For those who desire to have children, a cancer diagnosis, severe reproductive disorder, or other serious disease, can leave them feeling despaired, as their dreams of building a family are either put on hold, or seem unimaginable. For both men and women facing these conditions, fertility preservation becomes crucial, as aggressive treatment options can lead to infertility.

Chemotherapy and radiation treatments provide hope, but while killing cancer cells, it can also damage oocytes and sperm, resulting in secondary infertility in individuals who might otherwise have been fertile. Advancements in fertility preservation allow cancer survivors to look forward to their future life—beyond their disease. For fertility preservation, men may pursue sperm cryopreservation (sperm banking), testicular sperm extraction, or testicular tissue freezing. For women, fertility preservation options can include In Vitro Fertilization (IVF) and embryo cryopreservation, ovarian tissue banking, gonadal shielding, vitrification or oocyte freezing. While it is difficult for pre-pubertal girls and boys to take on the decision of parenthood at such a young age, oocyte and testicular freezing allow them to freeze their unfertilized eggs or testicular or ovarian tissue, which are stored for future use. Fertility preservation for pre-pubertal children is currently experimental and there is a significant need for additional technology development in the future to ensure a good likelihood of successful outcome when the child matures to adulthood.

The problem is that fertility preservation options are not routinely discussed when the patient receives their cancer diagnosis, and some patients undergo cancer treatment without knowledge of their fertility preservation options. Amongst the cancer centers in the Texas Medical Center, we are working to navigate patients through a streamlined care process that could eventually lead them on the path to parenthood. From the moment they are diagnosed with cancer and prior to any treatment and/or surgery, experts provide essential resources and support on fertility preservation as part of their treatment plan. This gives patients the autonomy in which they determine what they want to do with their eggs, sperm, or tissue based on their desire to be a parent.

As health, science, and medical professionals, it is our mission to equip patients with the appropriate resources, continue to translate our science into innovative treatment options, and provide comfort when they need it the most. Their dreams of having children hopefully will not be dashed by cancer, but through fertility preservation, biologic parenthood could become an exciting reality.
The American Society of Andrology (ASA) 42nd Annual Meeting aimed to stimulate scientific exchange and rejuvenate the science of male reproductive health and patient care. CRM members joined the meeting with a series of short talks, posters, and abstracts.

**TESTIS WORKSHOP TRAVEL AWARD WINNER:**

**“ADCY2 is a Candidate Gene for the Development of Congenital Genitourinary Anomalies Through Partial Disruption of Steroidogenesis”**

Marisol O’Neill, M.S.
Graduate Student, Lab of Dr. Dolores J. Lamb
Department of Urology

Genitourinary (GU) anomalies are among the most common types of birth defects, yet their genetic causes are poorly understood. We identified Adenyllyl Cyclase 2 (ADCY2) as a candidate gene for the development of GU anomalies using array comparative genomic hybridization. Through further analysis of patients with GU anomalies, we identified an enrichment of ADCY2 copy number variants compared to the general population.

Adcy2 is highly expressed in fetal Leydig cells suggesting a role in steroid biosynthesis. Overexpression of Adcy2 in murine Leydig cell lines resulted in ligand independent testosterone production and down regulation of the luteinizing hormone receptor. These results suggest Adcy2 duplications may be involved in dysregulation of steroidogenesis through a negative feedback loop.

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American Society of Andrology
42nd Annual Meeting
April 21 - 25, 2017

**New Concepts and Perspectives in Male Reproductive Health**

8 short talks & posters by 6 CRM members

- “Knockdown of IFT140 Decreases Testosterone Production in MTC-1 Cells”
  - Amin Herati, M.D. (AWARD WINNER)
- “PRSS50: A Serine Protease Required for Proper Sperm Flagellum Assembly”
  - Carolina Jorgez, Ph.D.
- “Effect of Sperm Morphology on Intruterine Insemination Pregnancy Success: A Systematic Review and Meta-Analysis”
  - Taylor Kohn (AWARD WINNER)
- “ADCY2 is a Candidate Gene for the Development of Congenital Genitourinary Anomalies Through Partial Disruption of Steroidogenesis” AND “MAZ Haploinsufficiency Alters Baculum Morphogenesis in Mice”
  - Marisol O’Neill, M.S. (AWARD WINNER)
- “Whole Exome Sequencing Identifies Genes and Pathways with Potential Involvement in Peyronie’s and Dupuytren’s Diseases”
  - Alexander Pastuszak, M.D., Ph.D.
- “Hmg5 Role in Testis Development”
  - Boryana Zhelyazkova (AWARD WINNER)

