In January 2016, the United States Department of Defense announced the implementation of a two-year pilot program which would provide fertility preservation benefits to members of the Armed Services. Due to catastrophic injuries to the pelvic region, chemical and heat exposure, potential illnesses, and other factors, soldiers can be left with life-long injuries that may affect their ability to conceive. This program is a significant family-building option for those who serve this country. It not only provides the resources necessary when seeking fertility preservation options, but it also brings peace of mind to those who desire a future of parenthood.

In the same way the military is providing soldiers fertility preservation options prior to deployment; we do this in cases of infertility, cancer-related secondary infertility, and advanced paternal aging. The key word here is “prior.” As reproductive specialists we aim to prepare men, women, and children with fertility preservation options, resources, and knowledge, prior to treatment.

This provides individuals and couples the opportunity to make a confident, well-informed decision when fulfilling their future family-building goals. By helping them understand beforehand that there are safe and available treatment options, it gives them hope and something to look forward to—a normal life, with healthy babies.

To honor National Infertility Awareness Week (NIAW) April 24 – 29, 2016, Center for Reproductive Medicine members shared factors and advice on understanding male and female infertility issues, and treatment and fertility preservation options. During the week, I delivered the keynote presentation, “Genetic Basis of Male Infertility,” at Augusta University’s Inauguration 2016 President’s Research Symposium, in Georgia. This memorable event designed to honor a superb reproductive endocrinologist, Dr. Virendra Mahesh, brought together distinguished leaders in science, health, and medicine to deliver research talks and celebrate discoveries. As the CRM moves forward, we will continue to have a presence on these platforms; thereby making an impact in the reproductive science community and in our patient’s lives.

This issue takes an in-depth look into the research labs of our CRM members. Topics include maternal-fetal medicine, male contraception, morphogenesis, and others. We also cover the Texas Forum for Reproductive Sciences 2016 and hear from the meeting’s organizers. Lastly, join us on June 2 for the CRM Quarterly Membership Meeting and Reception, and hear about the current research strides and developments moving through our labs.
A Genome Wide Association Study (GWAS) from a Global Cohort Identifies Common Variants in FSHB and SMAD3 Driving Spontaneous Human Dizygotic Twinning

Kjersti Aagaard, M.D., Ph.D.
Associate Professor, Department of OB/GYN

Although dizygotic (DZ) twins occur once every 70 live births and has long been suspected to be familial, the genetic loci driving human twinning have not yet been identified. We established the Twinning GWAS Consortium to characterize the genetic basis of natural DZ twinning in humans using robust discovery and replication datasets built from mothers of DZ twins.

Using a GWAS approach in a large, multinational cohort comprised of over 315,000 gravidae, we identified, for the first time, maternal genetic loci driving human dizygotic twinning.

The rs11031006 allele, located near FSHB, was significant in its association with maternal serum FSH. Conversely, rs17293443 (SMAD3) was not associated with FSH levels, but was associated with maternal age at last birth.

A Maternal High Fat Diet (HFD) During Gestation Alters the Neonatal Gut Microbiome in a Human Population Based Longitudinal Cohort

Derrick Chu, M.D./Ph.D. Candidate
Department of Translational Biology and Molecular Medicine

Evidence from our non-human primate model demonstrated that a maternal high fat diet in gestation alters the offspring gut microbiome. We thus sought to determine in a human cohort if the neonatal gut microbiome was similarly impacted by maternal gestational diet.

CONTINUED ON PAGE 3
A large cohort of mother-neonatal pairs was enrolled and infant stool samples were collected at delivery and at six-weeks. The maternal diet was assessed with a rapid dietary screener and the cohort was stratified into a high fat and low fat group (n=13/group).

We found that the neonatal gut microbiome varied by virtue of maternal fat intake, with a persistent decrease in *Bacteroides* in neonates exposed to a high fat diet.

Notably, *Bacteroides* have been shown to promote the healthy maturation of gut immune tissues. These findings warrant further studies to determine if these changes impact infant development.

**The Offspring Microbiome is Altered by Virtue of a High Fat Maternal Diet During Gestation**

**Amanda L. Prince, Ph.D.**
Department of OB/GYN

**AND**

**Derrick M. Chu, M.D./Ph.D. Candidate**
Department of Translational Biology and Molecular Medicine

Adult metabolic disease is associated with early life exposures, such as maternal diet during gestation and lactation, and dysbiosis of the gut microbiome is associated with adult metabolic disease. We previously demonstrated in our non-human primate model of maternal obesity that maternal diet is associated with alterations in the offspring gut microbiome at one year. Thus, we hypothesized that a fetal microbiome is present and is altered by maternal diet.

