NEURAL ENGINEERING
SEMINAR SERIES

Systems Analysis of Neural Immune Signaling in Neurodegenerative Diseases

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ABSTRACT: Dysregulated neural immune activity contributes to the pathogenesis of diverse diseases, including Alzheimer's disease, traumatic brain injury, and lysosomal storage disorders, among others. Understanding neural immune function and identification of strategies to restore healthy or homeostatic immune activity holds the potential to transform our ability to treat neurodegenerative diseases. Neural immune activity is a complex system, consisting of intracellular regulation of diverse immune genes by phospho-signaling cascades that ultimately control glial phenotypes and expression of extra-cellular signaling factors, such as cytokines, that communicate between cells and exacerbate dysfunction. Dr. Levi Wood will discuss the role of the blood factors heme and hemoglobin in potentiating Alzheimer's disease pathogenesis. His lab has found that elevation of these factors in Alzheimer's disease suppresses immune function of the brain's immune cells, astrocytes and microglia, including their abilities to clear amyloid beta, which is the hallmark protein that forms plaques in Alzheimer's brains. By integrating extracellular (cytokine) and intracellular (phospho-protein) signaling data, they have determined that heme and hemoglobin attenuate normal immune function by stimulating the PI3K/Akt pathway. Moreover, attenuation of the heme biosynthetic pathway reduced amyloid beta pathology in 5xFAD Alzheimer's disease mice. Together, these data illuminate an entirely new aspect of Alzheimer's disease pathogenesis and suggest a novel mechanism resulting in brain immune cell "fatigue," which may be treated by attenuating heme synthesis.

Next, Dr. Wood will discuss his work to identify neuroinflammatory signaling responsible for cognitive deficit after repetitive mild traumatic brain injury (mTBI). Using a non-invasive optical cerebral blood flow sensor, Dr. Wood and his team found that mice with acutely low cerebral blood flow after mTBI would suffer long-term memory deficit and had elevated acute microglial activation. Surprisingly, microglial activation was accompanied by neuronal pro-inflammatory phospho-signaling and cytokine expression, suggesting for the first time that neural immunity and cognitive deficit depends on the interplay between glia and neurons. Their ongoing studies suggest that inhibition of phospho-signaling using translationally relevant small molecules has the potential to restore cognitive function after repetitive mTBI.

BIOGRAPHY: Dr. Levi Wood is an assistant professor of mechanical and bioengineering at Georgia Tech. He completed his doctorate in mechanical engineering at the Massachusetts Institute of Technology and his postdoctoral studies in systems biology and molecular pathology at Massachusetts General Hospital and Harvard Medical School. Dr. Wood's lab uses computational analysis with large "omics" datasets from humans, mice, and cells to understand the roles of neural immune signaling in healthy brain and several neurological disorders, including Alzheimer's disease and traumatic brain injury. Dr. Wood has won institute teaching and junior faculty awards at Georgia Tech and recently received the National Science Foundation CAREER award for his work to conceptualize neuroinflammation as a dynamic process for treatment of Alzheimer's disease.

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