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## Innovation Grants Awarded

On December 5, 2007 a request for Innovation Grant proposals went to all members via the e-mail. The purpose of this grant program was to support proposals that advance the objectives of the CCMTR. The proposals that would benefit multiple investigators, promote of basic/clinical investigator interactions, and/or provide critical resources for submission of extramural, multi-investigator proposals were considered responsive to the RFP.

Recipient Grants include:

Upgrade of Compound Microscope Leica DM5000B and PC Workstation (Yoder)

Expansion of Flow Cytometry and Cell Sorting Laboratory Service Core (Tompkins, Dean)

Determining the Mechanism of Action of a Novel Small Molecule with Unique Teratogenic and Melanogenic Properties (Nascone-Yoder, Hauck, Deiters)

Canine B cell Lymphomas: Histopathologic, Cytologic, Flow Cytometric, Cytogenic, and Molecular Characterization (Suter, Breen, Tompkins, Neel, Matthew, Lascelles, Cullen, Ruslander, Valli, Vernau)

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## Highlighted Research – Dr. Char Farin

Dr. Charlotte Farin, a member of the clinical genomics core, is a newly appointed at-large member of the executive committee. She is currently a professor in the Department of Animals Science (CALs).



Dr. Farin's research covers two main related areas; examination of the effects of in vitro embryo production (IVP) systems on fetal development and gene expression in cattle; and the evaluation of mechanisms regulating in vitro maturation of mammalian oocytes.

Working in collaboration with Dr. Peter Farin, also a clinical genomics core member, Drs Farin and Farin have demonstrated that production of embryos using the embryo production in vitro systems can be associated with the abnormal fetal and placental development. In this work, their laboratories have assessed the effects of IVP on expression of mRNAs for the insulin-like growth factor family, a group of ligands, receptors and associated proteins that play an important role in regulating normal fetal and post-natal development. This growth factor family includes genes that are imprinted (*Igf2* and *Igf2r*) or non-imprinted (*Igf1*, *Igf1r*). Their data suggest that abnormalities in fetal growth associated with IVP reflect dysregulation of not only imprinted but also non-imprinted genes. Most recently, working in collaboration with Dr. Jorge Piedrahita's laboratory, their group has documented the existence of an antisense noncoding (nc) RNA to the *Igf2r* gene in cattle (bovine *AIR*, antisense to *Igf2r*). The murine homolog of this ncRNA has been implicated in regulation of imprinted expression of *Igf2r* in mice. Expression of bovine *AIR* ncRNA was shown to vary with stage of fetal development as well as with method of embryo production (in vivo vs. in vitro).

The second major area of Dr. Char Farin's research program is the examination of mechanisms regulating in vitro maturation of mammalian oocytes. In cattle, in vitro embryo production involves maturation of oocytes obtained from donor females. When oocytes are matured in vitro, however, their developmental competency is compromised. Understanding factors that regulate in vitro oocyte maturation is important for improving the efficiency of current IVP practices. Work in Farin's laboratory focuses on the use of specific transcriptional inhibitors to study follicle stimulating hormone-induced resumption of meiosis in cultured mammalian oocytes. The lab has successfully used approaches for gene expression profiling (mice: serial analysis of gene expression; cattle: differential display) to identify candidate genes involved in regulating the resumption of oocyte meiotic maturation in vitro. They have also used short interfering RNA approaches to disrupt candidate mRNA expression to verify the physiological functions of the

candidate genes with respect to their ability to regulate the initiation of oocyte meiosis.

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### **Novartis Gift to the Center**

The Center of Comparative Medicine and Translational Research is the recipient of a \$625,000 gift from Novartis Animal Health US, Inc., to help support the Clinical Trials Program.

Presented over a five-year period, the Novartis gift will fund a clinical trials veterinarian, a veterinary research technician, and laboratory space and equipment that will be dedicated to supporting clinical research studies involving patients in the CVM Veterinary Teaching Hospital.