The XXIV North American Testis Workshop at ASA
April 19 - 22, 2017

From Testis Differentiation to Sperm Production

3 short talks by CRM members

- “Knockdown of IFT140 May Disrupt Spermatogenesis by Dysregulating the NFkB Signaling Pathway”
  - Amin Herati, M.D.
- “ADCY2 is a Candidate Gene for the Development of Congenital Genitourinary Anomalies Through Partial Disruption of Steroidogenesis”
  - Marisol O’Neill, M.S. (AWARD WINNER)
- “Mrn1p is a Ubiquitously-Expressed Gene Required for Male Fertility”
  - Renata Prunskaite-Hyyrylainen, Ph.D.
Twenty three years after its initial inception as the Texas Forum for Female Reproduction (TFFR), the Texas Forum for Reproductive Sciences (TFRS) held April 27-28, 2017 in Houston, Texas showed its highest number of participants yet. With over 140 attendees and 85 abstracts submitted from all over Texas including Baylor College of Medicine, UT Southwestern Medical Center, Texas A&M Health Science Center, UT Medical Branch (UTMB), University of North Carolina School of Medicine, UT MD Anderson Cancer Center, Prairie View A&M University, and many others.

2017 TFRS Meeting Chairperson, Mala Mahendroo, Ph.D., Professor, Department of Obstetrics and Gynecology, Division of Basic Reproductive Biology Research, Member, Cecil H. and Ida Green Center for Reproductive Biology Sciences, UT Southwestern Medical School and Meeting Organizer, Chandra Yallampalli, Ph.D., DVM, Professor, Department of Obstetrics and Gynecology, Baylor College of Medicine, praised attendees on their strong dedication towards the science and research of male and female reproduction, and their support in bringing together the Texas reproductive science community.
CONGRATULATIONS!
CRM TFRS 2017 ABSTRACT WINNERS

ACHUTH PADMANABHAN, Ph.D.
Postdoctoral Associate, Dept. of Molecular & Cellular Biology
Second Place, Platform Winner
- “Deletion of the Mrnip Gene Causes Male Infertility”

JESSICA RUBIN, M.D.
Clinical Postdoctoral Associate, Dept. of OB/GYN
Third Place, Platform Winner

RENATA PRUNSKAITE-HYYRYLAINEN, Ph.D.
Research Scholar, Department of Pathology
Second Place, Poster Winner - “Deletion of the Mrnip Gene Causes Male Infertility”

SHORT TALKS BY CRM MEMBERS CONTINUED:

“An Ubiquitin Dependent Lysosome-Mediated Pathway Regulates the Turnover of p53-R157H Gain-of-Function Mutant Protein in Ovarian Cancer Cells”
Achuth Padmanabhan, Ph.D. - PLATFORM WINNER

“The Fetal Microbiome is Altered in Association with Maternal Diet during Gestation”
Amanda Prince, Ph.D.

“Can Preimplantation Genetic Screening (PGS) be Applied to Previously Untested Vitrified Blastocysts”
Jessica Rubin, M.D. - PLATFORM WINNER

“Hmgn5 Role in Testis Development”
Boryana Zhelyazkova

ENDOCRINE SOCIETY
ENDO 2017 MEETING
APRIL 1 - 4, 2017 | ORLANDO, FLORIDA

ENDO is the world’s largest event centered on the latest in endocrine science, research, and medicine. CRM Senior Advisory Committee and Translational Research Group Leaders led the following sessions:

Session: Nuclear Receptor Signaling: Master Regulator and Progeny
Presenter: Dr. Bert O’Malley, “The Master Co-Regulator”
Chair: Dr. Nancy Weigel

Session: Critical Steps of Sperm Under Scrutiny
Presenter: Dr. Martin Matzuk, “Genetic and Small Molecule Manipulation of Spermatogenesis and Sperm Function”

Additional 2017 Meetings Involving CRM Participation:

Frontiers in Reproduction (FIR)
April 29-June 11, 2017 | Woods Hole, MA

American Urological Association (AUA) 2017 Annual Meeting
May 12-16, 2017 | Boston, MA

American Association of Bioanalysts (AAB) Annual Meeting and Educational Conference
May 18-20, 2017 | Houston, TX

Society for the Study of Reproduction (SSR) 2017 Annual Meeting
July 13-16, 2017 | Washington D.C.

