



# REPRODUCTION MATTERS

A publication of the  
**Center for Reproductive Science**  
Northwestern University  
Evanston & Chicago

Fall 2005

## 26th Minisymposium on Reproductive Biology

This year, the 26th Minisymposium on Reproductive Biology took place on October 17. Attendees and participants came from across the Midwest to take part in this annual event. The keynote speaker and recipient of the second Neena B. Schwartz Lectureship award, was **Dr. J. David Puett**, Regents Professor and Head of the Department of Biochemistry and Molecular Biology at the University of Georgia. The title of Dr. Puett's keynote address was *hCG and the Lutropin Receptor: Expanding Horizons*.

Continuing a tradition begun last year, the event featured two alumni guest speakers, **Dr. Sonali Anand**, Unilever and **Dr. Angela Bauer-Dantoin**, University of Wisconsin Green Bay, who reflected on their years at Northwestern and offered advice to trainees currently pursuing careers in reproductive biology. Dr. Anand was formerly a graduate student in the Turek/Horton lab (1996-2002) and Dr. Bauer-Dantoin was a graduate student in the Levine lab (1988-1992) and a postdoctoral fellow in the Jameson lab (1993-1997).



Erv Goldberg, Neena Schwartz, J. David Puett and Geula Gibori

The winners of the Constance Campbell Memorial Research Awards in the Oral Division were: First Place - **Susan Park**, *Genetic Background of the C57BL/6J Mouse Strain Permits Male-to-Female Sex Reversal in*

*Dax1 Null Animals*; Second Place (tie) - **Melissa Chamberlin**, *Blockade of ATP-Sensitive Potassium Channels Restores Male Sexual Behavior in the Castrated Rat*; and Second Place (tie)- **Robert Cook**, *Structural Basis for a Functional Antagonist in the TGFbeta Superfamily*. Winners in the Poster Division this year were: First Place - **Christina Matulis**, *Structure-Function Analysis of the Nuclear Receptor Steroidogenic Factor 1 (SF-1) in Complex with its Target DNA Sequence in the Inhibin Alpha Promoter*; Second place- **Sarah Bristol-Gould**, *Postnatal Regulation of Germ Cells by Activin*; and Third Place- **Courtney Berkholtz**, *Differential Effects of FSH and Forskolin on Primary Mouse Follicles in Three-Dimensional In Vitro Culture*.

The 26th Minisymposium was sponsored in part by the Offices of the President and Vice President for Research at Northwestern University, the Robert H. Lurie Comprehensive Cancer Center and Serono. The generous sponsorship of these organizations helped CRS continue its tradition of offering trainees the opportunity to present their research and providing a forum for scientific exchange. The Minisymposium is organized by trainees and is open to the public. *More minisymposium pictures on page 2.*

### In this Issue:

Minisymposium 2005.....	1-2
From the Director.....	2
Research Notes.....	3
Recent Publications.....	4
CFAC.....	5
Upcoming Seminars.....	6
CRS Logo Contest.....	6

REPRODUCTION MATTERS  
Fall 2005

### Center for Reproductive Science

2205 Tech Drive  
Hogan 2-171  
Evanston, IL 60208-3520  
[www.northwestern.edu/research/crs/](http://www.northwestern.edu/research/crs/)

#### Director:

Kelly E. Mayo, PhD

#### Associate Director:

Mary Hunzicker-Dunn, PhD

#### Production Editor:

M. Lise Jinno



Sonali Anand and former co-advisor, Terry Horton



Jon Levine and Angela Bauer-Dantoin

## From the Director...

Over the years, I've come to associate the beginning of the new academic year with the Minisymposium on Reproductive Biology, and it's hard to believe that another one, our 26th, has come and gone. And yes, we are already planning for the 27th!

We got off to a great start this fall with a CRS reception following the internal seminar by Professor **Warren Tourtellotte**. The title of his talk was *Male germ cell maturation and testosterone biosynthesis regulated by early growth response transcription factors*. It was a great opportunity for students and faculty from both campuses to interact.

