Regulation of Metabotropic Glutamate Receptor Scaffolded Signaling Complexes

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Canada

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Regulation of Metabotropic Glutamate Receptor Scaffolded Signaling Complexes

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Research Abstract

Glutamate is the major excitatory neurotransmitter in the brain. Glutamate acts via two types of glutamate receptors families expressed at connections between neurons and allows for the transmission of information from one neuron to the next and is essential for memory and learning. This proposal focuses on the mechanism(s) by which the activity of metabotropic glutamate receptors is regulated by proteins that interact with these receptors inside of the cell. Alteration in the cellular regulation of metabotropic glutamate receptors has been associated with neuronal cell death in a variety of neurodegenerative diseases including: Huntington’s disease, Parkinson’s disease and Alzheimer’s disease. The present proposal focuses on

proteins that we have identified to interact with glutamate receptors and how these interactions affect the activity of the receptor proteins. Specifically, we have identified two important regulators of neuronal function that have been linked to memory and learning as glutamate receptor binding proteins (calmodulin-dependent protein kinase II and spinophilin). We propose to : 1) identify where these proteins interact the receptors to develop inhibitory peptides, 2) how they contribute to regulating the function of these receptors, and 3) to determine whether a loss of protein expression might effect cellular mechanisms underlying memory and learning. In addition, we propose to assess the contribution of glutamate receptors to the pathology associated with Alzheimer's disease in a Alzheimer mouse model. Specifically, we will assess whether glutamate receptor expression is upregulated in Alzheimer's disease and whether a loss of glutamate receptor expression will slow disease progression in mice. Understanding the role of mGluR signaling in Alzheimer's disease is essential for the development of new therapeutic targets for the treatment of Alzheimer's disease.

Further information available at:

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