Sample Abstract 1

Modeling the Vasopressin V2-Renal Reception and Predicting Interaction with Non Peptide Antagonists

Nicholas Callahan, Department of Biochemistry; Rosemarie M Dazard, Department of Biochemistry; and Menachem Shoham, Department of Biology, CWRU

Vasopressin is a peptide hormone implicated in kidney, heart and brain function. The Vasopressin-2 receptor is a seven-helix transmembrane G-protein coupled receptor, which plays a role in water reabsorption and vasodilatation. This research is concerned with creating a computer model of the Vasopressin-2-renal receptor, then using this model to predict how vasopressin and non-peptide antagonists dock to the receptor. We have also investigated how mutations in the receptor would alter the affinity of the antagonists to the receptor. Experiments are underway to experimentally measure the affinity of the compounds to wild type and mutant receptors. The antagonists are OPC21268, OPC31260, OPC41061 obtained from Otsuka Pharmaceuticals (Japan) and SR49059, SR121463B, and SSR149415 obtained from Sanofi Pharmaceuticals (France).

Project Mentor: Professor Menachem Shoham, Department of Biochemistry, CWRU

Sample Abstract 2

A Multiplex PCR-LDR Assay for Polymorphism Determination in Plasmodium falciparum pfmdr1 Gene

Eric Carnevale, Department of Biology; Dr. Peter Zimmerman, Global Health and Disease (CWRU).

Resistance to antimalarial drugs such as chloroquine (CQ) has significantly increased the mortality rate of malaria infections in the past several decades. Because of this a greater understanding of the mechanisms behind CQ resistance is required, and specifically the role played by the Plasmodium falciparum gene pfmdr1. Single nucleotide polymorphisms (SNPs) have been identified in this gene that is thought to contribute towards the parasite's ability to withstand treatment. Because of this we are developing an assay that can identify supposed resistance genotypes quickly, reliably, and with the capacity for processing many samples at once. A standard PCR amplifies target DNA, which is then followed by a ligase detection reaction (LDR). The LDR interrogates the SNP by binding an upstream probe that is allele specific and tagged with a 5' sequence to hybridize to a polystyrene bead, and a downstream probe that anneals to a conserved sequence and is bound to biotin on the 3' end to hybridize to a fluorescent molecule. Detection involves hybridizing the LDR product to fluorescent r-phycoerythrin for quantification, and to a unique, fluorescent, polystyrene bead for allele identification. The process has been shown to accurately identify the pfmdr1 genotype in five SNPs simultaneously, with up to a 100:1 signal to noise ratio. When fully developed, a single operator would be able to analyze samples at a rate of one per minute and a half, amounting to thousands per day. For malaria treatment, this translates to detailed and current knowledge of parasite resistance capabilities within a region or country, allowing governments and health ministries to effectively direct treatments, at a cost that would be feasible in the developing world.

Project Mentor: Dr. Peter Zimmerman, Global Health and Disease, CWRU
Faculty Sponsor: Professor Nancy Dilulio, Department of Biology, CWRU

Sample Abstract 3

The Ripple Effect: The Impact of ADHD-Associated Sleep Problems on College Students

Samia Ahuja, Psychology and Sociology

Attention-Deficit Hyperactivity Disorder (ADHD) is a neurodevelopmental disorder that includes symptoms of inattention, hyperactivity, and impulsivity. Symptoms often begin in childhood and continue into adulthood. Individuals with ADHD are more likely than their peers to have sleep problems, which often worsen with age. ADHD and sleep problems are closely linked, each making the other's symptoms worse. Among the individuals already diagnosed with ADHD, 55% of children and 80% of adults report sleep issues, including insomnia, difficulty falling asleep, staying asleep, daytime sleepiness, and poor sleep quality. As of 2024, approximately 25% of college students are diagnosed with ADHD. The purpose of this narrative literature review is to examine the ways in which sleep problems associated with ADHD impair the academic performance and executive functioning of college students. In this review, literature from the fields of psychology, sleep medicine, education, and occupational therapy was examined. The collective findings indicate that students with ADHD-associated sleep problems are constantly feeling tired and unfocused, unable to retain information and complete assignments on time. These students experience challenges with procrastination, prior organization, low motivation, and absenteeism, which makes it difficult for them to complete coursework and meet deadlines. Additionally, ADHD-associated sleep problems also impair their executive functioning skills, such as planning and organization, self-regulation, and time management. Lower motivation and self-esteem and reduced working memory as a result of sleep problems make it challenging for students to successfully meet the demands of college life. The implication of these findings shows the need for target interventions and support systems in higher education for students with ADHD-associated sleep problems.

