Weekly Colloquium

Tuesday, 07/19/2016, 12:30pm, Billings Building – Rosedale Conference Room

"Preclinical Modeling of repetitive mild TBI; platforms for drug discovery"

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TBI is recognized as the “signature wound” of the conflicts in Iraq and Afghanistan, and the high profile sports injuries and suicides of the last few years. An estimated 1.4 million TBI occur each year in the US, and approximately 5.3 million individuals are living with disabilities as a result of TBI. The dramatic long term health consequences of TBI have long been known to confer increased risk for neurodegenerative disease, and are now recognized as a major health concern. Our team has a long history of research in Alzheimer’s disease (AD), encompassing identification of the first genetic causes of AD (mutations in the APP gene) through target identification and drug discovery to an ongoing Phase III clinical trial in Europe with a repurposed pharmaceutical. Our interest in TBI grew from epidemiological data linking AD and TBI, and from the known risk conferred to both conditions by the APOE gene. For the last several years we have focused on the importance of mild TBI, and in particular repetitive mTBI. To that end we developed a novel mouse model of repetitive mTBI, and characterized this model neurobehaviorally and pathologically over the mouse lifespan (2 years post-TBI) demonstrating that repetitive versus single injury results in persistent cognitive deficits and progressive neuroinflammatory changes in the brain. Most recently we developed a chronic repetitive mTBI model, which demonstrates persistent TBI-dependent tau pathology (something which has proved elusive in the preclinical TBI research field) which we consider will be of great value for investigations of the pathogenic role of tau in TBI and in Chronic Traumatic Encephalopathy in particular. Both models are suitable platforms for therapeutic target identification and drug discovery, and we have been conducting preclinical studies of potential therapeutics in our mouse models of TBI, including a derivative of the AD drug we have in clinical trial, and a very potent anti-inflammatory compound. Both have shown efficacy in our models and we are pursuing further studies to advance these toward clinical testing. We continue to explore additional variables of relevance to human TBI, such as APOE genotype and dietary influences, in order to best facilitate translational research.

Recent Publications:
