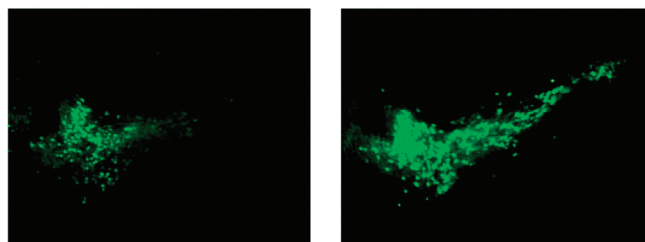


## Neuroprotection in Parkinson's Disease

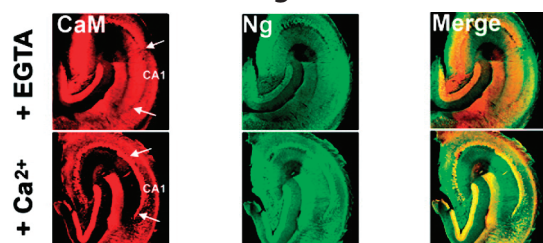


At present, there are no effective drugs for treating Parkinson's disease. In two research papers (DOI: 10.1021/cn1001107 and DOI: 10.1021/cn100109k), researchers led by Philip LoGrasso demonstrate that a novel inhibitor of a kinase enzyme is the first orally bioavailable, brain-penetrant small molecule that shows neuroprotection in mouse and rat models of Parkinson's disease.

A hallmark of Parkinson's disease is the loss of dopaminergic neurons in the substantia nigra pars compacta with projecting nerve fibers in the striatum. In cultured cells, the small molecule demonstrated protection against induced cell death. Further, in rodent models of Parkinson's disease, the small molecule protected primary dopaminergic neurons exposed to a neurotoxin. In addition, the neuroprotection resulted in reduction of dysfunctional motor responses characteristic of Parkinsonism.

The two studies describe a first-in-class small molecule which shows great promise as an early stage lead in the development of effective drugs for the treatment of Parkinson's disease.

## Calmodulin and Neurogranin Interactions



Two abundant neuronal proteins calmodulin and neurogranin are found in the forebrains of animals. The interactions between these proteins are involved in regulating synaptic response and plasticity. In mice, deleting the gene encoding for neurogranin causes deficits in cognition as well as behavioral aberrations. Now, Huang and Huang (DOI: 10.1021/cn200003f) investigate interactions between calmodulin and neurogranin in hippocampal neurons.

The authors utilize a low-calcium model of epilepsy in hippocampal slices and discover that these two proteins undergo calcium-sensitive translocation between soma and dendrites of hippocampal CA1 pyramidal neurons. Reducing the concentration of extracellular calcium causes a transient neuronal excitation concomitant with reduction of intracellular combination. Together, these may signal the movement of calmodulin and neurogranin, resulting in epileptic manifestations.