Indeed, we found a distinct fetal microbiome that clusters separately from maternal body sites but contains taxa similar to the placental microbiome. Furthermore, we detected changes in the fetal microbiome modulated by maternal diet.

Similar alterations associated with maternal diet were also detected at six months (pre-weaning), ten months (post-weaning), and three years of age, despite weaning offspring onto a control diet. Altogether, these data suggest that maternal diet is important for the developing microbiome.
Texas Forum for Reproductive Sciences (TFRS) 2016 meeting co-organizers, Marie-Claude Hofmann, Ph.D., Professor, Department of Endocrine Neoplasia and Hormonal Disorders, UT MD Anderson Cancer Center, and Chandra Yallampalli, Ph.D., DVM, Professor, Department of OB/GYN, Baylor College of Medicine, praised TFRS 2016 attendees on their outstanding research presented, and the forum’s continued mission to bring together the Texas reproductive science community. Beginning with TFRS 2016, Drs. Hofmann and Yallampalli will co-organize this annual meeting. Below they describe noteworthy elements from TFRS 2016.

The 22nd annual TFRS meeting was held on April 21 - 22, 2016 in the Onstead Auditorium at The University of Texas (UT) MD Anderson Cancer Center. This forum, originally named as the Texas Forum for Female Reproduction (TFFR), held its first meeting in 1995, and evolved into the current TFRS, to include both male and female reproductive sciences research. Annually, it brings scientists in reproductive sciences from all over Texas. We have had consistent participation from Baylor College of Medicine, UT MD Anderson, UT Houston, UT San Antonio, University of Texas Medical Branch (UTMB), UT Southwestern, Texas A&M University, Prairie View A&M University, Texas Tech University, and University of Houston, over the years. Dell Medical School UT Austin participated for the first time this year.

The major emphasis at this meeting is to provide a forum for trainees and junior faculty to showcase their research and present their best work. Prizes are given for the meritorious platform and poster presentations. In this Thursday through Friday meeting, we usually have two plenary speakers, 20 platform presentations, and about 50 posters presenting. We had a record setting meeting this year in both the number of registrants (over 125) and number of abstracts (69), and the feedback has been very positive.

In particular, newcomers noted the welcoming and interactive nature of the conference, as well as the feedback and opportunities for collaborations given to trainees and junior investigators.

We will continue to provide services to the forum to expand and encourage more participation, especially for the trainees. We are looking forward to next year’s meeting in April, and encourage members of BCM to participate more actively.

— Drs. Chandra Yallampalli and Marie-Claude Hofmann, TFRS 2016 Meeting Co-organizers

SAVE THE DATE: TEXAS FORUM FOR REPRODUCTIVE SCIENCES 2017
April 27 - 28, 2017
UT MD Anderson Cancer Center
Onstead Auditorium, Houston, TX
**Texas Forum for Reproductive Sciences**
April 21 - 22, 2016
Houston, TX

**TFRS 2016 MEETING CHAIRPERSON**
Marie-Claude Hofmann, Ph.D.
Professor, Department of Endocrine Neoplasia and Hormonal Disorders
UT MD Anderson Cancer Center

**TFRS 2016 MEETING ORGANIZER**
Chandra Yallampalli, Ph.D., DVM
Professor, Department of OB/GYN
Baylor College of Medicine

**5 TFRS 2016 Steering Committee**
Members from the CRM
- Marie-Claude Hofmann, Ph.D.
- Dolores J. Lamb, Ph.D., HCLD
- Joanne Richards, Ph.D.
- Ignatia Barbara Van den Veyver, Ph.D.
- Chandra Yallampalli, Ph.D., DVM

**2 CRM Platform Moderators**
- Meade Haller
  Graduate Student
  Department of Urology
- Diana Monsivais
  Postdoctoral Associate
  Department of Pathology

**2 Plenary Lecturers**
**Molecular Mechanisms of Estrogen Signaling**
W. Lee Kraus, Ph.D.
Director, Cecil H. and Ida Green Center for Reproductive Biology Sciences, Professor and Vice Chair of Basic Sciences, Department of OB/GYN, UT Southwestern

**Transplantation of Immune Privileged Sertoli Cells: More than Just Testicular Nurse Cells**
Janette Dufour, Ph.D.
Associate Professor, Associate Dean for Research, Department of Cell Biology and Biochemistry, Texas Tech University Health Sciences Center

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**CONGRATULATIONS TO OUR CRM POSTER WINNERS!**

**Uterine BMP7 Guides the Process of Embryo Implantation**
Diana Monsivais - First Place
Postdoctoral Associate, Department of Pathology

