Center for Reproductive Science

REPRODUCTION MATTERS

Spring 2006

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REPRODUCTION MATTERS

Spring 2006
is a publication of the
Center for Reproductive Science,
Northwestern University,
Evanston and Chicago.

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NORTHWESTERN UNIVERSITY

Domain Dinner Focuses on Reproductive Technologies

Since the initial application of in vitro fertilization with the birth of the first 'test tube baby' in 1978, there have been many advances in assisted reproductive technologies, opening up a range of fertility options to individuals who wish to bear children. Northwestern University's Office of Administration and Planning dedicated their recent Domain Dinner to an emerging field known as 'oncofertility', the preservation of fertility in patients with cancer who will undergo treatments that will save their lives but threaten their fertility.

Beginning in 1998, the Office of Administration and Planning has hosted Domain Dinners as an opportunity for faculty from different campuses, schools and departments to interact and to highlight the unique interdisciplinary nature of the University. Dinners are designed to focus on a faculty generated program that engages colleagues across multiple disciplines. On May 2, 2006 the program was "The Science and Ethics of Emerging Reproductive Technologies" .


Ralph Kazer, MD

The three speakers considered the application of current reproductive technologies in the fertility clinic, explored basic science in reproductive biology as it relates to preservation of the female germ line, and discussed the ongoing and emergent ethical and societal issues raised by reproductive technologies.


Teresa Woodruff, PhD

The presenters were: **Ralph Kazer**, Professor, Feinberg School of Medicine, Obstetrics and Gynecology, "Progress in Assisted Reproductive Technologies: Where are We Now and Where are We Going", **Teresa Woodruff**, Professor, Weinberg College of Arts and Sciences, Neurobiology and Physiology and Feinberg School of Medicine, Medicine, "Oncofertility: Preservation of Fertility Options for Women and Girls with a Cancer Diagnosis", and **Laurie Zoloth**, Professor, Feinberg School of Medicine, Medical Ethics and Humanities and Weinberg College of Arts and Sciences, Religion, "Consent in the Future Tense: Risks, Permission and Ethics in Reproductive Research". **Kelly Mayo**, Professor and Chair, Weinberg College of Arts and Sciences, Biochemistry, Molecular Biology and Cell Biology and Director, Center for Reproductive Science, served as moderator.


Laurie Zoloth, PhD


Kelly Mayo, PhD

All of the presenters are members of the Center for Reproductive Science. The event was held at the James L. Allen Center, on the Evanston Campus.

From the Director...

I often use this column to introduce new members of CRS, and am particularly pleased to report in this issue that Professor **Laurie Zoloth** is the newest member of CRS. Laurie is Professor of Medical Ethics and Humanities at the Feinberg School of Medicine, and of Religion in the Weinberg College of Arts and Sciences. She is also the Director of the newly formed Center for Bioethics, Science and Society at Northwestern University. Professor Zoloth is highly recognized national leader in ethics of biomedical research and of theories of justice in health care. With the emergence of new assisted reproductive technologies, and related issues such as the therapeutic use of stem cells, bioethics is playing a key role in the reproductive sciences, and we are pleased to have Professor Zoloth join CRS. As you will see in the cover article, Professor Zoloth was a featured speaker at our recent domain dinner *"The Science and Ethics of Emerging Reproductive Technologies".*

In the last issue of *Reproduction Matters*, I introduced our 'contest' to find a new CRS logo. As you will see in the article below, we have a winner, and a new CRS logo! I hope you will agree that it is a bit more modern, and brings a fresh look to CRS materials. And don't ask me what it represents- use your imagination!

We have just closed the books on calendar year 2005, with submission of the CRS annual report to the Vice President for Research. It was another terrific year for CRS, and I want to take this occasion to thank all of you for your many contributions to the Center. Your participation in our research grants, training programs, seminar series and outreach efforts make CRS the vibrant center that it is. As always, please let us hear from you with your ideas and suggestions for making CRS even better.

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

Kelly Mayo

Director, CRS

New Logo for CRS

We are pleased to announce that the CRS logo contest, announced in the last edition of Reproduction Matters, was a success. We received many submissions and the judges task of selecting the logo that best represents the Center, was a difficult one.

