CTSC Newsletter

Clinical & Translational Science Discovery at SUNY Downstate

Clinical & Translational Science Center

ISSUE 1, JANUARY 2017

OPENING OF THE CTSC AT DOWNSTATE

Please join us on Wednesday, January 11, 4:00-6:00 PM for a reception and tour of the Center. Light refreshments will be served: UHB, 5th floor CTSC

In October, 2016, Dr. Carlos Pato, Senior Vice President for Research and Dean, College of Medicine, announced the opening of the CTSC. Its mission is to provide a clinical laboratory and other support for clinical, basic, and translational scientists who conduct human subject research. Translational research beginning at the laboratory bench that leads to clinical studies performed at the CTSC should aim to translate basic scientific discoveries into novel diagnostic and therapeutic methods that improve health care. Collaborations between basic and clinical scientists are encouraged.

The CTSC is a Center within Downstate's Institute for Genomic Health (IGH; Dr. Michele Pato, Director). It is available to investigators in any of the SUNY Downstate Schools and Colleges. Dr. Richard Coico serves as Director of the CTSC and Dr. Michele Pato serves as Executive Director. The investigations carried out in the CTSC include studies of normal and abnormal human physiology and studies of the cause, prevention, control, and cure of diseases that afflict individuals of all ages, races and ethnic backgrounds. The CTSC also serves as a resource for teaching and training medical students, residents, fellows, and other health care professionals in the skills of clinical investigation.

In each CTSC Newsletter, we highlight investigations being carried out by members of the CTSC. Newsletters also feature a "Did you know...?" section that focuses on a disease and briefly discusses its epidemiology and how translational science is being used to develop new approaches for the diagnosis, treatment, or possible cure. In general, we will highlight diseases that disproportionately impact the SUNY Downstate patient population. This section of the Newsletter will also point readers to funding opportunities for those interested in studying the disease. Finally, in upcoming issues we'll also feature a translational scientist working to translate biomedical knowledge into therapies, techniques, and tools for treating human disease: from bench to bedside.

We plan to publish newsletters on a regular basis to inform everyone about new clinical and translational science research activities within the Center.

HOW CAN I USE THE CTSC TO SUPPORT MY RESEARCH PROGRAM AT DOWNSTATE?

Members of the faculty with IRB-approved studies who need to use outpatient space to perform research involving study subjects with informed consent are welcome to apply for CTSC membership. Membership provides individuals and their staff up to six-month renewable terms of use of CTSC facilities. The CTSC website provides more detailed information about how to apply for membership. Applications are reviewed by a CTSC committee that provides applicants with feedback within 10 days of submission.

CTSC Website:
http://www.downstate.edu/ctsc

WHAT'S HAPPENING AT THE CTSC?

CTSC Investigator: *Dr. Scott Miller*

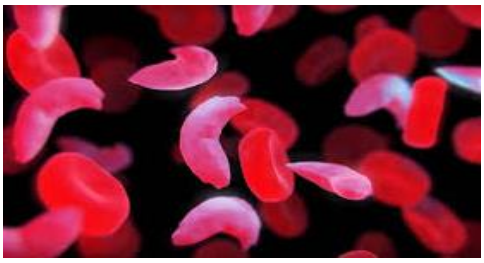
Dr. Miller is studying new ways to treat sickle cell disease (SCD). SCD is associated with a number of serious and potentially disabling conditions that have similar symptoms but vary in severity by genotype. Most notable is vaso-occlusive crisis (VOC), presumably resulting from acute ischemic tissue injury. Over the course of a year, about 60% of patients who are homozygous for the abnormal hemoglobin, Hb S. These individuals are referred to as SCD-SS. Patients with SCD-SS have at least 1 severe VOC, which typically presents as episodes of pain and inflammation. These pain crises, as VOC episodes are also known, are the clinical hallmark of SCD and are responsible for (>90%) of hospitalizations and result in significant morbidity, mortality, and interruption of daily functioning. Rivipansel is a pan-selectin antagonist that inhibits selectin binding *in vitro* as well as selectin-mediated effects *in vivo*. Inhibition of selectins offers potential promise as a useful therapeutic option for patients with SCD. Rivipansel has potent anti-inflammatory effects in several animal models, including the sickle cell mouse, in which it has been shown to normalize blood flow, reduce blood cell aggregation, and to improve survival in a model of VOC. This Phase 3 randomized, double-blind, placebo-controlled, parallel group multicenter study is designed to demonstrate the efficacy of rivipansel in treating subjects with SCD who are ≥ 6 years of age experiencing an acute VOC event necessitating hospitalization.

