The Neuroscience Graduate Program

presents:

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Advisor:

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in a PhD Thesis Defense

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11:00am in Auditorium K-207(2-6408)

The Role of Transglutaminase 2 in Neuronal Viability

Neuronal viability is dependent on various pathways induced by the extracellular environment. If these pathways are disturbed neurons are more susceptible to injury. A protein necessary for the survival of neurons is transglutaminase 2 (TG2). TG2 is a ubiquitously expressed, multifunctional protein present in the central nervous system. Previous studies from the lab demonstrate that expression of TG2 in neurons is protective after an ischemic injury, while expression of TG2 in astrocytes is detrimental.

The aim of this project was to further elucidate the role of TG2 in neurons during ischemic and normoxic conditions. Previous work has shown that the subcellular localization of TG2 can influence TG2's role in cell viability. Is important to note that the localization of TG2 is dependent on the cellular stressor. We explored the localization pattern of TG2 in neurons and astrocytes in response to hypoxia. We have found that the total levels of TG2 are increased in neurons in response to hypoxia, while they remain unchanged in astrocytes. Also, neuronal TG2 nuclear levels are increased after hypoxia, but astrocytic nuclear TG2 levels are reduced. TG2's role after hypoxia seems to be cell dependent.

In order to further explore the role of TG2 in neurons we investigated the effects of TG2 depletion in cell viability. We show that depletion of TG2 causes a robust decrease in cell survival. In order to expand upon this finding, high throughput next generation sequencing was used to assess the expression of genes in neurons depleted of TG2. We found that genes involved in extracellular matrix organization and focal adhesion were upregulated. Also, we found that depletion of TG2 reduces the length of neurites.

These studies have broadened our understanding of the required mechanisms to maintain neuronal cell integrity and of TG2's contributions to cell survival. This new understanding will allow us to develop new therapies.