Endocrinology-Reproductive Physiology at the University of Wisconsin-Madison

www.erp.wisc.edu

Celebrating 50 years of graduate training: 1959-2009

From the Director

Ian Bird, PhD
Program Director

Season's Greetings! It has been a great semester. Our fall alumni speakers have been well received, and we look forward to our spring guests (and warmer weather). Response to our first alumni survey has been very positive – if you have not yet responded, we would love to hear from you at www.erp.wisc.edu/alumni or by emailing tabachmann@wisc.edu. Finally, we have established a fund at the UW Foundation to support student activities when State funds fall short. A gift of any size is always appreciated and can be made online at www.erp.wisc.edu/giving.

Many thanks. Happy New Year!

Continuing our Lecture Series

3/13/08: Dr. David Miller, Univ. of Illinois-Urbana/Champaign
4/10/08: Dr. Ramesh Bhalla, University of Iowa
4/17/08: Dr. Robert Dailey, University of West Virginia
5/01/08: Dr. John Gibbons, Clemson University

All lectures are held from 3-4 p.m., 1360 Biotechnology Bldg, 425 Henry Mall, Madison.

Regeneration and restoration

Cut off a salamander's leg, and it grows back. When a child loses a fingertip, a new one takes its place. Once you reach adulthood, however, a fingertip lost is a fingertip gone forever.

Why this happens is the focus of ERP alumna Dr. Tanja Dominko's research. In her November 7th lecture in the Endocrinology and Reproductive Physiology program's 50th anniversary series, she spoke about "Fibroblasts – the Ultimate Stem Cell," covering her current research into wound healing and regeneration.

Dr. Dominko received her PhD from the ERP program in 1996, and is currently a research assistant professor at Worcester Polytechnic Institute in Massachusetts as well as president and chief scientific officer of CellThera Inc., a biotechnology start-up firm. Together, CellThera and WPI are conducting joint research to develop techniques for restoring tissue – including digits and limbs – damaged or lost due to traumatic injury.

After a brief introduction on the history of stem cells, Dr. Dominko went into detail on her work with fibroblast cells in salamanders. In the adult salamander limb, fibroblast cells orchestrate regeneration. In mammals, these same cells also respond

Dr. Tanja Dominko, courtesy Worcester Polytechnic Institute

to injuries, but with very different results. A greater understanding of these cells is the key to triggering a regenerative response in humans.

"Understanding how fibroblasts acquire, maintain and alter their function has unrealized potential to provide insights into regeneration," she said.

Working on a Defense Advanced Research Projects Agency (DARPA) grant, Dr. Dominko's research is particularly relevant to the hundreds of soldiers dealing with recent traumatic injuries caused by grenades, shrapnel and explosive devices. The key question, she says, is whether or not they can "reeducate" mammals' cells to regenerate.

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Preeclampsia: studying the science of stress

Dr. Scott Walsh learned many things from ERP program founder RK Meyer, but one of his favorite lessons came from a recalcitrant iguana.

"The iguana would not come out of its crate to the cage," Dr. Walsh recalled. "Dr. Meyer started running through everything he knew about iguana behavior and physiology, when the animal handler delivering the reptile suggesting putting it in the cold room to make it lethargic so it would be easier to move.

"The lesson – you can always learn from someone else. You just need to take the time to listen."

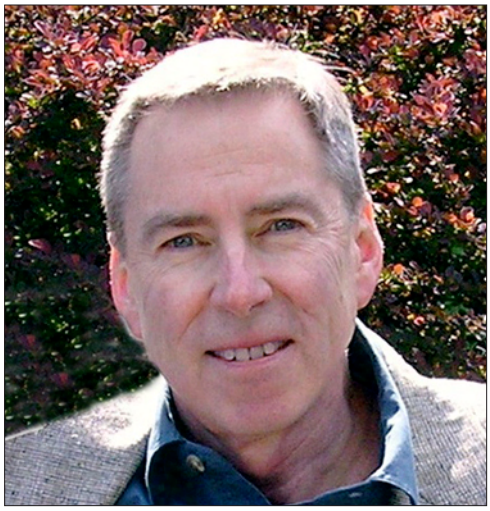
Dr. Walsh earned his MS and PhD degrees from the ERP program in 1972 and 1975 respectively. He is currently a tenured professor in the Department of Obstetrics and Gynecology at Virginia Commonwealth University, and he holds a joint appointment in VCU's Department of Physiology. In his contribution to the ERP's 50th anniversary lecture series, Dr. Walsh discussed his primary research interest: preeclampsia.

Preeclampsia, or hypertension during pregnancy, is a leading cause of fetal and maternal morbidity and mortality. Currently, there is no treatment other than delivery, despite the age or viability of the fetus. Dr. Walsh's research started at the placental production rates of arachidonic acids thromboxane and prostacyclin. In a normal placenta, the two acids remain somewhat in balance, but in a preeclamptic placenta, thromboxane outbalances prostacyclin by about seven to one. Such an imbalance leads to inflammation – and stress.

"Oxidative stress drives this imbalance," Dr. Walsh says. "It also appears to play a role in neutrophil production and migration into the vasculature."

Dr. Walsh and his research team examined placental tissue from non-pregnant, normal pregnant and preeclamptic pregnant women to look for neutrophil infiltration between endothelial cells. The results were significant, with preeclamptic cells samples four times as likely to show infiltration than healthy pregnant cells.

"Infiltration causes inflammation into the vascular smooth muscle and vasoconstriction," says Dr. Walsh. "The effects translate into the main markers of preeclampsia."



Dr. Scott Walsh

Discovering causes is one thing, but improving the ability to predict preeclampsia before symptoms occur is another.

"In my opinion, preeclampsia is occurring in women who are predisposed to it," he remarked. "Determining why they are predisposed to it – if it's genetic, lifestyle factors, etc – can make a tremendous difference in improving the number of healthy, successful pregnancies."

Dominko, continued

"I believe we can," she said. "Studies show these cells can be reprogrammed. The goal of this research is to develop methods for the de-differentiation of adult fibroblasts and encourage their participation in regeneration responses instead of scar formation."

Dr. Dominko and her colleagues in the study at UC-Irvine, Tulane University and University of Louisville have developed a model for this process and continue to test these ideas in the lab. Some of the important steps in this process are maintaining an environment that will support differentiation, and subsequently, examining these cells ability to induce tissue response.

"It is a great day to be a biologist," she said. "There is lots of interest in our work. The work behind trying to grow limbs and help amputees and burn victims is a very noble cause."