American Society for Human Genetics (ASHG) 2017 Annual Meeting
Oct. 17-21, 2017 | Orlando, FL

Sexual Medicine Society of North America (SMSNA) 2017 Annual Fall Scientific Meeting
Oct. 26-29, 2017 | San Antonio, TX

American Society for Reproductive Medicine (ASRM) 2017 Annual Meeting
Oct. 28-Nov. 1, 2017 | San Antonio, TX

For a full overview of 2017 meetings attended by CRM members:
bcm.edu/reproductivemedicine/meetings
PEGGY SMITH, PH.D., Director, Baylor Teen Health Clinic, Professor, Department of Obstetrics & Gynecology
In March 2017, Dr. Peggy Smith was honored with the 2017 David C. Wiley Award by the Texas Campaign to Prevent Teen Pregnancy, for her dedication towards teen pregnancy prevention efforts, and tireless work on behalf of young people in Texas.

In May 2017, Dr. Smith was named to the Houston Endowment Steering Committee for Reducing Maternal Mortality whose mission focuses on developing a comprehensive, community-wide plan to reduce maternal mortality in Houston and Harris County.

AMIN HERATI, M.D., Postdoctoral Fellow, Department of Urology
During the American Society of Andrology (ASA) 42nd Annual Meeting in April 2017, Dr. Herati received the NIH Trainee Travel Award AND Outstanding Trainee Investigator Award for his work on, “Knockdown of IFT140 May Disrupt Spermatogenesis by Dysregulating the NFκB Signaling Pathway.”

MARISOL O’NEILL, Graduate Student, Lab of Dr. Dolores Lamb, Department of Urology
During the American Society of Andrology (ASA) 42nd Annual Meeting in April 2017, Marisol O’Neill received the NIH Trainee Travel Award for her poster, “MAZ Haploinsufficiency Alters Baculum Morphogenesis in Mice” AND the North American Testis Workshop Travel Award for her work on, “ADCY2 is a Candidate Gene for the Development of Congenital Genitourinary Anomalies Through Partial Disruption of Steroidogenesis.”

BORYANA ZHELAYAZKOVA, Graduate Student, Lab of Dr. Dolores Lamb, Dept. of Molecular and Cellular Biology
During the American Society of Andrology (ASA) 42nd Annual Meeting in April 2017, Boryana Zhelyazkova received the NIH Trainee Travel Award for her poster, “Hmgn5 Role in Testis Development.”

TAYLOR KOHN, Medical Student
During the American Society of Andrology (ASA) 42nd Annual Meeting in April 2017, Taylor Kohn, received the NIH Trainee Travel Award for his abstract, “Effect of Sperm Morphology on Intrauterine Insemination Pregnancy Success: A Systematic Review and Meta-Analysis.”

BERT O’MALLEY, M.D., Chairman and Professor, Department of Molecular and Cellular Biology
In May 2017, Dr. Bert O’Malley received the 2017 Michael E. DeBakey Award for Excellence in Research. Named in honor of the college’s first president and pioneering heart surgeon, Dr. Michael E. DeBakey, this award is given to Baylor College of Medicine faculty members who have made the most significant published scientific contribution to clinical or basic biomedical research during the past three years. For additional information about his work see the Baylor press release.
Q | Take us back a little bit. What was your path like starting as an undergraduate at Oberlin College, then eventually inspiring you to pursue a career in reproductive medicine?

A | My career in science began by default and a whole lot of luck. From a wonderful life surrounded by the lakes, mountains, and seashore of New Hampshire, I went off to Oberlin College (Ohio) to become a French major. That changed my sophomore year when I had difficulty hearing words with earphones and because I got tired of analyzing French literature. Luckily, I was taking all the premed biology courses—not because I was intending to be a premed, but because biology was also an interest—eventually it became my major.

