# BiomedX Pitch Day Agenda

Wednesday May 31, 2023 | 8:30AM – 12:30PM

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| 8:30AM | **Welcome & Opening Remarks**<br>Meghan Pinezich, PhD<br>X. Edward Guo, PhD<br>Sam Sia, PhD |
| 8:50AM | **FASTr: Mobile Based AI to Accelerate Stroke Recognition**<br>(PI: James Noble, MD, MS; Presented by: Nirav Shah, MD) |
| 9:15AM | **Stool-based host RNA profling for gut disease diagnosis and monitoring**<br>(PI: Harris Wang, PhD; Presented by: Yiming Huang) |
| 9:40AM | **Optimization of personalized T cell based immunotherapy by characterization of morphology**<br>(PI: Lance Kam, PhD; Presented by: Xin Wang) |
| 10:05AM | **Massively multiplexed qPCR for genome-scale screening and diagnostics**<br>(PI: Wei Min, PhD; Presented by: Zhilun Zhao, PhD) |
| 10:30AM | **Networking Break** |
| 10:45AM | **Rapid point-of-care assays for detection of poliovirus and enterovirus D68**<br>(PI: Nischay Mishra, PhD) |
| 11:10AM | **MCI-ED Screen: A Speech-Processing Algorithm for Automatic Screening of Black Women Patients with Mild Cognitive Impairment and Early Dementia in Home Healthcare Setting**<br>(PI: Maryam Zolnoori, PhD) |
| 11:35AM | **CardiAIc: AI for better cardiac arrhythmia therapy**<br>(PIs: Christine Hendon, PhD & Deepak Saluja, PhD) |
| 12:00PM | **Ecological momentary assessment/intervention based mHealth app as treatment for post-acute sequelae of SARS-CoV-2**<br>(PI: Lawrence Purpura, MD, MPH, TM) |
| 12:30PM | **Adjourn for invited guests, closed door judging session** |

**FASTr: Mobile Based AI to Accelerate Stroke Recognition**

**PI:** James Noble, Associate Professor, Neurology

**Team:**
- Nirav Shah, Resident Physician, Medicine
- Jonathan Tiao, Resident Physician, Medicine
- Samuel Bruce, Resident Physician, Medicine

**Abstract:** Stroke is a leading cause of serious long-term disability in the US and costs $53 billion annually. It has the potential to devastate a patient and their family, meaningfully lowering their quality of life irreversibly. A key driver in the morbidity and mortality of strokes is delay between symptom onset and presentation to the hospital. Each minute of delay in treatment after stroke causes a patient to irreversibly lose 1.9 million neurons - within two hours this is the equivalent of 5 years of normal aging. Time to treatment is crucial, and delays lead to a lower chance of recovery. Excellent therapies for ischemic stroke, such as tissue-plasminogen-activator (tPA) and thrombectomy, have the potential to save patients and prevent debilitating neurological damage. However, for these treatments to be maximally effective, they must be given in a critical time window. Emergency response systems and hospitals are optimized to minimize delays. Unfortunately, strokes present with a wide range of symptoms, and lack of recognition continues to delay presentation, directly worsening outcomes. Extensive educational campaigns have failed because they lack the ability to intervene in real-time. As the at-risk, senior population rapidly grows over the next few decades, there is a need for a new mobile-based solution driven by (1) increasing ubiquity of smartphones amongst the elderly (2) advances in high resolution sensors on these smartphones capable of capturing signs of a stroke and (3) breakthroughs in cloud-based artificial intelligence (AI) capable of rapidly and accurately detecting stroke. We are building an AI powered smartphone application that is a patient-centered, seamless solution that will rapidly and accurately alert patients of stroke symptoms, accelerate EMS activation, and prevent long term disability and death.

