BIOGRAPHICAL SKETCH

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NAME: Meyerson, Joel Reuben

eRA COMMONS USER NAME (credential, e.g., agency login): jmeyerson

POSITION TITLE: Assistant Professor of Physiology and Biophysics

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Texas, Austin	B.S.	05/2007	Biomedical Engineering
University of Texas, Austin	B.A.	05/2007	Government
University of Cambridge	Ph.D.	04/2014	Biological Sciences
National Institutes of Health	Postdoctoral	08/2015	Structural Biology
HHMI / Brandeis University	Postdoctoral	02/2018	Ion Channel Biophysics

A. Personal Statement

The research in my lab is focused on understanding molecular mechanisms of glutamate receptor ion channel (iGluR) activity, modulation and organization in the context of human neurobiology and disease. I have a strong background in relevant areas which include iGluR structure, membrane protein biochemistry, electrophysiology, and cryo-electron microscopy (cryo-EM) imaging and image processing. This has given me training in the intellectual framework and methods needed for the proposed project. My previous work on the structure and mechanisms of iGluRs was foundational to ongoing efforts in the field to develop a comprehensive structural model for iGluR gating.

My lab at Weill Cornell Medical College is focused on developing a quantitative molecular mechanism for how the kainate receptors (KARs), which are one of three iGluR family members, respond to the neurotransmitter L-glutamate. With this I aim to form a ground level framework for understanding and interrogating the broader physiology of these receptors. The longer-term vision is to build on this foundation and develop a structural model for KAR supercomplexes composed of cytosolic, synaptic, and transmembrane auxiliary proteins organized around the receptors. This will be vital for a comprehensive understanding of how KAR physiology is shaped by its interactome. Throughout my research career I have successfully trained and mentored postdoctoral researchers, graduate students, technicians, undergraduates, and high school students. The training philosophy in my lab emphasizes quantitatively rigorous research in a diverse, inclusive environment, with the goal of preparing trainees for careers across the biomedical workforce. With this research and training background, recently-renovated lab space, a large start-up package, and strong intellectual and mentorship support in the biophysics and neuroscience community at Weill Cornell, I am equipped to successfully carry out the proposed research project.

B. Positions and Honors

Positions and Employment

2009-14 Research Assistant, MRC-MBU, University of Cambridge, Cambridge, UK
2014-15 Postdoctoral Fellow, National Cancer Institute, NIH, Bethesda, MD
2015-18 Postdoctoral Fellow, Department of Biochemistry, HHMI / Brandeis University, Waltham, MA

2018- Assistant Prof., Dept. of Physiology and Biophysics, Weill Cornell Medical College, New York, NY

Honors

2009-14 NIH-Cambridge Graduate Fellowship (PhD funding, 4 years)
2012-13 NIH Intramural AIDS Research Fellowship (PhD funding, 1 year)
2013-14 NIH Intramural AIDS Research Fellowship (PhD funding, 1 year)
2016 Award for Best Presentation, Gordon Research Seminar, Ligand Recognition and Molecular Gating
2016 Presenter, Gordon Research Conference, Ligand Recognition and Molecular Gating

C. Contributions to Science

1. My first scientific contributions focused on the HIV Envelope protein, and the mechanism by which it initiates HIV infection of CD4+ T-cells. At the time of this work, there was limited structural information about how native HIV Envelope trimers proceed through stepwise interactions with the CD4 receptor and co-receptor on the T-cell surface. Using cryo-electron tomography, I obtained 3D structures of the Envelope trimer on the virus surface in complex with an array of binding partners. The different structures and conformations contributed critically to a coherent model for the infection mechanism. Additionally, by using a panel of small (15 kDa) HIV-neutralizing proteins to probe this infection mechanism, we derived the basis of therapeutic activity for these molecules. Later, working with colleagues focused on influenza I successfully extended this experimental approach to studying neutralization of H1N1 influenza. Finally, this work gave me the opportunity to develop novel cryo-electron tomographic approaches that I will apply in my own lab.

