UNIVERSITY of WASHINGTON

Undergraduate Research Symposium May 19, 2017 Mary Gates Hall

Online Proceedings

POSTER SESSION 1

Commons West, Easel 11

11:00 AM to 1:00 PM

Agreement of Blood Pressure Measurements – Cuff Position

Sara De Rosier, Fifth Year, Nursing
UW Honors Program
Mentor: Elizabeth Bridges, Biobehavioral Nursing and Health Informatics

The accurate performance and measurement of blood pressure (BP) measurement is vital in hospitalized patients in evaluating treatment effects and assessing clinical condition. However, patients routinely return from the operating room with the BP cuff reversed in orientation so that the tubing is pointing up toward the patient's head, rather than down as is the manufacturer's recommendation. The purpose of this study was to determine whether orientation of the oscillometric BP cuff affects the accuracy of blood pressure measurements in healthy adults. A randomized controlled trial with repeated measures was conducted. Subjects served as their own control. Using an oscillometric cuff, the BP was measured with the tubing facing up and down (order randomized) on the right or left arm (arm randomized). Correct technique (arm position, cuff size and placement) was standardized. The tubing down was the standard for comparison. Thirty-eight healthy adults participated; one subject was excluded for a BP out of range. The mean difference and standard deviation between tubing down versus up was 1.3 $\pm$ 5.2 mm Hg (p = .032) for systolic blood pressure (SBP), for diastolic BP: 0.3 $\pm$ 3.1 mm Hg (NS), and 1.0 $\pm$ 4.0 mm Hg (p = .037) for mean arterial pressure (MAP). While SBP and MAP were statistically significant different, the difference was not clinically significant compared to international standards. The European Society of Hypertension protocol for BP measurement devices requires 74% of differences in SBP to be 5 mm Hg or less, and 88% of differences to be 10 mm or less – our data exceed these guidelines at 75% and 93% respectively. The results of our study suggest that in the clinical setting, orientation of the BP cuff does not impact BP measurement in healthy adults.

POSTER SESSION 2

Balcony, Easel 114

1:00 PM to 2:30 PM

An Organotypic Brain Slice Model of Glutamate Excitotoxicity

Belinda Garana, Senior, Chemical Engineering
Mary Gates Scholar
Mentor: Elizabeth Nance, Chemical Engineering

Less than 3% of therapeutics can cross the blood-brain barrier, and the lack of penetration of therapeutics into the brain is the most cited failure for neurological clinical trials. In order to assess the efficacy of developing therapeutics which have the potential to address these issues, we are working towards establishing a high-throughput organotypic ex vivo brain slice model. We are specifically interested in developing a model that allows us to study and characterize the brain in the presence of glutamate excitotoxicity. Glutamate excitotoxicity is cell death due to an excess of the excitatory neurotransmitter glutamate, and is a common disease hallmark in neurological injury. The slice model we developed consists of cultured newborn rat brain slices to simulate an *in vivo* brain environment. However, in slice form, we have the ability to systematically study key pathophysiological variables, such as exposure to various excitotoxins that induce glutamate excitotoxicity. We use quantitative assessments of cytotoxicity (cell death) through cellular staining and imaging, as well as assays for lactate dehydrogenase (LDH), an enzyme released from the cytoplasm during cell death. We have established percent cytotoxicity profiles for both healthy untreated and maximum death control brain slices, and developed a protocol for testing excitotoxins to simulate glutamate excitotoxicity. With this slice platform, we will be able to compare the efficacy of potential therapeutics based on the decreases in rates of cell death they produce in brain slices with induced glutamate excitotoxicity. This research represents a promising platform to assay behavior, mechanism, and efficacy of therapeutics in development for the treatment of neurological disorders associated with glutamate excitotoxicity.

