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TITLE: Molecular & Genetic Investigation of Tau in Chronic Traumatic Encephalopathy

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<b>14. ABSTRACT</b> Repetitive mild TBI leads to chronic traumatic encephalopathy (CTE), but the underlying molecular changes remain unclear. Here, biochemical and genetic studies that deepen our understanding of the pathogenesis of CTE will be performed, facilitating diagnosis and therapeutic development. This award has been in the transfer process from Columbia University to the Icahn School of Medicine at Mount Sinai until 10/28/2015, thus no funds have been available to initiate the project. Now that funds are available, work will commence.					
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**INTRODUCTION:**

Repetitive mild traumatic brain injury leads to neurological symptoms and chronic traumatic encephalopathy (CTE). The molecular changes underlying CTE are unknown, but our data demonstrate a spectrum of pathology with accumulation of aggregates of the microtubule-associated protein tau. Our preliminary data indicates an association between CTE and the tau gene (*MAPT*) H1 haplotype. How *MAPT* haplotypes contribute to CTE is unclear, but differences in transcription, mRNA splicing and translation may participate. The objective of this proposal is to validate the association of CTE with *MAPT* and characterize differences the expression of tau protein and tau-associated proteins in CTE patients. We hypothesize that the tau H1 haplotype increases CTE risk by increasing expression of abnormal tau. We will test this hypothesis by performing biochemical and genetic studies of CTE. Understanding the mechanisms that underlie changes in tau in CTE will enable biomarkers and treatments. These studies will deepen our understanding of how genetic and biochemical alterations in tau contribute to CTE, facilitating diagnosis and therapeutic development.

**KEYWORDS:**

Chronic traumatic encephalopathy, tauopathy, tau haplotype, *MAPT*, tau isoform

**ACCOMPLISHMENTS:**

*Nothing to report\**

**IMPACT:**

*Nothing to report\**

**CHANGES/PROBLEMS:**

*Nothing to report\**

**PRODUCTS:**

*Nothing to report\**

**PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS**

*Nothing to report\**

**APPENDICES:**

*Nothing to report\**

**\*NOTE:** This award had been in the transfer process from Columbia University Medical Center to the Icahn School of Medicine at Mount Sinai until 10/28/2015. As such, no funds were available to conduct any work. As such, no financial report is included. The project will now commence given the very recent successful transfer of the award.