“Clinical studies are integral to the advancement of veterinary medicine,” says Dr. Gregg Dean, director of the Center. “Such studies investigate risk factors for disease as well as methods to prevent, treat, or cure illnesses that affect both animals and humans. The Novartis gift will fund resources that are critical to helping the CCMTR ensure an effective Clinical Trials Program.”

Dean says the CCMTR Clinical Trials Program (CTP) enables clinical investigators the opportunity to evaluate novel approaches to diagnose and treat disease and deliver innovative solutions that enhance animal and human health. The CTP promotes research collaboration by serving as a liaison between clinical investigators, basic researchers, referring veterinarians, pet owners, and industry scientists. In addition, participating in the program may help interest DVM students and residents in exploring careers in translational medicine.

The CTP can assist with or independently design and implement all organizational and technical aspects of clinical trials including case recruitment, patient enrollment, patient visits, sample collection and processing, and patient follow-up and data analysis. There are currently 19 ongoing investigations in seven hospital clinics: Cardiology, Dermatology, Internal Medicine, Neurology, Oncology, Pain Management, and Surgery.

According to Dean, a dedicated clinical trials enterprise is an essential component of an evidence-based medicine approach to determine the standard of care. Such trials, he says, enable clinical investigators to determine the best way to treat specific medical conditions while offering patients access to the most advanced diagnostic and therapeutic technology available.

“It’s critical for the CVM to play a leading role in performing well-controlled trials designed to advance the quality of patient care,” says Dean. “The Novartis support will allow us to continue to build a clinical trial framework that will become self supporting as it matures into a premiere national veterinary clinical trials program. We envision that the CTP will also conduct trials that will have implications for the treatment of people, making the program unique in the veterinary and human medical fields.”

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### **Flow Cytometry Service Core Expands Service**

The NCSU Flow Cytometry and Cell Sorting Laboratory Service Core, located on the third floor of the College of Veterinary Medicine main building, is expanding its services.

The laboratory currently provides instrumentation and assistance for multi-parameter flow cytometric analysis and sorting. The laboratory operates as a by-appointment, fee-for-service laboratory.

Dr. Mary Tompkins is the Director of the Core and Ms. Janet Dow is the supervisor who oversees the day-to-day operation. In the past, the laboratory consisted of only three flow cytometers. Two Becton-Dickinson instruments which are used for analysis only, including a three-color capability FACScan and a four-color capability FACScalibur. The third, a Beckman Coulter MoFlo is a state-of-the-art, high speed cell sorter, equipped with three lasers and 10-color capability.

One of the instruments to be added to the core includes the Xenogen Lumina in vivo imaging system. This instrument is designed for detection of fluorescence or luminescence in live animals (mice, rats, piglets). The second instrument is a Becton-Dickinson LSRII analytical flow cytometer currently equipped with two lasers (488nm and 633 nm) providing 6 color capability. This is a state-of-the-art fiber-optic, digital

instrument. Through our recent Innovation Grants, the LSRII has been upgraded in order to increase the services available in the Flow Cytometry and Cell Sorting Service Core. A third Violet laser (20mW, 405nm) and the necessary photomultiplier tubes and filter sets required to provide up to 3 additional colors have been added.

This upgrade now allows for cutting edge flow cytometry that requires the analysis of very small, rare samples and/or very specifically defined cell types identified by multiple cell surface molecules. For either application, many colors are needed.

These two additional pieces of equipment will be housed in room 257 of the CVM Research Building. There is a plan to add a part-time technician.

Future plans for expansion include the possibility of offering new services such as custom conjugation of antibodies. This would be particularly useful in the CVM environment where few directly-conjugated antibodies are available for veterinary species.

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### **Pilot Grant Research-in-Progress Symposium**

The Pilot Grant Research-in-Progress Symposium will be held on **May 15, 2008**. This year the symposium will be held at The Dorothy and Roy Park Alumni Center on Centennial Campus. The symposium is scheduled to begin at **1 p.m.** with the eight recipients of the pilot project grants presenting their research.

The symposium will be followed by a reception. Reservations will be required. Information regarding the reservation process will be circulated via e-mail.