The Importance of Endocytosis to Neuregulin1 Back Signaling: Implications in Neuropsychiatric and Neurodegenerative Disorders

Massa, Scott

There is currently no cure for neurological disorders such as schizophrenia and Alzheimer’s disease. These disorders have been linked to impairments in critical cellular pathways including Neuregulin1 (Nrg1) back signaling, which regulates neuronal gene expression. This pathway may provide a new avenue for treating neurological disorders. The details of Nrg1 back signaling mechanisms are not understood, and it has been unclear whether endocytosis is required for effective Nrg1 back signaling. This study tested whether endocytosis is necessary for Nrg1 intracellular domain (ICD) translocation in ErbB4-mediated, depolarization-mediated, and basal level Nrg1 back signaling. ImageJ was used to quantify nuclear translocation of ICD based on confocal microscopy images after immunostaining and to quantify ICD production levels based on infrared images after protein immunoblotting. Endocytosis inhibition led to a statistically significant decrease in nuclear ICD levels in ErbB4-mediated Nrg1 back signaling samples ($P = 0.01$) while ICD production levels were consistent among all samples. In this study, it was demonstrated that deficits in ErbB4 endocytosis result in impaired ErbB4-mediated Nrg1 back signaling and may therefore be associated with the onset of neurological disorders. Deficient ErbB4 endocytosis is a cellular malfunction to be targeted for potential treatments or cures for schizophrenia and Alzheimer’s disease.

Awards Won:
Second Award of $2,000