CTSC Newsletter

Translating Research into Practice to Improve Human Health

Clinical & Translational Science Center

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WHAT'S HAPPENING AT THE CTSC?

CTSC Investigator: Dr. Jason Lazar –
HIV-Related Coronary Heart Disease

Dr. Lazar, Professor of Medicine and Director of Non-Invasive Cardiology, is investigating the impact of combination antiretroviral therapy (cART) on heart function as people with HIV age. cART has improved life expectancy in people infected with HIV, but this has been accompanied by an increase in chronic non-infectious diseases, notably coronary heart disease (CHD). Chronic HIV-related inflammation has been linked to subclinical systolic and diastolic left ventricular (LV) heart abnormalities, as has prior CHD. However, the impact of HIV and its treatment on cardiac function in women, who make up half of HIV-infected people worldwide, remains understudied. The advent of novel ultrasound techniques to study myocardial abnormalities now allows for improved assessment of subclinical cardiac disease. As part of the Bronx and Brooklyn NIH-supported Women's Interagency HIV Study (WIHS), Dr. Lazar's group has compared cardiac function in hundreds of HIV-infected vs. uninfected women with myocardial abnormalities and shown that the former group displays a greater LV mass index and low LV ejection fraction but similar LV diastolic dysfunction. Ongoing follow-up studies of current study participants together with expansion of the subject population is focused on enhanced evaluation of subclinical LV disease. This will be complemented by cardiac MRI for myocardial fibrosis and steatosis in a subset of subjects to characterize the basis for LV function abnormalities. Ultimately, the group plans to follow study participants over a 12-year period to: (a) compare the echocardiographic prevalence of LV systolic dysfunction as measured by global longitudinal strain, and (b) examine development of LV diastolic dysfunction using conventional measures, in HIV+ and HIV- women. They will also assess myocardial fibrosis and lipids by CMR in HIV+ and HIV- women. Ultimately, these studies will help to identify specific HIV-associated factors associated with myocardial abnormalities in HIV+ women.

CTSC Investigator: Dr. Tonya Taylor –
Healthy Aging in HIV-Infected Women

Dr. Taylor, Assistant Professor of Medicine and member of the Special Treatment and Research (STAR) Program, is investigating the biopsychosocial and interpersonal challenges faced by older women living with HIV disease. With near universal access to antiretroviral therapy, people aging with HIV are living longer and healthier lives. Despite treatment efficacy, studies show that people aging with HIV evidence significant burdens of disease seen in a higher frequency of non-HIV related comorbidities, such that multimorbidity and poly-pharmacy are the rule and not the exception. Aging-related stressors, such as chronic illnesses, changing physical function, pill burden, and social losses can undermine health outcomes. For many, these stressors are exacerbated by poverty, unemployment, housing and food insecurity, as well as stigma driven discrimination and social isolation. Notwithstanding these challenges, people aging with HIV can achieve *Healthy HIV Aging* by maintaining physical and psychosocial function and sustaining viral suppression. There are no programs that help individuals to optimally age with HIV or that address gender and biopsychosocial needs. Using findings from an NIH study to identify the prevention needs of older (50+) women with HIV (OWLH), Dr. Taylor developed and piloted a novel peer-delivered and gender- and generationally-tailored program entitled, *THE CHANGE* (a euphemism for menopause extended to optimal aging) to address the complex biopsychosocial and interpersonal challenges that OWLH face as they age. *Healthy HIV Aging* is assessed using the Veterans Aging Cohort Study (VACS) Index – a predictive measure of 5-year mortality and morbidity among people with HIV using indicators of HIV disease and organ system injury. Commenting on the history and progress of the program, Dr. Taylor notes, "We first piloted the program in a group format with 33 OWLH, and implemented 7, 2-day programs and 7 monthly booster sessions. We further developed the program by integrating new tailored components to address barriers to behavior change, and adapted the curriculum for an individual format in the clinic or home. We re-piloted a group and six individual programs with 8 OWLH with inconsistent viral suppression. Through the tailored approach, 88% of the participants have reduced their VASC score at 3-month follow up."

DID YOU KNOW…?

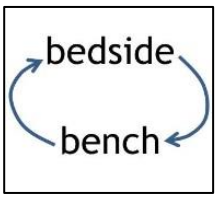
Disease: ***HIV/AIDS***

Epidemiology: Approximately 36.9 million people are living with HIV globally. Since the epidemic began in the early 1980s, 1.2 million people have been diagnosed with AIDS in the US, with 1.1 million people living with HIV. www.CDC.gov

Translational Science Aimed at HIV/AIDS:
Where to begin? So many discoveries have been made over the past few decades that have resulted in new therapies to treat HIV. Today, there are more than 25 drugs to control HIV and currently, biologicals used as therapeutics (monoclonal antibodies) are entering the clinical trials arena. New research from The Rockefeller University and the NIH suggests that treatment with two anti-HIV antibodies immediately after infection enables the immune system to effectively control the virus, preventing its return for an extended period.
http://www.nature.com/nature/journal/v543/n7646/abs/nature21435.html?foxtrotcallback=true

TRANSLATIONAL RESEARCH AT DOWNSTATE

Investigator: Dr. Henri Tiedge –
Regulatory RNAs in Cancer



Work in the Tiedge lab is directed at mechanisms of translational control of gene expression. Such mechanisms are especially important in neurons where gene expression has to be individually regulated at thousands of heterogeneous synapses, often at considerable distances from soma and nucleus. The Tiedge group and others have shown that translational machinery is present in synapto-dendritic domains, and that various types of mRNAs are specifically targeted there. It is important that these mRNAs are only translated at the right time, for instance following synaptic stimulation, as dysregulated local protein synthesis may result in impaired synaptic function. Regulatory RNAs of the BC (brain cytoplasmic) type control local synaptic translation by reversibly repressing translation initiation. In the basal state, BC RNAs inhibit recruitment of small ribosomal subunits to mRNAs through interactions with eukaryotic initiation factors (eIFs) 4A and 4B. Upon receptor activation, eIF4B is rapidly dephosphorylated at serine 406, causing dissociation of regulatory BC RNAs and derepression of local translation. Given their functional role at the synapse, it was anticipated, and experimentally confirmed, that BC RNAs are neuron-specific and are typically not expressed in any other somatic cell type. An exception to the neuron-specific role of BC RNAs is provided by a subset of malignant tumors, in particular adenocarcinomas of the breast. High levels of human BC200 RNA are expressed in ductal carcinoma cells, potentially causing translational dysregulation. It appears that BC200 RNA expression in such cells is associated with invasive or metastatic potential. In agreement with this hypothesis, substantial levels of BC200 RNA were detected in circulating tumor cells (CTCs) in peripheral blood from invasive ductal carcinoma patients. Current work in the Tiedge lab is directed at the utility of CTC detection in the diagnosis and prognosis of breast cancer.

Question: (MA Banerji) I need to recruit subjects for diabetes research. Does anyone have access to subjects who might want to participate?
Answer: (M.T. Pato) Yes. All of my research subjects in the GPC - genomic study are queried about history of diabetes and 98% have given consent to be contacted about other studies. Send emails to michele.pato@downstate.edu
Question: (S. Levine) I have partial funding for a research coordinator. Anyone interested in sharing a coordinator to hire someone full-time?
Answer: (R. Coico) The CTSC facilitates networking among investigators to address questions such as this one. Send emails to richard.coico@downstate.edu.

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 Michele Pato | Carlos Pato | Michael Reinhardt | 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

CTSC Newsletter comments, questions or suggestions? Email Dr. Richard Coico, CTSC Director: richard.coico@downstate.edu