CRS welcomes 2 new investigators as members this fall. Professor **Lonnie Shea** in the Department of Chemical and Biological Engineering and Professor **Eugene Xu** from the Department of Obstetrics and Gynecology. You can read about some of Professor Shea's work in this edition's Research Notes. Professor Xu has just joined the Northwestern faculty following training at the University of California San Francisco. We welcome both of them to the CRS family!

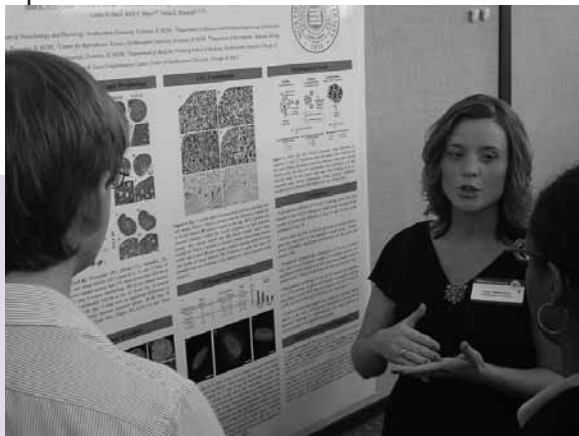
You will find on the back of the newsletter an article describing an open contest to design a new CRS logo. The current one has served us well, but in all things some change is good, and we look forward to seeing your ideas. I know we have a lot of creative and talented people, so I hope many of you will participate!

Finally, remember- with growing concern about an increasing world population and a deteriorating environment- reproduction matters!

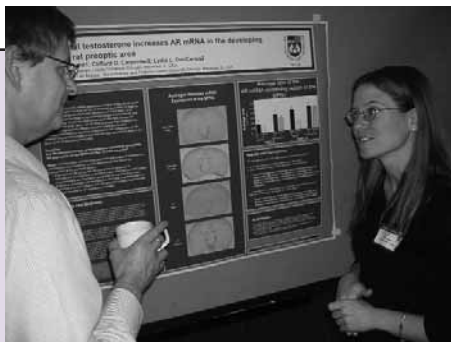
Dr. Kelly E. Mayo  
Director, Center for Reproductive Science



Susan Park, Northwestern University, first place in the Oral Division with Kelly Mayo, CRS Director.



Sarah Bristol-Gould, Northwestern University, second place poster winner.



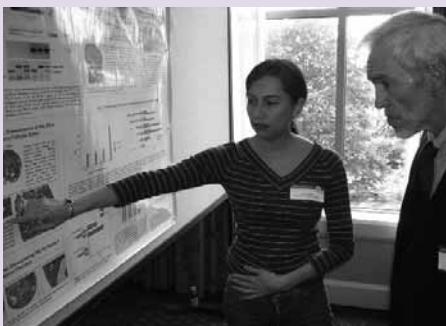
David Abbott, University of Wisconsin-Madison and Sarah Hund, Loyola University.



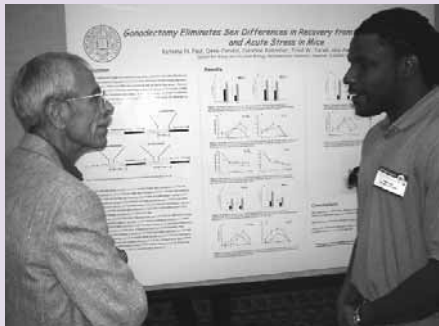
Christina Matulis, Northwestern University, explains her poster. Christina won first place in the poster division.



Jason Hickok, University of Illinois, gives his talk.



Julia Halperin, University of Illinois-Chicago discusses her poster with keynote speaker, J. David Puett.



Bela Piacsek, Marquette University and Ketema Paul, Northwestern University.



Courtney Berkholtz, Northwestern University, talks to Martha McClintock, University of Illinois-Chicago.