POSTER SESSION 2

Balcony, Easel 116

1:00 PM to 2:30 PM

Characterization of Quantum Dot Toxicity for Potential Use as a Biomarker in Brain Injury

Kate Hildahl, Senior, Chemical Engineering
Mary Gates Scholar
Mentor: Elizabeth Nance, Chemical Engineering
Mentor: Mengying Zhang, Molecular Engineering and Science

Quantum dots (QDs), fluorescent semiconductor nanocrystals, can be used as a biomarker and diagnostic tool because of their unique optical and electrical properties, including high luminescence, resistance to photobleaching, and broad excitation and emission spectrums. But in order to use QDs as biomedical imaging devices, particularly in sensitive organs such as the developing brain, toxicity must be adequately characterized. Little is known about the toxic effect of QDs on the brain, especially on the neonatal brain. QDs consist of a metal core, typically cadmium selenide, and a shell to protect the core. Cadmium is known to be highly toxic to many of the body's systems, including the central nervous system. However, expanding the shell and attaching functional biomolecules prevents cadmium release and changes the characteristics of the particles. In our study, several surface ligands were tested at variable concentrations and periods of exposure to measure the toxic potential of QDs on an *ex vivo* organotypic brain slice model. Three methods of characterization were used: a lactate dehydrogenase (LDH) assay, a propidium iodide stain, and a fluoro-jade C stain. The cellular stains were evaluated using confocal microscopy. Results showed that toxicity is a function of QD exposure time, surface chemistry, and concentration. Several QD conjugations displayed minimal or no toxic effect after 24 h of exposure. The results of this study will be useful in identifying a QD conjugate as nontoxic in a biological setting. QDs can then be tailored to site and cell-specific uptake in the brain, thereby improving the selectivity of current imaging techniques and providing a powerful diagnostic with regards to diseased cell fate.

POSTER SESSION 2

Balcony, Easel 115

1:00 PM to 2:30 PM

Stability of Biologically Safe, Surfactant-Coated Nanoparticles in Complex Media: Implications for Drug Delivery

Andrew (Andy) Kirk, Senior, Chemical Engineering
Mentor: Elizabeth Nance, Chemical Engineering

For a nanoparticle to become a pharmaceutical transport device, it must have shelf life stability and avoid aggregation. Spontaneous aggregate formation, or particle sedimentation, can render a therapeutic nanoparticle ineffective and potentially harmful as a pharmaceutical. Using a biologically safe material that provides steric stabilization (i.e Pluronic F127) may slow or eliminate aggregation, improving shelf life and potential for pharmaceutical use. The use of a surfactant coating instead of a chemically conjugated method will improve ease of nanoparticle formulation. To determine aggregation kinetics, various surfactant-coated nanoparticles (SCNP) have been compared in a number of medias, including standard measuring media (10mM NaCl), known aggregate media (30:70 methanol:water solution by volume), as well as in complex media such as artificial cerebral spinal fluid (aCSF) and high ion concentration media like phosphate buffered saline (PBS). These SCNP's have been compared to stock carboxylated-polystyrene nanoparticles, as well as polyethylene glycol-coated polystyrene nanoparticles. Characterizing SCNP behavior can have significant implications for nanoparticle design for drug delivery.

SESSION 2F

POLITICS AND CULTURE

Session Moderator: John Wilkerson, Political Science

MGH 242

3:30 PM to 5:15 PM

* Note: Titles in order of presentation.

Civil Control of Defence Forces in Ireland

Laurel Kunkel, Senior, Political Science
Mentor: Elizabeth Kier, Political Science

Ireland generally does not come to mind when debating military doctrine or civil-military relations; nevertheless, the Irish military has seen battle both abroad and at home since the British relinquished their legal domain over the nation in the 1920's. Despite this short history, the nature of Ireland's civilian relationship with its Permanent Defence Forces, or Óglaigh na hÉireann, is worth inspection due to its professional respect for civilian authority and successful minimal force policy which can serve as a comparison to our own military in the United States. This research uses political scientist Samuel Huntington's terms of formal authority and informal influence to assess the success of the Irish Permanent Defence Forces via the quality of its relationship to both the Irish Parliament and the general Irish civilian population. I measure the formal relationship by the level, unity, and scope of influence, whereas I measure the informal relationship by group affiliation, economic resources, post-military occupations, and level of prestige. Following analysis of these several factors, the paper concludes that the informal de-politicized and formal subordinate role of the Irish military serves the state as a successful instrument of defense. The Defence Forces hold fairly little informal influence in terms of prestige, post-military occupations, economic resources, and group affiliation, yet this may serve in the best interests of the state. It has little to no formal autonomy to

manipulate political affairs, yet very structural, stable control over the breadth of its own military responsibilities with internal avenues for releasing tension or for incurring incremental, thoughtful administrative change as necessary. The Irish military is constantly reminded of its subordination to the civilian government while at the same time accorded a fair degree of autonomy over its own regions of authority. These factors combined have created a peaceful and efficient civil-military relationship within Ireland.

