



WHAT'S HAPPENING AT THE CTSC?

Dr. Subodh Saggi –

Treatment of Chronic Kidney Disease

Dr. Saggi, Professor of Medicine, is conducting a phase 3 study to evaluate the safety and efficacy of daprodustat compared to FDA-approved recombinant human erythropoietin (rhEPO) in the treatment of anemia associated with chronic kidney disease in subjects on dialysis. Anemia has also been implicated as a contributing factor in many of the symptoms associated with reduced kidney function. These include fatigue, depression, reduced exercise tolerance, dyspnea, and cardiovascular consequences, leading to increased risk of morbidity and mortality, principally due to cardiac disease and stroke. Associations, however, do not prove causality; thus, these associations may reflect underlying comorbid conditions and severity of illness that contribute to both the severity of anemia, reduced responsiveness to erythropoietin-stimulating agents, and poorer outcomes. Anemia is a very common clinical problem in patients with chronic kidney disease and is associated with increased morbidity and mortality in these patients. Erythropoietin is a hormone synthesized in the kidney which is responsible for stimulating red blood cell maturation in the bone marrow. It is deficient in the majority of patients with advanced kidney disease thereby predisposing these individuals to anemia. rhEPO has been used to successfully treat anemia in patients with chronic kidney disease causing mean hemoglobin and hematocrit to rise steadily. In this study, Daprodustat which is an oral hypoxia inhibitory factor that can raise endogenous levels of erythropoietin, is being compared with rhEPO to examine its safety and efficacy in the treatment of chronic kidney disease. Daprodustat has a longer half-life than rhEPO and can be administered orally in contrast to rhEPO which is administered intravenously.



Drs. Michael Reinhardt and Carl Cohen –

Amyloid PET Scans in Alzheimer's Disease

Dr. Reinhardt, Assistant Professor of Psychiatry, and Dr. Cohen, Professor of Psychiatry, are participating in a multi-center study to examine brain amyloid status among patients suffering from dementia in diagnostically uncertain cases. Amyloid PET scans allow accurate detection of amyloid plaques -- one of the hallmarks of Alzheimer's disease (AD) -- in living people. The hypothesis is that in such diagnostically uncertain cases, knowledge of amyloid status will lead to significant changes in patient management, and that this will translate into improved long-term outcomes. The study aims to investigate whether the impact of amyloid PET testing on short-term patient management leads to a meaningful change between intended and actual patient management plan. Cumulative endpoints consist of: AD drug therapy, other drug therapy, and counseling about safety and future planning. Secondary objectives of the study will assess the impact of amyloid PET results on clinical diagnosis and prevention of unnecessary diagnostic procedures and treatments. Medicare claims data is being used to compare medical outcomes at 12 months for patients enrolled in the longitudinal cohort with that from a matched control cohort of patients who have never undergone amyloid PET imaging. Here, the primary objective is to determine if amyloid PET testing in the amyloid PET-known cohort of patients is associated with a reduction in hospitalizations and emergency room visits in comparison to the matched amyloid PET-naïve patients. Secondary objectives are to examine whether knowledge of amyloid PET status reduces hospitalizations related to ambulatory-sensitive conditions, whether the association between amyloid PET knowledge and health outcomes varies by baseline cognitive status and amyloid status (amyloid positive versus negative). In pursuing these Aims, investigators will generate valuable observational data on clinical utility that will inform future use of this technology in diagnostic algorithms, and develop a cohort of patients who undergo amyloid PET and can serve as a foundation to address future research questions.

DID YOU KNOW...?

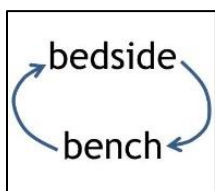
Translational Research Using Zika Virus

Zika virus was discovered in 1947. It hit the headlines in 2016 when an epidemic of the virus began quickly spreading through parts of South and Central America. The virus, spread by mosquitoes, rarely causes serious problems in adults, but it can lead to birth defects, specifically microcephaly if a woman contracts the virus when pregnant. The virus has the ability to cross from the blood into the brain, prompting researchers at UCSD and Washington University to see if it could be used to treat glioblastoma. In preclinical studies using cell culture methods and in mice they showed that Zika virus preferentially infected and killed glioblastoma stem cells (GSCs) relative to differentiated tumor progeny or normal neuronal cells. The virus potently depleted patient-derived GSCs grown in culture. Moreover, mice with glioblastoma survived substantially longer and at greater rates when the tumor was inoculated with a mouse-adapted strain of Zika virus. The investigators speculate that genetically modified Zika strains that further optimize safety could have therapeutic efficacy for adult glioblastoma patients.

<http://jem.rupress.org/content/early/2017/09/05/jem.20171093>

TRANSLATIONAL RESEARCH AT DOWNSTATE

Investigator: Dr. Sabina Hrabetova



The main focus of the Hrabetova lab is to quantify structural parameters of brain extracellular space and to understand how these parameters influence brain function and wellbeing. In brain, extracellular space is a system of interconnected pores that channels chemical signals between cells and is an essential route for delivery of nutrients and drugs. Properties of the extracellular space may be quantified by analyzing the diffusion of a set of chosen molecules. Two macroscopic structural parameters of the ECS are determined: the

extracellular volume and the hindrance imposed on the diffusing molecules by the tissue. The extracellular compartment has been generally viewed as static and functionally less significant than neuronal and glial compartments. Current work in the Hrabetova lab, focused on newly discovered extracellular space dynamics in the sleep-wake cycle and in seizures, is challenging such a view and it highlights the role of extracellular space in CNS function and dysfunction. Projects are based on two new discoveries about extracellular space dynamics on time scales ranging from many hours (in the case of the sleep-wake cycle) to a few seconds (in the case of epilepsy). First, they found that macromolecules spread much more slowly when the brain is awake than when it is asleep. Second, they observed rapid, transient pulsations of the extracellular volume, coincident with the epileptic activity, which suggests a close relationship between the recurrent decreases in the extracellular volume and the epileptiform discharges. Translational aspects of this basic science research include clearance of endogenous macromolecules from brain (e.g., amyloid β implied in Alzheimer's disease and α -synuclein implied Parkinson disease), drug delivery during a sleep-wake cycle and new therapeutic strategies in epilepsy.

Q&A

Q: How can I access Downstate's electronic health records (EHR) to perform an IRB-approved research study?

A: In 2018, the CTSC will offer several research methodology seminars including one on the use of EHR to mine data in IRB-approved studies. We will also offer seminars on how to use REDCap and how to perform a meta-analysis. Announcements regarding seminars will be distributed campus-wide.

CTSC MEMBERS

Ovadia Abulafia | MaryAnn Banerji | Ivan Bodis-Wollner | Carl Cohen | Jack DeHovitz | Olga Dvorkina | Ellen Ginzler | Arthur Grant
Deborah Gustafson | John Kral | Jason Lazar | Yi-Chun Lee | Steve Levine | William Litman | Scott Miller | Howard Minkoff | Carlos Pato
Michele Pato | Michael Reinhardt | Subodh Saggi | Yalini Senathirajah | Iuliana Shapira | Tonya Taylor | Jessica Yager | Shahriar Zehtabchi

HOW TO BECOME A CTSC MEMBER

The CTSC is a Center within the Institute for Genomic Health (IGH), Dr. Michele Pato, Director (michele.pato@downstate.edu). Downstate faculty conducting IRB-approved studies are welcome to apply for CTSC membership. There are no fees associated with membership.

For more information, visit <http://www.downstate.edu/ctsc>