The University of Maryland Physician Scientist Training Program Residents

Mark Kvarta, MD, PhD – PGY3 PSTP Resident

Project: Dynamic integration of stress and genetics to reward circuit dysconnectivity in depression.

Primary Mentor: Elliot Hong, MD

Depression is a devastating, deadly, and costly disease. It is most commonly treated, often unsatisfactorily, by manipulating synaptic serotonergic tone, yet the key substrates that mediate antidepressant efficacy are largely unknown and a better understanding of the etiology and neurobiological pathophysiology is needed. My doctoral work focused on the role of chronic stress in causing excitatory synaptic dysfunction within the hippocampus and ultimately downstream at the corticolimbic interface with the reward system in the nucleus accumbens, resulting in reward deficits including anhedonia in rodents. I described how chronic stress and successful antidepressant treatment bidirectionally altered excitatory synaptic strength using electrophysiology and molecular and behavioral techniques. With my current project I aim to extend these findings into human populations and study circuit dynamics between these key brain areas using functional imaging (fMRI) and electrophysiology (EEG) in depressed and non-depressed individuals. Furthermore, I am investigating the role of major stressors experienced at different time points throughout life, and the interaction of this stress with genetic vulnerability towards altering circuit function and ultimately depressive symptomatology. Understanding how these brain regions communicate with each other and are perturbed by genetics and environment in depression are critical in order to develop meaningful biomarkers and the next generation of therapeutics.

My PSTP Experience

As an MD/PhD trainee graduating from the University of Maryland, I knew firsthand the strength of neuroscience research housed at the University of Maryland SOM, the key attraction that brought me here over a decade ago. The training towards clinical excellence is only further sharpened by the unique partnership with Sheppard-Pratt Hospital as a joint residency. The formal research track in psychiatry through the PSTP has been a unique opportunity to bridge these two strengths of clinical and research distinction. The outpouring of support and enthusiasm as a research-track resident I have constantly enjoyed has been remarkable, even more so for the broad scope of clinical training taking place in tertiary, state, private and community hospitals, forensic settings, psychotherapy offices, substance abuse clinics, and emergency rooms. I am fortunate to have developed mentorship from faculty of all interests and experience, from purely clinical to purely research and everywhere in between, extending well beyond the mentorships formally arranged. It is clear there is a shared vision to advance psychiatry through development and translation of cutting-edge neuroscience with a new generation of biological psychiatrists. Most importantly, the mix of freedom and guidance has been seamlessly individually

tailored as I develop my own personal toolbox to meet my own goal of developing into an independent translational researcher and physician-scientist.

Eric Luria Goldwaser, DO, PhD, - PGY2 PSTP Resident

Project: Development stress and blood-brain barrier integrity in schizophrenia.

Primary Mentor: Elliot Hong, MD, and Peter Kochunov, PhD

Secondary Mentor:

Endothelial cell monolayers are shared within the body's many vascular systems. A peripheral assessment may provide surrogate information on the blood-brain barrier (BBB) endothelial function in schizophrenia. My doctoral research project was focused on the assessment of endothelial dysfunction in Alzheimer's disease at the molecular and cellular level of the BBB. This current project will extend my prior research experiences in BBB endothelial integrity to schizophrenia at the clinical biomarker level during my PSTP training. The primary goals of this project are to: 1) test the central and peripheral endothelial integrity in schizophrenia which can be assessed with state-of-the-art neuroimaging for BBB integrity, ophthalmologic tools for blood-retina barrier function, and peripheral endothelial assays, and 2) ascertain developmental insults as a significant contributor to the endothelial dysfunction in schizophrenia. Neurocircuitry involved in aberrant processing and connectivity may further be explored at the junction between perfusion and metabolism utilizing various diffusion MRI sequences, and to carve out putative targets for non-invasive neuromodulation.

My PSTP Experience

Clinically, what was important to me in a residency program was that I would develop my interest that drew me to psychiatry initially, insight-oriented psychotherapy. My interests in research have grown from the more basic and translational neuroscience level using animal models and cell culture into human, clinical applicability. My background work was in blood-brain barrier damage in the context of neurocognitive and neuropsychiatric disorders, namely Alzheimer's disease and post-operative delirium, which has developed into an interest in neuroimaging tools to investigate the neurovascular unit on a structural and functional level. Since the beginning of my PGY-1 year, the level of support and encouragement as part of the PSTP has been nothing short of exceptional. Importantly, the funding for a serious research project is available and accessible, the mentorship and collaborations are rich and meaningful, and the protected time to conduct the research is real, from the start. More than anything, however, I find myself having developed a project that I am passionate about, and that I am eager to build the rest of my clinical neuroscience career on. My goals are to develop the skills needed for a robust clinical trial assessing the neuroanatomy of behaviors, neuroimaging biomarkers of psychotherapeutic interventions, and carving out neuromodulatory circuits amenable to non-invasive assays and brain stimulation as a possible adjuvant to psychotherapy.