MSN, RN, ACNP-BC, Thomas Pool, PhD and Shahryar Kavoussi, MD, MPH
Austin Fertility & Reproductive Medicine
(Presented By: Parviz Kavoussi, MD)

Introduction: In males with congenital adrenal hyperplasia (CAH) there is an impaired production of cortisol and mostly of aldosterone resulting in increased pituitary adrenocorticotropic hormone (ACTH) production leading to hyperplasia of the adrenal glands and overproduction of adrenal androgens. Some men with CAH will develop benign testicular adrenal rest tumors (TART’s), which are typically bilateral and originate in the rete testis. TARTs commonly result in obstructive azoospermia and destruction of normal testicular tissue with growth and may cause orchialgia. There have been reports of testicular aspiration for use with in−vitro fertilization/intracytoplasmic sperm injection (IVF/ICSI) with the tumors in situ and reports of men remaining azoospermic after tumor resections. Our objective was to evaluate the effectiveness of concomitant sperm retrieval and tumor resections with the goal of minimizing the numbers of procedures in these men.

Methods: Case report with chart review.

Results Obtained: 35 year old male with the diagnosis of CAH and bilateral TARTs with bilateral orchialgia was found to be azoospermic. He had been on treatment with dexamethasone and human chorionic gonadotropin (HCG) was found to be azoospermic on two separate semen analyses. He underwent concomitant bilateral testicular tumor resection and open testicular sperm extraction. His sperm retrieval was successful and was cryopreserved for future use with IVF/ICSI and his orchialgia resolved after resection. Pathology revealed architecture consistent with adrenal rests.

Conclusions: To our knowledge, this is the first case reported of men with CAH and bilateral TARTs undergoing a successful sperm retrieval concomitantly with bilateral tumor resection. As it has previously been shown that men remain azoospermic following tumor resections, sperm retrieval and tumor resection in one surgical setting would seem to be the optimal approach rather than subjecting such patients to two separate procedures.

93
WHY WE ESTABLISHED THE MALE CONTRACEPTION INITIATIVE
David Sokal, MD and Aaron Hamlin, MEd, MPH, JD
Male Contraception Initiative
(Presented By: David Sokal, MD)

Introduction: Resources for research and development of new, reversible male contraceptives are limited. Currently women have 15 modern contraceptive methods to choose from, while men have only two. Fifty years of research on male hormonal methods have not led to a marketed product. The Gates Foundation supports the development and marketing of new female contraceptives, but has stated it would not fund research on new male methods. The Michaelson Foundation is supporting a $100 million effort to develop new contraceptives for dogs and cats. No similar effort is focused on men, yet at least five promising methods await funding to move forward. Although women bear most of the consequences of unintended pregnancy, unintended fatherhood also has economic and mental health consequences. Given recent advances in biotechnology, it seems timely to explore novel approaches for new reversible, non−hormonal male contraceptives.
**ABSTRACTS**

### 94 RAPID SELECTION OF MOTILE SPERM WITH HIGH DNA INTEGRITY USING MICROFLUIDICS

Krista Zeidan, MSc¹, Maria C. San Gabriel, MSc, PhD¹, Reza Nosrati, PhD candidate², Lise Eamer, MSc², Marion Vollmer, PhD², David Sinton, PhD, P Eng² and Armand Zini, MD¹

¹McGill University; ²Toronto University

(Presented By: Maria C. San Gabriel, MSc, PhD)

**Introduction:** Microfluidic technology has found wide application in the biomedical field particularly in cell sorting. We have previously reported on the application of a microfluidic device (MFD) that selects motile spermatozoa with high DNA integrity. The MFD processes raw semen and involves a simple one-step protocol without the need for centrifugation. The goal of this study was to further evaluate the ability of a 7.5 mm MFD to select sperm with high vitality and DNA integrity at different run times.

**Methods:** Sperm samples were obtained from volunteer donors. After testing successive devices and evaluating sperm recovery from earlier models, we focused on testing the 7.5 mm MFD. One ml of raw semen was loaded into the device and spermatozoa from the outlets were collected at 10 and 20 min run times. Sperm DNA integrity was assessed by the SCSA (sperm chromatin structure assay) and results expressed as %DFI (measure of DNA damage) and %HDS (measure of chromatin compaction). Viability was determined using eosin-nigrosin stain.

**Results:** Spermatozoa collected from the 7.5 mm MFD outlets had significantly higher viability after 10 and 20 minute run times (99±7% and 96±8%, respectively) compared to raw semen (88±3%) (P-value=0.0042). Spermatozoa collected from the 7.5 mm MFD outlets had significantly lower levels of DNA damage (%DFI=9.8±4.8% [Raw] vs. 4.1±3.9% [10 min] and 1.6±1.3% [20 min], P-value 0.002) and a lower percentage of poorly compacted nuclei (%HDS=3.2±1.0% [Raw] vs. 1.1±1.4% [10 min] and 0.9±1.0% [20 min], P-value 0.0014).

**Conclusions:** The 7.5 mm channel MFD allows for the recovery of motile sperm populations with significantly higher viability and DNA integrity than raw semen. The 10 and 20 minute run times yielded comparable results. Our study demonstrates that this MFD could be used for selecting viable and highly motile sperm with good quality DNA for potential use in assisted reproductive technologies.

### 95 COMPARATIVE STUDY OF MICROFLUIDIC DEVICE (MFD) AND DENSITY GRADIENT CENTRIFUGATION (DGC) IN SELECTING SPERM WITH HIGH DNA INTEGRITY

Maria C. San Gabriel, MSc, PhD¹, Krista Zeidan, MSc¹, Khalid Alrabeelah, MD¹, Reza Nosrati, PhD candidate², Lise Eamer, MSc², Marion Vollmer, PhD², David Sinton, PhD, PEng² and Armand Zini, MD¹

¹McGill University; ²Toronto University

(Presented By: Maria C. San Gabriel, MSc, PhD)

**Introduction:** Assisted reproductive technologies (ARTs), such as ICSI (intracytoplasmic sperm injection), have revolutionized the management of infertile couples. Nonetheless, the search for improved sperm selection methods is of paramount importance to ensure that only good quality sperm are used for ARTs. We have previously reported on a microfluidic device (MFD) that selects sperm with high DNA integrity. The goal of this study was to further evaluate the MFD and compare its ability to select sperm with high vitality and DNA integrity to that of conventional density gradient centrifugation (DGC).

**Methods:** Semen samples were obtained from healthy donors (n=10) and allowed to liquefy. A 1 ml aliquot of semen was loaded onto a 6 mm MFD and another 1 ml aliquot was layered on top of a two-step Percoll density gradient (40–80%). Spermatozoa were collected from the MFD outlet after a 30 min runtime and from the density gradient pellet after centrifugation at 300g for 25 min. The recovered spermatozoa were tested for vitality (by eosin/nigrosin staining), DNA integrity (reported as %DFI using the SCSA – sperm chromatin structure assay) and chromatin compaction (reported as %HDS using the SCSA). We also assessed the % sperm recovery in the MFD outlet and DGC pellet.

**Results:** The mean (±SD) percentage of viable spermatozoa was significantly higher in sperm recovered from the MFD and DGC (98 ± 2% and 97 ± 4%, respectively) compared to raw semen (91 ± 10%) P value=0.034. The %DFI and %HDS were both significantly lower in sperm recovered from the MFD and DGC (%DFI= 3.6 ± 1.8% and 3.0 ± 2.2% and %HDS= 0.7 ± 0.3% and 0.8 ± 0.5%, respectively) compared to raw semen (%DFI=12.3 ± 8.4%, [P value=0.0004] and %HDS=3.1 ± 1.6% [P value=<0.0001]). However, the percent sperm recovery was significantly higher using DGC than with the MFD (98 ± 6.5% vs. 6.0 ± 0.4%, respectively) P value=<0.0001.

**Conclusions:** Our results indicate that the 6 mm MFD and DGC yield comparable results in terms of selecting sperm with good viability and DNA integrity. However, DGC yielded a higher percent sperm recovery than the MFD.
PROTEOMIC PATHWAYS OF OXIDATIVE STRESS IN THE HUMAN SEMINAL PLASMA.

Paula Intasqui, MSc¹, Mariana Camargo, MSc¹, Mariana P. Antoniassi, BSc¹, Karina H. M. Cardozo, PhD², Valdemir M. Carvalho, PhD² and Ricardo B. Bertolla, DVM, PhD¹

¹Department of Surgery, Division of Urology, Sao Paulo Federal University; ²Fleury Group

(Submitted By: Paula Intasqui, MSc)

Introduction: Oxidative stress is widely considered one of the main cellular mechanisms of male infertility. It promotes negative effects on sperm function mainly through lipid peroxidation and oxidation of seminal plasma and sperm proteins. Thus, our aim was to investigate if the seminal plasma proteome may reflect semen lipid peroxidation (LPO) levels.

Methods: We performed a cross-sectional study with 156 normozoospermic patients. Semen was collected by masturbation, analyzed according to WHO 2010 guidelines and centrifuged for seminal plasma separation. LPO levels were assessed using a colorimetric assay for malondialdehyde, a by-product of LPO, and patients were grouped as low LPO levels (control group, bottom 15%, n=23) and high LPO levels (study group, top 15%, n=23). Seminal plasma proteomics was performed by a label-free quantitative approach, in which 50ug of total proteins were pooled, digested into trypic peptides and analyzed by liquid chromatography followed by tandem mass spectrometry (LC-MS/MS). Four pools were prepared for each group, including biological variation between the pools, and these were run in technical triplicates. Significant proteins (Student’s T test) were used for functional enrichment analysis and confirmed by logistic regression and discriminant analysis.

Results: LPO levels (mean ± standard deviation) were 14.9 ± 1.60 ng/mL in controls and 32.0 ± 2.68 ng/mL in the study group (p<0.001). Progressive motility and total motility were statistically (p<0.05) lower, while immotility was higher in the study group. 629 proteins were quantified, of which 4 were absent, 19 were downexpressed, 8 were exclusive and 63 were overexpressed in the study group, with several enriched functions (Figure 1). The logistic regression model presented a total predictive value of 91.7%, and an area under the ROC curve of 99.3%. We suggest Mucin−5B (MUC5B_HUMAN) as a biomarker of semen oxidative stress.

Conclusion: The seminal plasma proteome and post-genomic pathways reflect semen LPO levels, mainly with the enrichment of reactive oxygen species detoxification. MUC5B may be a semen biomarker of LPO damage.

Support: FAPESP (process 2011/14631−7) and CNPq (process 472941/2012−7).

TIME FOR PUBLIC HEALTH ACTION ON INFERTILITY: UPDATES FROM THE CENTERS FOR DISEASE CONTROL AND PREVENTION

Steven Schrader, PhD¹, Lee Warner, PhD, MPH², Richard Wang, MD³ and Hubert Vesper, PhD³

¹CDC/NIOSH; ²CDC/NCCDPHP; ³CDC/NCEH

(Presented By: Steven Schrader, PhD)

Introduction: Infertility has become a public health issue in the US. Recently, the nation’s premier public health agency, the Centers for Disease Control and Prevention (CDC) released the long anticipated “National Public Health Action Plan for the Detection, Prevention, and Management of Infertility” This presentation will describe highlights of the action plan and what CDC is doing to further promote the issue of infertility as a public health problem for both men and women.

Methods: To describe the development and contents of the national public health action plan as well as ongoing surveillance, research and programmatic efforts surrounding infertility.

Results: The plan, released in July 2014, was coordinated by CDC in consultation with many stakeholders including governmental and non–governmental organizations, professional societies, health care professionals, academic programs, and individuals affected by infertility. Its goal is to highlight the need to better understand and address issues at a population level that contribute to and are caused by infertility and that may affect the health of the resulting pregnancy. This plan represents the first major effort by the agency to consider the broader implications of infertility from a public health perspective. Overall goals include promoting healthy behaviors that can help maintain and preserve fertility; promoting prevention, early detection, and treatment of medical conditions that can threaten fertility, and reducing exposures to environmental, occupational, infectious, and iatrogenic agents that can threaten fertility. Several publicly available, population–based surveys conducted by CDC, including the National Survey of Family Growth (NSFG), National Health and Nutrition Examination Survey (NHANES), National Health Interview Survey (NHIS), National Vital Statistics System (NVSS), and Pregnancy Risk Assessment Monitoring System (PRAMS) can be used to examine key aspects of or risk factors for infertility.