## RESEARCH NOTES

*Research Notes features the recent laboratory findings of CRS members. This issue we focus on the laboratories of **Lonnie Shea, PhD** and **Teresa Woodruff, PhD**.*

### Small Steps toward Making Egg Banks a Reality

For over fifty years, techniques to cryopreserve sperm have allowed for the establishment of sperm banks. However, women do not yet possess the equivalent of this option because of difficulties in growing oocytes *in vitro*. In a close collaboration between engineering and the basic sciences, the laboratories of Lonnie Shea and Teresa Woodruff have pioneered a method to support follicle development and oocyte maturation *in vitro*. The follicle is the functional unit of the ovary that houses the female gamete, the egg. The research method developed by CRS faculty is based on the use of an alginate hydrogel, where follicles are encapsulated in beads made of alginate, a natural polysaccharide isolated from seaweed. Compared with collagen or other biopolymers, alginate can gently envelop the follicle without damaging it. The promise of this method lies in the ability to mimic the natural ovary. Soluble factors that dynamically regulate the growth and maturation of the granulosa cells and oocyte can be added to meet the needs of the follicle. Furthermore, the bead provides a three-dimensional environment that maintains the necessary somatic-germ cell and provides desirable cell-matrix interactions.

Through the work of the Shea and Woodruff laboratories, their unique methodology has proven successful in mice. Follicles grown *in vitro* are identical to those grown *in vivo*. Along with the follicle, oocytes have also been matured normally, to a point where they can be fertilized. Using the follicles cultured in the alginate system, mice embryos were transplanted into foster mothers. The transplantation resulted in live births from 20% of the transferred embryos. This exciting step forward demonstrates

that immature follicles can direct oocyte maturation when maintained in a three-dimensional alginate system. Such progress suggests that follicles isolated from human ovarian tissue could be matured *in vitro* utilizing an alginate scaffold and later used with *in vitro* fertilization and embryo transplantation procedures. This technology is being applied to humans through the Center for Families After Cancer (*See related article, page 5*). Egg banks are thus an option at Northwestern for women who must undergo fertility-threatening cancer treatments.



NUage and NUgene with their foster mother

In addition to the promise of this new methodology in fertility preservation, the alginate scaffolding creates a unique system for studying follicle development and oocyte maturation. The effects of growth and differentiation factors, as well as harmful agents like environmental toxins, on follicles and oocytes can be investigated systematically. The work of Drs. Shea and Woodruff's laboratories will continue to expand what is known regarding follicle development and oocyte maturation in hopes of translating their research into meaningful ways of preserving female fertility. *Article contributed by Carrie Nieman*



NUage and NUgene, the mouse pups that resulted from follicles cultured in the alginate system

