



Reproduction and Perinatology Update

A publication of the D.H. Barron Reproductive and Perinatal Biology Research Program and the Center for Perinatal Outcomes Research

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Fall 2015 Warnick Lecturer – Peter Sutovsky



Dr. Peter Sutovsky, professor of Animal Science and Obstetrics, Gynecology and Women's Health at the University of Missouri, will present the 6th Warnick Lecture on November 4 at 4:00 PM as part of the Reproductive & Perinatology Seminar Series.

During his career, which has included a position at Oregon Regional Primate Research Center and, since 2001, the University of Missouri, Sutovsky has developed several new concepts in human and animal reproduction, fertilization and development that are now widely accepted.

He was the first to describe the role of the ubiquitin-proteasome system (UPS) in the

regulation of mitochondrial DNA inheritance in mammals. As an outgrowth of this work, he developed the concept of the extracellular UPS system. He demonstrated the importance of sperm-borne proteasomes for mammalian fertilization and the role of UPS in epididymal sperm quality control.

Sutovsky's work on in vitro fertilization and intracytoplasmic sperm injection influenced the optimization and prompted the safeguarding of human assisted reproductive technologies. At the same time, he mapped out the post-fertilization fate of important sperm accessory structures such as the centriole and perinuclear theca. Recently, he has used his knowledge of sperm biochemistry to develop new approaches for improving quality of sperm used for artificial insemination and assisted reproduction in animals and humans.

Dr. Sutovsky received the MS from Slovakia Agricultural University

University and the PhD from the Institute of Animal Physiology and Genetics, Czech Academy of Sciences. He completed a postdoc at the University of Wisconsin.

Sutovsky is the author of more than 150 papers, holds eight patents and has been recognized often for his research accomplishments. He, received the University of Missouri Chancellor's Award for Outstanding Research and Creative Activity in the Biological, and was inducted into the National Academy of Inventors.

The Alvin C. Warnick Lecture Series was created by the Dept. of Animal Sciences to recognize the achievements of Dr. Alvin C. Warnick. One of the founders of the Reproductive and Perinatal Biology Group, Dr. Warnick has made important contributions to the improvement of the livestock industry through research, extension, and teaching.

Faculty, Student, Postdoc and Alumni News

Contribute IDC to Support Our Program

Our reproductive biology effort is supported by the Center for Perinatal Outcomes Research. This is a source of funds that are generated by indirect costs from us - up to 7.5% of IDC that otherwise goes to the Deans Office can be designated to the Center (Code - 00047347). These funds are used to invite speakers to campus, organize retreats and are used as a source of seed grants. Please consider designating some of your IDC to the Center

Identify Our Program on Your Next Paper

Please consider including the D.H. Barron Reproductive and Perinatal Biology Research Program as one of your affiliations

John Bromfield (Animal Sciences) was appointed to the Editorial Board of the *Journal of Assisted Reproduction and Genetics*.

Two new clinical fellows in Maternal Fetal Medicine have joined the program. **Anushka Chelliah** will be mentored by Mark Atkinson and Clive Wasserfall and **Oluseyi Ogunleye** will be mentored by Kirk Conrad.

Greg Christman (Ob/Gyn) will present a plenary talk entitled "Gene therapy in reproductive medicine" at the 1st Meeting on Controversies in Preconception, Preimplantation and Prenatal Genetic Diagnosis (CoGEN), September 25-27, 2015 in Paris, France. The talk will focus on the prevention of mitochondrial disease transmission and the potential future of CRISPER/Cas 9 gene editing in human embryos.



Kyle Dobbs, who received the PhD in 2014 while in the lab of **Pete Hansen**, has taken a position with Thermo-Fisher as a technical application scientist II in the molecular biology department. He is based in San Diego.

Elizabeth Ann Jannaman has joined **Pete Hansen's** laboratory (Animal Sciences) as an IVF lab technician. Previously, she worked in human ART at Reproductive Associates of Delaware, located in Newark DE.

Vitor Mercadente recently completed his PhD in Animal Sciences with **Cliff Lamb** and will be taking a faculty position as assistant professor in

the Dept. of Animal and Poultry Science at Virginia Tech University.