Conclusion: The national public health action plan provides a foundation and framework for discussion and collaboration between stakeholders and CDC regarding the prevention, management and treatment of male and female infertility in the United States.

CRYOPRESERVATION OF SPERMATOZOA: OPTIMIZATION OF MOTILITY WITH A NONPERMEABLE CRYOPROTECTANT

Jie Liu, PhD, Cigdem Tanrikut, MD, Diane Wright, PhD, Gloria Lee, Mehmet Toner, PhD and Thomas Toth, MD

Massachusetts General Hospital and Harvard Medical School, Boston, MA

(Presented By: Cigdem Tanrikut, MD)

Introduction: Cryopreservation of sperm from men with severe male factor infertility eliminates the need for repeat surgical extractions in azoospermic men and the risk of inadequate viable sperm the day of oocyte retrieval in men with cryptozoospermia. However, current sperm cryopreservation techniques do not reliably freeze/thaw very low numbers of sperm. In an effort to help solving this problem, we
used trehalose and silica micro-capillaries with a 2 µl capacity to preserve sperm from healthy men and optimized post thaw motility.

**Methods:** Motile sperm were isolated with 80%/40% density gradients from fresh ejaculates. Only those samples with 80% or greater motility were used. Aliquots from 8 samples (three repeats per sample per treatment) were diluted 1:1 with a freezing medium consisting of human tubal fluid (HTF), 5% human serum albumin (HSA), and varying concentrations of trehalose: 0.0M, 0.125M, 0.25M, 0.5M, and 1M. Two microliters of the suspension were loaded into each 200 µm silica capillary. After sealing each capillary end with Tygon tubing, the capillary was incubated in liquid nitrogen (LN2) vapor for 5 minutes before being plunged into LN2. To thaw, each capillary was quickly immersed into a room temperature (~22°C) water bath. Capillary contents were expelled into a drop of 12 µl HTF with 5% HSA on a glass slide, then covered with a coverslip and motility of the sperm was examined. Sham controls consisted of sperm/freezing medium suspension were loaded into capillaries and expelled immediately for assessment without freezing.

**Results:** When 0.0M, 0.125M, 0.25M, 0.5M, and 1M trehalose was supplemented into the freezing medium, recovered motility (post thaw motility/pre−freeze motility × 100%) of the sperm was 41.0%, 62.0%, 67.8%, 52.3%, and 29.1%, respectively. For sham controls corresponding to the above trehalose concentrations, sperm motility was 98.0%, 98.9%, 98.9%, 93.8%, and 84.2%, respectively. The freezing medium containing 0.25M trehalose achieved the highest recovered motility among all media.

**Conclusion:** Trehalose is an effective nonpermeable cryoprotectant in preserving sperm using silica capillaries. This protocol eliminates washing after thawing, avoiding unintended sperm loss. We have demonstrated a system potentially beneficial to preserve small numbers of sperm from azoospermia and oligozoospermia patients.

### 99 NON−MOTILE SPERM CELL SEPARATION USING A SPIRAL CHANNEL

Jiyoung Son, MS¹, Raheel Samuel, PhD², Kristin Murphy, PhD³, Douglas Carrell, PhD², Bruce Gale, PhD³ and James Hotaling, MD²
¹Electrical and Computer Engineering of University of Utah; ²Urology Division, Department of Surgery, University of Utah School of Medicine; ³Mechanical Engineering of University of Utah

**Introduction:** Microfluidic sperm sorting has historically relied on sperm motility. However, motility−based sperm separation technology will not work when viable non−motile sperm need to be separated in from testicular tissue from testicular sperm extraction (TESE) and microdissection TESE techniques. Here, we demonstrate the use of inertial microfluidic technology using spiral channels to separate sperm. The separation method is label−free does not rely on sperm motility for sorting.

**Methods:** Basic principles of spiral channel separations were used to define specific channel and flow parameters for separating non−motile sperm, including the ratio of inertial lift and Dean drag (Rf), the ratio of particle and channel dimension (Î) and the aspect ratio of the channel cross−section. When Rf, Î, and the aspect ratio are >−0.08, >0.07 and 3:1 respectively, theory suggests that the sperm could be focused and separated from red blood cells (RBCs). Channels to implement these features were designed and validated. Mixed samples of RBCs and sperm were used to test the device. The inlet flow rate ranged from 0.1−0.3ml/min. The processed sample contained 2 million (M)/ml of sperm and 5.3M/ml of RBC in a 1 ml volume. The original sample was diluted for some later experiments to avoid interference between the different particles. After running the sample through the spiral channel, the samples were collected from four different splitter outlets, and were inspected using microscopy.

**Results:** For a 0.3ml/min injection, sperm concentration was focused at outlet 1 (1.7M/ml) and outlet 2 (2.4) with lower concentrations at outlet 3 (0.4) and outlet 4 (0.45). In terms of concentration ratio the overall collected sperm at outlet 1~4 were 34, 48, 8, and 9%, respectively. In contrast, the concentration of RBCs was clearly higher at outlet 3 (0.85M/ml) and outlet 4 (10.3) than at outlet 1 (0) and outlet 2 (0.4). The concentration ratio of the overall collected RBC at outlet 1~4 were 0, 3.4, 7.3 and 89.2%, respectively.

**Conclusion:** Sperm and RBCs were successfully separated from each other in a microfluidic spiral device with over 96% of RBCs removed from the sample and 82% of the non−motile sperm recovered, suggesting that this technique might be useful for separating non−motile sperm found in TESE and mTESE samples.

### 100 QUANTITATIVE EVALUATION OF EXPRESSION OF THE CATSPER CHANNEL IN HUMAN SPERM AND RELATION WITH FUNCTIONAL PARAMETERS

Lara Tamburrino, Sara Marchiani, Cambi Marta, Forti Gianni, Muratori Monica and Elisabetta Baldi
Dept. of Biomedical, Experimental and Clinical Sciences, University of Florence, Italy

(Presented By: Elisabetta Baldi)

**Introduction:** CatSper is a sperm−specific calcium channel activated by progesterone (P) in human spermatozoa, and has been indicated as putative progesterone sperm receptor (Strunker et al, 2011; Lischo et al, 2011). KO mice for any of the Catsper family genes, fail to acquire hyperactivated motility (HA) and are infertile. Less clear is the role of CatSper in human sperm hyperactivated/activated motility and in asthenospermia. Here, we re−examined the involvement of CatSper in sperm motility parameters, intracellular calcium levels and acrosome reaction (AR) by directly investigating their relationship with CatSper expression.

**Methods:** We set up a method for quantitative evaluation of CatSper expression in sperm by immunofluorescence/flow cytometry. CatSper expression was found reduced in asthenozoospermic men (53.3±16.0%, p=24 vs 68.3±17.1% in normozoospermic, n=85, p<0.01) and was significantly correlated with progressive (r=0.31, p<0.01), total (r=0.36, p<0.01) and hyperactivated (r=0.44, p<0.01) motility. Besides a higher percentage of sperm not expressing CatSper, asthenozoospermic men showed a larger amount of sperm with localization of the immunofluorescence signal in the midpiece (44.9±1.9%) respect to normozoospermic (27.7±4.3%, p<0.005). By using a probe to distinguish live and dead cells, expression of CatSper was found to be prevalent in live sperm (53.3±14% vs 20.4±0.2 % in dead).

**Results:** A significant correlation was found between CatSper expression and the increase of [Ca2+]i in response to progesterone (r=0.4, p<0.05) but not with basal [Ca2+]i. No correlation was found with AR, either basal or in response to progesterone. Receiver operating characteristic analysis demonstrated that at the threshold
of 73%, CatSper expression discriminates subjects with 10% hyperactivation (a value distinguishing between fertile donors and sub–fertile patients) with an accuracy of 77%, a sensitivity of 87% and a specificity of 61%.

Conclusion: Our results demonstrate that CatSper expression is a prerequisite for human sperm activated and hyperactivated motility, highlighting a role in the pathogenesis of asthenozoospermia. Evaluation of CatSper expression in semen might represent an additional parameter to routine semen analysis in the elucidation of the pathogenesis of male infertility and in the management of infertile couples.

101 - WITHDRAWN

102 THE GENERAL METHOD OF PLACING THE RESERVOIR IN INFLATABLE PENILE PROSTHESIS OPERATION
Chen Bin, MD, Zhan Junxin, Chen Chaoyue, Huang Fengjin and Zhu Xihong
(Presented By: Chen Bin, MD)

Introduction: Objective: To summarize the basal putting method of reservoir to retropubic space (bladder before), is carried out in the IPP operation.

Methods: 20 cases of IPP surgery, adopt the “blind” way for putting the water sac to retropubic space (bladder before).

Results: the anatomical position, osseous marks, puncturing technique for the back–membrane of inguinal canal, the temperature change of entering into the retropubic space, and how to determine the correct position, were summarized.

Conclusion: The basal method of putting reservoir to retropubic space, should be standardized. We think the reservoir can be placed in the right place if using our general method in IPP.

103 FAILURE TO ATTAIN STRETCHED PENILE LENGTH AFTER INTRACavernosAl INJECTION OF A VASODILATOR AGENT IS PREDICTIVE OF VENO–OCCLUSIVE DYSFUNCTION ON PENILE DUX Doppler Ultrasoundography
Faysal A. Yafi, MD, FRCS, Ian R. McCaslin, MD, Russell P. Libby, MD, PremSant Sangkum, MD, Suresh Sikka, PhD and Wayne J.G. Hellstrom, MD, FACS
Tulane University School of Medicine
(Presented By: Faysal A. Yafi, MD, FRCS)

Introduction: Penile duplex Doppler ultrasound (PDDU) is frequently used to assess the etiology of erectile dysfunction (ED). Peak systolic velocity (PSV), end–diastolic vascular velocity (EDV), and resistive index (RI) are commonly used PDDU parameters. We sought to assess whether reaching stretched penile length (SPL) at peak erection after intracavernosal injection (ICI) of vasodilator during PDDU had any correlation with the etiology of ED.

Methods: We performed a retrospective review of 278 consecutive patients who underwent PDDU for the work–up of ED or Peyronie’s disease (PD) between 2011 and 2013. Flaccid and stretched penile length and circumference were measured by standardized ruler, prior to ICI and at peak erection during PDDU. All measurements were performed by the expert ultrasonographer (SS) using standardized protocol (Sikka et al, JSM 2013). Collected data included patient demographics, vascular, and anatomic parameters.

Results: The mean age of our population was 54 years (median 56.0, range 18–80). SPL matched with peak length after ICI in 171 patients (62%, group 1) and did not in 103 (38%, group 2). There were no significant differences between the 2 groups in terms of age, presence of Peyronie’s disease, degree or direction of curvature, IIEF–5 score, percent rigidity or tumescence, and vasodilator dose used. Surprisingly, patients who did not match SPL at peak erection were found to have more veno–occlusive dysfunction (VOD) (62% vs. 42%, p=0.0013). On multivariate analysis, failure to reach SPL was predictive of VOD (OR 0.480, CI 0.271–0.850, p=0.0118) in these patients.

Conclusion: Failure to reach SPL during PDDU after ICI of a vasodilator agent appears to be predictive of VOD which is independent of rigidity and tumescence.

104 THE HISTORY OF PENILE ENHANCEMENT – TO CUT A SHORT STORY LONG
Paul Cleaveland, MBChB, Zubei Ali, MBChB and Ian Pearce, MBChB
Royal Preston Hospital; South Manchester Teaching Hospitals NHS Trust; Central Manchester Teaching Hospitals
(Presented By: Paul Cleaveland, MBChB)

Introduction: Throughout history the penis has been a sign of masculinity characterised by its length, shape and performance. Insecurity regarding penile dimensions and methods of penis enlargement are well reported. We present the various methods of penile enhancement from ancient times to modern day era.

Methods: A literature search was conducted describing penis size and methods for penile enhancement throughout history. We reviewed the evolution of these techniques and present our findings.