## RECENT PUBLICATIONS

- Rzadzinska A, Schneider M, Noben-Trauth K, **Bartles JR**, Kachar B. Balanced levels of Espin are critical for stereociliary growth and length maintenance. *Cell Motil Cytoskeleton*. 2005 Oct 3;62(3):157-165.
- Moore C, Shalet S, Manickam K, Willard T, Maheshwari H, **Baumann G**. Voice abnormality in adults with congenital and adult-acquired growth hormone deficiency. *J Clin Endocrinol Metab*. 2005 Jul;90(7):4128-32. Epub 2005 May 3.
- Turek FW**, Joshi C, Kohsaka A, Lin E, Ivanova G, McDearmon E, Laposky A, Losee-Olson S, Easton A, Jensen DR, Eckel RH, **Takahashi JS**, **Bass J**. Obesity and metabolic syndrome in circadian Clock mutant mice. *Science*. 2005 May 13;308(5724):1043-5.
- Amsterdam LL, Gentry W, Jobanputra S, Wolf M, Rubin SD, **Bulun SE**. Anastrozole and oral contraceptives: a novel treatment for endometriosis. *Fertil Steril*. 2005 Aug;84(2):300-4.
- Chatterton RT Jr**, Mateo ET, Hou N, Rademaker AW, Acharya S, Jordan VC, Morrow M. Characteristics of salivary profiles of oestradiol and progesterone in premenopausal women. *J Endocrinol*. 2005 Jul;186(1):77-84.
- Sam S, Legro RS, Bentley-Lewis R, **Dunaif A**. Dyslipidemia and metabolic syndrome in the sisters of women with polycystic ovary syndrome. *J Clin Endocrinol Metab*. 2005 Aug;90(8):4797-802.
- Gussin HA, Sharma AK, **Elias S**. Culture of cells from maternal circulation, in conditions favoring fetal endothelial cell expansion, does not facilitate the preferential expansion of circulating fetal cells. *Fetal Diagn Ther*. 2005 Jan-Feb;20(1):64-9.
- Hirsch E**, Wang H. The molecular pathophysiology of bacterially induced preterm labor: insights from the murine model. *J Soc Gynecol Investig*. 2005 Apr;12(3):145-55.
- Horton TH**. Fetal origins of developmental plasticity: animal models of induced life history variation. *Am J Hum Biol*. 2005 Jan-Feb;17(1):34-43.
- Park Y, Maizels ET, Feiger ZJ, Alam H, Peters CA, **Woodruff TK**, Unterman TG, Lee EJ, **Jameson JL**, **Hunzicker-Dunn M**. Induction of cyclin D2 in rat granulosa cells requires FSH-dependent relief from FOXO1 repression coupled with positive signals from Smad. *J Biol Chem*. 2005 Mar 11;280(10):9135-48.
- Raverot G, **Weiss J**, Park SY, Hurley L, **Jameson JL**. Sox3 expression in undifferentiated spermatogonia is required for the progression of spermatogenesis. *Dev Biol*. 2005 Jul 1;283(1):215-25.
- Park SY, Meeks JJ, Raverot G, Pfaff LE, **Weiss J**, Hammer GD, **Jameson JL**. Nuclear receptors Sf1 and Dax1 function cooperatively to mediate somatic cell differentiation during testis development. *Development*. 2005 May;132(10):2415-23.
- Kuzawa CW**. Fetal origins of developmental plasticity: are fetal cues reliable predictors of future nutritional environments? *Am J Hum Biol*. 2005 Jan-Feb;17(1):5-21.
- Zhang X, Jafari N, Barnes RB, Confino E, **Milad M**, **Kazer RR**. Studies of gene expression in human cumulus cells indicate pentraxin 3 as a possible marker for oocyte quality. *Fertil Steril*. 2005 Apr;83 Suppl 1:1169-79.
- Kim JJ**, Buzzio OL, Li S, Lu Z. Role of FOXO1A in the regulation of insulin-like growth factor-binding protein-1 in human endometrial cells: Interaction with progesterone receptor. *Biol Reprod*. 2005 Oct;73(4):833-9.
- Zhang Q, Rubenstein JN, Jang TL, Pins M, Javonovic B, Yang X, Kim SJ, Park I, **Lee C**. Insensitivity to transforming growth factor-beta results from promoter methylation of cognate receptors in human prostate cancer cells (LNCaP). *Mol Endocrinol*. 2005 Sep;19(9):2390-9.
- Schneider JS, Burgess C, Sleiter NC, DonCarlos LL, Lydon JP, O'Malley B, **Levine JE**. Enhanced sexual behaviors and androgen receptor immunoreactivity in the male progesterone receptor knockout mouse. *Endocrinology*. 2005 Oct;146(10):4340-8.
- Foeking EM, Szabo M, **Schwartz NB**, **Levine JE**. Neuroendocrine consequences of prenatal androgen exposure in the female rat: absence of luteinizing hormone surges, suppression of progesterone receptor gene expression, and acceleration of the gonadotropin-releasing hormone pulse generator. *Biol Reprod*. 2005 Jun;72(6):1475-83.
- Burkart AD, Mukherjee A, Sterneck E, Johnson PF, **Mayo KE**. Repression of the inhibin alpha-subunit gene by the transcription factor CCAAT/enhancer-binding protein-beta. *Endocrinology*. 2005 Apr;146(4):1909-21.
- McDade TW**. Life history, maintenance, and the early origins of immune function. *Am J Hum Biol*. 2005 Jan-Feb;17(1):81-94.
- Ahmadiyeh N, Churchill GA, Solberg LC, Baum AE, Shimomura K, **Takahashi JS**, **Redei EE**. Lineage is an epigenetic modifier of QTL influencing behavioral coping with stress. *Behav Genet*. 2005 Mar;35(2):189-98.
- Gleyzer N, Vercauteren K, **Scarpulla RC**. Control of mitochondrial transcription specificity factors (TFB1M and TFB2M) by nuclear respiratory factors (NRF-1 and NRF-2) and PGC-1 family coactivators. *Mol Cell Biol*. 2005 Feb;25(4):1354-66.
- Groten T, Pierce AA, Huen AC, **Schnaper HW**. 17 beta-estradiol transiently disrupts adherens junctions in endothelial cells. *FASEB J*. 2005 Aug;19(10):1368-70.
- Kreeger PK, Fernandes NN, **Woodruff TK**, **Shea LD**. Regulation of mouse follicle development by follicle-stimulating hormone in a three-dimensional in vitro culture system is dependent on follicle stage and dose. *Biol Reprod*. 2005 Jun 29.
- Shulman LP**. The use of triphasic oral contraceptives in a continuous use regimen. *Contraception*. 2005 Aug;72(2):105-10.
- Symowicz J, Adley BP, Woo MM, Auersperg N, Hudson LG, **Stack MS**. Cyclooxygenase-2 functions as a downstream mediator of lysophosphatidic acid to promote aggressive behavior in ovarian carcinoma cells. *Cancer Res*. 2005 Mar 15;65(6):2234-42.
- Yoo SH, Ko CH, Lowrey PL, Buhr ED, Song EJ, Chang S, Yoo OJ, Yamazaki S, Lee C, **Takahashi JS**. A noncanonical E-box enhancer drives mouse Period2 circadian oscillations in vivo. *Proc Natl Acad Sci U S A*. 2005 Feb 15;102(7):2608-13.
- Whitehead J, Keller-Peck C, Kucera J, **Tourtellotte WG**. Glial cell-line derived neurotrophic factor-dependent fusimotor neuron survival during development. *Mech Dev*. 2005 Jan;122(1):27-41.
- Easton A, Meerlo P, Bergmann B, **Turek FW**. The suprachiasmatic nucleus regulates sleep timing and amount in mice. *Sleep*. 2004 Nov 1;27(7):1307-18.
- Urbanek M**, Woodroffe A, Ewens KG, Diamanti-Kandarakis E, Legro RS, Strauss JF 3rd, **Dunaif A**, Spielman RS. Candidate gene region for polycystic ovary syndrome (PCOS) on chromosome 19p13.2. *J Clin Endocrinol Metab*. 2005 Aug 9.
- Xiao W, Jiang F, **Wang Z**. ELL binding regulates U19/Eaf2 intracellular localization, stability, and transactivation. *Prostate*. 2005 Aug 20.
- Thompson TB, Lerch TF, Cook RW, **Woodruff TK**, Jardetzky TS. The structure of the follistatin:activin complex reveals antagonism of both type I and type II receptor binding. *Dev Cell*. 2005 Oct;9(4):535-43.
- Kenny HA, **Woodruff TK**. Follicle size class contributes to distinct secretion patterns of inhibin isoforms during the rat estrous cycle. *Endocrinology*. 2005 Sep 29.
- Cooke BM, **Woolley CS**. Gonadal hormone modulation of dendrites in the mammalian CNS. *J Neurobiol*. 2005 Jul;64(1):34-46.

