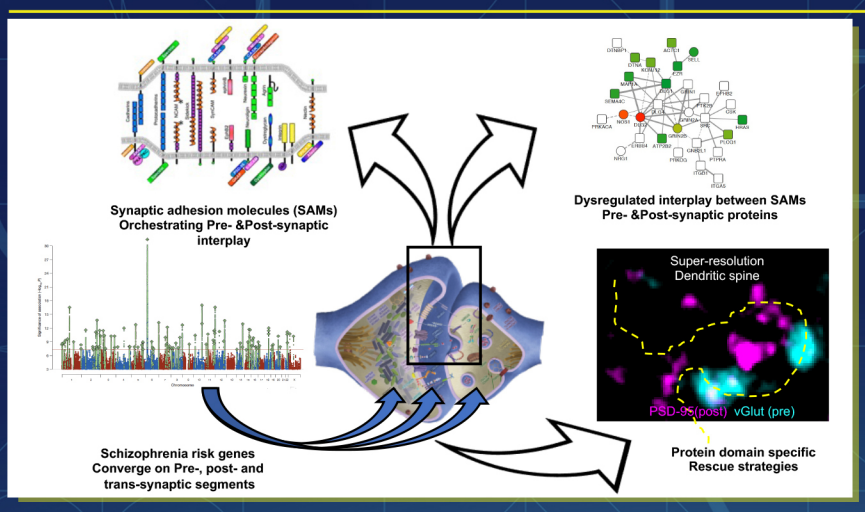
RESEARCH AFFAIRS OFFICE FUNDS THREE THOMAS JEFFERSON UNIVERSITY TEAMS PURSUING NIH P AND U GRANTS

In December, the Provost's Research Affairs Office released an RFA offering pilot funding to groups planning NIH P or U grant submissions in 2021/2022. Four proposals were received and reviewed by a panel of senior Jefferson's faculty. Three of the proposals were deemed worthy of funding at this time and awards were made in amounts ranging from $47,000 to $105,000. The teams represent some of University's leading areas of programmatic strength; neurological disease, vaccine development, and squamous cell carcinoma of the head and neck. The teams and their research are described below.

Brian Squilla, MBA
Sr. VP for Administration
Chief Research Officer

Steven McMahon, PhD
Senior Associate Provost
Programmatic Science

Transsynaptic mechanisms impacting structural plasticity in schizophrenia



Among the most remarkable discoveries in schizophrenia research is that hundreds of genes play causative roles for the illness. Strikingly, dysregulation of many of these genes converge on the synapse, a site of communication between brain cells. Our goal is to examine the molecules that bridge between the cells proximal or distal to synapse (pre- and postsynaptic cells), called synaptic adhesion molecules (SAMs), as candidates for therapeutic targets in schizophrenia. In post-mortem brain studies, we will characterize how SAMs are dysregulated and they impact on synapse (Project 1). Using systems biology approaches, this will be further expanded to a genomewide basis and reduced to specific protein domains for possible therapeutic intervention (Project 2). Finally, SAMs will be examined for their impact on changes in synaptic ultrastructure shown in patients and their specific domains for therapeutic modifications (project 3). Results from these studies will provide novel insights into disease mechanism and will likely lead to new avenues for therapeutic approaches.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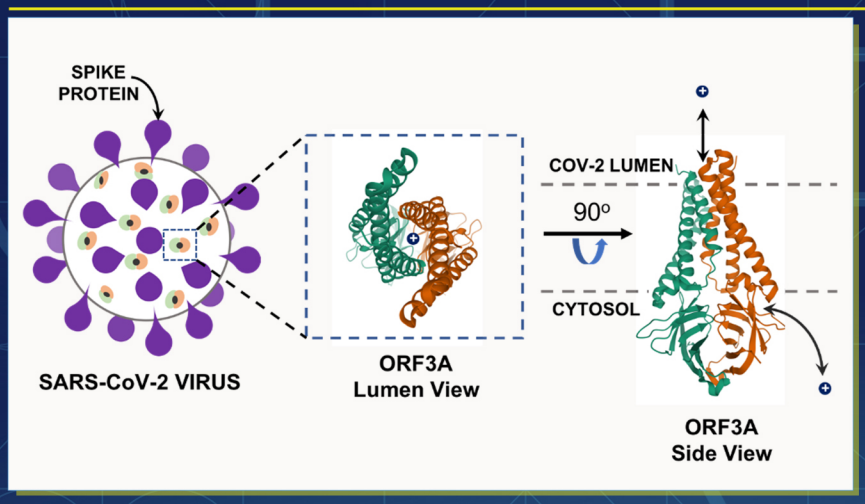
Structure and function of SARS-CoV-2 viroporins