Results: Procedures employed for male enhancement date back to ancient rituals, such as the African custom of hanging weights from genitals and the Topinama tribesmen (Brazil) practice of increasing penile size by allowing a snake to bite the penis. Approaches to penis enlargement have since evolved, with more sophisticated methods currently employed. A vacuum device utilising a compression ring was first patented in 1917. The first recorded penis augmentation procedure was performed in 1971 for the treatment of microphallus in bladder extrophy children. Over the years, division of the suspensory ligament in cosmetic surgery has become established. Other initiatives include penile rings, penile extenders/traction devices, and jelqing. The mainstream of girth enhancement is fat injection into the penis, described in 2006. These methods have various degrees of success as well as associated morbidity.

Conclusion: Penile enhancement is an interesting and controversial subject. It is clear that since ancient times across cultural divides, penile dimensions have been topical. The evolution of the techniques currently available to enhance penile size is ongoing fuelled by intrigue and demand.

105 THE EFFECT OF AN AQUEOUS TYPHA CAPENSIS EXTRACT ON THE AGEING MALE REPRODUCTIVE SYSTEM
Nicole Haines-Arries, MSc, Abdulkarem Ilfergane, MSc and Ralf Henkel, PhD
University of the Western Cape
(Presented By: Ralf Henkel, PhD)

Introduction: In traditional African medicine, an aqueous Typha capensis rhizome extract (TCE) is recommended to males as it is believed to enhance male reproductive function although few studies
exist focusing mainly on the phytochemistry of this plant. Thus, there is a definite need to investigate this plant in terms of its beneficial effects on male reproductive health.

**Methods:** Data obtained from an in vitro study led to a pilot study, which investigating the effect of TCE on 1-year-old, male rats. The treatment group (32 mg TCE kg−1 body weight (BW)) was force-fed daily at a maximum volume of 200 µl while the control group received a similar volume of tap water over a period of 14 days. At termination, weights of back fat and the gastrocnemius muscle, as well as testosterone (T) and luteinizing hormone (LH) concentrations were determined.

This study was repeated over a 52-day period and animals were divided into a high-dose (32 mg TCE kg−1 BW per day) (HD), a low-dose (2 mg TCE kg−1 BW per day) (LD) and control group. At termination, in addition to the previous parameters, weights of testis, prostate, epididymis, seminal vesicles, liver, kidney, adipose tissue and gastrocnemius muscle were recorded. In addition, progesterone (P) and estradiol (E) were determined.

**Results:** Data from the pilot study showed no difference for the BW (P=0.0532) and adipose tissue weight (P=0.2239) between control and TG. However, the average BW and adipose tissue weight in the TG decreased by 14.28% and 29.26%, respectively, compared to the control. Although there was no significance difference (P=0.1429) in average muscle weight and T (P=0.3777) between the control and TG, increases in muscle weight (4.8%) and T (30%) were noted. There was no difference for LH levels.

After 52 days of treatment, BW in the LG (P=0.0350) increased and no difference (P=0.3447) was observed in the HG, although a slight increase in BW was observed. No difference was observed for weights of the reproductive organs, liver, kidney, adipose tissue and gastrocnemius muscle for both, LG and HG. No difference was observed for LH levels.

**Conclusion:** Results suggest that TCE affects the parameters tested. Higher dosages can cause negative feedback. Further studies are underway to determine if TCE may be used as herbal remedy to alleviate aging males’ symptoms.

**ABSTRACTS**

106 ASSOCIATION BETWEEN ERECTILE FUNCTION AND SUBCLINICAL ATHEROSCLEROSIS: A STUDY BASED ON MIDDLE-AGE HEALTHY MEN FROM THE GENERAL POPULATION

Babak Rezanezhad, Rasmus Borgquist, MD, PhD, Ronnie Willenheimer, MD, PhD and Saad Elzanaty, MD, PhD

(Presented By: Babak Rezanezhad)

**Introduction:** Epidemiological studies suggest atherosclerosis as a common risk factor between cardiovascular diseases and erectile dysfunction (ED). We aimed, therefore, to determine the association between erectile function (EF) and biomarkers of subclinical atherosclerosis in 119 healthy men from the general population.

**Methods:** The EF was assessed using the International Index of Erectile Function–5 (IIEF–5). Serum levels of biomarkers of atherosclerosis; Apolipoprotein A (ApoA), Apolipoprotein B (ApoB), fibrinogen, and C-reactive protein (CRP) were measured. In addition, the body mass index (BMI) was calculated.

**Results:** The mean (SD) of age was 55 years (±4.0). The prevalence of ED was 50 %. There was a negative significant correlation between EF and CRP, and BMI (r = −0.20, p = 0.02), (r = −0.20, p = 0.03), respectively. No significant correlations between EF and ApoA, ApoB, and fibrinogen were found (p > 0.05). A positive significant correlation was found between BMI and CRP (r = 0.30, p = 0.001). Finally, in a multivariate logistic regression model with EF as the dependent variable, CRP was the only biomarker that predicted ED (odds ratio = 0.343; 95 % CI: 0.122–0.963).

**Conclusion:** These results indicate a direct causal association between subclinical atherosclerosis and ED. This association seems to be related to the increased values of BMI among such men.
ORAL TREATMENT WITH A COMBINATION OF 4 NUTRACEUTICALS (GINGER, L–CITRULLINE, MUIRA PUAMA AND PAULLINIA CUPANA) THAT UPREGULATE THE NO–CGMP PATHWAY CAN DELAY THE ONSET OF AGING ASSOCIATED ERECTILE DYSFUNCTION

Su M. Hlaing, BS, Andre Chan, BS, Jorge N. Artaza, MS, PhD and Monica G. Ferrini, PhD¹,²
¹Department of Internal Medicine, Charles R. Drew University of Medicine & Science, Los Angeles, CA 90059; ²Department of Health and Life Science, College of Science and Health, Charles R. Drew University of Medicine & Science, Los Angeles, CA 90059
(Presented By: Monica G. Ferrini, PhD)

Introduction: Aging associated erectile dysfunction (ED) is characterized by a progressive apoptosis of the smooth muscle cells and collagen deposition in the corpora cavernosa which leads to an impairment in erectile function. High local output of nitric oxide (NO) via inducible nitric oxide synthase (iNOS) has been shown to inhibit corporal fibrosis and this effect of iNOS may be further enhanced by treatment with PDE5 inhibitors. Nutraceuticals are substances that offer medicinal benefit, including prevention and/or treatment of diseases. The nutraceuticals ginger, muira puama and paullinia cupana have been shown in some studies to enhance NOS activity similar to that seen with the PDE5 inhibitors. We therefore evaluated whether the daily oral administration for 2 months with a combination of ginger, paullinia cupana, muira puama as well as L–citrulline, (COMP–4) can effectively delay the ongoing corporal fibrosis, smooth muscle cell loss and cavernosal veno–occlusive dysfunction (CVOD) seen in middle aged rats and compared these results to those receiving tadalafil only.

Methods: 10 Month old Fisher 344 rats were treated orally for two months with either vehicle (controls), COMP–4 (ginger 45 mg/Kg B.W, L–Citrulline 133 mg/Kg B.W, Muira Puama 45 mg/Kg B.W), or tadalafil (2.5 mg/Kg B.W). CVOD was determined by dynamic infusion cavernosometry. Penile sections of the corpora cavernosa were subjected to Masson trichrome staining to evaluate fibrosis, immunohistochemistry followed by image analysis was used for both iNOS and desmin, a marker of smooth muscle content.

Results: A decline in the control rats’ erectile function is evident by 10–12 months of age (ICPAP: 30% decrease; drop rate 1.7 fold increase) and is accompanied by a decrease in the corporal smooth muscle content (52%) and an increase in corporal fibrosis by 70%. The daily treatment for two months with COMP–4 increases iNOS expression, preserves corporal smooth muscle content, and decreases corporal fibrosis resulting in the preservation of normal erectile function. These results with COMP–4 parallels those obtained with daily tadalafil.

Conclusion: An oral combination of ginger, Muira Puama, Paullinia cupana and L–citrulline seems to be as effective as a daily PDE5 inhibitor in delaying and/or reversing the onset of the histological and functional characteristics of aging related ED.

THE SECONDARY HYPOGONADISM POPULATION THAT CAN BE TREATED WITH ENCLOMIPHENE CITRATE AND RESULTS

Ronald Wiehle, PhD, Gregory Fontenot, PhD and Jaye Thompson, PhD Repros Therapeutics
(Presented By: Ronald Wiehle, PhD)

Introduction: Men with secondary hypogonadism are characterized by low normal LH and low serum testosterone. Men have been treated with exogenous testosterone products such as gels and injections but also Clomiphene Citrate off–label to raise their serum testosterone. Exogenous testosterone suppresses testicular serum testosterone production and sperm counts. We have seen that the trans isomer of Clomiphene Citrate, enclomiphene citrate, can similarly raise serum T without decreases in sperm counts and have been developing it with the intention that it can be approved for use in men. We have conducted a series of phase 1, 2, and 3 clinical trials to evaluate the utility of enclomiphene citrate in men with secondary hypogonadism as indicated by two low morning serum values and low-to-normal LH. We have found that many men with secondary hypogonadism are obese or have BMIs in the overweight range.

Methods: Multiple clinical trials in men. We usually have an active–treatment arm. Sometimes we have shown a placebo arm and/or an active–control arm. The breakdown of our clinical trial population is given in the table.

Results: Enclomiphene Citrate is able to raise LH and FSH in men with secondary hypogonadism in essentially all men to whom it has been given: 85% of all men see an increase in serum T into the normal range. When we have done the comparison, about 75% of the men have seen retention of sperm counts. We see a decrease in serum cholesterol, We have seen a decrease in serum IGF−1. We see a preservation of testes size. Enclomiphene citrate appears to be neutral on bone over one year.

Conclusion: Obese men with secondary hypogonadism achieve a normalization of LH, FSH, and T with enclomiphene citrate. Weight loss has not been apparent. The effects of enclomiphene appear to be initiated on the hypothalamus with a stimulation leading to release of LH and FSH from the pituitary with down-stream effects of the Leydig Cells (testosterone production) and Sertoli cells of the testes (maintenance of sperm counts.) This work was supported entirely by Repros Therapeutics.
110

3-ADRENERGIC RECEPTORS ARE INVOLVED IN REGULATING NITRIC OXIDE SIGNALING AND NEUROGENIC FORCE OF CONTRACTION IN CORPUS CAVERNOSUM OBTAINED FROM PATIENTS WITH ERECTILE DYSFUNCTION
Serap Gur, MD¹, Faysal Yafi, MD², Suresh Sikka, MD², Philip Kadowitz, MD² and Wayne Hellstrom, MD³
¹Ankara University; ²Tulane University School of Medicine
(Presented By: Faysal Yafi, MD)

Introduction: 3-adrenergic receptors (3-ARs) play a physiological role in mediating penile erection. Earlier data in human corpus cavernosum (HCC) from male-to-female transsexual surgical procedures showed that activation by a selective 3-receptor agonist elicits marked relaxation by a cyclic guanosine monophosphate (cGMP)-dependent but nitric oxide (NO)-independent mechanism. The aim of the study was to analyze whether 3-ARs were also functional in the HCC of men with erectile dysfunction (ED).

Methods: HCC specimens were obtained from patients (aged 53–69 years, n=7) with ED undergoing penile prosthesis surgery. HCC strips were mounted in organ baths and tested for changes in isometric tension in response to a 3-AR agonist, BRL−37344 (0.01–100 µM) on phenylephrine (Phe)−induced contraction. The influence of 3 agonists on nitricergic relaxations induced by either electrical field stimulation (EFS, 1–40 Hz) or acetylcholine (ACh, 10µM) was studied in HCC. The effects of BRL−37344 on neurogenic contractions evoked by EFS were investigated. The specificity of action of BRL−37344 on 3-adrenergic receptors was verified using SR 59230A(10 µM), a selective 3-AR antagonist.

Results: Phenylephrine−induced contraction in HCC was inhibited by BRL−37344 (77.2 ± 7.1%, at 100 µM). The biphasic relaxation in response to EFS changed in a monophasic response in the presence of BRL−37344. In HCC strips, ACh (100 µM)−induced relaxation responses were increased by 36%. The EFS−induced contractile response at 40 Hz was remarkably decreased by 83% with BRL−37344. BRL−37344’s inhibition of the amplitude of neurogenic contractions was antagonized with SR 59230A.