**Stool-based host RNA profiling for gut disease diagnosis and monitoring**

**PI:** Harris Wang, Associate Professor, Systems Biology

**Team:**

- Alejandro Chavez (Co-PI), Associate Professor, Pediatrics
- Yiming Huang, Postdoctoral Research Scientist, Systems Biology
- Marley Giddins, Graduate Research Assistant
- Kristin Beiswenger, Scientific Program Director, Systems Biology

**Abstract:** Development of real-time, low-burden, and cheap monitoring methods for gut health, signaling, and inflammatory status can improve the management of inflammatory bowel disease (IBD). Current methods for management of IBD involve colonoscopies, which are resource intensive and invasive, and stool or blood tests, which only measure a limited number of biomarkers such as calprotectin and lactoferrin and do not directly evaluate gut cells. Unfortunately, these strategies do not provide the necessary sensitivity nor insight into disease pathology required to inform clinical decisions nor ongoing drug development efforts. In order to overcome these limitations, we have developed a non-invasive and inexpensive method, Exfo-seq, to measure the gastrointestinal transcriptome directly from stool to track disease state and response to therapy over time in large patient cohorts for less than $30 per sample. Exfo-seq can be used to profile gut health, level of inflammation, disease pathway activity, and therapeutic response, and holds great potential as a non-invasive method to guide early stage drug development efforts and personalized clinical management for individuals with IBD.

**Optimization of personalized T cell based immunotherapy by characterization of morphology**

**PI:** Lance Kam, Professor, Biomedical Engineering
**Team:**

- Jia Guo (Co-PI), Professor, Neurobiology (in Psychiatry)
- Xin Wang, PhD Student, Biomedical Engineering
- Justin Tso, Master Student, Biotechnology/Biological Science

**Abstract:** T cells have shown tremendous promise as "living drugs". T cell-based immunotherapy, particularly Chimeric Antigen Receptor (CAR) T cell therapy, has been revolutionary for cancer treatments. However, production of high-quality T cells remains a barrier to full deployment of such therapies since disease impacts cell function in diverse ways that are detrimental to their use. For example, CAR T cell therapy is not appropriate for about 30% of chronic lymphocytic leukemia (CLL) patients due to T cell deficits in activation and proliferation that limit manufacture of clinically relevant numbers of cells. Early characterization of T cell state with respect to this exhaustion is important for optimization and deployment of clinical treatment directions. Conventional technologies including biomarkers only capture molecular components of cellular function and do not provide sufficient information to predict T cell performance in disease therapy. Our technology introduces an AI-based platform called ImmunoVision to evaluate T cell function and optimize T cell production for personalized immunotherapy. We propose a deep learning model which analyzes images of short-term interaction of cells with a test surface to characterize T cell response. The cell-material interface mimics the immune synapse (IS) contact site between T cells and antigen-presenting cells, which plays an important role in T cell activation. As a starting point, we have leveraged deep learning to classify cell into healthy or chronic lymphocytic leukemia (CLL) groups based on cell morphology. It will be further applied to predict T cell proliferative capacity and the optimal growth condition for T cell production, which would make treatment of difficult CAR-T therapy cases possible. Compared to existing approaches, our technology is fast, inexpensive, does not require extensive training and most importantly, has predictive power.

**Massively multiplexed qPCR for genome-scale screening and diagnostics**

**PI:** Wei Min, Professor, Chemistry

**Team:**

- Zhilun Zhao, Postdoctoral Fellow, Chemistry
- Naixin Qian, PhD Candidate, Chemistry

**Abstract:** Nucleic acid identification and measurement is a fundamental methodology in bioscience, with various technologies developed to meet this need. However, there is a gap between the number of targets that can be simultaneously detected and the cost and turnaround time associated with the technology. To bridge this gap, a massively multiplexed qPCR technique (mmqPCR) has been developed that allows for genome-wide qPCR with a low cost and quick turnaround time. This invention has broad applications in basic science research, drug discovery, diagnostics, and more. For drug discovery, measuring gene expression levels is crucial, but current techniques are limited in their multiplexity. The low cost and rapid turnaround of qPCR are only suitable for a few targets, while the comprehensiveness of NGS is associated with a high cost and slow turnaround time. The mmqPCR technique allows for the systematic understanding of biological responses to stimuli, such as drug treatment, in drug screening studies. Infectious diseases account for a significant proportion of deaths and financial losses worldwide. The current diagnostic process involves multiple steps, which are increasingly expensive and time-consuming, and can lead to misdiagnosis. A fast, comprehensive, and cost-effective diagnostic tool is needed to address these issues. The mmqPCR technique has the potential to revolutionize infectious disease diagnostics, enabling fast and comprehensive pathogen detection at a low cost. This would improve patient outcomes, reduce costs for hospitals, insurers, and patients, and help to address healthcare inequalities.