## The Center for Families After Cancer: Uniting Clinical Care with Fundamental Discovery in the Reproductive Sciences

Through a partnership between the Shea and Woodruff laboratories, an alginate scaffolding system has been developed that allows for the development and maturation of follicles *in vitro* (See related article, page 3). After maturation, the oocyte can be isolated and brought to a state where *in vitro* fertilization and embryo transplantation are possible. Such a system has led to the live births of mice, an encouraging accomplishment that lays the foundation for the utilization of this technology in creating human egg banks. Although egg banks could benefit healthy women wanting to preserve their fertility, egg banks could also provide a practical way for women to protect their fertility in the face of follicle-threatening chemo- or radiation therapy. It is the latter promise that has led Dr. Woodruff to develop the Center for Families After Cancer (CFAC), which is dedicated to helping cancer survivors have a family later in life.

CFAC has four major objectives: 1) to encourage research that can protect or preserve fertility options for survivors of cancer, 2) to apply the research findings to clinical practice, 3) to understand better the decision making process leading to patient acquisition of fertility options, and 4) to serve as an educational resource for cancer-caused, fertility-related questions by the community. In order to achieve these goals, CFAC is composed of a team that draws its strength from departments across disciplines and campuses. Although its origins stem from the reproductive sciences, CFAC was a CRS and Robert H. Lurie Comprehensive Cancer Center initiative which brings together leaders in the fields of oncology, assisted reproductive technologies, medical ethics, communication, social policy, among others.