Conclusion: These results further support the hypothesis that 3-AR mechanisms may play an important role in the nitricergic and adrenergic neurotransmission processes in HCC. The 3-AR system may maintain the biological activity of exogenous NO in the presence of adrenergic stimulation. Thus, while 3-ARs likely play a dynamic role in modulating HCC smooth muscle tone, 3-AR agonists may be promising candidates for the clinical treatment of men with ED.

111

EARLY EXPERIENCE WITH MICRO SURGICAL SPERMATIC CORD DENERVATION FOR CHRONIC ORCHALGIA IN A CANADIAN CENTRE.
Darby Cassidy, MD
University Hospital of Northern British Columbia
(Presented By: Darby Cassidy, MD)

Introduction: Microsurgical spermatic cord denervation (MSCD) is an effective surgical technique for the management of chronic orchalgia but has not been readily adopted by Canadian Urologists. This paper reviews the early experience of a single Urologist in Canada.
114 TRANSCRIPTIONAL REGULATION OF HUMAN SPERM-ASSOCIATED ANTIGEN 16 BY S-SOX5
Ling Zhang, PhD¹, Junpin Liu, MD¹, Wei Li, MD², Jerome Strauss III, MD, PhD³ and Zhibing Zhang³
¹Wuhan University of Science & Technology; ²Virginia Commonwealth University; ³Virginia Commonwealth Univ/OB/Gyn
(Presented By: Zhibing Zhang)

Introduction: The mammalian sperm-associated antigen 16 gene (SPAG16) encodes an axoneme central apparatus protein that regulates cilia/flagella motility. It is highly abundant in the testis. The gene is also expressed in most somatic tissues, particularly in the tissues with motile cilia, such as tracheal and brain. Human and mouse SPAG16 gene promoters contain multiple potential binding sites for the transcription factor SOX5, which has homology to the high mobility group box region of the testis-determining factor, SRY.

Methods: Given that both the mouse and human SOX5 genes encode a 48-kDa SOX5 protein (S-SOX5) that is only present in tissues containing cells with motile cilia/flagella, we hypothesized that SPAG16 is regulated by S-SOX5. Thus, human SPAG16 gene regulation by S-SOX5 was investigated in BEAS-2B cells, a line derived from human bronchial cells.

Results: S-SOX5 stimulated human SPAG16 promoter function in BEAS-2B cells, but the effect was abrogated when the SOX5 binding sites were mutated. The SPAG16 message was up-regulated when S-SOX5 was overexpressed in BEAS-2B cells, and silencing of S-SOX5 down-regulated SPAG16 transcripts. Chromatin immunoprecipitation experiments demonstrated that S-SOX5 directly associates with the SPAG16 promoter.

Conclusion: The present study demonstrates that SPAG16 is a S-SOX5 target gene. We have previously reported that S-SOX5 also regulates sperm-associated antigen 6 (SPAG6), a gene that encodes another axoneme central apparatus protein. Thus, S-SOX5 may be a master transcription factor that controls expression of a suite of genes related to motile cilia/flagella. Its in vivo role is being studied by generating a conditional mutant mouse model that targets only S-Sox5.

115 MULTIDRUG RESISTANT BACTERIAL ISOLATES CAUSING NOSOCOMIAL URINARY TRACT INFECTION IN A TERTIARY CARE HOSPITAL, NEPAL
Manoj Sah, Master of Science in Clinical Microbiology¹ and Shyam Mishra, MScClinical Microbiology²
¹Kathmandu University, Kantipur Dental College, Kathmandu, NEPAL; ²TU, Nepal
(Presented By: Manoj Sah, Master of Science in Clinical Microbiology)

Introduction: Nosocomial infection is becoming a leading problem in medical practitioners now-a-days placing an extra burden on individual patients worldwide. Nosocomial urinary tract infection caused by multidrug resistant (MDR) pathogens is a major threat of the patients in developing country which are increasing numbers in Nepal. The aim of this study was to determine the etiology of nosocomial urinary tract infection caused by multidrug resistant bacterial pathogens.

Methods: A total of one hundred twenty two bacterial strains isolated from the patients diagnosed of nosocomial urinary tract infection were studied during 2011-2012 at Tribhuvan University Teaching Hospital (TUTH). Antibiotic sensitivity test was determined by modified Kirby Bauer Disc Diffusion method as described by Clinical and Laboratory Standards Institute (CLSI)

Results: Nosocomial urinary tract infection was caused by Escherichia coli 51(41.8%) was found to be more predominant which was followed by Acinetobacter calcoaceticus baumannii (Acb) complex 19(15.6%), Klebsiella pneumoniae 11(9%) Enterococcus spp. 18(14.8%) and Staphylococcus aureus 11(9%). Of the total isolates, 74.6% was MDR which is much higher in Klebsiella pneumoniae 100% which was followed by Escherichia coli 90.1%. Data were analyzed by using SPSS version 17.0

Conclusions: The emergence of MDR bacterial strains causing nosocomial urinary tract infection are increasing in number. The high prevalence of MDR has demanded the special attention to the management of such patients and prevention of dissemination of such strains into hospitals.

116 CRISP3 IS PRO-TUMORIGENIC IN THE PROSTATE
Moira O’Bryan, PhD¹, Marianna Volpert, BSc (hons), PhD², Duangporn Jamsai, BSc, PhD², Gail Risbridger, BSc (hons), PhD² and Luc Furic, BSc (hons), PhD²
¹Monash University; ²The Department of Anatomy and Developmental Biology, Monash University
(Presented By: Moira O’Bryan, PhD)

Cysteine-rich secretory protein 3 (CRISP3) is a vertebrate-specific member of the CRISP clade of the CRISP, Antigen 5, Pathogenesis-related (CAP) superfamily. Within healthy mammals it is expressed predominantly in the salivary glands and in components of the immune system. In instances of human prostate cancer, however, it is up-regulated several hundred fold and has been proposed as a potential marker of progression to advanced disease. Within this study we have assessed the mechanism of CRISP3 action in prostate cancer. We show that recombinant CRISP3 promotes both the migration and invasion of PC3 cells in the XCelligence system. Further, and consistent with the up-regulation of CRISP3 in human prostate cancer, CRISP3 is highly up-regulated with advanced disease in the Hi-MYC mouse models of prostatic adenocarcinoma. Importantly the deletion of Crisp3 leads to the delayed transition of prostatic intraepithelial neoplasia to carcinoma in situ and a complete blocking of progression to invasive disease. Collectively these data define CRISP3 as pro-tumorigenic in the prostate with a role in invasion.

117 – WITHDRAWN
Introduction: Varicocele is considered one of the most common identifiable causes in men with infertility complaint, affecting about 15% of the general population, and up to 40% of fertile men or sub-fertile. One of the biggest challenges in the surgical approach of varicocele is the identification of subjects who will show improvement of the fertile potential. Objective: To identify a histological pattern with predictive prognostic value of improved fertility in patients undergoing microsurgical varicocelectomy.

Methods: This retrospective study consisted of 16 testicular biopsies with histological analysis of men in a specialized clinic of male fertility between the years 2006 and 2012. Were included men in reproductive age with a diagnosis of infertility and presence of varicocele and excluded patients with azoospermia, sexually transmitted diseases and neoplasms of the genitourinary tract. The patients were submitted to urological physical examination with diagnosis of varicocele, performed by careful palpation of the pampiniform plexus with the patient standing, followed by Valsalva maneuver to evaluate the degree of varicocele. In addition, semen analyzes and hormonal measurements were performed. For the determination of a histological pattern can predict the improvement of fertility, cut-off points were created that combine Johnsen’s score, LH, FSH and prolactin serum levels to improved semen parameters.

Results: For improvement of sperm concentration, Johnsen’s score must be greater than 6.45 (right testis) and LH <0.48; to a satisfactory predictor of progressive motility, Johnsen’s score >9.15 in the right testis and >5.9 in the left testis. In the evaluation of sperm morphology, left Johnsen’s score should be greater than 9.3.

Conclusion: We suggest that the creation of histological patterns with predictive values of improved fertile potential, as demonstrated in this study, may benefit patients candidates for microsurgical varicocelectomy.

119 PROTEOMIC PROFILING OF DETERGENT RESISTANT MEMBRANES (LIPID RAFTS) OF PROSTASOMES AND THEIR REVESICULATION
Louise Dubois, Göran Ronquist, Bo Ek, Gunnar Ronquist and Anders Larsson
Uppsala University, Sweden
(Presented By: Göran Ronquist)

Introduction: Prostasomes are exosomes derived from prostate epithelial cells through exocytosis by multivesicular bodies. Prostasomes have a bilayered membrane and readily interact with sperm. The membrane lipid composition is unusual with a high contribution of sphingomyelin at the expense of phosphatidylcholine and saturated and monounsaturated fatty acids are dominant. Lipid rafts are liquid–ordered domains that are more tightly packed than the surrounding non–raft phase of the bilayer. Lipid rafts are proposed to be highly dynamic, submicroscopic assemblies that float freely within the liquid disordered membrane bilayer and some proteins preferentially partition into the ordered raft domains. We asked the question whether lipid rafts do exist in prostasomes and, if so, which proteins might be associated with them.

Methods: Prostasomes of density range 1.13–1.19g/mL were subjected to sucrose density gradient ultracentrifugation fabricated by PBS containing 1% Triton X–100 with capacity for banding at 1.10g/mL, i.e. the classical density of lipid rafts. Prepared prostasomal lipid rafts (by gradient ultracentrifugation) were analyzed by mass spectrometry and electron microscopy. The clearly visible band on top of 1.10g/ml sucrose in the Triton X–100 containing gradient was subjected to LC–MS/MS and more than 350 lipid raft associated proteins were identified. Among them several were involved in intraluminal vesicle formation e.g. tetraspansins, ESCRRTs and Ras–related proteins.

Results: This is the first comprehensive LC–MS/MS profiling of proteins in lipid rafts derived from exosomes. Ultrastructurally, prostasomal lipid rafts and control prostasomes displayed similar spherical shapes although the former were more electron lucent than the controls. Prostasomal lipid rafts also presented a bilayered membrane. Therefore, we hypothesized that prostasomal lipid rafts underwent revesiculation in hypertonc sucrose (1.10g/mL), and later the enveloped sucrose rendered them an osmotic lysis and another revesiculation in PBS.

Conclusion: We conclude that prostasomes contain lipid rafts that may be functional vesicular entities.
Results: To identify a novel PSA cleavage site, cleaved galectin-3 H64P98 was incubated with PSA, and the extent of cleavage was quantitated. The four galectin-3 variants generated by the SNPs rs4644 and rs4652 were compared using Kaplan-Meier analysis to compare age-at-diagnosis. Furthermore, the galectin-3 genotype and covariates with increased odds of PCa were evaluated using logistic regression analysis. Results suggest that heterozygosity for the SNPs H64P98 and P64T98 is a risk factor for PCa and that tobacco use and the galectin-3 SNP genotype are synergistic covariates for increased odds of PCa. Significantly, tobacco use has not previously been associated with PCa risk. Protease assay results indicate that the galectin-3 phenotype determines the susceptibility of galectin-3 to proteolytic cleavage by PSA. We anticipate that these studies will provide the groundwork towards personalized medicine approaches for the prevention and treatment of PCa.

121 IMPACT OF GALECTIN-3 SINGLE NUCLEOTIDE POLYMORPHISM (SNP) ON INCREASED ODDS OF PROSTATE CANCER (PCA) AND ON PROTEOLYSIS BY PROSTATE SPECIFIC ANTIGEN (PSA)

Matthew Kovak, MS¹, David Schoen, BS¹, Horace Spencer, MS², Sarika Saraswati, PhD³ and Alan Diekman, PhD¹
¹Department of Biochemistry and Molecular Biology, College of Medicine, University of Arkansas for Medical Sciences; ²Department of Biostatistics, College of Public Health, University of Arkansas for Medical Sciences; ³Department of Pathology, Microbiology, and Immunology, College of Medicine, Vanderbilt University

Introduction: Galectin-3 is a carbohydrate-binding protein implicated in numerous human diseases, including PCa. In the male reproductive tract, galectin-3 function is regulated by proteolytic processing by PSA. Galectin-3 cleavage in the prostate tumor microenvironment is associated with cancer progression. The SNPs rs4644 and rs4652 generate proline (P)→histidine (H) and threonine (T)→P polymorphisms in galectin-3 at amino acids 64 and 98, respectively. The objectives of this study were to evaluate the impact of galectin-3 SNPs on the odds of PCa and on the susceptibility of galectin-3 to proteolysis by PSA.

Methods: Heterozygosity for the SNPs rs4644 and rs4652 was associated with >63% higher odds of PCa than homozygosity. Moreover, heterozygosity for either SNP was associated with a 3-year-earlier age-at-diagnosis of PCa. Covariate analysis indicated that tobacco users heterozygous for either SNP had a nearly two-fold higher odds of PCa than non-tobacco users or homozygous tobacco users. Cleavage analysis indicated that galectin-3 H64 variants were up to 3.5-fold more susceptible to PSA cleavage than the P64 variants. Moreover, the H64 variants exhibited an additional cleavage product not observed for the P64 variants. Edman degradation of PSA-cleaved galectin-3 H64P98 indicated that PSA cleaves galectin-3 H64 variants between Y63–H64.

Conclusion: Results suggest that heterozygosity for galectin-3 H64P98 and P64T98 is a risk factor for PCa and that tobacco use and the galectin-3 SNP genotype are synergistic covariates for increased odds of PCa. Significantly, tobacco use has not previously been associated with PCa risk. Protease assay results indicate that the galectin-3 phenotype determines the susceptibility of galectin-3 to proteolytic cleavage by PSA. We anticipate that these studies will provide the groundwork towards personalized medicine approaches for the prevention and treatment of PCa.

122 ULTRASOUND FOR PALPABLE SCROTAL MASSES: WHAT ARE WE FINDING?

Marah Hehemann, MD¹, James Kashanian, MD², Christopher Morrison, MD², Daniel Mazur, MD³, Valary Raup, MS4², Brian Trinh, MS³, Mohammed Said, MS³, Andrew Choi, MS³ and Robert E. Brannigan, MD²
¹Loyola University Health Systems; ²Northwestern University

Introduction: Scrotal ultrasound (US) is the most common adjunctive test performed in the assessment of patients with palpable scrotal abnormalities. We hypothesize that the majority of scrotal US performed for the evaluation of a palpable scrotal abnormality exhibit findings that are consistent with benign processes. On the other hand, we also hypothesize that the majority of testicular neoplasms detected on US coincide with a palpable mass on physical exam. Additionally, we predict that a small fraction of all testicular neoplasms are found incidentally.

Methods: After receiving IRB approval, we performed a retrospective review of all scrotal US performed from 2002 to 2014 at our tertiary care institution. We separately examined A) scrotal US performed for a clinical history of a palpable scrotal mass, nodule or swelling and, B) scrotal US with findings of intra-testicular mass suspicious for neoplasm. Individual US results were reviewed and analyzed. We hypothesize that the majority of scrotal US performed for the evaluation of a palpable scrotal abnormality exhibit findings that are consistent with benign processes. On the other hand, we also hypothesize that the majority of testicular neoplasms detected on US coincide with a palpable mass on physical exam. Additionally, we predict that a small fraction of all testicular neoplasms are found incidentally.

Methods: After receiving IRB approval, we performed a retrospective review of all scrotal US performed from 2002 to 2014 at our tertiary care institution. We separately examined A) scrotal US performed for a clinical history of a palpable scrotal mass, nodule or swelling and, B) scrotal US with findings of intra-testicular mass suspicious for neoplasm. Individual US results were reviewed and analyzed. We hypothesize that the majority of scrotal US performed for the evaluation of a palpable scrotal abnormality exhibit findings that are consistent with benign processes. On the other hand, we also hypothesize that the majority of testicular neoplasms detected on US coincide with a palpable mass on physical exam. Additionally, we predict that a small fraction of all testicular neoplasms are found incidentally.

Results: A total of 18,593 scrotal US were performed from 2002 to 2014 at our institution. There were 3,487/18,593 (18.7%) US performed for palpable abnormality (Group A). Of this group only, 198/3487 (5.68%) US identified discrete intratesticular masses concerning for malignancy. A total of 259/18,593 (1.4%) discrete testicular masses (group B) were identified on US for any indication. Of this group, 198/259 (76.4%) were performed because of a palpable abnormality and the remaining 61/259 (23.5%) were found incidentally on US. The 61 incidentally found intra-testicular masses accounted for just 0.33% of all US performed.
Conclusion: To our knowledge, this is the largest study addressing findings of scrotal ultrasound. Based on our 12 year retrospective analysis, we found that only a small minority (5.68%) of US performed for scrotal masses on physical exam confirmed a discrete intratesticular mass concerning for malignancy. Based on these results, we believe that patients presenting with a palpable testicular mass should undergo initial scrotal US to rule out malignancy. Interestingly, though, the vast majority (94.3%) of palpable abnormalities correspond to non-malignant US findings. Finally, incidentally found intra-testicular masses are extremely rare (0.33%).

Results: Age (mean ± SD) was 33.6 ± 8.4 and 34.2 ± 3.0 in men with and without varicocele, respectively. Results are shown in Table 1. Sperm parameters and mitochondrial activity were lower, and concentrations of IL−1 and caspase−1 were higher, in semen of men with, versus without, varicocele. Ninety days after repair, significant improvements were seen in volume, morphology and caspase−1, but these improvements did not reach values of men without varicocele until 180 days after repair, at which time mitochondrial activity, DNA fragmentation and caspase−1 also reached values of men without varicocele.

Conclusion: Our results indicate that varicocele in adults is associated with evidence of inflammatory activity that improves after varicocele repair. Varicocelectomy is associated with early improvement in sperm morphology and late improvement in ejaculate volume, sperm DNA fragmentation, and mitochondrial activity. Future studies will determine if these findings are present in a broader group of varicocele patients, and if these outcomes are associated with improved spermatogenesis and testicular function.

Funding: FAPESP (2012/15039−7) and Capes (005555/2014−00) (Brazil).
Objective: to investigate the protection of resveratrol against the reproductive side effects caused by BEP-treatment.

Methods: From the 36th day post partum (dpp), rats were resveratrol-treated (gavage) with a daily dose of 300mg/kg, per 5 days; from 41st dpp, the co-administration of R and BEP (R-BEP group) was applied for three weeks: etoposide (3.50mg/kg) and bleomycin (0.70mg/kg) for 5 consecutive days/week and bleomycin (0.35mg/kg; every 2nd day of each week); drugs were injected by intraperitoneal route (ip). Three other groups were treated with: 1)BEP (BEP group); 2)Resveratrol (R group) and 3–carboxi–methyl–cellulose (R vehicle, gavage) and 0.9% physiologic solution (ip route; SC– Sham–Control group). Body weight, sperm quantitative and qualitative (morphology and motility) evaluation, sperm mitochondrial activity and DNA fragmentation and acrosome integrity were investigated, as well as the dosage of sex hormones, apoptotic germ cell frequency (TUNEL) and testicular oxidative stress.

Results: BEP group presented higher frequency of TUNEL–positive germ cells when compared with the other three groups. Sperm anomalous forms, low mitochondrial activity and acrosome integrity, along with a reduction in intratesticular testosterone were noted in the BEP group when compared to the R–BEP group. Sperm motility was altered in BEP and R–BEP groups but the parameter reflecting sperm flagellar beating was only altered in BEP group. The plasma testosterone, lipid peroxidation and sperm DNA fragmentation of BEP and R–BEP groups were altered. The germ cell apoptosis frequency reduction and the improvement of the mitochondrial activity, flagellar beating, morphology and acrosome integrity in the R–BEP group point out to a reduction of the reproductive damage caused by BEP–treatment. Using such protocol, we did not observe any differences in sperm DNA fragmentation.

Conclusion: Additional studies are on the way to better clarify the chemoprotective action of resveratrol on the spermatogenesis.

Introduction: Testicular cancer is the most common cancer affecting men of reproductive age (15–35 years). BEP Protocol, which includes bleomycin, etoposide and cisplatin, has been promoting up to 90% chance of cure in patients with testicular cancer. However, side effects on the reproductive health of patients have been reported. Resveratrol (R), a fitoalexin, has anti–apoptotic and antioxidant properties. Objective: to investigate the protection of resveratrol against the reproductive side effects caused by BEP–treatment.

Methods: From the 36th day post partum (dpp), rats were resveratrol-treated (gavage) with a daily dose of 300mg/kg, per 5 days; from 41st dpp, the co-administration of R and BEP (R–BEP group) was applied for three weeks: etoposide (3.50mg/kg) and cisplatin (0.70mg/kg) for 5 consecutive days/week and bleomycin (0.35mg/kg; every 2nd day of each week); drugs were injected by intraperitoneal route (ip). Three other groups were treated with: 1)BEP (BEP group); 2)Resveratrol (R group) and 3–carboxi–methyl–cellulose (R vehicle, gavage) and 0.9% physiologic solution (ip route; SC– Sham–Control group). Body weight, sperm quantitative and qualitative (morphology and motility) evaluation, sperm mitochondrial activity and DNA fragmentation and acrosome integrity were investigated, as well as the dosage of sex hormones, apoptotic germ cell frequency (TUNEL) and testicular oxidative stress.

Results: BEP group presented higher frequency of TUNEL–positive germ cells when compared with the other three groups. Sperm anomalous forms, low mitochondrial activity and acrosome integrity, along with a reduction in intratesticular testosterone were noted in the BEP group when compared to the R–BEP group. Sperm motility was altered in BEP and R–BEP groups but the parameter reflecting sperm flagellar beating was only altered in BEP group. The plasma testosterone, lipid peroxidation and sperm DNA fragmentation of BEP and R–BEP groups were altered. The germ cell apoptosis frequency reduction and the improvement of the mitochondrial activity, flagellar beating, morphology and acrosome integrity in the R–BEP group point out to a reduction of the reproductive damage caused by BEP–treatment. Using such protocol, we did not observe any differences in sperm DNA fragmentation.

Conclusion: Additional studies are on the way to better clarify the chemoprotective action of resveratrol on the spermatogenesis.
126
FLUORESCENCE IN−SI T U HYBRIDIZATION DETECTS INCREASED SPERM ANEUPLOIDY IN MEN WITH RECURRENT PREGNANCY LOSS
Ranjith Ramasamy, Jason Scovell, BA, Jason Kovac, MD, Peter Cook, BA and Dolores Lamb, PhD
Baylor College of Medicine
(Presented By: Ranjith Ramasamy)

Introduction: Objective: To investigate, in men presenting with recurrent pregnancy loss (RPL), the prevalence of sperm autosomal and sex chromosome aneuploidy.

Methods: Design: Retrospective Study. Setting: Male infertility clinic at a tertiary referral center. Patients: 140 men with recurrent pregnancy loss provided semen samples and five normozoospermic controls provided 140 semen samples for comparison. RPL, documented in the female partners, was defined as a prior miscarriage and/or recurrent IVF/ICSI failure. Interventions: Fluorescent In situ hybridization (FISH) was used to detect numerical abnormalities in sex chromosomes (X,Y) and autosomes (13, 18, 21) in ejaculated sperm. Main Outcome Measures: Sperm aneuploidy in men with RPL and normozoospermic controls.

Results: Men with RPL had a greater percentage of sperm aneuploidy within the sex chromosomes, chromosomes 18 and 13/21 (1.04% vs. 0.38%, p=0.015; 0.18% vs. 0.03%, p=0.001, 0.26% vs. 0.08%, p=0.002). In total, 40% of men with normal sperm density and motility had abnormal sperm aneuploidy in the all the chromosomes analyzed. Men with abnormal sperm density and motility had a higher proportion of sperm sex chromosome aneuploidy than men with normal density/motility (62% vs. 45%, p=0.042). Men with normal strict morphology (>4%) had lower rates of sex chromosome and sperm aneuploidy than men with abnormal strict morphology (28% vs. 57%, p=0.038). There was no association between sperm DNA fragmentation and sperm aneuploidy.

Conclusion: Men with RPL have increased sperm aneuploidy compared to controls. A total of 40% of men with RPL and normal sperm density/motility had abnormal sperm aneuploidy. Men with oligoasthenospermia and abnormal strict morphology had greater percentage of sperm aneuploidy compared to men with normal semen parameters.