I went to graduate school to become a high school biology teacher through the Master’s in Arts and Teaching (MAT) Program at Brown University. I learned the first day of practicing teaching that I had absolutely no disciplinary powers whatsoever! I knew instantly that this was not my calling. Luckily, the program required research experience.
That evolved into applying for the Ph.D. program in Physiological Chemistry, or Biochemistry at Brown. This was my first exposure to research and research in the ovary, with a focus on enzymes (NAD kinase) controlling steroidogenesis and electron microscopy. After a brief time in the Biology Department at the University of North Dakota, I joined the Reproductive Endocrinology Program (fondly known as REP) at the University of Michigan, Ann Arbor. This is where my career in reproductive endocrinology started.

“Radioimmunoassays had been discovered and for the first time allowed endocrinologists to quantitate peptide and steroid hormones in serum! What a revolution. This led to radioreceptor assays and the realization that not only hormones, but also receptors for these hormones were regulated, changed during follicular development and controlled what follicles would eventually ovulate.”

FROM 1970 - PRESENT

These early discoveries led to our studies on the molecular events that control LH mediated induction of ovulation and the essential role of specific genes that control cumulus cell-oocyte complex (COC) expansion. These events included LH induction of the EGF-like factors (in collaboration with Dr. Espey, Trinity University and Dr. Masayuki Shimada, Hiroshima University) and activation of the EGF receptor and the downstream kinases, ERK1/3. By targeted depletion of Erk2 in Erk1 null mice, we documented unequivocally that ERK1/2 control a master switch that suppresses the FSH-driven molecular program in granulosa cells of growing follicles and induces COC expansion, meiotic resumption in oocytes, ovulation, and luteinization in preovulatory follicles. By targeted depletion of Cebpα and Cebpβ, we documented further that these transcription factors are obligatory for ovulation and the regulation of specific genes controlling ovulation and luteinization.

Q| What is the next step for you and your lab?
A| More recently, my laboratory has developed novel mouse models of ovarian surface epithelial (OSE) cancer and granulosa cell cancers. These models have led to our keen interest in the roles of specific GOF mutants of the tumor protein 53 (TP53 or p53), how these mutants can be targeted and how they impact the tumor-immune cell microenvironment in human and mouse ovarian cancer.

Specifically, using our OSE mutant mouse models we have shown that: 1) wild type (WT) tumor protein 53 (p53) enhances ovarian surface epithelial tumor survival and growth;
2) depletion of p53 in our mice leads to markedly reduced tumor growth and the appearance of only small lesions; 3) the p53 depleted mice respond dramatically to estradiol with rampant growth and metastasis to the peritoneal cavity indicating the loss of WT p53 renders the tumors in these mice more responsive to steroid hormones and that steroids can impact ovarian cancer metastasis; 4) expression of the gain-of-function (GOF) R172H mutant in our mouse strain leads to early tumor formation, rapid metastasis to the omentum, and responsiveness to estradiol; and 5) mice expressing heterozygous R172H and WT alleles not only develop serous OSE tumors, but by 12 weeks of age also present with mucinous ovarian tumors, providing the first mouse model of this ovarian type.

“A major goal of our current studies is to determine how the GOF R175H, R273H, and R248Q mutant p53 alleles that are over-represented in human ovarian cancer control tumor growth. We have shown that these GOF p53 mutants are...

...essential for tumor cell viability, and therefore, we are analyzing the response of human and mouse ovarian cancer tumors to specific cytotoxic drugs that reduce GOF mutant p53 protein levels and lead to cell death.”

We have shown that the R175H mutant is ubiquitinated and degraded by novel lysosomal pathway and not by proteasomes as is WT p53. We are also analyzing the interactions of ovarian cancer cells with immune cells on the omentum and how this unique ovarian cancer microenvironment supports and promotes tumor initiation and progression.

We have recently analyzed and identified inflammatory events associated with peri-ovulatory events in follicles of PCOS patients undergoing IVF. These studies have led to our current interest in how androgens, immune cells, and cytokines interact to control ovarian follicular development, the follicular microenvironment, and the ovarian stroma.
Reproductive senescence is a hallmark of aging. As aging progresses, functional decline in the reproductive system is accompanied by increased risk of infertility and birth defects. The delay in childbearing is a current trend in western societies, resulting in high risk of subfertility, fetal and perinatal mortality, which is also associated with developmental disabilities and diseases of early childhood. Hence, how to improve reproductive health during aging represents a new challenge for public health.