**Rapid point-of-care assays for detection of poliovirus and enterovirus D68**

**PI:** Nischay Mishra, Assistant Professor, Epidemiology

**Team**:

- Kiran T. Thakur (Co-PI), Assistant Professor, Neurology
- Amy Rosenfeld (Co-PI), Research Scientist, Virology

**Abstract:** One in 200 infections with poliovirus (Enterovirus-C) leads to irreversible paralysis. The mortality rate in paralyzed patients ranges from 5-10%. Poliomyelitis cases began to drop dramatically worldwide in 1961 with the introduction of an oral-vaccine containing attenuated/weakened virus. Although many predicted that this advance would lead to the eradication of poliomyelitis, recent vaccine-reluctance led to increase number of confirmed diagnoses of circulating vaccine-derived-polioviruses-type-2 (cVDPV2). A 2022 survey revealed that approximately 25% of 45 million children in the USA (>11 million) are not fully protected. Thus, the risk of infection and disease is again increasing. In July-2022, a young-adult in Rockland (NY) developed cVDPV2-associated-poliomyelitis. Wastewater samples collected in the area tested positive for the same strain, suggesting a risk of a polio outbreak. EV-D68 (Enterovirus-D) can also cause paralytic illness; acute flaccid myelitis (AFM). AFM was first reported in the children in USA in 2014 (700 documented cases reported by the CDC). There is currently no vaccine for EV-D68. Diagnostic tests are urgently needed to restrict contagion by identifying individuals with infectious poliovirus or EV-D68 and identify those who may benefit from early medical intervention. The objective of this program is to build rapid, sensitive tests for early detection of poliovirus and EV-D68. The enabling technology derives from work reported in 2019 wherein we identified antibodies (Abs) to specific short-peptide sequences in the EV-D68-VP-1-capsid-protein and poliovirus-VP1-capsid-protein using a high-density peptide microarray. We raised Abs in rabbits by immunizing these synthetic peptides with KLH-conjugate, and measured reactivity, specificity, and utility of these Abs in ELISAs with cognate biotinylated-peptides and multiple enterovirus isolates. We will isolate and produce recombinant-monoclonal Abs (rmAbs) from immunized rabbits, use these rmAbs for poliovirus and EV-D68 detection in rapid antigen tests. We will establish sensitivity and specificity of rapid antigen tests using clinical specimens for the regulatory approvals.

**MCI-ED Screen: A Speech-Processing Algorithm for Automatic Screening of Black Women Patients with Mild Cognitive Impairment and Early Dementia in Home Healthcare Setting**

**PI:** Maryam Zolnoori, Research Scientist, Nursing

**Team**:

- Julia Hirschberg (Co-PI), Professor, Computer Science
- Maxim Topaz, Nursing

**Abstract:** Mild cognitive impairment (MCI) and early-stage dementia (ED) affect one in five older adults over 60, leading to frequent utilization of healthcare services. Despite efforts to diagnose MCI-ED, more than 50% of patients remain undiagnosed and undertreated. Black patients, particularly Black women, face higher risks due to healthcare access barriers, racial biases in neurological examination, and lower health literacy. The proposed project aims to develop an innovative algorithm for early identification of MCI-ED in Black women using data from electronic health records and audio-recorded verbal communication during routine home healthcare encounters. Current biomarkers for detecting MCI-ED such as magnetic resonance imaging are limited by high costs and invasiveness, but recent studies suggest that spoken language can act as an early biomarker of cognitive decline. Existing speech processing algorithms are not sufficient as they were trained on limited data from predominantly White patients. The proposed MCI-ED screening algorithm for Black women will be cost-effective, non-invasive, and unbiased, with potential for integration into the home healthcare workflow. The project is based on pilot studies conducted at VNS Health, and aims to refine the performance of our existing speech processing algorithm on a sample of audio-recorded Black women patients' verbal communication. The killer experiment will involve a sample of ≈80 Black women patients, with 40 in the MCI-ED case group and 40 in the control group. The experiment is expected to be completed within a year, with support from Columbia University and VNS Health. The MCI-ED screening algorithm has significant market potential, addressing a serviceable obtainable market of USD 6.39 billion for Black women with MCI-ED in the home healthcare setting. This study's future plan involves incorporating the MCI-ED Screen algorithm into home healthcare, evaluating its efficacy through a clinical trial, and seeking an STTR grant from the NIA for support.