127
STUDY OF RNA BIOMARKERS OF NORMAL SPERMIOGENESIS IN NORMAL SEMEN AND SPERM VIA TRANSCRIPTOME ANALYSIS.
Alexander Yatsenko, MD, PhD, Archana Kishore, PhD, Andrew Georgiadis, Randy Beadling, Ettia Volk, Joseph Sanfilippo, Thomas Jaffe, James Lyons-Weiler and Tamanna Sultana MWRI
(Presented By: Alexander Yatsenko, MD, PhD)

Introduction: Previous studies have indicated that mature human sperm contains a complex population of RNAs that have been implicated in past and coming events such as spermatogenesis, fertilization, and possibly early embryonic development. Recent attempts were made to identify those RNAs associated with good fertility and good sperm quality. Here, we report the transcriptome analysis of normal semen and sperm based on total RNA−seq study.

Methods: Equimolar RNA from five semen and 6 mature sperm samples were studied. To increase efficiency of total RNA sequencing analysis we excluded ribosomal RNA via rRNA reduction. Preliminary, our RNA seq analysis detected a total of ~19,900 and ~17.00 genes in 2 RNA samples. After normalization, we identified 16,898 transcripts that were common to both samples. Using more stringent criteria with average sequence read coverage of >1, we identified ~10,000 transcripts and 5,000 transcripts in two samples, where ~4,500 transcripts were shared between the two samples. We classified these transcripts as protein coding, non−coding and pseudogenes. To reveal the functional annotation and pathways of these genes, all protein coding genes were subjected to Ingenuity Pathway Analysis and PANTHER analysis.

Results: This annotation resulted in 14 major categories, including DNA replication/repair, gene expression regulation, post−transcriptional regulation, post−translational modification, cellular maintenance, cellular structure, molecular transport, cell movement, cell signaling, cell cycle regulation, apoptosis, metabolism, spermatogenesis, and embryogenesis. Based on number of genes involved, IPA identified the top pathways including, translation regulation, cellular growth, cell cycle, DNA repair, apoptosis and transcription regulation. A number of novel transcripts were also identified in this study, however their role in spermatogenesis remain to be explored.

Conclusion: Our study suggests the presence of important sperm RNAs that could serve as informative biomarkers of male germ cell quality and potentially predict fertilization and early embryonic development outcome in IVF/ICSI procedures.

128
THE RELATIONSHIP BETWEEN SOME SEMEN QUALITY MEASUREMENTS, SCROTAL CIRCUMFERENCE, BODY WEIGHT AND FERTILITY OF AWASSI RAMS
Basim J. Awda¹, Luma W. Abdul Latif², Abdul Jabbar AL-Khazraji³, Hussein O. Kready³ and Mahaba R. Ali³
¹Department of Medical and Molecular Biotechnology, College of Biotechnology, Al-Nahrain University; ²Department of Applied Biotechnology, College of Sciences, Al-Nahrain University, Baghdad, Iraq; ³Ministry of Science and Technology, Baghdad, Iraq
(Presented By: Basim J. Awda)

Introduction: Great efforts have been taken in recent years for improving reproductive efficiency in Awassi sheep. Semen quality and testicular measurements are important parameters for fertility evaluation in rams and ewes as well. Despite there being studies on biological factors associated with these traits, little is known about the potential relationships between reproductive efficiency andram fertility traits in Awassi sheep. The objective of this study was to examine the relationship between conception rate and ram fertility traits (sperm motility, ejaculate volume (EV), pH, sperm concentration, scrotal circumference (SC) and body weight (BW)).
ABSTRACTS

Methods: SC and BW were measured and semen collected from 4 mature Awasi rams [2.88 ± 0.24 yr old; 65.25 ± 1.93 kg (mean ± SE)] using the electroejaculation method. The ejaculates were placed in a thermost (35 °C) immediately after collection. The collected semen samples were then evaluated for EV, pH, sperm motility, and sperm concentration. Each ejaculate was extended and used immediately to inseminate 3–4 Awasi ewes/ram [2.05 ± 0.29 yr old; 48 ± 1.44 kg (mean ± SE)]. Ram fertility percentage was calculated based on non–return to estrus following 17 days post insemination. Conception rates and litter size were determined by real time ultrasonography at 34, 44 and 60 days post insemination. Data were analyzed using the CORR procedure and Tukey–Kramer multiple comparisons to test for trait effect.

Results: SC, BW, sperm motility, EV, pH, sperm concentration did not correlate significantly with ram fertility (P>0.05). However, ewes BW negatively correlated (r = 0.99; P<0.05) with ram fertility percentage. There were no significant differences in fertility percentage or ram fertility traits between the two groups of rams based on ewes litter size (pregnancy type; single vs. twin).

Conclusion: In conclusion, this study suggests that fertility of Awasi ram may be affected by ewe’s BW, and further studies are needed to evaluate the relationships between the ram fertility traits and the conception rate of Awasi ewes.

129 THE RELATIONSHIP BETWEEN SOME BLOOD PARAMETERS MEASUREMENTS, SCROTAL CIRCUMFERENCE, BODY WEIGHT AND FERTILITY OF AWASSI RAMS
Basim J. Awda1, Mahaba R. Ali2, Hussein O. Kready3, Adul Jabbar AL-Khazraji1 and Luma W. Abdul Latif2
1Department of Medical and Molecular Biotechnology, College of Biotechnology, Al-Nahrain University; 2Department of Applied Biotechnology, College of Sciences, Al-Nahrain University, Baghdad, Iraq; 3Ministry of Sciences and Technology, Baghdad, Iraq (Presented By: Basim J. Awda)

Introduction: Great efforts have been taken in recent years for improving reproductive efficiency in Awasi sheep. Semen quality, testicular measurements and biochemical properties of blood serum are important parameters for fertility evaluation in rams and ewes as well. Despite there being studies on biological factors associated with these traits, little is known about the potential relationships between fertility and biochemical properties of blood parameters in Awasi rams. The objective of this study was to examine the relationships between ram fertility percentage and some biochemical properties of blood serum, scrotal circumference (SC) and body weight (BW) in Awasi rams.

Methods: SC and BW were measured; semen and blood samples were collected from 4 mature Awasi rams [2.88 ± 0.24 yr old; 65.25 ± 1.93 kg (mean ± SE)]. Semen samples were collected using the electroejaculation method. Each ejaculate was extended and used immediately to inseminate 3–4 Awasi ewes/ram [2.05 ± 0.29 yr old; 48 ± 1.44 kg (mean ± SE)]. Blood samples were analyzed for packed cell volume (PCV), erythrocyte sedimentation rate (ESR) and haemoglobin concentration (Hb). Blood serum was analyzed for glucose concentration, glutamic oxaloacetic transaminase (GOT) and glutamic pyruvic transaminase (GPT) activities and total proteins (TP). Ram fertility percentage was calculated based on non–return to estrus following 17 days post insemination. Conception rates and litter size were determined by real time ultrasonography at 34, 44 and 60 days post insemination. Data were analyzed using the CORR procedure and Tukey–Kramer multiple comparisons to test for trait effect.

Results: PCV, Hb (r = −0.97; P<0.1) and ewes BW (r = −0.99; P<0.05) were negatively correlated with the fertility percentage. There were no significant differences in fertility percentage between the two groups of rams based on ewes litter size (pregnancy type; single vs. twin). However, GPT activity in single group was greater than that of twin group [38.05 ± 0.43 vs. 33.66 ± 0.62 U/L (mean ± SE); P<0.1] and WBC(cells/µ) was significantly greater in twin group than that in single group [P<0.05; 12800 ± 141.42 vs. 8500 ± 100 (mean ± SE)].

Conclusion: In conclusion, this study suggests that fertility of Awasi ram may be affected by PCV, Hb and ewe’s BW and GPT activity and WBC number could be markers for pregnancy type in Awasi sheep. Further studies are needed to evaluate these relationships in Awasi sheep.
testis identified 17,829 phosphorylation sites in 3,955 phosphoproteins. Although only approximately half of the phosphorylation sites enriched by IMAC were also captured by TiO2, both the phosphoprotein datasets identified by the two methods significantly enriched the functional annotation of spermatogenesis. Thus, the phosphoproteome profiled in this study is a highly useful snapshot of the phosphorylation events in spermatogenesis. To further understand phosphoregulation in the testis, the site–specific kinase–substrate relations (ssKSRs) were computationally predicted for re–constructing kinase–substrate phosphorylation networks (KSPNs). A core sub–KSPN among the spermatogenesis–related proteins was retrieved and analyzed to explore the phosphoregulation during spermatogenesis. Moreover, network–based analyses demonstrated that a number of protein kinases such as MAPKs, CDK2 and CDC2 with statistically more ssKSRs might have significantly higher activities and play an essential role in spermatogenesis, and the predictions were consistent with previous studies on the regulatory roles of these kinases. In particular, the analyses proposed that the activities of POLO–like kinases (PLKs) might be dramatically higher, while the prediction was experimentally validated by detecting and comparing the phosphorylation levels of pT210, an indicator of PLK1 activation, in testis and other tissues. Further experiments showed that the inhibition of PLKs decreases cell proliferation by inducing G2/M cell cycle arrest.

Conclusion: Taken together, this systematic study provides a global landscape of phosphorylation in the testis, and should prove to be of value in future studies of spermatogenesis.

131 THE EFFECT OF PULSATILE TREATMENT OF FSH AND TESTOSTERONE ON DIFFERENTIAL GENE EXPRESSION IN RATSERTOLICELLS DURING POSTNATAL TESTICULAR MATURATION

Indrashis Bhattacharya, PhD¹, Mukkesh Gautam, PhD², Bholashankar Pradhan, PhD³ and Subeer Majumdar, PhD³
¹HNB Garhwal University, Srinagar, India; ²The Ken & Ruth Davee Department of Neurology, Northwestern University, Chicago, USA; ³Division of Cellular Endocrinology, National Institute of Immunology, New Delhi, India
(Presented By: Indrashis Bhattacharya, PhD)

Introduction: The alarming rise in male infertility merits an immediate attention. Testicular Sertoli cells (Sc) regulate spermatogenesis under the control of FSH and testosterone (T). Postnatal maturation of Sc in terms of appropriate hormonal responsiveness is prerequisite for the pubertal onset of spermatogenesis. However, limited knowledge about the extent of hormone (both T and FSH) responsive gene expression during the different phases of Sc maturation, restricts our understanding about the molecular events necessary for male fertility.

Methods: Sc were isolated, cultured from neonatal (5 days old), pre–pubertal (12 days old) and adult (60 days old) rat testes and were stimulated with pulsatile FSH and T (in combination) treatment. The hormone induced differential gene expression data obtained from Sc of 12 days and 60 days of age were compared with that of Sc obtained from 5 days old rats using microarray technology. The array data was also revalidated further by Q–PCR for some of the genes selected from all three age groups.

Results: Our data revealed that hormone induced gene expression was significantly higher with pulsatile treatment of hormones as compare to that of the constant exposure at 24hr. Moreover, the magnitude of hormone mediated augmentation in gene expression was on its peak at 11hr. Microarray analysis indicated that genes like Igf1r, Igf2r, Fgf9, Acvr1B, Bmpr1b, Tgfb1r and Itga4, were upregulated in immature Sc. Ntf3, Nrg1, BDNF, SCF, GDNF and CXCL12 were upregulated in maturing Sc. Mature adult Sc were found to express genes involved in glucose metabolism, phagocytosis, and cytoskeleton structuring for the maintenance of spermatogenesis. The expression profiles of some of such genes like Aass, Unc 5c, Ccl5, RoBo, Fat3, Tlr, Wisp, Msln, Spz, Pwwp1 and Testin etc were validated by qPCR that authenticated the reliability of the array data further.

Conclusion: Taken together, our data suggested that the pulsatile hormone treatment is a better choice over the conventional constant hormonal exposure to primary culture of Sc for studying hormone induced gene expression. The differential transcriptome data provide an important resource to reveal the molecular network of Sc maturation which is necessary to govern male germ cell differentiation, hence, will improve our current understanding of the etiology of some forms of male infertility.

132 HISTONE H4K20 DEMETHYLASE REGULATES SPERMATOGENESIS

Charlie Degui Chen
(Presented By: Charlie Degui Chen)

Introduction: It is well known that the amount of heterochromatin increases with the differentiation of spermatogonia, however, the role of heterochromatin in this process is not defined. Because heterochromatin formation is regulated by methylation in histone H4 lysine 20 (H4K20me), we set out to identify histone demethylases for this heterochromatin mark. Objectives: To identify a demethylase for H4K20 and examine its role in the differentiation of spermatogonia.