Jacklyn Quinlan (PhD, Univ. of Montreal) has started a postdoctoral fellowship in the Department of Anthropology in the laboratory of **Connie Mulligan**.

James L Resnick was recently promoted to professor in the Dept. of Molecular Genetics & Microbiology

Eduardo de Souza Ribeiro completed his PhD in the AMCB graduate program under the supervision of **Jose Santos** in summer 2015. The title of his dissertation was *Molecular Features of Reproductive Biology Associated with Fertility in Lactating Dairy Cow*.

Ricarda Santos, a visiting professor from Federal University of Uberlândia in Brazil, recently finished her sabbatical in the laboratory of **Jose Santos**.

New Graduate Students

Name	Origin	Major	Degree sought	Major Professor
Arnold, Danielle Marianne	Canada	Animal Sciences	PhD	Mortensen
Chris Clukay	Florida	Anthropology	PhD	Mulligan
Fabris, Thiago	Brazil	Animal Sciences	MS	Dahl
Fontes, Pedro	Brazil	Animal Sciences	MS	Lamb
Jumutayeva, Gulnur	Kazakhstan	Animal Molecular & Cellular Biology	MS	Hansen
Lopera Higueta, Camilo	Columbia	Animal Sciences	MS	Santos
Oosthuizen, Nicola	South Africa	Animal Sciences	MS	Lamb
Zolini, Adriana	Brazil	Animal Molecular & Cellular Biology	PhD	Hansen/Block

Awards and Recognitions

Rafael Bisinotto (Animal Sciences) received the National Milk Producers Federation Richard M. Hoyt Award from the American Dairy Science Association.

G. Cliff Lamb (Animal Clinical Sciences) was the recipient of the 2015 Animal Management Award from the American Society of Animal Science.

Natalia Martinez-Patino (Animal Sciences) received the 2015 Alltech Inc. Graduate Student Paper Publication Award from the American Dairy Science Assn.

Christopher Mortensen (Animal Sciences) was recently awarded the College of Agricultural and Life Sciences Teacher of the Year for 2014-2015.



Natalia Martinez-Patino and her major professor, Jose Santos



Rafael Bisinotto



Cliff Lamb

Recent Extramural Grants and Contracts

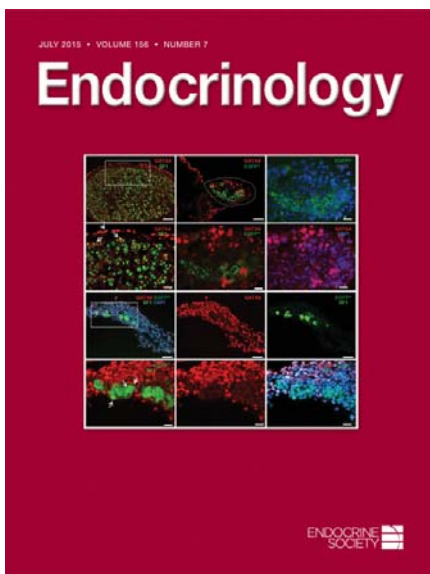
National Science Foundation. Wild Discoveries, zooming into the scientific method. CJ Mortensen, AC Thoron, JK Miot, \$199,098.

Select Sires. Improving calving rates in dairy cows by infusion of seminal plasma proteins at the time of artificial insemination. JJ Bromfield, GC Lamb, PJ Hansen, J Block, \$14,900.

USDA-NIFA AFRI. Impact of heat stress on cellular events in the mammary gland during the dry period. GE Dahl, S. Wohlgemuth and S. Tao. 2015-67015-23409, 2015-2018, \$450,000.



Christopher Mortensen with Dean Elaine Turner, Dean of the College of Agricultural & Life Sciences, at the Teacher of the Year Awards Ceremony



The July 2015 cover of *Endocrinology* highlighted the work of the Sergei Tevosian laboratory (Physiological Sciences) described in their paper entitled “Adrenal development in mice requires GATA4 and GATA6 transcription factors”.

