CENTER FOR GENOMIC MFDICINE

Science | Community | Administration

CGM #GiveHealthy & Get Healthy Challenge

We are excited to announce the CGM #GiveHealthy & GetHealthy challenge. The challenge is twofold;

#GiveHealthy:

The CGM is hosting a Food Drive to support the Greater Boston Area Food Bank! #GiveHealthy is a movement to change how and what people donate. #GiveHealthy enables people to donate fresh fruits, vegetables and other healthy food to ensure that others facing hunger have greater access to the nutrition they need to live active, healthy lives.

No need to lug cans and boxes of food in! Participation is easy, simply click **HERE** to donate!!! Please help the CGM reach its goal of donating 250 pounds of healthy food!

GetHealthy:

This summer, we are challenging the CGM to GetHealthy. In addition to the reinvented summer steps challenge, there will be opportunities to learn ways to eat healthy, incorporate exercise into your daily lives, set diet/exercise goals for yourself, and build community with others who are looking to GetHealthy too!

This summer, the CGM challenges you to #GiveHealthy and GetHealthy!!

Be on the lookout for more information in the coming weeks.

Message from the Director

Dear Colleagues,

In our strategic plan for CGM, we committed to taking steps to "complete the cycle" and test the viability/applicability of "genomic medicine". Towards this goal, I want to describe a demonstration project that we have successfully launched. We have initiated a research study to assess the feasibility of implementing Whole Genome



implementing Whole Genome Sequencing (WGS) as a diagnostic tool within MGH.

We plan to recruit 500 patients from various genetic clinics at MGH, including the Cardiovascular Genetics Program, Gastrointestinal Cancer Clinic, Ataxia Unit, general pediatric and adult Medical Genetics Program, and Endocrine Tumor Genetics Clinic. The 500 participants will be randomized 1:1 to 'standard of care' genetic testing (n=250) ordered by their clinical genetics provider versus standard of care plus WGS (n=250). In addition, for pediatric participants, we will perform full trio genomic sequencing (proband + parents) to increase diagnostic yield in pediatric populations. The primary aims of this study are to develop a process for ordering WGS and returning results to patients being seen across multiple genetic programs and to compare diagnostic yield of WGS to that of standard of care testing. By incorporating a randomization component, the study team will be able to assess downstream impact of WGS information on health care utilization within a hospital system such as MGH.

After a year of planning, the first patient was successfully recruited in March 23, 2018 and we are excited to complete the study within the next 18 months. I want to thank Deanna Brockman, Caroline Harley, Candace Patterson, Miriam Udler, and Krishna Aragam for their leadership in planning and executing this project.

Best, Sek



Spotlight on the Kimberly Lab



W. Taylor Kimberly, MD PhD is Faculty in the CGM, Associate Chief of the Division of Neurocritical Care & Emergency Neurology at MGH, Associate Director of the Neuroscience Intensive Care Unit at MGH, and Associate Professor of Neurology at HMS.

Taylor received his MD from Harvard Medical School, and his PhD from the Program in Neuroscience at Harvard Graduate School of Arts and Sciences, studying the gamma-secretase

enzyme in the pathogenesis of Alzheimer's disease in the laboratory of Dennis Selkoe, MD. Taylor completed an internship in medicine at MGH, and a neurology residency and neurocritical care fellowship at the BWH/MGH Partners program. His clinical interests focus on the critical care management of acute neurological and neurosurgical diseases, including stroke, subarachnoid hemorrhage and traumatic brain injury.

The Kimberly lab studies mechanisms of secondary brain injury after acute stroke and subarachnoid hemorrhage. His laboratory develops novel biomarker tools to characterize the types of secondary brain injury and link them to molecular pathways in observational and randomized patient cohorts. The long-term research goal is to understand the underlying biology of brain edema, and define neuroinflammatory mechanisms that drive its formation. A key aspect of our work is to design and lead multicenter clinical studies targeting brain edema. These are connected to Dr. Kimberly's leadership in the conduct of multicenter, randomized clinical trials, including the GAMES-Pilot (NCT01268683) and GAMES-RP (NCT01794182) trials. He is also currently co-PI of the global phase 3 RCT, the CHARM (NCT02864953) trial.