However, it remains poorly understood the molecular mechanisms by which genetic and environmental factors interact and cooperate to modulate the onset and progression of reproductive senescence. We carried out the first functional genomic analysis of reproductive senescence, and identified a series of new genes that regulate reproductive longevity. Many of these genes are well conserved across different species, and thus these studies provide new insights into the molecular control of reproductive aging.

We also discovered a neuroendocrine nexus linking olfactory sensation and reproductive senescence in response to environmental variations. We found that environmental inputs are perceived by specific neurons, and consequently regulate age-related reproductive outcomes.

These findings reveal the significance of neuroendocrine regulation in maintaining reproductive health, and shed new light into the understanding of gene-environmental interactions in promoting reproductive health.

March 9, 2017

“Genetic and Environmental Regulation of Reproductive Strategies”

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These findings reveal the significance of neuroendocrine regulation in maintaining reproductive health, and shed new light into the understanding of gene-environmental interactions in promoting reproductive health.
April 13, 2017

“Hedgehog Signaling Receptor Patched1 in S100a4 Cell Lineages is Critical for Fertility”

One out of eight couples in the United States suffers from infertility and in about a third of these couples the cause is not known. Although the hypothalamic-pituitary-gonadal axis is the main endocrine regulatory system that controls female and male fertility, this axis is influenced by many other physiological and pathological conditions, including metabolic status, aging, chronic inflammation, and infection. Understanding of how these conditions impact the reproductive system will assist in the diagnosis and treatment of many infertility cases.

Using a genetically engineered mouse model, we show that disruption of the hedgehog signaling pathway receptor protein PATCHED1 in the hematopoietic (immune) cell lineage leads to female infertility with alterations in pituitary and ovarian functions.

These observations suggest that specific immune cells are essential for fertility at the pituitary and/or ovarian level and thus they act as modulators of reproductive success.

NATIONAL INFERTILITY AWARENESS WEEK 2017
APRIL 23 - 29, 2017

National Infertility Awareness Week (NIAW) is the perfect time to help those who are struggling to build a family, and reduce the stigma behind infertility. During NIAW 2017, CRM members helped raise awareness, provided support, and educated the community. Activities included:

DOC TALK
April 25, 2017

“Understanding Infertility: Causes and Treatment Options”

AMY SCHUTT, M.D.
Assistant Professor, Department of OB/GYN

Along with treatment options, male factors, age-related considerations, and myths of female fertility, Dr. Schutt emphasized upon three major categories when evaluating couples with infertility. This included ovarian function (ovulation, egg quantity vs. egg quality, and hormonal assessments), female pelvic anatomy, and sperm parameters. Dr. Schutt also addressed that women often feel alone when facing infertility. However, with the proper knowledge and resources, they may be able to find an appropriate path or decision best suited for them.

WATCH THE VIDEO

“He Said, She Said: Infertility”
youtu.be/BcbSO9O0tyA

Dr. Larry Lipshultz, Professor and Chief, Scott Department of Urology and Dr. Amy Schutt, Associate Professor of OB/GYN, discuss infertility from both male and female perspectives, including the realities of the disease at various ages.

SEE THE PRESS RELEASE

“Facing the Hard Realities of Infertility”

TERRI WOODARD, M.D.
Assistant Professor, Department of OB/GYN

bcm.edu/news/reproductive-health/facing-the-hard-realities-of-infertility
Over his 30 years at Baylor, former Associate Director of the Center for Reproductive Medicine, Francesco (Franco) DeMayo, Ph.D., started off as a postdoctoral fellow, training in reproductive and molecular biology, then rose through the ranks to become tenured Professor. During that time, Dr. DeMayo was Professor of Molecular and Cellular Biology and Pediatrics; he held the Dan L. Duncan Cancer Center and Gordon Cain Professorships; was Director of the Genetically Engineered Mouse Core; and Director of the NIH-funded Center for Reproductive Biology U54 cooperative research grant. He has received numerous awards and achievements, including the Michael E. DeBakey Award for Excellence in Research (2006) and the Society for the Study of Reproduction (SSR) Research Award (2011). Dr. DeMayo brings a wealth of knowledge, and is dedicated not only to the field of reproductive medicine and cancer research, but also to mentoring the next generation of young investigators. Here Dr. DeMayo reflects upon his days as a postdoctoral fellow, and how that experience has evolved into his current work in uterine function.