Schedule Fall Seminar Series

Reproductive & Perinatal Biology Seminar

Wednesday 4:00-5:00 PM

D.H. Barron Conference Room Medical Sciences Building M-304

sponsored by the D. H. Barron Reproductive & Perinatal Biology Research Program
and the Center for Perinatal Outcomes Research

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|---------------|--|--------------|---|
| September 16: | Hideko Kasahara, MD, PhD
Associate Professor of Physiology & Functional Genomics, College of Medicine, University of Florida | November 4: | Peter Sutovsky, MD
Warnick Lecturer
Professor of Animal Science and of Obstetrics, Gynecology & Women's Health, University of Missouri-Columbia |
| September 23: | Karen Racicot, PhD
Assistant Professor of Obstetrics, Gynecology and Reproductive Biology, Michigan State University | | <i>Spermatozoa – The Good, The Bad, and The Ugly: Lessons from sperm phenotypes of livestock animals and their translation to human male infertility</i> |
| September 30 | James Resnick, PhD
Professor of Molecular Genetics & Microbiology, College of Medicine, University of Florida | November 18: | Klibs Galvão, DVM, MPVM, PhD, DACT
Assistant Professor of Large Animal Clinical Sciences, College of Veterinary Medicine, University of Florida, Gainesville |
| October 7: | Nancy Denslow, PhD
Professor of Physiological Sciences, College of Veterinary Medicine and of Biochemistry & Molecular Biology, College of Medicine, University of Florida | December 2: | Jim Segars, MD |
| October 14: | Marty Cohn, PhD
Professor of Molecular Genetics and Microbiology, College of Medicine, University of Florida | December 9: | Melissa Mann, PhD
Associate Professor of Obstetrics & Gynecology and of Biochemistry, University of Western Ontario Schulich School of Medicine and Dentistry |
| October 21: | José Santos, DVM, PhD
Professor of Animal Sciences, University of Florida | | |
| October 28: | Veronica Negron-Perez, MS
PhD Student, Department of Animal Sciences, University of Florida | | |

Work in Progress Meetings

Organized by Kirk Conrad, the purpose of the Work in Progress Conference is to present new ideas and new data, in order to solicit feedback from one's peers, educate trainees, and find common ground for new NIH R01 and P01 applications.

We meet at the New Deal Café from 4 to 6 PM on approximately one Friday each month. Beverages and hors d'oeuvres are provided! It is preferred that presentations should be really informal and spontaneous, with NEW IDEAS and data to back

them up, if you have any (not necessary). PowerPoint and screen are available, but you are encouraged to use them sparingly. There is also a white board with markers. Dates for fall semester are Oct. 16, Oct. 30, Dec. 4 and Dec. 18.

Research Highlight 1 - Establishing Maternal Allele Identity

James L Resnick, Department of Molecular Genetics & Microbiology

Prader Willi and Angelman syndromes are neurobehavioral disorders arising from a cluster of imprinted genes at 15q11-q13. Similar to other imprinted domains, this region harbors an imprinting center (IC) that regulates gene silencing as well as parent-of-origin allele identity. The IC for this region is unique in that it is defined by overlaps of small deletions in people with imprinting defects, rather than by engineered mutations in mice. Two separate sequences comprise this IC, the PWS-IC and the AS-IC. The PWS-IC activates expression of genes on the paternal chromosome in somatic cells. The AS-IC acts in oocytes to epigenetically inactivate the PWS-IC so that paternal genes are not transcribed from the future maternal allele. Failure of the AS-IC to silence the PWS-IC results in AS. The PWS-IC is conserved in many mammals but lack of sequence homology has impeded research into molecular characterization of the AS-IC. However using mouse transgenes we previously demonstrated that AS-IC activity consists of oocyte transcription across the PWS-IC, leading to PWS-IC epigenetic inactivation. In the current paper, we investigated the molecular function of the human AS-IC sequence, an 880 bp region deleted in some people with AS. Using diverse approaches, we demonstrate that the human AS-IC functions as an oocyte-specific promoter that drives transcripts across the PWS-IC. To confirm and extend this finding we also examined bovine oocytes, a species to which the human AS-IC sequence exhibits about 65% conservation. We found that the bovine AS-IC sequence also functions as an oocyte-specific promoter. These results strongly suggest a model in which most individuals with AS imprinting defects arose from oocytes in which lacked inactivating transcription across the PWS-IC.

