

[SYM-M-034] REGULATION OF PLASMINOGEN ACTIVATOR ACTIVITY IN THE CENTRAL NERVOUS SYSTEM

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The regulation of proteolytic activity within the central nervous system (CNS) is essential in both normal and pathological processes. However, the precise role that proteolysis plays in the CNS is not well established. Recent work from many laboratories has indicated that the serine protease tissue-type plasminogen activator (tPA) is involved in a number of important processes both during development and in the adult brain. These include events associated with synaptic plasticity such as long term potentiation (LTP), motor learning and anxiety-like behavior, all processes which are thought to involve synaptic remodeling. TPA has also been implicated in neuronal death following excitotoxic injury, seizure and stroke. The primary inhibitor of tPA within the CNS is the serine protease inhibitor (serpin) neuroserpin. The tissue distribution of neuroserpin indicates that it is predominantly expressed in neurons in areas where either tPA message or activity has also been localized. Neuroserpin is also found in areas known to have the highest susceptibility to ischemic injury, and neuroserpin is neuroprotective in stroke and seizure. Like tPA, neuroserpin has also been suggested to regulate anxiety-like behavior since both over-expression and complete deficiency of neuroserpin in mice results in anxiety-like behavior and neophobia. These data suggest that tPA and neuroserpin can rapidly and directly regulate activity-dependent neuronal processes possibly through associations that promote synaptic remodeling and/or enhanced synaptic transmission. This talk will examine this general hypothesis by addressing the basic cell biology of tPA and neuroserpin in the CNS. The subcellular localization and regulated secretion of neuroserpin and tPA will be examined. Lawrence DA. REGULATION OF PLASMINOGEN ACTIVATOR ACTIVITY IN THE CENTRAL NERVOUS SYSTEM. *J Thromb Haemost* 2007; **5** Supplement 2: SYM-M-034

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