Q| How did your Fellowship training and research at Baylor prepare you for your career?  
A| I was a postdoctoral fellow in the laboratory of Dr. David Bullock (Department of Cell Biology) in 1983. At that time there were few labs generating transgenic mice. “My fellowship consisted of establishing the transgenic mouse system to investigate the hormonal regulation of the rabbit uteroglobin gene in vivo. I was given the freedom to develop the system since no one at Baylor had the capability at the time.”

I was exposed to labs doing cutting-edge molecular biology and was able to interact with many investigators. The experience was exciting and fun.

Q| Can you describe one or two fond memories you had from your time here at Baylor?  
A| The two fondest memories I had were: developing an X-ray film of a Southern Blot that confirmed I had generated my first transgenic mouse; and the collaboration I had with Dr. John Lydon to generate the PRCre mouse model. This opened up the field on the genetic analysis of uterine biology.

Q| What are some of your contributions to reproductive medicine?  
A| My laboratory has generated the tools to conduct in vivo analysis of the molecular pathways that regulate uterine fertility. We used these tools to investigate the pathways regulated by the hormone progesterone.

“Additionally, we have used these tools to identify the critical pathways that regulate embryo implantation, the ability of the uterus to support the developing fetus, and the pathways that are altered in infertility and uterine diseases such as endometrial cancer and endometriosis.”

Q| What advice do you have for a starting scientist or medical/science professional?  
A| My advice to starting scientists is to “Think Big.” “Once you have identified the big picture in which you want to focus your career, you can easily identify what you have to do to achieve that goal.”

Q| Where would you like to see your research go in the future?  
A| I see the future of my research as identifying the factors that regulate uterine differentiation and function. I will then identify how the environment can influence uterine biology by interacting with these factors. Ultimately my research should develop the approaches to repair or engineer a uterus that can support embryo implantation in pregnancy.
“Man Up” Male Health Fair
Finnigan Community Center | April 29, 2017

On April 29, the Houston Parks and Recreation Department hosted its first annual “Man Up” Male Health Fair to motivate men of all ages to take charge of their bodies by staying healthy, happy, and educated. Attendees had the opportunity to meet with 40 public health and education officials from Houston-area institutions. Representing the CRM and joining David McBride, Project Coordinator and Chair, Male Empowerment Coalition of the Baylor Teen Health Clinic were third-year medical students in Urology—Jordan Krieger, Taylor Kohn, and Javier Santiago (pictured above from left to right).

Kohn and Santiago provided a special informational session directed towards male teens—“Young Men Need Urologists Too.” They guided high school athletes through various urologic trauma conditions and their after effects, sexually transmitted infections (STIs), testicular cancer and the importance of self-examinations, plus prevention and treatment options to lead a healthy and sound lifestyle. Krieger volunteered at the Teen Health Clinic booth to provide important health education information to inquiring teens on pregnancy, STIs, urologic health, resource hot lines, guidance and career-planning advice, and other materials.

Sexuality, Science & Sandwiches
April 21, 2017

“Male Anorgasmia: From No to Go!”
Alexander Pastuszak, M.D., Ph.D.
Assistant Professor, Department of Urology

On April 21, Dr. Pastuszak met with Houston-area public health and science officials interested in sexuality-related research and scholarship within various disciplines, fields, and agencies. Focusing on delayed ejaculation (DE)/anorgasmia— inability to achieve orgasm after persistent sexual stimulation—he addressed its causes and treatment options, as this issue can lead to personal distress.

SAVE THE DATE

CRM QUARTERLY MEMBERSHIP MEETING AND RECEPTION

Thursday, June 15, 2017
4 – 6 p.m.
Alkek Building, Room N317
Refreshments served

CRM Director, Dr. Dolores Lamb, along with our Translational Research Group Leaders will share a recap of our spring 2017 efforts, including notable research strides and developments, and current research moving forward within their labs and the reproductive field. Afterwards, enjoy a networking reception, and connect with colleagues old and new. Kindly RSVP to jyotip@bcm.edu.

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