

## Online Proceedings

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### POSTER SESSION 2

Balcony, Easel 109

1:00 PM to 2:30 PM

#### **Do Not Ignore the Role of Astrocytic Inwardly Rectifying K<sup>+</sup> Channel (Kir4.1) In Targeting Alzheimer's Disease and Parkinson's Disease**

*Eric Shaban Thorland, Junior, Pre-Sciences*

*Mentor: Jing Zhang, Pathology*

*Mentor: Lifu Sheng, Department of Pathology*

Astrocytes are a type of glial cells in the central nervous system, play a critical role in protecting neuronal signaling by regulating brain homeostasis, synaptic plasticity and transmission, and blood brain barrier functioning in central nervous system. Accumulating evidence has indicated that abnormal behaviors of astrocytic functions, including astrodegeneration and astrogliosis, are implicated as the primary factors contributing to a number of chronic neurodegenerative diseases such as Alzheimer's disease (AD) and Parkinson's disease (PD). Kir4.1 is an inwardly rectifying K<sup>+</sup> channel expressed on the projections of astrocytes, which serve important roles in the neuroprotective function of astrocytes, such as maintaining K<sup>+</sup> homeostasis and regulating extracellular glutamate. Abnormal expression of Kir4.1 has been reported in certain neurodegenerative diseases, including Amyotrophic lateral sclerosis (ALS) and Huntington's disease (HD), suggesting a vital role in the development of pathophysiology. However, the association between the molecular mechanism and expression of Kir4.1 and the underlying pathogenesis of AD and PD has been largely uninvestigated. In this study, we have had the critical opportunity to access human post-mortem brain tissue, provided by the University of Washington Alzheimer's Disease Research Center, and conducted confocal microscopy studies. Through a quantitative immunofluorescence staining approach, we expect to demonstrate a distinct expression pattern of Kir4.1 in various brain regions of AD and PD post-mortem tissues when compared to control subjects. Determining the role this protein has in neurodegeneration may provide new insight into the development of therapeutic targets to ameliorate the progression of AD and PD.

### SESSION 2R

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#### **NEW TREATMENTS FOR OLD DISEASES**

*Session Moderator: Benjamin Freedman, Medicine/Nephrology*

**JHN 111**

3:30 PM to 5:15 PM

\* Note: Titles in order of presentation.

#### **Chitosan-Based Tissue Scaffolds for High-Throughput Screening of Human Glioblastoma Therapeutics**

*Colin Alexander Lester, Senior, Mat Sci & Engr: Nanosci & Moleculr Engr*

*Mentor: Miqin Zhang, Materials Science & Engineering*

*Mentor: Olivia FC Chang, Materials Science and engineering*

Glioblastoma multiforme (GBM) is a highly aggressive variant of brain cancer that has been a focal point of chemotherapeutic development for years. However, initial drug screening using traditional *in vitro* culture of GBM cells frequently produces encouraging results that do not translate well to animal models and clinical application. To address this disparity, implementation of three-dimensional tumor modeling can better emulate the microenvironment that tumor cells experience *in situ*, improving accuracy of early *in vitro* screening. We developed two chitosan-based polymer blends to produce biocompatible, porous scaffolds that mimic the extracellular matrix and promote cell adhesion. Scaffold production was done in 96-well cell culture plates for high-throughput drug screening with a large sample size. These scaffolds were used to grow human GBM cell lines U-118 MG, U-87 MG and GBM6 for 14 days, confirming cell compatibility with the materials and promoting formation of tumor spheroids. The cultures were treated with the established chemotherapeutic agent temozolomide (TMZ) for 72 hours, and cells were then tested for metabolic activity using the Alamar Blue resazurin assay. We demonstrated increased resistance to chemotherapeutics in cells with this induced morphology relative to cells grown in two-dimensions for all cell lines and both scaffold compositions. Additionally, based on gene and protein expression analysis, GBM cell spheroids more strongly expressed cancer stem cell characteristics and greater malignancy. The presence of GBM resistance to chemotherapy and

enhanced characteristics associated with *in situ* tumors indicates the potential of using chitosan-based tissue scaffolds for more accurate high-throughput screening of novel GBM treatments.

