

Synaptic vesicle recycling and Parkinson's disease

<https://www.neurodegenerationresearch.eu/survey/synaptic-vesicle-recycling-and-parkinson%c2%92s-disease/>

Name of Fellow**Institution****Funder**

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Contact information of fellow**Country**

EC

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Synaptic vesicle recycling and Parkinson's disease

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Parkinson's disease & PD-related disorders

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Synapse | neurotransmitter | vesicle cycle | Pink1 | Parkinson | reactive oxygen species | nitric oxide | NOA1 | α -Synuclein | Drosophila

Research Abstract

The nervous system consists of a complex network of neurons interconnected by chemical synapses. Recycling of neurotransmitter filled vesicles at these synapses enables neurons to maintain communication during periods of intense activity. There is accumulating evidence that

synaptic dysfunction is, at least in part, responsible for common neurodegenerative diseases such as Alzheimer's, Huntington's and Parkinson's disease. I therefore set out to find genes involved in the synaptic pathogenesis of these diseases by performing a forward genetic screen in *Drosophila melanogaster*. I isolated more than 86 mutants in a screen for non-canonical vesicle recycling and found that one of the them genetically interacts with the Parkinson's related gene *pink1* in a secondary screen. I mapped this mutation to the *Drosophila* ortholog of NOA1, a conserved gene encoding a mitochondrial protein whose function remains largely enigmatic. Since both proteins, PINK1 and NOA1 are reported to localize in mitochondria and interact with Complex I of the respiratory chain, I hypothesize that they function in the same pathway. Here, I describe experiments to determine the exact nature of the interaction between *Drosophila* PINK1 and NOA1 and present plans to examine the molecular function of *Drosophila* Noa1 at the synapse. In addition, I will further characterize the remaining mutants for interactions with α -Synuclein, a protein known to be involved in Parkinson's disease. In this way, I will find new components of the vesicle recycling machinery that interact with Parkinson's disease-related proteins which will not only further our understanding of the mechanisms underlying synapse function, but also identify possible new therapeutic targets for this disease.

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