**Steroid Receptor Coactivator-2 is a Critical Regulator of Endometrial Cancer Cell Metabolism**
Maria Szwarc - Third Place
Research Assistant/Graduate Student
Department of Molecular and Cellular Biology

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*TXFRRS 2016 Plenary Lecturer, Dr. Janette Dufour, explains her lab’s research focus in Sertoli cells.*
Held at the UT MD Anderson Cancer Center Onstead Auditorium in Houston, Texas, the Texas Genetics Society’s 43rd Annual Meeting brought together geneticists and all persons with an interest in genetics to a three-day forum. Attendees were encouraged to foster the development of, exchange ideas, and teach those with an interest in genetics research or genetic services. CRM members contributed short talks and posters on topics covering infertility, genitourinary hypoplasias, and testosterone research.

Invited Address:
**Genetic and Genomic Mechanisms of Human Male Infertility**
Dolores J. Lamb, Ph.D., HCLD  
Director  
Center for Reproductive Medicine

**Contributed Papers Session:**
**Deregulation of the 16p11.2 Transcription Factor MAZ Results in Genitourinary Hypoplasias**
Meade Haller  
Graduate Student/Research Assistant  
Department of Urology

**Technician Poster Presentation:**
**The Down Expression of NPAS2 Predicts Low Testosterone Levels Due to Decreased Expression of StAR**
Cenk Cengiz, B.S.  
Research Tech II  
Department of Urology

NPAS2 interacts with BMAL1 and functions via an E-box (enhancer box) element, a specific sequence in the promoter region of many circadian rhythm genes. A homologous mutation in NPAS2 was identified by whole exome sequencing in two non-obstructive azoospermic brothers in a consanguineous family.

NPAS2 affects the expression of steroidogenic pathway genes, including the rate-limiting gene for steroid biogenesis, Steroidogenic Acute Regulatory Protein (StAR). The absence of NPAS2 would therefore be expected to negatively affect the expression of StAR and predicted to impact steroid production.

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**CRM MEMBER AWARDS**

**AMIN HERATI, M.D.**  
Postdoctoral Fellow, Department of Urology

In April 2016, Dr. Amin Herati received the **2016 NIH Trainee Travel Award** during the 41st Annual American Society of Andrology (ASA) Conference for his abstract, *IFT140 is a Novel Candidate Gene for Impaired Spermatogenesis: Identification by Whole Exome Sequencing and Validation with Sanger Sequencing.*

**CENK CENGIZ, B.S.**  
Research Tech II, Department of Urology

During the Texas Genetics Society 43rd Annual Meeting in April 2016, Cenk Cengiz received the **Best Technician Poster Presentation Award** for his poster, *The Down Expression of NPAS2 Predicts Low Testosterone Levels Due to Decreased Expression of StAR.*
Development of a Non-obese Mouse Dietary Model of Gestational Diabetes and What We Can Learn From It

Gestational Diabetes Mellitus (GDM) is a common obstetrical complication affecting an estimated 18% of all pregnancies. Women who suffer from GDM are more likely to develop metabolic syndrome, including type II diabetes and cardiovascular disease, later in life. The mechanisms regulating the programming effect of GDM on maternal long-term health and disease are poorly understood.

Our laboratory has worked to develop a mouse model of GDM that recapitulates these long-term maternal health complications later in life. Preliminary data suggests that pancreatic islet vasculature expansion is impaired in GDM pregnancies and that this impairment persists later in life. Current studies in the laboratory are focusing on the mechanisms regulating pancreatic vascular expansion during pregnancy and determining if impairment of this process leads to the development of GDM and the resulting long-term maternal health complications.

Fig 1. Intra-islet vasculature is decreased in islets from GDM dams (B, E, & H) at day 13.5 (A-C) and 17.5 of pregnancy (D-F) and 12-weeks post-partum (G-H) compared to controls (A, D & G). Insulin (red), CD31 (green), nuclei (blue).
CRM AND MCB R&D WORKSHOP SERIES CONTINUED

ANNA MARIE SOKAC, Ph.D.
Assistant Professor
Department of Biochemistry & Molecular Biology
Anna Sokac Lab, Baylor College of Medicine
April 14, 2016

**Stress Resistance is Regulated by F-actin Stability During Morphogenesis**

Every embryo develops under its own unique set of challenges, with variable and sometimes dangerous inputs coming from mother, father, and the environment. Despite these challenges, healthy offspring reliably emerge. This amazing feat is accomplished due to a biological property called “robustness.” Unfortunately, this robustness can be overwhelmed, ending in miscarriage, premature birth, and structural and functional birth defects.