a. Moulaei T, Alexandre KB, Shenoy SR, Meyerson JR, Krumpe LR, Constantine B, Wilson J, Buckheit RW Jr, McMahon JB, Subramaniam S, Wlodawer A, O'Keefe BR. Griffithsin tandemers: flexible and potent lectin inhibitors of the human immunodeficiency virus. *Retrovirology*. 2015 Jan 23;12:6.
b. Harris AK, Meyerson JR, Matsuoka Y, Kuybeda O, Moran A, Bliss D, Das SR, Yewdell JW, Sapiro G, Subbarao K, Subramaniam S. Structure and accessibility of HA trimers on intact 2009 H1N1 pandemic influenza virus to stem region-specific neutralizing antibodies. *Proc Natl Acad Sci U S A*. 2013 Mar 19;110(12):4592-7.
c. Meyerson JR, Tran EE, Kuybeda O, Chen W, Dimitrov DS, Gorlani A, Verrips T, Lifson JD, Subramaniam S. Molecular structures of trimeric HIV-1 Env in complex with small antibody derivatives. *Proc Natl Acad Sci U S A*. 2013 Jan 8;110(2):513-8.
d. White TA, Bartesaghi A, Borgnia MJ, Meyerson JR, de la Cruz MJ, Bess JW, Nandwani R, Hoxie JA, Lifson JD, Milne JL, Subramaniam S. Molecular architectures of trimeric SIV and HIV-1 envelope glycoproteins on intact viruses: strain-dependent variation in quaternary structure. *PLoS Pathog*. 2010 Dec 23;6(12):e1001249.

2. The second phase of my research career has focused on the molecular mechanics of ionotropic glutamate receptors (iGluRs) which are integral to myriad neurobiological processes and implicated widely in central nervous system pathophysiology. Specifically, I contributed to understanding how the receptors traverse their key functional states – resting, active, and desensitized. My first major contribution in this area provided structures of these three states by single particle cryo-EM, from which my colleagues and I derived a molecular model for receptor activity at the synapse. My second significant contribution asked and addressed the basic question of how iGluRs mediate conflicting structural needs during desensitization. My current work builds on this foundation with questions focused on the molecular mechanisms of kainate receptor iGluRs and how they are organized and modulated at the synapse.

a. Meyerson JR, Chittori S, Merk A, Rao P, Han TH, Serpe M, Mayer ML, Subramaniam S. Structural basis of kainate subtype glutamate receptor desensitization. *Nature*. 2016 Sep 22;537(7621):567-571.
b. Meyerson JR, Rao P, Kumar J, Chittori S, Banerjee S, Pierson J, Mayer ML, Subramaniam S. Self-assembled monolayers improve protein distribution on holey carbon cryo-EM supports. *Sci Rep*. 2014 Nov 18;4:7084.
c. Meyerson JR, Kumar J, Chittori S, Rao P, Pierson J, Bartesaghi A, Mayer ML, Subramaniam S. Structural mechanism of glutamate receptor activation and desensitization. *Nature*. 2014 Oct 16;514(7522):328-34.

Complete List of Published Work in MyBibliography

https://www.ncbi.nlm.nih.gov/myncbi/1ziJ7Xd0kyWI3f/bibliography/public/

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

Leon Levy Foundation Neuroscience Fellowship Meyerson (PI) 02/01/20 – 01/31/21
The overall goal of this proposal is to use cryo-electron microscopy to develop structural models for how kainate receptors respond to their ligand, L-Glutamate, and how they receptors are organized and modulated by partner proteins at the synapse.

STARR Cancer Consortium Grant. Meyerson (co-PI) 01/01/20 – 12/31/21
This project aims to image mammalian cells by correlative fluorescence and cryo-electron microscopy, with the goal of understanding how chimeric antigen receptor (CAR) T-cells form immunological synapses with, and initiate killing of, target cancer cells. The work is in collaboration with Michel Sadelain (MSKCC), Morgan Huse (MSKCC), and Gregory Alushin (Rockefeller University).

Weill Cornell Medical College Institutional Start-up Funds Meyerson (PI) 03/01/18 – 02/28/22
Funds have been used to initiate my research effort. This includes setting up a protein biochemistry facility complete with tissue culture resources and instrumentation for protein purification and analysis, setting up computational infrastructure for cryo-EM analysis, and recruiting personnel and purchasing lab supplies.

Completed Research Support
N/A