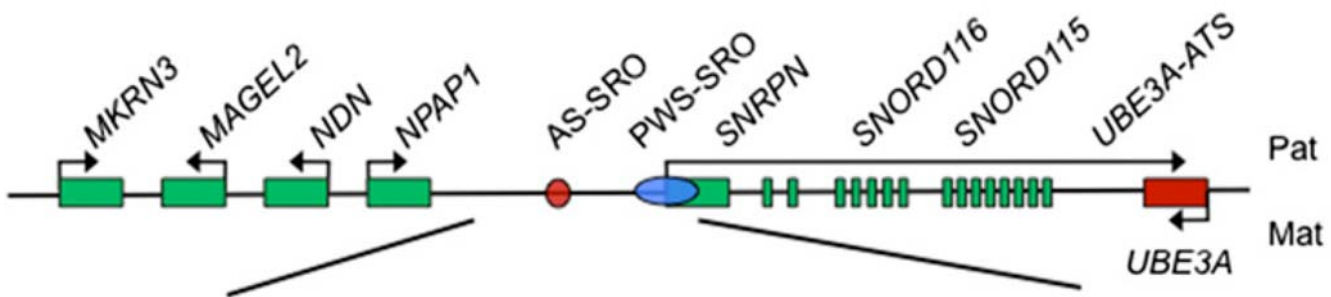


Figure 1. Map of the human AS-PWS-imprinted domain.

Selected Publications

Bisinotto RS, Lean IJ, Thatcher WW, Santos JEP. Meta-analysis of progesterone supplementation during timed AI programs in dairy cows. *J. Dairy Sci* 2015; 98:2472-2487.

Bromfield JJ, Santos JE, Block J, Williams RS, Sheldon IM. Uterine infection: Linking infection and innate immunity with infertility in the high-producing dairy cow. *J Anim Sci* 2015; 93:2021-2033.

Denicol AC, Leão BC, Dobbs KB, Mingoti GZ, Hansen PJ. Influence of sex on basal and dickkopf-1 regulated gene expression in the bovine morula. *PLoS One* 2015;10:e0133587.

Diamond MP, Legro RS, Coutifaris C, Alvero R, Robinson R, Casson P, Christman GM, Ager J, Huang H, Hasen KR, Baker V, Usadi R, Seundamrong A, Bates GW, Rosen RM, Haisenleder D, Krawetz S, Barnhart K, Trussell JC, Jin Y, Santoro N, Eisenberg E, Zhang H. Assessment of multiple intrauterine gestations from ovarian stimulation (AMIGOS) trial: baseline characteristics. *Fertil Steril* 2015; 103:962-973.

Greco LF, Neves Neto JT, Pedrico A, Ferrazza RA, Lima FS, Bisinotto RS, Martinez N, Garcia M, Ribeiro ES, Gomes GS, Shin JH, Ballou MA, Thatcher WW, Staples CR, Santos JEP. Effects of altering the ratio of dietary n-6 to n-3 fatty

acids on performance and inflammatory responses to a lipopolysaccharide challenge in lactating Holstein cows. *Dairy Sci* 2015; 98:602–617.

Lewis MW, Brant JO, Kramer JM, Moss JI, Yang TP, Hansen PJ, Williams RS, Resnick JL. Angelman syndrome imprinting center encodes a transcriptional promoter. *Proc Natl Acad Sci USA* 2015;112:6871-6875.

Mesa AM, Warren LK, Sheehan JM, Kelley DE, Mortensen CJ. L-arginine supplementation 0.5% of diet during the last 90 days of gestation and 14 days postpartum reduced uterine fluid accumulation in the broodmare. *Anim Reprod Sci* 2015; 159:46-51.

Mortensen CJ, Nicholson AM. The flipped classroom stimulates greater learning and is a modern 21st century approach to teaching today's undergraduates. *J Anim Sci* 2015; 93:3722-3731.

Padua MB, Jiang T, Morse DA, Fox SC, Hatch HM and SG Tevosian. Combined Loss of the GATA4 and GATA6 transcription factors in male mice disrupts testicular development and confers adrenal-like function in the testes. *Endocrinology* 2015; 156:1873-1886.