The Sokac Lab has a long-term goal of understanding how robustness is achieved for mechanical events like embryonic morphogenesis. Graduate student, Liuliu Zheng, has made a major advance, identifying two, evolutionarily conserved, F-actin binding proteins that influence robustness during morphogenesis in fruit fly embryos: Zheng et al. show that F-actin stability is reduced in thermally stressed embryos, leading to morphogenesis failures. F-actin is destabilized by stress-dependent upregulation of an F-actin severing protein, Cofilin.

Conversely, Cofilin destabilization is antagonized by an F-actin stabilizer, Serendipity-α, to promote stress resistance. Thus, the Sokac Lab shows for the first time that F-actin stability determines stress resistance and so promotes robust morphogenesis.

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RAMAKRISHNA KOMMAGANI, Ph.D.
Research Instructor, Department of Molecular & Cellular Biology
March 24, 2016

**The Roles of Steroid Receptor Coregulators in Endometrial Function and Dysfunction**

Failure of an embryo to correctly implant into the endometrium is a common cause of pregnancy failure or early embryo miscarriage. Dr. Ramakrishna Kommagani discussed the importance of steroid hormone receptors and coregulators in this aspect of embryo implantation. Dr. Kommagani emphasized that the development of a receptive endometrium requires steroid receptor coactivator-2, a factor which modulates the response of an endometrial cell to the pregnancy hormone, progesterone. Specifically, Dr. Kommagani discussed how SRC-2 increases progesterone-dependent glycolysis in the endometrial cell to provide energy and biomolecules for supporting the embryo growth within the endometrium.

Dr. Kommagani focused on identifying the mechanisms that underlie the steroid hormones action in endometrial function and dysfunction. Outcomes from his research focus will not only provide mechanistic insights on early embryo miscarriage, but also on endometrial disorders associated with infertility.

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Heat map displays metabolites that are significantly altered with SRC-2 knockdown in decidualizing human endometrial stromal cells.
Over the past 50 years, women have had the ability to choose from various forms of contraception best suited to their hormonal balances, body systems, and unique needs. However, men have not had the ability to do the same. Now the question remains, will men be able to control their own fertility one day?

*In the future, there should be a large number of opportunities, whether it’s for men or women, to have contraception.*

Martin Matzuk, M.D., Ph.D. Director, Center for Drug Discovery at Baylor College of Medicine, to Houston Matters on Houston Public Media radio in November 2015

Research conducted within the Baylor College of Medicine labs of Dr. Martin Matzuk and David Lonard, Ph.D., Associate Professor, Department of Molecular and Cellular Biology, are looking to pinpoint a protein or small molecule that can be translated into the derivation of a male contraceptive. Each lab is taking its own approach in developing a safe and effective method.

Dr. Matzuk’s lab is focused on targeting a small molecule that would only affect spermatogenesis, thereby inhibiting sperm function or motility. Dr. Lonard’s lab is concentrating on the reaction between small molecule inhibitors and steroid receptor coactivators into producing a non-hormonal male contraceptive. Here they describe their current research efforts in male contraception.

**MARTIN MATZUK, M.D., PH.D.**

Director, Center for Drug Discovery  
Stuart A. Wallace Chair and Professor, Department of Pathology and Immunology  
Baylor College of Medicine  
Director, Clinical Chemistry, Ben Taub General Hospital

Although oral contraceptives have been available to women for the last 55 years, contraceptive choices for men (condoms and vasectomy) have been unchanged since World War II. One of the research goals of the Matzuk laboratory is to increase the contraceptives choices for men. Using the mouse as a model, Dr. Martin Matzuk showed that oral contraceptives for males are possible.
In his groundbreaking work (Matzuk et al., Cell 2012), Dr. Matzuk demonstrated that the small molecule JQ1 reversibly inhibits the activity of the bromodomain testis-specific (BRDT) protein, preventing fertility in 100% of male mice that were administered the drug.

JQ1 demonstrates reversible male contraception with no effect on testosterone levels or changes in libido; however, JQ1 also targets other related bromodomain proteins expressed in tissues throughout the body.

With his establishment of the Center for Drug Discovery (CDD) at Baylor College of Medicine, Dr. Matzuk and his collaborators are working to find derivatives of JQ1 that will only interact with BRDT.

The Steroid Receptor Coactivators (SRC-1, SRC-2, and SRC-3) are master regulators for estrogen, progesterone, androgen, and other nuclear receptors and play key roles in the regulation of both the male and female reproductive systems. Specifically, SRC-2 is required for normal Sertoli cell function and SRC-2 knockout male mice become infertile shortly after the onset of puberty. This suggests that selective targeting of SRC-2 function in Sertoli cells could serve as a strategy to block sperm production.