Methods: high–content cell–based screening of a cDNA library containing 4,500 nuclear proteins one by one, in vitro enzymatic assays, ChIP–seq coupled with RNA–seq, and gene knockout study.

Results: Ectopic expression of KDM9 led to a reduction in the global level of H4K20me1. ChIP–Seq experiments revealed that KDM9 demethylated H4K20me2 and H4K20me3 at specific genomic loci in vivo. In vitro, KDM9 specifically demethylated H4K20me1/2/3 and generated formaldehyde, and the enzymatic activity required Fe(II), −ketoglutarate and ascorbic acid as cofactors. RNA–seq demonstrated that KDM9 regulated the transcription of repetitive elements, but not protein coding genes. KDM9 knockout blocked spermatogenesis in mice.

Conclusion: We identified a histone demethylase for H4K20 that regulates spermatogenesis. Since the protein sequence of the catalytic domain of KDM9 is different from LSD1 and JmjC domain–containing proteins, the two known classes of histone demethylases, this enzyme represents a new class of histone demethylase.

133 – WITHDRAWN
NR4A1 EXPRESSION IS REGULATED BY THE CALCIUM SIGNALING PATHWAY THROUGH DISTINCT API/CREB AND MEF2 ELEMENTS IN LEYDIG CELLS

Nicholas Robert, Houssein Salem Abdou, PhD and Jacques J. Tremblay, PhD
CHUQ Research Centre - Laval University
(Presented By: Nicholas Robert)

Introduction: The nuclear receptor NR4A1 (NUR77) is expressed in steroidogenic Leydig cells where it plays pivotal roles by regulating the expression of several genes involved in steroidogenesis and male sex differentiation including Star, HSD3B2, and InsI3. Activation of the cAMP and Ca2+ signaling pathways in response to LH stimulation leads to a rapid and robust activation of Nr4a1 gene expression that requires CAMKI kinase. We recently showed that disruption of the Ca2+ signaling pathway impair steroidogenesis in MA−10 Leydig cells through to a decrease in STAR and NR4A1 expression and promoter activity. While the cAMP/PKA and Ca2+/CAMKI signaling pathways are important for Nr4a1 expression, the specific transcription factor(s) mediating the effects of the Ca2+ signaling pathway in Leydig cells remain poorly characterized. We previously showed that the Nr4a1 proximal promoter (−331 to +50 bp) contains three important regions (NIR) with distinct activities: NIR−A (−331 to −233 bp) and NIR−C (−121 to −65 bp) are hormone/cAMP responsive while NIR−B (−233 to −121 bp) mediates most of the basal promoter activity.

Methods: In order to identify potential Ca2+/CaM effectors that regulate Nr4a1 expression, MA−10 Leydig cells were treated with forskolin to increase endogenous cAMP levels, calmidazolium (Cdz) to increase intracellular Ca2+ influx, dantrolene to inhibit endoplasmic reticulum Ca2+ release, and/or W7 to inhibit CaM activity. Using a Luciferase−based promoter analysis, we identified Ca2+−responsive elements mainly located in the NIR−A and NIR−C regions of the Nr4a1 promoter, which contains binding sites for several transcription factors such as AP1, CREB and MEF2.

Results: We found that one of the three API/CRE sites located at −255 bp is the most responsive to the Ca2+ signaling pathway as well as the two MEF2 binding sites at −315 and −285 bp. Furthermore, we found that the hormone−induced recruitment of the co−activator p300 to the Nr4a1 promoter requires the Ca2+ pathway.

Conclusion: Together our data indicate that the Ca2+−signaling pathway increases Nr4a1 expression in MA−10 Leydig cells, at least in part, by enhancing the recruitment of the co−activator most likely through the MEF2, AP1, and CREB transcription factors. In conclusion, these data demonstrate an important interplay between the Ca2+ and cAMP pathways in regulating Nr4a1 expression through distinct promoter elements that ultimately modulate co−activators recruitment.

Funding: Supported by NSERC.

Intraflagellar Transporter Protein IFT20 is Essential for Spermiogenesis in Mice

James Foster¹, Zhengang Zhang, MD, PhD², Wei Li, MD³, Yong Zhang, MD, PhD⁴, Hongfei Li, MD⁴, Ling Zhang, MD, PhD⁵, Maria Teves, PhD⁶, Gregory Pazour, PhD⁷, Rex Hess, PhD⁷, Jerome Strauss III, MD, PhD⁷ and Zhibing Zhang, MD, PhD⁷
¹Randolph-Macon College; ²Huazhong University of Science and Technology; ³Virginia Commonwealth University; ⁴Huazhong University of Science & Technology; ⁵Wuhan University of Science & Technology; ⁶University of Massachusetts; ⁷University of Illinois
(Presented By: James Foster)

Introduction: Intraflagellar transport (IFT), originally discovered in Chlamydomonas, is an evolutionarily conserved mechanism thought to be essential for the assembly and maintenance of all eukaryotic cilia and flagella. IFT polypeptide orthologues were also found in mice, and mutations in IFT proteins have been shown to cause several ciliopathies. In mouse testis, IFT20 is present in Golgi, the manchette, and the basal body of differentiating germ cells, key structures in ciliogenesis, suggesting that IFT20 might be also essential for spermatogenesis.

Methods: To investigate the role of IFT20 in male germ cells, the floxed Ift20 mice were bred to Stra8−cre mice so that the Ift20 gene is disrupted in spermatocytes/spermatids.

Results: The Ift20:Stra8−cre mutant mice did not show any gross abnormalities, all of the mutant mice survive to adulthood. There was no difference between testis weight/body weight between controls and mutant mice. Fertility of six week−old mutant was dramatically reduced, and adult mutant males were completely infertile. Sperm number, the percentage of motile sperm in the cauda epididymis, and sperm motility were dramatically reduced compared to the controls. Histological examination of the testes and epididymis revealed abnormally shaped elongating spermatid heads starting with step 10, and bulbous round spermatids in the lumen of seminiferous tubules. Spermatids appeared to be unable to form cytoplasmic lobes and residual bodies; resulting in necrosis or apoptosis and sloughing of cytoplasm. Some cells appeared to begin tail formation, but the tails were short, with only a few tails extend into the tubule lumen. Increased amount of cytoplasmic vesicles were observed in the mutant cells. Golgi body formation and chromatin condensation appeared to be normal. The epididymes contained round bodies of cytoplasm, probably derived from the sloughing of the cytoplasmic lobes and residual bodies. Some sperm with attached heads appeared normal, but tails were short and kinked. Immunofluorescence staining demonstrated that key sperm flagella components, including ODF2 and SPAG16L failed to be incorporated into sperm tails of the mutant mice.

Conclusion: Collectively, our findings suggest that IFT20 is essential for normal spermiogenesis.
ANABOLIC STEROIDS AND HYPOGONADISM IN ADVANCED CANCER: TO TREAT OR NOT TO TREAT

Domenico Fuoco, PharmD, PhD¹, Robert D. Kilgour, PhD, FACSM² and Antonio L. Vigano, MD, MSc¹

¹Supportive and Palliative Care Service, McGill University Health Centre, McGill Nutrition and Performance Laboratory. ²Department of Exercise Science, Concordia University, Montreal, Canada

(Presented By: Domenico Fuoco, PharmD, PhD)

Introduction: Hypogonadism (or testosterone deficiency) is prevalent in advanced cancer and is shown to contribute to decreased bone density and muscle wasting. These patients can benefit from a multimodal therapeutic approach to treatment that could include the administration of an anabolic steroid (testosterone or one of its numerous analogues). The clinical rational for this intervention not only favours the anabolic effect of testosterone, but the improvement of cognitive function and the reduction of the symptom burden that is frequently associated with advanced cancer patients. However, there is an ongoing controversy regarding the use of testosterone supplementation as a safe treatment intervention in hypogonadic patients, especially those with prostate cancer. Support for this argument is found in studies that have shown the absence of prostate cancer in those subjects that are naturally hypogonadic or after the surgical removal of the testes. Clinicians have been reluctant to prescribe any androgenic / anabolic steroid because of a perceived lack of evidence based medicine that would confirm its safe and effective use in advanced cancer patients. On the other hand, new theory and medical evidence are proving that testosterone administration in relatively high concentrations has a protective effect on the prostate.

Methods: We reviewed the historical and current literature (1940-the present) regarding testosterone and its utilization as a therapeutic intervention. We compared several algorithms and medical recommendations from different andro-endocrinological societies. Finally, we have elaborated upon a new risk / benefit ratio framework for advanced cancer patients.

Results: The landmark study by Huggins et al (1941) appears to have been the only published study that recommended the avoidance of testosterone especially as a treatment for patients with prostate cancer. This recommendation apparently has been based on the results from 3 male adult subjects. Current medical evidence suggest that the risk / benefit ratio favors the use and positive benefits provided by anabolic / androgen replacement therapy. At least over the last 15 years, junior clinicians have continued to question the use of testosterone therapy. Recently, the result of large clinical trials, epidemiological studies and more informed interpretations of drug precaution concepts are providing us with the rational to use testosterone for our patients. as valid pharmacological choice. In fact, researchers are now demonstrating that testosterone replacement therapy can serve as a safe and valid pharmacological alternative that can ameliorate the quality of life and survival of advanced cancer patients.

Conclusion: There appears to be a paradigm shift that supports the use of anabolic steroid therapy in hypogonadic patients. This new pharmacological approach will positively change the clinical outcome of patients in palliative care.
ASA 2014 – 2015 COMMITTEE LISTING

ANDROLOGY LABORATORIES
Charles H. Muller, PhD; Seattle, WA
Ainiela Bollendorf, MT; Philadelphia, PA
Anna - Marie Bort; Cleveland, OH
David S. Karabinus, PhD, HCLD; Manassas, VA
Angela Reese, TS; Alliance, OH
Susan Ann Rothmann, PhD, HCLD; Cleveland, OH
D. Allen Shrader, MD; Salina, KS
Suresh C. Sikka, PhD, HCLD; New Orleans, LA
Carol S. Sloan, MS; Hillsborough, NC

ARCHIVES & HISTORY COMMITTEE
Steven M. Schrader, PhD; Cincinnati, OH
Naazish Alladin, BSc; Toronto, ON Canada
James Ford Jr., PhD; Mattawan, MI
Jean L. Fourcroy, MD, PhD, MPH; Bethesda, MD
Rex A. Hess, MS, PhD; Urbana, IL
David S. Karabinus, PhD, HCLD; Manassas, VA
Sophie La Salle, PhD; Downers Grove, IL
Angela Reese, TS; Alliance, OH
Camilla Ribeiro, PhD; Sao Paulo, Brazil
Susan Ann Rothmann, PhD, HCLD; Cleveland, OH
Carol S. Sloan, MS; Hillsborough, NC
Anna Steinberger, PhD; Houston, TX

AWARDS COMMITTEE
Barry R. Zirkin, PhD; Baltimore, MD
John K. Amory, MD, MPH; Seattle, WA
Robert Edward Brannigan, MD; Hinsdale, IL
Terry R. Brown, PhD; Baltimore, MD
Gail A. Cornwall, PhD; Lubbock, TX
Martine Culty, PhD; Montreal, QC Canada
Erwin Goldberg, PhD; Evanston, IL
Sarah Kimmins, PhD; Ste-Anne-de-Bellevue, QC Canada
Dolores J. Lamb, PhD, HCLD; Houston, TX
Kat Loveland, PhD; Clayton, VIC Australia
Stephanie T. Page, MD, PhD; Seattle, WA
Sally Perreault Darney, PhD; Cary, NC
Gail S. Prins, PhD; Chicago, IL
Bernard Robaire, PhD; Montreal, QC Canada
Kenneth P. Roberts, PhD; Spokane, WA
James F. Smith, MD, MS; San Francisco, CA
William Wright, PhD; Baltimore, MD

BASIC SCIENCE WORKSHOP
Kate Loveland, PhD; Clayton, VIC Australia
Thomas Garcia, PhD; Houston, TX
Matthew Kovak, MS; Little Rock, AR
Sophie La Salle, PhD; Downers Grove, IL
Peter Liu, MBBS, PhD; Torrance, CA
Cristian O’Flaherty, PhD; Montreal, QC Canada
Elizabeth Snyder, PhD; Bar Harbor, ME
Margarita Vigodner, PhD; New York, NY

