

## Neurodegeneration

Other proteins of interest in our lab are the presynaptic proteins CSP $\alpha$ ; (cysteine string protein alpha) and  $\alpha$ -synuclein. CSP $\alpha$ ;, first discovered in *Drosophila*, is an abundant protein at nerve terminals known to function as a regulatory protein for Ca<sup>2+</sup>-dependent exocytosis. CSP $\alpha$ ; target chaperone complexes to attend other proteins in the process of folding (e.g. SNAP25), and hence facilitates the formation of the exocytotic machinery. While in humans mutations in the CSP gene cause autosomal-dominant adult onset neuronal ceroid lipofuscinosis, motor and sensory deficits are described in the mice that lack the protein. Such characteristics include massive lethal neurodegeneration of photoreceptors in the mouse retina that become apparent at P14 as monitored by ERGs.<http://www.pnas.org/content/103/8/2926.long>

Electrophysiological recordings of mouse motor nerve activity show that in the absence of CSP $\alpha$ ;, fast Ca<sup>2+</sup>-triggered release is not affected at postnatal day (P)14 but is dramatically reduced at P18 and P30 without a change in release kinetics during the third week of life. <http://www.ncbi.nlm.nih.gov/pubmed/18598257> On the other hand,  $\alpha$ -synuclein is a 14 kDa protein which mutation's (A30P, A53T, and E46K) causes the protein aggregations observed in synucleinopathies such as PD, AD and dementia with Lewy bodies. Although  $\alpha$ -synuclein KO mice are viable, past studies showed that due to its localization the protein has important functional roles in vesicle exocytosis and maintenance of nerve terminal function. Moreover, these functional properties of  $\alpha$ -synuclein become apparent under conditions of stress. Such example is the neuroprotective role of protein against neurodegeneration in CSP deficient mice emphasized by the overexpression of  $\alpha$ -synuclein<sup>A30P</sup>. Our aim is to elucidate how the overexpression of this mutated form of  $\alpha$ -synuclein influences the neurodegeneration process.