

**Stony Brook University
The Graduate School**

Doctoral Defense Announcement

Abstract

The role of annexin II in tPA-dependent microglial activation

By

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Overt neuronal excitation in the course of many different neurodegenerative diseases can lead to neuronal dysfunction and death, a process termed excitotoxicity. Experimentally, this process can be mimicked by injection of excitatory pharmacological agents into the brains of rodents. Mice deficient in the serine protease tissue Plasminogen Activator (tPA) are more resistant to such agents and protected from neuronal death. This is partially attributed to the perturbed function of the brain resident immune cells, the microglia. Microglia respond to brain injuries of variable nature in a stereotypical process called activation, which can exacerbate the injury, potentially in an attempt to prevent the development of secondary dysfunction resulting from survival of injured neurons. tPA acts as a message, or cytokine, on microglia allowing them to become activated. The microglial protein annexin II has been implicated as the cell surface binding partner for tPA that mediates this cytokine-like function.

In the current study we investigated whether annexin II is present on the surface of microglia, whether it interacts with tPA physically and if microglia which do not express annexin II show activation defects similar to those of tPA deficient ones. We studied the expression of tPA and annexin II and the secretion of tPA in the temporal course of microglial activation. Demonstration of the presence of annexin II on the microglial cell surface and of the physical interaction of annexin II with tPA proved technically challenging. Microglia with lower or no expression of annexin II exhibited, although inconclusively, a slight overactivation compared to wild type ones. The nature of the microglial cell surface binding partner for tPA is still under investigation.

Date: March 16, 2007

Time: 1:00 pm

Place: BST, T8-180

Program: Molecular and Cellular Pharmacology

Dissertation Advisor: Stella E. Tsirka, PhD