COMMUNICATIONS AND MEDIA COMMITTEE
Jacques J. Tremblay, PhD; Quebec City, QC Canada
Janice L. Bailey, PhD; Quebec, QC Canada
Rex A. Hess, MS, PhD; Urbana, IL
Sarah Kimmins, PhD; Ste-Anne-de-Bellevue, QC Canada
Marvin L. Meistrich, PhD; Houston, TX
Katja Teerds, PhD; Wageningen, Netherlands
Paul Jacob Turek, MD; San Francisco, CA

CONSTITUTION AND BYLAWS COMMITTEE
Jannette Dufour, PhD; Cincinnati, OH
Terry R. Brown, PhD; Baltimore, MD
Daniel G. Cyr, PhD; Lavel, QC Canada
Erma Z. Drobnis, PhD; Columbia, MO
Mohit Khera, MD; Houston, TX
Moira K. O’Bryan, BSc, PhD; Clayton, VIC Australia
Jennifer Venditti-Roadarmel, PhD; Bloomington, PA

DIVERSITY COMMITTEE
Maria Christina W. Avellar, PhD; Sao Paulo, Brazil
George L. Gerton, PhD; Philadelphia, PA (Vice Chair)
Naazish Alladin, BSc; Toronto, ON Canada
Christiaan de Jager, BSc, MSc, PhD; Pretoria, South Africa
Folami Iderabedullah, PhD; Kannapolis, NC
Carolina Jorgez, PhD; Houston, TX
Carol C. Linder, MA, PhD; Las Vegas, NM
Peter Liu, MBBS, PhD; Torrance, CA
Patricia A. Martin-DeLeon, PhD; Newark, DE
Patricia L. Morris, PhD, MS; New York, NY
Camilla Ribeiro, PhD; Sao Paulo, Brazil
Hooman Sadri-Ardekani, MD, PhD; Lewisville, NC
Ana Maria Salicioni, PhD; Amherst, MA
Terry T. Turner, PhD; Charlottesville, VA
Pablo E. Visconti, PhD; Amherst, MA
Humphrey Hung-Chang Yao, PhD; Research Triangle Park, NC

ENDOWMENT COMMITTEE
Susan Ann Rothmann, PhD, HCLD; Cleveland, OH
Rudi Ansbacher, MD; Ann Arbor, MI
Gail A. Cornwall, PhD; Lubbock, TX
Erwin Goldberg, PhD; Evanston, IL
Mohit Khera, MD; Houston, TX
Deborah A. O’Brien, PhD; Chapel Hill, NC
Dana Alan Ohl, MD, PhD; Ann Arbor, MI
Michael A. Palladino, PhD; West Long Branch, NJ
Sally Perreault Darney, PhD; Cary, NC
Gail S. Prins, PhD; Chicago, IL
Bernard Robaire, PhD; Montreal, QC Canada
Steven M. Schrader, PhD; Cincinnati, OH
Richard J. Sherins, MD; Washington, DC
Paul Jacob Turek, MD; San Francisco, CA
Terry T. Turner, PhD; Charlottesville, VA
Donna L. Vogel, MD, PhD; Baltimore, MD
ASA 2014 – 2015 COMMITTEE LISTING

ETHICS COMMITTEE
Ronald W. Lewis, MD, FACS; Augusta, GA
Rudi Ansbacher, MD; Ann Arbor, MI
Keith D. Smith, MD; Houston, TX
Finance COMMITTEE
Michael A. Palladino, PhD; West Long Branch, NJ
Gail A. Cornwall, PhD; Lubbock, TX
Erwin Goldberg, PhD; Evanston, IL
Rex A. Hess, MS, PhD; Urbana, IL
Patricia L. Morris, PhD, MS; New York, NY
Donna L. Vogel, MD, PhD; Baltimore, MD

FUTURE MEETINGS COMMITTEE
John McCarrey, PhD; San Antonio, TX
Janice L. Bailey, PhD; Québec, QC Canada
Nina Sarah Davis, MD, MD; Portland, OR
Alan Diekman, PhD; Little Rock, AR
Janice P. Evans, PhD; Baltimore, MD
Erwin Goldberg, PhD; Evanston, IL
Charles H. Muller, PhD; Seattle, WA
Michael A. Palladino, PhD; West Long Branch, NJ

INDUSTRIAL RELATIONS COMMITTEE
Mohit Khera, MD; Houston, TX
Joseph P. Alukal, MD; New York, NY
Tobias S. Kohler, MD, MPH, FACS; Springfield, IL
Kirk C. Lo, MD, FRCSC; Toronto, ON Canada
Allen D. Seftel, MD, FACS; Camden, NJ

INTERNATIONAL LIASON COMMITTEE
Patricia S. Cuasnicu, PhD; Buenos Aires, Argentina
Maria Christina W. Avellar, PhD; Sao Paulo, Brazil
Elisabetta Baldi, PhD; Florence, Italy
Catherine Itman, PhD; Callaghan, NSW Australia
Robert Sullivan, PhD; Quebec, QC Canada
Christina Wang, MD; Torrance, CA

JOURNAL COMMITTEE
Rex A. Hess, MS, PhD; Urbana, IL
John K. Amory, MD, MPH; Seattle, WA
Gail A. Cornwall, PhD; Lubbock, TX
Marvin L. Meistrich, PhD; Houston, TX

JOURNAL EDITORS
Douglas T. Carrell, PhD, HCLD; Salt Lake City, UT (Editors-In-Chief)
Ewa Rajpert-De Meyts, MD, PhD, DMSc; Copenhagen, Denmark (Editors-In-Chief)
Laboratory Science Forum
David S. Karabinus, PhD, HCLD; Manassas, VA
Aniela Bollendorf, MT; Philadelphia, PA
Charles H. Muller, PhD; Seattle, WA
Robin Pillow, BS, CT (ASCP); Cleveland, OH
David Quiceno; Bogota, Colombia
Angela Reese, TS; Alliance, OH
Suresh C. Sikka, PhD, HCLD; New Orleans, LA
Carol S. Sloan, MS; Hillsborough, NC

LIAISON COMMITTEE
Cristian O’Flaherty, PhD, DVM; Montreal, QC Canada
Martine Culty, PhD; Montreal, QC Canada
Michael Louis Eisenberg, MD; Stanford, CA
Sophie La Salle, PhD; Downers Grove, IL
Ajay K. Nangia, MBBS, FACS; Kansas City, KS
James F. Smith, MD, MS; San Francisco, CA
Christina Wang, MD; Torrance, CA

MEMBERSHIP COMMITTEE
Alan Diekman, PhD; Little Rock, AR
Sijo J. Parekkattil, MD; Clermont, FL (Co-Chair)
Ina Dobrinski, DVM, PhD; Calgary, AB Canada
Benoit Guyonnet, PhD; Lubbock, TX
Michael K. Holland, PhD; Westlake, QLD Australia
Jennifer Hughes; Davis, CA
Catherine Itman, PhD; Callaghan, NSW Australia
Matthew Kovak, MS; Little Rock, AR
Peter Liu, MBBS, PhD; Torrance, CA
Kirk C. Lo, MD, FRCSC; Toronto, ON Canada
Christopher Payne, PhD; Chicago, IL
Wei Yan, MD, PhD; Reno, NV
Zhibing Zhang, MD, PhD; Richmond, VA

NOMINATING COMMITTEE
Erwin Goldberg, PhD; Evanston, IL
Robert Edward Brannigan, MD; Hinsdale, IL
Gail A. Cornwall, PhD; Lubbock, TX
Kate Loveland, PhD; Clayton, VIC Australia
Gail S. Prins, PhD; Chicago, IL
Steven M. Schrader, PhD; Cincinnati, OH
Donna L. Vogel, MD, PhD; Baltimore, MD

2015 PROGRAM COMMITTEE
Edward D. Kim, MD; Knoxville, TN (Co-Chair)
William Wright, PhD; Baltimore, MD (Co-Chair)
John K. Amory, MD, MPH; Seattle, WA
Maria Christina W. Avellar, PhD; Sao Paulo, Brazil
Robert Edward Brannigan, MD; Hinsdale, IL
Patricia S. Cuasnicu, PhD; Buenos Aires, Argentina
Jurrien Dean, MD; Bethesda, MD
Alan Diekman, PhD; Little Rock, AR
George L. Gerton, PhD; Philadelphia, PA
Michael D. Griswold, PhD; Pullman, WA
Mary Ann Handel, PhD; Bar Harbor, ME
Wayne J.G. Hellstrom, MD, FACS; New Orleans, LA
Mohit Khera, MD; Houston, TX
Sarah Kimmins, PhD; Ste-Ann-de-Bellevue, QC Canada
Sophie La Salle, PhD; Downers Grove, IL
Peter Liu, MBBS, PhD; Torrance, CA
Martin M. Matzuk, MD, PhD; Houston, TX
John McCarrey, PhD; San Antonio, TX
Jon M. Oatley, PhD; Pullman, WA
Sally Perreault Darney, PhD; Cary, NC
Bernard Robaire, PhD; Montreal, QC Canada
Jay I. Sandlow, MD; Milwaukee, WI
Paul Ray Shin, MD; Washington, DC
Donald J. Tindall, PhD; Rochester, MN
Jacqueta M. Trasler, MD, PhD; Dorval, QC Canada
Wei Yan, MD, PhD; Reno, NV

© 2015 American Society of Andrology and European Academy of Andrology
ASA 2014 – 2015 COMMITTEE LISTING

PUBLIC AFFAIRS AND POLICY COMMITTEE
Ajay K. Nangia, MBBS, FACS; Kansas City, KS
Joseph P. Alukal, MD; New York, NY
Robert Edward Brannigan, MD; Hinsdale, IL
Dolores J. Lamb, PhD, HCLD; Houston, TX
Patricia L. Morris, PhD, MS; New York, NY
Cigdem Tanrikut, MD; Boston, MA

SPECIAL SYMPOSIUM
Mohit Khera, MD; Houston, TX (Co-Chair)
Tobias S. Kohler, MD, MPH, FACS; Springfield, IL (Co-Chair)

TRAINEE AFFAIRS
Peter Liu, MBBS, PhD; Torrance, CA (Co-Chair)
Sophie La Salle, PhD; Downers Grove, IL (Co-Chair)
Mahmoud Aarabi, MD, PhD; Verdun, PQ Canada
Alexandra Amaral; Coimbra, Portugal
Alan Diekman, PhD; Little Rock, AR
James Foster, PhD; Ashland, VA
George L. Gerton, PhD; Philadelphia, PA
Barry T. Hinton, PhD; Charlottesville, VA
Catherine Itman, PhD; Callaghan, NSW Australia
Matthew R. Marcello, PhD; New York, NY
Edward Nguyen, PhD; Oklahoma City, OK
Michael A. Palladino, PhD; West Long Branch, NJ
Genevieve Plante, BSc; Varennes, QC Canada
Budhan S. Pukazhenthi, DVM, PhD; Front Royal, VA
Ranjith Ramasamy, MD; Houston, TX
Mara Roth, MD; Seattle, WA
Ana Maria Salicioni, PhD; Amherst, MA
Erick Jose Ramo Silva, PhD; Sao Paulo, SP Brazil
Elizabeth Snyder, PhD; Bar Harbor, ME
Chantal M. Sottas, BA; New York, NY
Donna L. Vogel, MD, PhD; Baltimore, MD
Ping Ye, PhD; Pullman, WA
Mary Katherine Sampfaski, MD; Los Angeles, CA
   (Trainee Representative)
Luke Simon, PhD; Salt Lake City, UT (Trainee Representative)

If you are interested in serving on any of the committees, please contact the respective chairs.
Table of Contents

Schedule at a Glance
President’s Welcome
Past Presidents
State of Utah Governor Gary Herbert Letter
Salt Lake City Mayor Ralph Becker Proclamation
ASA Officers
General Information
Special Events
Message from the Program Co-Chairs
ASA Lecturer Award
Distinguished Andrologist Award
Distinguished Service Award
Matthew P. Hardy Young Andrologist Award
Outstanding Trainee Investigator Award
Thanks to Donors and Sponsors
Course Objectives & CME Credit Information
Schedule of Events
Speaker Abstracts
Poster Session I
Poster Session II
Index of Abstract Authors
Abstracts Full Text
Committee Listing