Faculty Mentor: Anastasia Dimitropoulos, Department of Psychological Sciences

Sample Abstract 4

Effects of a Combination Therapy Targeting the Meningeal Lymphatic Vasculature on Alzheimer's Disease Physiopathology

Ankita Bhatnagar, Neuroscience and Psychology; Dr. Antoine Louveau, Department of Neurosciences, Cleveland Clinic Lerner Research Institute

Alzheimer's Disease (AD) is a devastating neurodegenerative disorder that still suffers from limited therapeutic offer. Previous studies in the laboratory have shown that the degeneration of the meningeal lymphatic vasculature, a network of vessels ensuring homeostasis of the fluid dynamic and immune populations, is a central factor in age-associated cognitive dysfunction. We found that we can prevent age-associated cognitive decline through the boost of lymphatic vessel growth via providing an exogenous source of VEGFc (the main lymphatic growth factor), or removing CD49a, which is an integrin that limits lymphatic function with aging. Preliminary data, however, suggest that either of these treatments only has limited to no effect on AD physiopathology using the 5xFAD mouse model of AD. Given that VEGFc and CD49a regulate lymphatic function through independent pathways and mechanisms, we want to investigate how combinatorial therapy may further improve lymphatic function and affect AD physiopathology. In this study, 5xFAD mice at age 4 either received VEGFc treatment, removed CD49a from their lymphatic vessels, or a combination of both treatments. Two months later, tissues were harvested from these mice. Meningeal lymphatic morphology and function was assessed, and the amyloidosis pathology of the 5xFAD mice was assessed using histology. The aim of this project is to determine if the degree by which lymphatic function is improved is a factor determining the efficiency of targeting the meningeal lymphatic system for the treatment of AD.

Project Mentor: Dr. Antoine Louveau, Department of Neurosciences, Cleveland Clinic Lerner Research Institute
Capstone Instructor: Dr. Ashley Nemes, Department of Neuroscience

Sample Abstract 5

Interactive Fluid Simulation Web App

Sean Brown, Data Science and Computer Science; **Chase Shriver,** Engineering Physics; **Liam McCall**, Engineering Physics; **Olugbadebo Adesina**, Computer Science

Fluid dynamics describes the flow of liquids and gasses. It allows engineers and scientists to model phenomena such as airflow over wings, water currents, and drag and lift forces. Especially for complex components, computer-assisted fluid simulation is a critical part of the design process. Existing fluid simulators, however, are not very accessible to the average person. They are often complex, hard to understand, and expensive. Many high-fidelity fluid simulators require a deep knowledge of math and physics. Just setting up a simulation requires extensive parameter tuning, which amateurs or hobbyists will likely struggle with. Popular simulators, like ANSYS Fluent and COMSOL Multiphysics, come with high licensing fees and require considerable computing resources, making them hard to run on a standard laptop or desktop.

We created an interactive fluid simulation web app that lowers the barriers to entry, emphasizing user friendliness and real-time interactivity. Our project allows users to model a flow system in real-time. Given an initial state, users can place objects in a fluid and see how they behave. They can customize the parameters and get instant feedback on how the behavior changes. One of the most common applications of fluid simulation is predicting aerodynamic performance, where the lift and drag are critical factors in wing design. Using their cursor, users can draw their own wing, see its performance, and quickly make changes if necessary. This process is much more accessible and easier for beginners than it is in existing simulators, where merely creating an object to test can be quite involved.

Project Mentor: Shuai Xu, Department of Computer and Data Sciences

Sample Abstract 6

Altered Neural Dynamics and Sleep Patterns in Epilepsy and the Effect of Potassium Buffering

Faith Ferry, Neuroscience; Dr. Vipin Kumar, Department of Neurosciences; Dr. Masashi Tabuchi, Department of Neurosciences

This project sought to characterize the neural alterations invoked by epileptogenesis, to further explore the potential of omega fatty acids to rescue these disturbances, and to observe the effects of a novel glial ion channel on epileptiform activity. In order to elucidate the underpinnings of unstable dynamics in epileptic neural circuitry, we cultured hiPSCs and analyzed various electrophysiological properties. As expected, epileptic hiPSC cultures exhibited increasing spiking activity and local variance in spiking patterns. Higher order analysis also revealed changes to metastable brain states and state transition patterns. Previous research utilizing a Drosophila model reported decreased seizure activity in bang-sensisitve mutant flies when their food was supplemented with omega-3 and omega-6 fatty acids, thus provoking our interest in their effects on cell lines. We found that supplementation did not alter firing rates or local variance of spike patterns. However, differences were observed in higher order analysis that revealed changes to transition patterns and state stability, potentially suggesting that the alterations observed in the Drosophila may have been induced by an alternative mechanism. Further delving into the processes underlying seizure activity, we decided to investigate a pH sensitive chloride channel that serves a role in alkaline taste sensation in Drosophila. The channel (Alka) has been shown to be present in both neurons and astrocytes, as well as in regions of the brain particularly involved in sleep mechanisms. The channel, in the Drosophila brain, serves a role in potassium buffering, an important aspect of mediating hyperexcitability that can invoke seizures. Therefore, we will use Drosophila expressing this channel and mutations to it to analyze their sleep patterns and compare them with those observed in bang-sensitive flies. Through this data collection, we aim to determine a potential relationship between this channel and epileptogenesis.

Project Mentor: Dr. Masashi Tabuchi, Department of Neurosciences
Capstone Mentor: Dr. David Friel, Department of Neurosciences