**Artificial intelligence for atrial isthmus prediction**

**PI:** Deepak Saluja, Associate Professor, Medicine Cardiology

**Team**:

- Christine Hendon (Co-PI), Associate Professor, Electrical Engineering
- Elaine Y. Wan, Associate Professor, Medicine
- Edward J. Ciaccio, Senior Research Scientist, Medicine
- Jonah Abrams Majumder, Graduate Research Assistant, Biomedical Engineering
- Ziyi Huang, Graduate Research Assistant, Electrical Engineering
- Lawrence Zeldin, Postdoctoral Residency Fellow, Medicine

**Abstract:** Cardiac arrhythmias are common and cause significant morbidity and mortality, and cardiac ablation has developed as a commonly used tool to treat arrhythmias. A common mechanism of arrhythmia generation involves circus-movement rotation of electricity called reentry. The critical component, or isthmus, of such a circuit is typically an area of diseased tissue that is isolated from the rest of the myocardium by functional or anatomic barriers, such as regions of scarring or a valve annulus. A common goal of an ablation procedure is to identify and eliminate such isthmuses. We showcase that electroanatomic data recorded during ablation procedures can be analyzed with custom software to extract electrical features from the points samples. These features and their associated anatomical positions are applied to train a deep learning network to recognize which features are associated with points located on a critical isthmus. This information can then be used to prospectively predict the location of isthmuses. This product has the potential to improve in ablation outcomes for a substantial number of patients, by identifying where to ablate within the critical circuit.

**Ecological momentary assessment/intervention based mHealth app as treatment for post-acute sequelae of SARS-CoV-2**

**PI:** Lawrence Purpura, Assistant Professor, Medicine

**Team:**

- Saleena Subaiya (Co-PI), Clinical Researcher, Psychiatry
- Michael Yin, Associate Professor of Medicine
- Belinda Tan, MD, PhD Co-CEO & Co-Founder of People Science
- Noah Craft, MD, PhD Co-CEO & Co-Founder of People Science

**Abstract:** Long COVID affects up to 65 million individuals worldwide, and with ongoing transmission of SARS-CoV-2 is projected to increase in prevalence over time. As Long COVID is a novel condition without an established treatment, there are many gaps in care. Anecdotally, nonpharmacological therapies are effective; these include pacing to prevent post-exertional malaise, salt-tablets for dysautonomia, and mindfulness-based strategies for psychiatric symptoms. Due to long clinic wait times, many patients self-initiate care, relying on support groups and other internet resources for direction. Mobile health (mHealth) apps have been used successfully to track chronic illness while providing 'just-in-time' interventions to manage symptoms. In partnership with the award-winning company, People Science, we propose refining the existing mobile health app, Chloe, to create "Long COVID MD" – a mobile health app for Long COVID patients, providers, and scientists. Long COVID MD will obtain ecological momentary assessments to track daily symptoms, provide 'just-in-time' interventions for symptom management that include pacing recommendations, relaxation exercises, and sleep hygiene recommendations, and a dashboard for patients, physicians, and researchers to track data. Our "killer-experiment" will be designed in three stages: 1) semi-structured interviews with patients and providers to design content, 2) group usability testing, 3) beta version piloting to assess acceptability, feasibility, and adherence. Our 12-month goal is to create an mHealth platform that can be adapted for three tiers of use: patients, care providers, and researchers. With a Service Obtainable Market of 2.75 million people in the US and $60/year subscription fees, total anticipated sales are $165 million per year. Our long-term goals are to adapt Long COVID MD for other chronic illnesses that are similar in nature to Long COVID symptoms and their management.