Kimberly Lab Research Areas:

Clinical trials for the prevention of brain edema. Through collaborative efforts with academic investigators and industry, we design, lead and execute multicenter clinical trials that evaluate novel pharmacotherapies for brain edema and brain injury. Our primary focus is the prevention of cerebral edema, testing the hypothesis that the sulfonylurea receptor 1 (Sur1) mediates edema formation after stroke. The clinical development of the Sur1 inhibitor, intravenous glyburide, began with a Phase 2a pilot clinical trial (GAMES-Pilot Trial), which evaluated the safety and efficacy of intravenous glyburide for the prevention of edema after large hemispheric stroke. The results from this effort was followed

Kimberly Lab Members

Zsuzsanna Ament, PhD is a Postdoctoral Research Fellow in the Kimberly Lab. Her background is in analytical chemistry and she leads our metabolomics and small molecule biomarker discovery platform, using a liquid chromatography-tandem mass spectrometry instrument.

Matthew Bevers, MD, PhD is an Instructor of Neurology in the Kimberly Lab, and a Neurointensivist at BWH. He leads the translational and clinical studies of ST2 in ischemic and hemorrhagic stroke.

Christina Hansen, BA is a Clinical Research Coordinator in the Kimberly Lab. She is responsible for patient enrollment in our ongoing biorepository studies and clinical trials. She is also studying the galectin-3 pathway in relation to post-stroke recovery.

Matt Koch, MD is a Neurosurgery resident at MGH. He studies markers of cerebral vasospasm after aneurysmal subarachnoid hemorrhage.

Cristina Sastre, PhD is a Postdoctoral Research Fellow. She studies the role of brain endothelial cells in regulating ST2 and dissecting the mechanism of its effect in cell culture and animal models of stroke.

Pongpat Vorasayan, MD is a Visiting Research Fellow. He is a neurologist from Bangkok, Thailand who is developing new neuroimaging tools to quantify brain water content using serial brain scans.

by a national, randomized, multi-center, double-blind Phase 2b trial in patients with large hemispheric stroke, GAMES-RP. The Kimberly laboratory has served as the pharmacokinetic and biomarker coordinating center for these clinical studies. In order to definitively test efficacy, a randomized, international, double-blind Phase 3 trial will begin in the summer of 2018. The CHARM trial will enroll stroke patients at centers in North America, Australia, Japan and Europe.

Metabolite profiling in cerebrovascular disease. The Kimberly laboratory also studies how the brain utilizes energy metabolites in the setting of ischemia. The major tool that we use is metabolite profiling ("metabolomics"), a liquid chromatography-tandem mass spectrometry technique that measures numerous small molecule analytes from biological specimens. Using this approach, we have identified a specific endocannabinoid candidate that is linked to early brain injury and delayed cerebral ischemia after aneurysmal subarachnoid hemorrhage. We have also used the method to identify an adverse metabolic profile highlighting inefficient oxidative phosphorylation in association with cardioembolic stroke. These findings raise the possibility that atrial fibrillation-related stroke may in part result from disordered metabolism within the atrial myocardium. Our analyses have also highlighted that this adverse profile is linked to a subgroup of cryptogenic stroke patients, indicating that metabolite profiling may assist with risk stratification of embolic stroke of undetermined source.

Post-stroke inflammation and brain edema formation.

Although inflammation after ischemic stroke is a well-described phenomenon and hypothesized to play a key role in secondary injury, the underlying mechanisms are not well understood. Our approach to identifying novel candidate mechanisms is two-fold. First, we develop novel neuroimaging tools to better quantify brain edema and blood-brain barrier integrity in the setting of cerebral ischemia. By creating highly specific methods using non-invasive imaging, we have advanced our understanding of the role brain edema plays in modulating neurological recovery after stroke. We then leverage these methods as quantitative phenotypes for biomarker screens. Those studies have identified



ST2 as a leading inflammatory marker that strongly and independently predicts brain edema formation, risk for early mortality, and long-term functional neurological recovery.