CTSC Investigator: ***Dr. Shahriar Zehtabchi***

Status Epilepticus (SE) is a life-threatening condition in which the brain is in a state of persistent seizure. Dr. Zehtabchi is participating in a multicenter, randomized, blinded, comparative effectiveness study of fosphenytoin, valproic acid, or levetiracetam in the emergency department treatment of patients with benzodiazepine-refractory status epilepticus. The primary objective is to determine the most effective and/or the least effective treatment of benzodiazepine-refractory status epilepticus (SE) among patients older than 2 years. There are three active treatment arms being compared: fosphenytoin (FOS), levetiracetam (LEV), and valproic acid (VPA). The second objective is comparison of three drugs with respect to secondary outcomes. The final objective is to ensure that the trial is informative for treatment of established SE in children by describing the effectiveness, safety, and rate of adverse reactions of these drugs in children.

DID YOU KNOW…?

Disease: Sickle Cell Disease (SCD)



Epidemiology: SCD refers to a group of inherited red blood cell disorders. It is the most common genetic disease in the U.S. An estimated 70,000-80,000 Americans have sickle cell disease. Persons with sickle cell trait (SCT) are heterozygous carriers of an abnormal ß-globin gene that results in the production of abnormal hemoglobin, Hb S. These individuals are usually asymptomatic. Homozygotes (SS individuals) who have inherited HbS alleles from both parents suffer from sickle cell anemia as many as 1.5% of babies born in the United States have SCT. All states now screen all newborns for SCT. In the U.S. Approximately 1 out of 10-12 African Americans have SCT, and 1 out of 400-500 African American newborns have the disease. Approximately 1 out of 1,000-1,400 Hispanic newborns has the disease.

Translational Science Aimed at SCD: Currently, the only cure for SCD is a bone marrow or stem cell transplant. The promising use of gene editing technology (CRISPR), however, may offer a new approach for a cure. CRISPR stands for Clustered Regularly Interspaced Short Palindromic Repeats. The discovery of the prokaryotic CRISPR "immune system" has allowed for the development for an RNA-guided genome editing tool. The Downstate community was treated to a Furchgott seminar last November by Dr. Jennifer Doudna (University of California, Berkley) who, in 2012, discovered CRISPR while working with her collaborator, Dr. Emmanuelle Charpentier. At her November seminar, Dr. Doudna noted that translational opportunities using CRISPR gene editing technologies are emerging at a rapid pace. One example is described in a recent study led by Mark DeWitt at UC Berkley. Using CRISPR technology to investigate the feasibility of editing out the mutated hemoglobulin gene that causes SCD and replacing it with a normal gene, they demonstrated that engraftment of hematopoietic stem/progenitor cells (HSPCs) possessing the edited gene into immunocompromised mice restored normal hemoglobulin synthesis. These results demonstrate that this approach can mediate efficient HSPC genome editing and suggest a path toward the development of new gene editing treatments for SCD and other hematopoietic diseases.
http://stm.sciencemag.org/content/8/360/360ra134
http://www.cdc.gov/ncbddd/sicklecell/facts.html

Sickle Cell Disease Funding Opportunities
http://wepsicklecell.org/

Current CTSC Members & Research Areas

Mary Ann Banerji -Diabetes
Ivan Bodis-Wollner - Parkinson Disease
Jack DeHovitz - HIV in Women
Jeanette Jakus - Acne Vulgaris
John Kral – Diabetes
William Litman – Parkinson Disease
Scott Miller - Sickle Cell Disease
Carlos Pato - Genomic Psychiatry
Michele Pato - Genomic Psychiatry
Richard Sinert – Parkinson Disease & Stroke

We welcome your comments and suggestions. Email all communications to Dr. Richard Coico, CTSC Director, Newsletter Editor: richard.coico@downstate.edu