The winning logo was designed by Cheri Fakes. Cheri is a senior at Northwestern who is double majoring in Performance Studies and Art Theory & Practice. When asked about the vision behind her design Cheri comments, “I knew that I wanted to make it an abstract design...abstract enough so that someone could glance at it and think, ‘That's a really cool graphic’ without needing any context behind it, and yet representative enough so that when put into context it would be an artful and tasteful way of depicting a sperm and an egg in union. I thought it appropriate to put the CRS acronym in the "egg" sphere of the drawing since CRS is involved or ‘gets into’ the mechanism and regulation of reproductive processes on a cellular and molecular level.”

The enthusiastic and creative response to the contest was fantastic. We received submissions from graduate students, postdoctoral fellows, undergraduates, faculty and staff as well as people outside the Northwestern community. We’d like to thank Cheri and everyone who participated in the contest and hope you enjoy the fresh, new look of CRS!

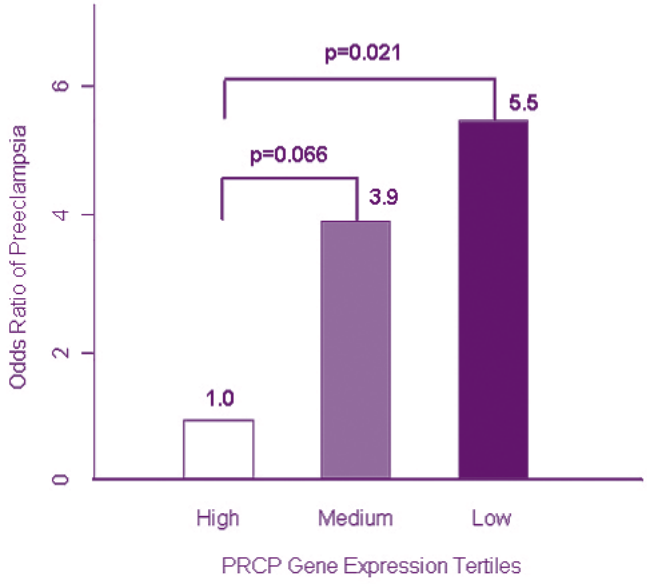
RESEARCH NOTES

Research Notes features the recent laboratory findings of CRS members.
This issue we focus on the laboratory of Dr. Xiaobin Wang.

Prolylcarboxypeptidase Gene, Chronic Hypertension, and Risk of Preeclampsia

Lin Wang[1*], Yan Feng[1*], Yan Zhang[1], Huanyu Zhou[1], Shanqun Jiang[1], Tianhua Niu[1, 2], Lee-Jen Wei[3], Xin Xu[1†], Xiping Xu[1†], Xiaobin Wang[4†]

Preeclampsia, affecting 3-5% of pregnancies in the United States, is a multisystem disorder characterized by hypertension and proteinuria that occurs after 20 weeks of pregnancy[1-3]. It causes a higher risk of intrauterine growth restriction, preterm birth and associated morbidities and mortality in the fetus, and a higher risk of seizure (eclampsia), hemolysis, elevated liver enzymes, low platelet count (HELLP) syndrome, renal failure, pulmonary edema, stroke, and mortality in the mother. Currently, women who are at an increased risk for preeclampsia are identified on the basis of epidemiologic factors[3], such as primiparity, previous history of preeclampsia, multiple gestation, higher body mass index (BMI), work-related psychosocial strain during pregnancy, poor social background, mother's age and own low birthweight and prematurity[4-6] as well as history of chronic hypertension, diabetes mellitus, coagulation abnormalities, and dyslipidemia[7, 8]. However, these risk factors are neither sensitive nor specific as predictors of preeclampsia. Of note, chronic hypertension is a well-known risk factor of preeclampsia. Its prevalence in pregnant women varies from 1 to 5 percent. The rates are higher in older, obese, or black women[9]. The link between chronic hypertension and preeclampsia suggests a possible molecular relationship and may be influenced by inheritance[7, 8, 10].



Risk of preeclampsia by tertiles of PRCP transcript level. Height of bar and numbers on top of the bars represent the odds ratio of preeclampsia. All those 74 women with RNA expression data were divided into 3 tertile groups according to PRCP transcript level: high, medium, and low. Statistically significance in each tertile group compared to the high group (reference group), as determined by logistic regression, is indicated.