### POSTER SESSION 3

MGH 241, Easel 139

2:30 PM to 4:00 PM

#### Optimization of Iron Oxide Nanoparticles as a Safe Contrast Agent for MRI

*Matthew Michael (Matt) James, Senior, Mat Sci & Engr: Nanosci & Moleculr Engr*

*Mentor: Miqin Zhang, Materials Science & Engineering*

*Mentor: Richard Revia, Materials Science and Engineering*

Nuclear magnetic resonance (MR) is a phenomenon which may be harnessed to provide high resolution images of the soft tissues of the body and aid in the diagnosis of many diseases. MR imaging relies on measuring the alignment, perturbation, and realignment of the magnetic dipole moments of hydrogen nuclei composing water molecules. Differing rates of realignment, or relaxation, of the magnetic moments of the hydrogen nuclei after perturbation creates contrast in MR images. This contrast can be enhanced by the introduction of magnetic field disturbances in the vicinity of hydrogen atoms. Clinically, contrast enhancement in MR imaging is achieved with chelates of the strongly paramagnetic metal, gadolinium. However, increasing evidence indicates that gadolinium can cause nephrogenic systemic fibrosis in patients with renal damage. Iron oxide nanoparticles (NPs) may be safer alternatives than gadolinium-based contrast agents given iron's biodegradability and physiological role in hemoglobin. This research optimizes iron oxide NPs for use as contrast agents in MR imaging. We evaluate two important MR imaging parameters, the transverse and longitudinal relaxivity, of iron oxide NPs as a function of core size at two different magnetic field strengths. Our findings show that both the transverse and longitudinal relaxivities of iron oxide NPs decrease with decreasing core size at a low field strength, but transverse relaxivity decreases while longitudinal relaxivity increases at high field strength. Furthermore, we find that the transverse relaxivity component is more strongly influenced by core size than the longitudinal relaxivity. These trends in MR parameters as a function of core size will allow for the optimization of iron oxide NP as contrast agents for MR imaging.

### POSTER SESSION 3

MGH 241, Easel 138

2:30 PM to 4:00 PM

#### Engineering Iron-oxide Nanoparticle-Based T1 Contrast Agent for Magnetic Resonance Imaging

*Manjot Singh, Senior, Bioen: Nanoscience & Molecular Engr, Public Health-Global Health*

*UW Honors Program*

*Mentor: Miqin Zhang, Materials Science & Engineering*

*Mentor: Mike Jeon, Materials Science and Engineering*

Magnetic Resonance Imaging (MRI) is an invaluable imaging modality that allows physicians to quickly analyze the anatomical and physiological processes of the body. To improve contrast efficiency, MRI contrast agents are frequently administered to patients. However, the most commonly used T1 contrast agent – gadolinium-based contrast agent (GBCA) – has been associated with many adverse health effects, such as reduced white blood cell count, increased serum levels of inflammatory cytokines, and vacuolar degeneration. As such, there is an urgent need to design a T1 contrast agent that has a short half-life and that does not produce toxic endpoints in patients. To address this need, the present study developed an iron-oxide nanoparticle (IONP)-based T1 contrast agent by synthesizing 4 nm oleic acid-coated IONP and reacting them with phosphine oxide-PEG. Next, this study characterized the biological and the magnetic properties of the generated IONP system in vitro in order to determine its suitability as a T1 contrast agent. Finally, this study also analyzed the synthesized contrast agent's use in other biomedical applications, specifically targeted drug delivery. Previous research has shown that cells can undergo ferroptosis – a regulated form of cell death – upon loss of activity of the lipid repair enzyme glutathione peroxidase 4 (GPX4). As such, a silencing RNA (siRNA) that can mark GPX4 mRNA for degradation was conjugated to these IONPs in order to downregulate GPX4 expression in mesenchymal stem cell – a type of stem cell that are particularly involved in cancer progression and that are especially resistant to radiotherapy – and sensitize them to radiotherapy. Ultimately, the findings of this study not only offer a safer alternative to GBCAs but also provide a foundation for a versatile, tunable IONP system that can be used in a variety of biomedical settings.

### POSTER SESSION 4

Balcony, Easel 93

4:00 PM to 6:00 PM

#### Heats of Adsorption of N<sub>2</sub>, CO, Ar and CH<sub>4</sub> versus Coverage on the Zr-Based MOF NU-1000: Measurements and DFT Calculations

*Graeme Oliver Vissers, Senior, Biochemistry*

*Mentor: Oscar Vilches, Physics*

*Mentor: Charles Campbell, Chemistry*

*Mentor: Wei Zhang, Chemistry*

Metal-organic frameworks (MOFs) represent an important

new class of adsorbent materials, catalysts, and catalytic supports. As such, it is important to fundamentally understand its adsorption capacity and selectivity of simple gases. NU-1000 is a prototypic zirconium-based MOF which has shown to be thermally stable up to 250 C and has a number of interesting catalytic and adsorbent properties. It is composed of zirconium oxide nodes connected by pyrene linkers with COO- end groups. We determined the isosteric heats of adsorption ( $Q_{st}$ ) versus coverage of four gases (N<sub>2</sub>, CO, Ar, and CH<sub>4</sub>) on NU-1000 by measuring volume-pressure equilibrium isotherms at very low coverages (under 0.1 monolayer) and above 90K. We then compared our experimental measurements to density functional theory (DFT) calculations of adsorption enthalpies at 77 K for the zero-coverage adsorption of the same gases at seven different types of sites of the MOF lattice. These comparisons showed remarkable agreement between the measured and theoretical isosteric heats in trend as well as reasonable agreement in magnitude, indicating that the sites predicted by DFT calculations are populated sequentially in order of decreasing absolute enthalpy. This study further increased our understanding of adsorption on this prototype MOF at very low coverages and reaffirmed the accuracy of theoretical calculations.