Spotlight on David Niles

Boston native, David Niles, joined the CGM community in the Fall of 2016 as the technical support specialist. David joined Partners Healthcare in 2014 where he worked at the Service Desk. David studied at the University of Massachusetts Boston where he graduated with a BA in Sociology in 2016. Currently he is taking classes towards a Masters of Professional Studies in Informatics at Northeastern University.

Among many passions he enjoys cooking, singing and Pinterest DIY projects. When time permits he also enjoys traveling. This summer he will be traveling to Punta Cana, DR and Los Angeles.

Fun facts – He is the oldest of 6, has a Maltese named Brooklyn, and studied classical music performance at Boston Arts Academy and briefly at the University of New Hampshire.

Do you have suggestions for the CGM?

Members of the CGM can submit their comments & ideas on how the CGM can improve its daily functions by completing the anonymous survey <u>HERE</u>.

CGM Email Addresses

To report your weekly time, please email:

TimeKeepingCGM@mgh.harvard.edu

To submit reimbursement requests, please email: reimbursementCGM@mgh.harvard.edu

For IT help requests, please email:

help@cgm.mgh.harvard.edu

For Facilities requests, please email:

facilities@cgm.mgh.harvard.edu

Important Dates

June 15, 2018-August, 15, 2018: CGM Food Drive for the Greater Boston Food Bank

Monday, June 18, 2018: 4pm, CGM Yoga

Wednesday, June 20, 2018: 11:30am, MGH Summer Picnic

Wednesday, July 4, 2018: MGH Holiday, Independence Day

Wednesday, July 11, 2018: 12pm, CGM All Post-Doc Networking lunch

Sunday, July 15, 2018: CGM GetHealthy Challenge Begins

Wednesday, August 26, 2018: 12pm, CGM Summer Ice Cream Social

Monday, September 3, 2018: MGH Holiday, Labor Day

Friday, September 21, 2018: CGM Retreat

Monday, October 8, 2018: MGH Holiday, Columbus Day

For a complete listing of events, click **HERE**.

CGM All Post-Doc Networking Lunch

Calling all Post-Docs!!

In addition to the smaller, monthly Post-Doc networking lunch, the CGM has organized an ALL Post-Doc networking lunch on Wednesday, July 11th at 12pm in Simches 3.110. If you would like to attend this lunch, please RSVP, **HERE**, by June 22nd (RSVP is required and all CGM Post-Docs are invited to attend).

Come, enjoy lunch, and network with other Post-Docs!

If you are a Post-doc and have not already received information regarding this lunch, please sign up for the CGM post-doc distribution list by emailing Shannon (SSTRATTON2@mgh.harvard.edu).

CGM Awards and Honors

Florian Eichler, MD, was presented with the Herbert Pardes Clinical Research Excellence Award by The Clinical Research (CR) Forum on April 18th. The CR Forum presents its annual Top Ten Clinical Research Achievement Awards to highlight outstanding research advances that involve both innovation and impact on human diseases. Congratulations to Dr. Eichler!

Please also join us in congratulating the following:

Dr. Jose Florez on his recent promotion to Professor of Medicine at Harvard Medical School.

Dr. Rakesh Karmacharya on his recent promotion to Associate Professor of Psychiatry at Harvard Medical School.

Dr. Taylor Kimberly on his recent promotion to Associate Professor of Neurology at Harvard Medical School.

Save the Date - CGM Annual Retreat

Please mark your calendars for the 2018 CGM annual retreat!

The retreat will be held on Friday, September 21, 2018 at the Partners Healthcare West building at Assembly Row (399 Revolution Dr., Somerville, MA 02145).

The CGM and the co-chairs of this year's retreat, Patricia Musolino, MD, PhD and Jonathan Rosand, MD, MSc, are excited to release more details in the coming months.