The Renin-Angiotensin System (RAS) plays an important role in the regulation of blood pressure and the etiology of preeclampsia. We investigated the association between five variants in angiotensiongen (AGT), angiotensin-converting enzyme (ACE), and prolylcarboxypeptidase (PRCP) genes and the risk of preeclampsia in 125 preeclamptic and 1040 non-preeclamptic black women enrolled at the Boston Medical Center. We used logistic regression models to estimate the risk for preclampsia associated with each marker and its interaction with chronic hypertension. Of the five gene variants, we found that PRCP E112D (rs2298668) D allele alone and its interaction with chronic hypertension were associated with a significantly higher risk of preeclampsia. Compared to women with homozygous EE genotype and without chronic hypertension, higher risks of preeclampsia were observed in DD women without chronic hypertension (OR=3.7, 95%CI: 1.2-12.4) and EE women with chronic hypertension (OR=9.1, 95%CI: 4.7-17.6). Women with both D allele and chronic hypertension had the highest risk (OR=158, 95% CI: 25-infinite). We further compared the PRCP transcript levels in peripheral blood cells of 23 preeclamptic and 51 non-preeclamptic women 2-3 days after delivery. The PRCP transcript levels were lower in ED/DD women than in EE Women (p=0.03) and lower in preeclamptic women than in non-preeclamptic women (p=0.007). Our study suggests that chronic hypertension coupled with PRCP D allele is a strong predictor of preeclampsia. Gene expression assays lent further support for the functional significance of PRCP in the etiology of preeclampsia.

It would be interesting to examine this association independently in other study populations and ethnic groups. To date, there are few clinically useful screening tests to identify women at high risk of developing preeclampsia. If confirmed, E112D could be a highly sensitive and specific early predictor of preeclampsia among women with chronic hypertension, even long before pregnancy.

Full article to be published in American Journal of Obstetrics and Gynecology (expected publication in April 2006)

RECENT PUBLICATIONS

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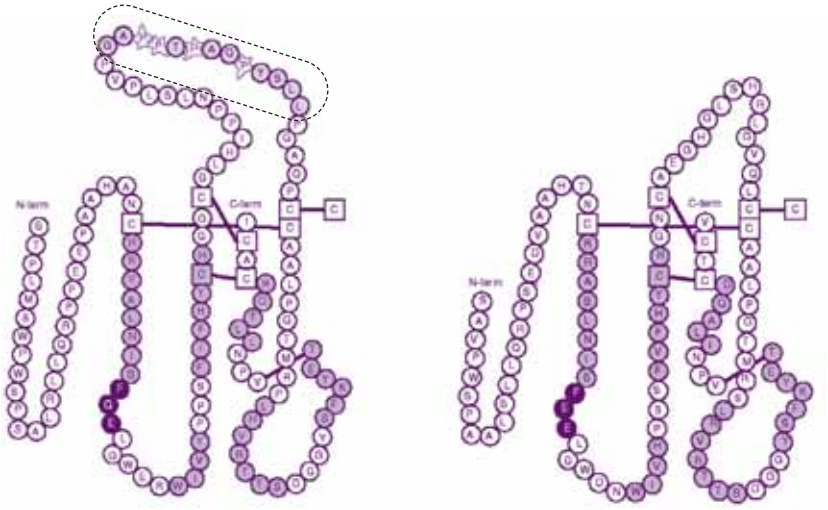
Introducing "The Interdisciplinary Committee on Evolutionary Processes"

"Nothing in biology makes sense except in the light of evolution"
Theodosious Dobzhansky (The American Biology Teacher March 1973 35:125-129)

Darwin's Theory of Evolution by Natural Selection stands with the discoveries of Kepler, Galileo, and Newton in its significance and enduring impact on modern science as well as anthropological, sociological, philosophical, and literary thought. The study of Evolutionary Processes is thus the ideal integrative topic for a liberal education. It was with this in mind that the Weinberg College of Arts and Sciences approved the formation of the Interdisciplinary Committee on Evolutionary Processes (ICEP), under the direction of Professor Teresa Horton, Neurobiology and Physiology, and the offering of an undergraduate minor in the study of Evolutionary Processes (MSEP) this year. Evolution is also critical to the understanding of reproductive processes and vice versa. The central mechanism of evolution is differential reproductive success; thus organisms descendent from a common ancestor diverge in response to environmental challenges. It is this simple mechanism that explains both the diversity and unity of life.