Polotsky AJ, Allshouse AA, Casson P, Coutifaris C, Diamond MP, Christman GM, Schlaff WD, Alvero R, Trussell JC, Krawetz SA, Santoro N, Eisenberg E, Zhang H, Legro RS for the Reproductive Medicine Network. Impact of male and female weight, smoking and intercourse on live birth in pregnancy in women with polycystic ovary syndrome. *J Clin Endocrinol Metab* 2015; 100:2405-2412.

Tevosian SG, Jiménez E, Hatch HM, Jiang T, Morse DA, Fox SC, Padua MB. Adrenal development in mice requires GATA4 and GATA6 transcription factors. *Endocrinology* 2015;156:2503-2517.

Research Highlight 2 – Heat Stress In Utero Alters Lactation Phenotype in Adulthood

Geoffrey E Dahl, Department of Animal Sciences

In lactation, heat stress (HS) effects are well known and include lower dry matter intake (DMI) and metabolic shifts that reduce milk production efficiency. When dry cows are HS they reduce DMI, but maintain normal metabolic profiles despite lower DMI. Late gestation HS reduces mammary growth, possibly due to suboptimal placental function. Dry period HS alters immune function and those impacts persist into lactation, resulting in a poorer transition outcome. Thus, a relatively brief duration of heat stress at a specific phase of the production cycle can have dramatic, negative outcomes on multiple physiological systems and overall productive efficiency. A recent focus has been on the effects of late gestation heat stress on calf survival and performance, with a series of studies to examine pre-weaning growth and health, and later reproductive and productive responses, to quantify acute and persistent impacts of in utero HS. Calves born to dams HS when dry have lower birth weight and remain lighter up to 12 mo of age vs. calves from dams that are cooled (CL) when dry. Calves HS in utero have lower immune status compared with those from CL dams, beginning with poorer apparent efficiency of IgG absorption and extending to lower survival rates. Relative to CL calves, HS calves also have shifts in metabolism that lead to greater peripheral accumulation of energy and less lean growth vs. those from CL dams. Comparing reproductive performance in HS vs. CL calves, we observe that the CL heifers require fewer services to attain pregnancy and are pregnant at an earlier age. Finally, milk yield in calves HS vs. those CL in utero reveals a 5 kg/d reduction in yield through 35 wk of lactation (Figure 2, next page), despite similar bodyweight at calving. These observations indicate that a relatively brief period of HS in late gestation dramatically alters the health, growth, and performance of calves. Thus, environmental factors can program shifts in physiological systems in a sustained manner to the detriment of productive efficiency.

