Online Proceedings

Poster Session 2

Commons East, Easel 77

1:00 PM to 2:30 PM

Gravitational Billiards

Nvida (N'vida) Yotcho, Junior,
Mentor: Jayadev Athreya, Mathematics

For many, mathematics is just the language of numbers. But, what people forget is that the universe is made of numbers, thus mathematics is its language. That is why we used a mathematical approach to study the long-term behavior of a moving ball influenced by the Earth's gravitational field. For our purpose, we experimentally defined gravitational billiards to be vertical billiards in which the earth gravitational field affects the billiards ball's motion. We also assumed that the billiards boundary could be any mathematical function of our choice, and the experimental system was conservative. Once in motion, the billiards ball followed a two-dimensional projectile trajectory until collision with the boundary occurred. After that, the ball engaged in a new projectile trajectory. As a matter of fact, each trajectory between two points of ball-boundary collision could be considered as an isolated two-dimensional gravitational motion with its own set of conditions. We took advantage of that aspect to build different simulations in parabolic, circular, paraboloidal and spherical gravitational billiards. The long-term behavior of the ball under gravity in our different gravitational billiards presented some aspects that so far corroborated the physics behind our study.

Poster Session 3

MGH 241, Easel 162

2:30 PM to 4:00 PM

Examining Mutations in Presenilin 2 Associated with Alzheimer's Disease

Leah Ariel Osnis, Senior, Biochemistry
UW Honors Program
Mentor: Suman Jayadev, Neurology
Mentor: Susan Fung, Neurology

Mutations in the gene Presenilin 2 (PSEN2) cause familial Alzheimer's disease (fAD). FAD shares clinical and pathological features of sporadic, late onset AD thus fAD cell models can be useful to study mechanisms relevant to all forms of AD which is critical to developing effective AD therapeutics. Presenilin 2 protein (PS2) forms the catalytic subunit of the γ-secretase complex, which cleaves amyloid precursor protein and releases Aβ1-42, considered a pathogenic contributor to Alzheimer's disease (AD). Our laboratory is interested in a fAD associated PSEN2 mutation, a frameshift two base-pair deletion (PSEN2 K115Fx) . The PSEN2 K115Fx is predicted to either lead to a truncated protein suggesting that the mutation may create a shortened peptide that interferes with normal cellular function (dominant negative or toxic gain of function) or result in degradation of the RNA transcript and subsequent loss of normal amount of PS2 protein (loss of function). To better understand how PSEN2 mutations cause disease, we have two objectives. The first aim of this project is to determine if the PSEN2 K115Fx does indeed result in a truncated protein or influence levels of wildtype PS2. I will be collecting human cultured fibroblasts isolated from AD patients with the PSEN2 mutations or controls and prepare cell lysate for analysis by Western blot. My colleague will also be analyzing mRNA levels from those same samples to determine the stability of the PSEN2 mutant and wildtype transcripts in all cases. The second aim is to determine the impact of the mutation on PS2 enzymatic activity. I will culture the cells described above, then infect with a luciferase based enzyme reporter assay to compare the impact of PSEN2 mutations on γ-secretase mediated cleavage of APP. My work will help identify the candidate mechanisms by which the PSEN2 K115Fx mutation causes AD.

Poster Session 3

MGH 241, Easel 161

2:30 PM to 4:00 PM

Mechanisms of Alzheimer's Disease Mediated by Mutations in Presenilin 2

Michelle Hong, Senior, Neurobiology, Psychology
Mary Gates Scholar, UW Honors Program
Mentor: Suman Jayadev, Neurology
Mentor: Carole Smith

There is an urgent need to clarify the causes of Alzheimer's Disease (AD) so targeted treatments can be developed. Mutations in Presenilin 2 (PSEN2) cause an inherited form of AD, but the mechanism for this relationship is not fully understood. PSEN2 protein (PS2) has been found to regulate

pro-inflammatory microglial response and the expression of microRNA miR146, an innate immune regulator. These findings led us to pursue the effects of PSEN2 mutations on microglia function, peripheral immunity, and AD. Our aim is to study mechanisms of microglia-induced neuron injury in AD. We hypothesize that PS2 mutation-expressing microglia contribute to neuroinflammation in AD by cytotoxicity and synaptic pruning mechanisms. To study the impact of stimulated microglia on neurons, we employ co-cultures, where microglial (BV2) and neuronal (SY5Y) cell lines are cultured together. We used a lactose dehydrogenase (LDH) cytotoxicity assay to measure levels of microglia-induced neuronal death. After initial assay optimizations, we measured LDH of a BV2/SY5Y coculture to quantify baseline LDH and optimize the ratio of neuron to microglia plating. Fluorescent microscopy was used to observe microglia and neuron interactions morphologically and flow cytometry quantified the levels of neuron phagocytosis of microglia. Using these methods, we were able to demonstrate interactions between the cells and these same methods can be used to later study synaptic pruning. From here, we will determine whether there is a difference in synaptic pruning levels and cytotoxicity between microglia from a control mouse and a mouse expressing mutated PSEN2 transgene when co-cultured with neurons. If our hypothesis holds true, we expect to see increases in both cytotoxicity and synaptic pruning induced by mutated microglia. Determining and understanding PSEN2's role in causing AD could lead to the development of targeted treatment for patients with these mutations.