The key participants in ICEP come from the departments of Anthropology, Computer Science, Geologic Sciences, Physics and Astronomy, and the Program in Biological Sciences. In addition to these core participants, there are a large number of scholars, representing a broad range of disciplines (e.g., Chemistry, History, Philosophy, Physics and Astronomy, Political Science, Psychology, Sociology, and Religion) who conduct research in some aspect of evolutionary processes at Northwestern University. However, prior to the formation of ICEP no administrative unit had the scholarly investigation of Evolutionary Process as its central theme. The goal of ICEP is to provide an intellectual home for these investigations.



Secondary structure of the human (left) and chicken (right) inhibin subunits. Divergent amino acid sequences in the proline-rich (circled) and N-terminal regions of the human subunit suggest an evolution of the protein as placental reproductive systems developed. Image courtesy of Robert Cook

ICEP offers quarterly seminars and monthly colloquia which are open to all. The seminars are formal events for which leading researchers from outside NU are invited to speak on topics that highlight recent advances in evolutionary studies. The colloquia are informal events; faculty members, graduate students, and postdoctoral fellows present data from recent studies or ideas that are under development for new studies. Because of the interdisciplinary nature of the group, the presenter is challenged to describe their results in terms that explain the significance of the work to a wide audience. The diversity of expertise represented by the participants often leads to new insights and interesting discussions. At a recent presentation, Robert Cook, a graduate student in Teresa Woodruff's laboratory explained x-ray crystallography results on the structure of inhibin to the uninitiated while presenting data on the structural difference between mammalian and non-mammalian inhibin (*see figure above*). There was a lively discussion about the techniques used to build cladograms, or diagrams illustrating "family tree", and many offers of help and support. The bottom line is we work hard and have a good time!

ICEP also offers a Minor in the Study of Evolutionary Processes (MSEP). The minor provides a comprehensive, interdisciplinary curriculum in the study of Evolutionary Processes. There are many courses offered by NU faculty that fall under the rubric of evolutionary biology, but many students miss these opportunities because the courses are widely dispersed throughout a number of departments. Bringing them together under the heading of a minor increases their visibility. The minor also facilitates the interactions among students with faculty who are conducting research on evolution, including population based studies, enabling the development of undergraduate research projects in these areas. The minor also requires the students to participate in at least one field or collections based course, thereby taking advantage of NU's increasing collaborations with the Field Museum of Natural History and the Chicago Botanic Garden.

For more information, please see the ICEP website at: http://www.wcas.northwestern.edu/evolution/

FACULTY HONORS AND AWARDS

Caroline Bledsoe was named Melville J. Herskovits Professor of African Studies

Andrea E. Dunaif, received the Berthold Medal from the German Endocrine Society. She has also received an honorary doctorate from the University of Athens, Athens, Greece.

Sherman Elias, was recognized as a Research Honoree, Jonas Salk Health Leadership Awards, March of Dimes Foundation

Erwin Goldberg was invited to receive an Honorary Doctor of Science Degree from the State University of New York (Binghamton University) at their 2006 Commencement Ceremonies in May 2006

Mary Hunzicker-Dunn was the recipient of the 2005 Society for the Study of Reproduction Research Award for scientific accomplishments during the past six years

J. Larry Jameson was elected a member of the Institute of Medicine founded in 1970 by the National Academy of Sciences to honor professional achievement in the health sciences. Dr. Jameson has also joined the board of directors of the American Board of Internal Medicine.

Julie Kim was the 2005-2006 recipient of the Young Investigator Award from the Northwestern Memorial Foundation

Kelly Mayo was named a "Model Laboratory Leader" in the HHMI/BWF publication "Making the Right Moves: A Practical Guide to Scientific Management for Postdocs and New Faculty".

John Sciarra was named a guest professor by Peking University Health Science Center.

Lonnie Shea was selected to participate in National Academy of Engineering's 2005 U.S. Frontiers of Engineering Symposium

H. William Schnaper has been appointed Deputy Director for Academic Development for Children's Memorial Research Center (CMRC).

Xiaobin Wang was elected as a Fellow of the American Academy of Pediatrics (FAAP). She also became a member of the Institute of Medicine Committee on Understanding Premature Birth and Assuring Healthy Outcomes.

Teresa K Woodruff was elected a fellow of the American Association for the Advancement of Science

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