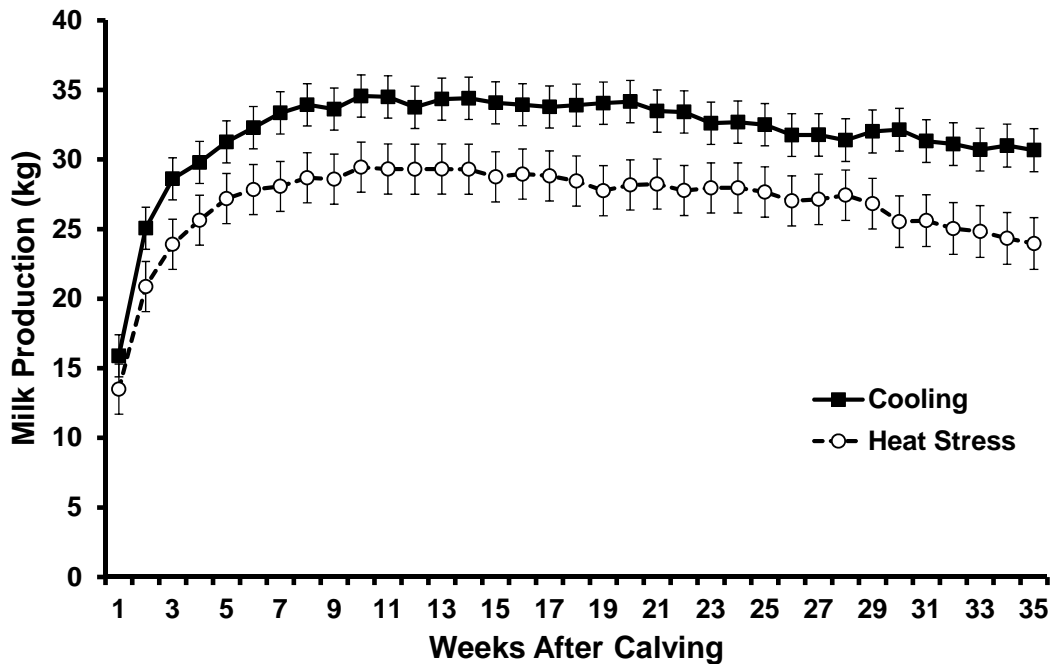


Figure 1. Effect of maternal heat stress (n = 29) or cooling (n = 35) during late gestation on milk production in the first lactation. Data from calves born over five consecutive years were analyzed. All calves were managed identically after birth and through the first lactation regardless of in utero treatment. Heifers born to cows in heat stress during the dry period produced less milk up to 35 weeks postpartum compared with those born to cows exposed to cooling (P = 0.03).

Death of Howard Jones, IVF Pioneer

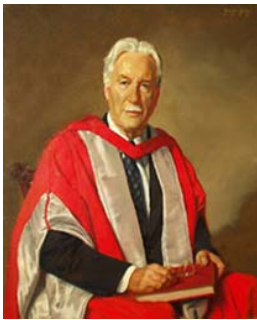
Dr. Howard W. Jones Jr., the father of in vitro fertilization (IVF) in the United States, died on July 31, 2015, aged 104.



Jones in 2010 (Wikipedia)

Dr. Jones and his wife, the late Dr. Georgeanna Jones, founded the Jones Institute for Reproductive Medicine at Eastern Virginia Medical School in 1978 and oversaw the birth of the first baby born as a result of IVF in the United States in 1981. The baby, named Elizabeth Jordan Carr, was born following 41 failed attempts. A photograph of Jones visiting with Carr as an adult can be viewed at <http://media.hamptonroads.com/cache/files/images/137581.jpg>

In his earlier career at Johns Hopkins, Jones was the physician who first treated Henrietta Lacks and collected biopsies of her tumor that were used to obtain HeLa cells.



DH Barron Reproductive & Perinatal Biology Research Program

University of Florida

Repro & Perinatal
Update is issued each
August and January

Send items of interest to
P.J. Hansen at
Hansen@animal.ufl.edu

We're on the Web!
www.perinatal.ufl.edu

About the D.H. Barron Reproductive and Perinatal Biology Research Program

History: The Repro program was founded in 1969 by Donald Henry Barron, Fuller Bazer and others. Seminars have been held continuously since that time. Donald Henry Barron (1905-1993) came to UF as the J. Wayne Reitz Professor of Reproductive Biology after a career at Cambridge and Yale. His research in fetal physiology lead to his being referred to as the Father of Scientific Obstetrics and the Father of Fetal-Placental Physiology. Known to his colleagues and students as "Dr. B.", his portrait is on the masthead. In 1969, Fuller Bazer, currently the O.D. Butler Chair in Animal Science at Texas A&M University, was an assistant professor in the Dept. of Animal Sciences. Since then, he has become one of the pioneers in understanding the nature of communication between the embryo and mother. Among the many recognitions he has received was the Wolf Prize in Agriculture in 2003.

Mission: To foster collaborative, multidisciplinary, and integrative approaches to basic and translational research that (i) improves the health of pregnant women and their babies, (ii) enhances the reproductive success of agriculturally important animals and wildlife, and (iii) prepares the next generation of scientists in these research disciplines.

Scope: Basic, translational and clinical research aimed at understanding (i) the biology of reproduction in humans and animals from fertilization to delivery and early postnatal development, and (ii) genetic, epigenetic or environmental influences that cause abnormal pregnancy outcomes, including those influences that predispose the mother and offspring to adult diseases.



The first calf born in the United States as a result of artificial insemination. The calf was born in February, 1939 at the Schomp Farm in Stanton, NJ. People in the photograph (left to right) are Richard Schomp, the owner, Dr. James Henderson, the veterinarian who collected semen and performed artificial insemination, and Dwight Babbitt, the Hunterdon County Extension Agent. At the time, the calf was considered the most photographed cattle in the world. Image is from <http://www.animalimagegallery.org/>