Reconstitution of Exocytosis Using Synthetic Vesicles in Intact Cells

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Neurons communicate with each other by the release of small molecules, the neurotransmitters. Upon arrival of an action potential within a nerve terminal, voltage-gated calcium channels open and trigger exocytosis of synaptic vesicles, during which the stored transmitter molecules are discharged. In recent years, the molecular components responsible for exocytosis have been identified. However, it is still unclear how these proteins cooperate to mediate exocytosis. To better understand how the proteins mediating exocytosis operate, the reconstruction of exocytosis in a "naive" cell is planned. Two doctoral students will carry out the experiments using an approach to micro-inject either purified native secretory vesicles or artificial vesicles containing defined components into intact cells and monitor the conditions under which these vesicles are capable of docking and fusion. Jahn's project expects fundamental insights into the requirements of vesicle docking and fusion in general and into the specific conditions for calcium-dependent exocytosis in neurons.

Jahn's team plans to reconstruct regulated, neuron-like exocytosis by testing the hypothesis as to whether it suffices to equip a non-neuronal cell with the correct SNARE proteins required for exocytosis in order to reconstitute calcium regulated

exocytosis of artificially introduced vesicles. It is hoped that this project will provide answers to basic and longstanding questions in the field, including what it takes to convert a standard, non-secretory cell into a cell capable of undergoing regulated exocytosis, and furthermore, what the minimal requirements for a vesicle to function as a synaptic/secretory vesicle in calcium-dependent exocytosis are.

The project will be carried out in the Department of Neurobiology at the Max Planck Institute for Biophysical Chemistry, Göttingen, Germany. Two doctoral students will work collaboratively under the supervision of the Principal Investigator, Reinhard Jahn. The first student will be mainly involved with the generation, characterization and labeling of the vesicles. This part will also involve in-vitro imaging of the vesicles after surface immobilization. The second student will mainly carry out microinjection experiments and perform the microscopic analysis for vesicle transport, docking and fusion.

The start of the project was set as 1 October 2017, and it is planned to end in the fall of 2020. Results of this work will be published in peer-reviewed scientific journals, and the Balzan Foundation will be acknowledged as funding source.