SESSION 2Q

CENTRAL NERVOUS SYSTEM DISEASE MODELS

Session Moderator: Gwenn Garden, Neurology
JHN 026
3:30 PM to 5:15 PM
* Note: Titles in order of presentation.

Glial Cell Characterization in an mGluR5 Knockout Rat Model of Autism Spectrum Disorders
Holly Lin (Holly) Sullivan, Senior, Chemical Engineering
Amgen Scholar, Mary Gates Scholar, UW Honors Program, Undergraduate Research Conference Travel Awardee
Mentor: Elizabeth Nance, Chemical Engineering

Autism Spectrum Disorder (ASD) affects 1 in 68 children and has been steadily growing in incidence in recent years. As a developmental disability, ASD causes social, communication, and behavioral challenges. ASD is as mysterious as it is diverse—no two cases are the same. This not only complicates treatment methods but also makes physical characterization of the autistic brain a tedious challenge. As the number of ASD cases begins to increase, so does the urgency for answers at the developmental and biological level that may unravel this condition and lead to more effective and targeted treatment. Microglia and astrocytes are key non-neuronal cells that exhibit altered activity levels in the autistic brain. The changes in behavior and the role these cells play in ASD, and many other neurological diseases, make them potential therapeutic targets. Leveraging this fact, the focus of my research is to study the morphology and distribution of glial cells in wild type and knock-out (autistic-like) mGluR5 rats using confocal microscopy. Regions of interest for changes in cell behavior and morphology include the hippocampus, cortex, and thalamus. Rats with ASD have microglial cells with enlarged soma, retracted and thickened processes, and processes encircling neurons. Fluorescent antibody stains are used to visualize these cells and structures. By defining a physical distinction between healthy and autistic brains, a new wave of therapeutics that target and mitigate the overactivation and inflammation of microglia and astrocytes can be explored.

SESSION 2Q

CENTRAL NERVOUS SYSTEM DISEASE MODELS

Session Moderator: Gwenn Garden, Neurology
JHN 026
3:30 PM to 5:15 PM
* Note: Titles in order of presentation.

Quantum Dot Localization in Glia and Neuronal Cells in the Developing Brain
Binh Dang, Senior, Chemical Engineering
Mary Gates Scholar
Mentor: Elizabeth Nance, Chemical Engineering
Mentor: Mengying Zhang, Molecular Engineering and Science

Quantum dot (QD) semiconductor nanocrystals offer significant advantages over conventional fluorescent markers due to broad excitation spectrum, narrow emission spectrum, and very high photo stability, which enables long term visualization. Because of this, there is great interest in using QDs as biomarkers, where cellular uptake of QDs play an important role. In this study, we aim to characterize QD uptake in neuronal and glial populations in the developing brain as a function of QD surface functionality. Previous research has shown that the behavior of QDs in biological systems can be dictated by surface functionality; however, this has not been systematically studied, particularly in the developing brain. Here, we used cadmium-selenide (CdSe) QDs with either cadmium-sulfide (CdS) or zinc-sulfide (ZnS) shell. These QDs are coated with a layer of surface ligands to protect the core-shell and minimize their hydrophobicity. We set out to examine five different surface coatings, including: mercaptoundecanoic acid (MUA), mercaptopropionic acid (MPA), polyethylene glycol-amine (PEG-NH2), polyethylene glycol-methoxy (mPEG) and carboxylic acid (COOH). We incubated organotypic neonatal rat brain slices in 0.1 and 0.01 μM of QDs over a 24 h period. Using immunohistochemistry and co-localization analysis, we observed QDs with PEG-NH2 functionality localize in neurons, whereas QDs with MUA or MPA surface functionality remain in the brain extracellular space. High resolution confocal imaging is used to visually assess the stained brain slices, and the degree of colocalization with cell stains can be quantified using ImageJ. Furthermore, we investigated the region-dependent of QD-PEG-NH2 localization in neurons. This provides insight into the mechanism of uptake for future studies, which include using QDs as biomarkers of inflammatory processes, mediated by glia, in the developing brain.