Currently, CFAC coordinates a research study for women who are diagnosed with cancer. The study offers the opportunity to preserve ovarian tissue before beginning cancer treatment. With a non-invasive laparoscopic surgery, one ovary is removed and cryopreserved. This affords the woman the opportunity to preserve her fertility and undergo *in vitro* fertilization and embryo transplantation at a later time of her choosing. While this research study is being offered to women 18 years of age and older, girls with childhood cancer could also greatly benefit from ovarian tissue cryopreservation. In order to better understand the issues involved with childhood cancer, a series of focus groups were conducted with childhood cancer survivors and their parents through cooperation with the STAR (Survivors Taking Action & Responsibility) program. The focus groups concentrated on what survivors and their parents know about the late effects of cancer treatment, particularly infertility, as well as the decision making processes that occur within the family during diagnosis and treatment. With a team of epidemiologists and clinical psychologists, the focus group data is being analyzed and will be used to develop a plan of how to bring this fertility-preserving option to patients with childhood cancer. Several other projects are being designed in collaboration with the Childhood Cancer Survivor Study (CCSS) group. One project will be a longitudinal study of ovarian reserve in childhood cancer survivors. Another will investigate cellular aging in parents of childhood cancer survivors, the key decision-makers during diagnosis and treatment. Decision making for cancer patients and their loved ones, the ethical considerations of fertility research as well as legal issues are all under investigation by CFAC investigators. As CFAC works to improve the reproductive outlook of cancer survivors, the Center will continue to expand, uniting the laboratory and clinic in powerful new ways. *Article contributed by Carrie Nieman*

### Center Services

- ~ **Germline Preservation Program for Female Cancer Survivors**
- ~ **Sperm Archive**
- ~ **Strategies for Follicle Development**
- ~ **Education and Social Policy**
- ~ **Bioethics of Fertility**
- ~ **Germline Transplant**
- ~ **Emergency IVF**
- ~ **Preservation**

**CFAC's new website can be found at <http://www.cancer.northwestern.edu/CFAC/index.cfm>.**

**UPCOMING SEMINARS**

- 12/12/2005 **David Albertini, PhD**  
Professor of Molecular & Integrative Physiology  
Kansas University Medical Center
- 12/19/2005 **Geula Gibori, PhD**  
Professor of Physiology and Biophysics  
University of Illinois at Chicago
- 01/9/2006 **Wayne Hendrickson, PhD**  
Professor of Biological Sciences  
Columbia University
- 02/13/2006 **Jill Schneider, PhD**  
Professor of Biological Sciences  
Lehigh University
- 03/13/2006 **Marco Conti, MD**  
Professor of Obstetrics & Gynecology  
Stanford School of Medicine
- 04/10/2006 **Tony Plant, PhD**  
Professor of Cell Biology & Physiology  
University of Pittsburgh
- 05/08/2006 **Laurinda Jaffe, PhD**  
Professor of Cell Biology  
University of Connecticut Health Center

*All seminars will take place on the Northwestern Evanston Campus,  
2058 Cook Hall, at 3:45 pm.*

**CRS LOGO CONTEST!!**

The time has come to bid farewell to the CRS logo that has served us faithfully for many years. Please help us come up with a new CRS logo!! Submissions should be in GIF or JPEG format with a resolution of at least 600 pixels per inch. The logo should be around 1.5" -2" and include the letters "CRS". It should also reflect the mission and essence of CRS. Submissions must be received by February 1, 2006. A \$200 prize will be awarded to the person with the winning submission and they will be acknowledged in the next issue of *Reproduction Matters* and at the 2006 Minisymposium. The winning logo will become the property of CRS and will be displayed on all CRS print and web media. Logo submissions and questions should be sent to CRS@northwestern.edu.



NON PROFIT  
ORGANIZATION  
US Postage  
PAID  
Northwestern University  
Permit Number 205

CENTER FOR REPRODUCTIVE SCIENCE  
Northwestern University  
2205 Tech Drive, Hogan 2-171  
Evanston, IL 60208-3520