Supporting this concept, we found that the compound gossypol, which was already known as a male contraceptive agent, functions as a SRC-2 inhibitor. However, due to unacceptable side effects, gossypol was abandoned as a viable contraceptive agent. My laboratory is engaged in the development of small molecule inhibitors (SMIs) against SRCs, including the development of SRC-2 SMIs for potential use as male contraceptive agents.

To identify new SRC-2 SMIs we have executed a high throughput screening campaign of more than 400,000 compounds. These efforts have led to the identification of a number of promising lead compounds that can inhibit SRC-2 function at low nanomolar concentrations.

Currently, we are actively engaged in medicinal chemistry efforts to improve the drug-like properties of these lead compounds and are evaluating them in cell culture and animal model systems. Steroid receptor coactivators function as pleiotropic transcriptional regulators that control metabolism and frequently drive cancer growth in addition to their roles in reproduction. Ultimately, we expect that the SMIs that we develop against SRCs will find broad use for the treatment of cancer, metabolic disorders, and other disease states, in addition to potential as non-hormonal contraceptive agents.
CRM Aphrodisiac Cocktail Party
February 11, 2016
Baylor St. Luke’s Medical Center
The Bobby R. Alford Educational Center

In celebration of Valentine’s Day, the CRM invited Baylor College of Medicine’s Partnership Board and Advisory Board members to Sweets With My Sweetie, an Aphrodisiac Cocktail Party, hosted by Dr. Dolores J. Lamb, on February 11, 2016.

Board members enjoyed aphrodisiac-inspired hors d’oeuvres and sweets, made with aphrodisiac ingredients such as avocados, chocolate, raspberries, peppers, and shrimp. Dr. Lamb shared her favorite aphrodisiac food stories and why they are thought to have aphrodisiac properties.

Board members were surprised when the singing quartet, S.L.E.D., performed a series of love songs, including one by Elvis Presley, during the Aphrodisiac Cocktail Party.

Baylor Teen Health Clinic Health Resources Fair and Fish Fry
March 5, 2016
Finnigan Park Community Center

The Male Empowerment Coalition of the Baylor Teen Health Clinic held its annual Health Fair and Fish Fry at Finnigan Park Community Center on March 5. Over 30 vendors gathered to provide local youth and their families with free health screenings, check-ups, and career and family development advice.

CRM members, Marisol O’Neill, Research Assistant/Graduate Student, Department of Molecular and Cellular Biology, and Peter Butler, Laboratory Tech II, Center for Reproductive Medicine, joined the Health Fair to provide expert urologic advice and sexual health education information to local teens and their families.

CRM members joined the Baylor College of Medicine community in celebrating Women’s Health Month on February 5, 2016! #goredforwomen
CRM MEMBERS IN THE NEWS

CRM Members continue to contribute and share their research endeavours with local, national, and international news channels, and across the BCM community. Click on link below to be taken to the article.

NATIONAL AND INTERNATIONAL NEWS

Conceiving After Cancer

Houston Traffic Pollution Linked to Preterm Birth

Microbes in Placenta Also Found in Mouth

Pregnant Women and Doctors in Houston Worry Summer Could Bring Local Threat of Zika

4 Things Doctors Wish They Knew About Infertility

Sperm Function Score Informs Fertility Evaluation

American Urological Association Spring 2016 Newsletter: Distinguished Mentor in Urology and Infertility: Dolores J. Lamb, Ph.D.

Mother’s Microbiome Shapes Offspring’s Immunity

BCM PRESS RELEASES

International Research Collaborative Discovers Genes Linked to Twinning and Reproductive Fitness

Sperm Banking – Preserving Fertility Before Cancer Treatment

New Research Supports Previous Findings in the Placental Microbiome

Experts Warn HPV Related Cancer on the Rise in U.S.

BCM MOMENTUM BLOG

What You Need to Know About Infertility

For additional news features by CRM members: bcm.edu/reproductive-medicine/news-and-announcements

UPCOMING EVENT

CRM Quarterly Membership Meeting and Reception

Thursday, June 2, 2016
4 – 6 p.m.
Alkek Building, Room N317

Refreshments served

As we head into summer 2016, join us for the CRM Quarterly Membership Meeting and Reception.

CRM Director, Dorrie Lamb, along with our Translational Research Group Leaders and members will share a recap of our spring 2016 efforts, including current research strides and developments moving through their labs and the reproductive field.

Afterwards, enjoy a networking reception with light appetizers and refreshments, and meet with fellow CRM members.

RSVP to Jyoti Patel at jyotip@bcm.edu.