The SARS-CoV-2 virus expresses proteins that play important roles in its life cycle. The spike protein is well known for its role in the infection process. However, other proteins found in the lipid membrane of the virus are also important for its replication and release from infected cells. CoV-2 viroporins are ion channels thought to play these roles. In this program project, we are investigating the structure and function of the ORF3a viroporin and proteins that interact with it to eventually identify therapeutic targets that could be exploited to effectively treat Covid-19.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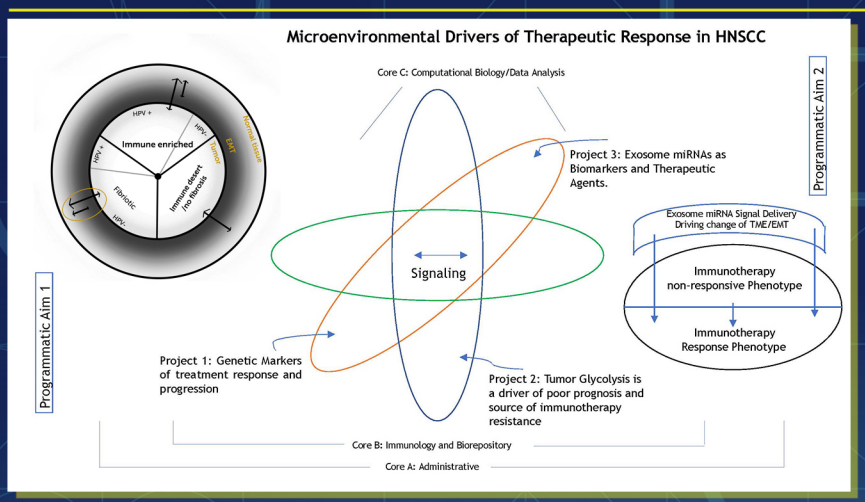
Microenvironmental drivers of therapeutic response in head and neck squamous cell carcinoma



Head and Neck Squamous Cell Carcinoma (HNSCC) is etiologically and phenotypically complex with a high burden of disease worldwide. Minimal improvement of overall survival has been seen in the past 20 years, and immune oncology strategies offer significant promise despite modest responses to monotherapy. Further advances will require a deeper understanding of how tumor phenotypes dictate response and identifying key regulatory pathways will guide combinatorial immune therapeutic approaches. The overall goal of this Research Program is to categorize HNSCC phenotypes (HPV status, EMT, immune, and metabolic) to aid clinical trial design and more accurately predict immunotherapy resistance. The overarching aims are to 1) Understand the epithelial mesenchymal transition in different subtypes of HNSCC including HPV+ vs – and how immunotherapy alters phenotypic behaviors to growth and clinical outcomes and 2) Test a biomarker strategy to predict therapeutic responses based on microenvironment profile and investigate ways to shift a phenotype to one that is responsive to treatment through metabolic decoupling and engineered extracellular vesicle delivery targeting IL-6 and IL-8 pathways.


Adam Luginbuhl, MD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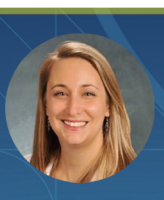
Andrew South, PhD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