

Catherine McKENZIE

Thesis supervisor: Harald JANOVJAK

MolTag Associate Student, Institute of Science and Technology Austria

Defensio: 08. August 2018

Title of the PhD thesis:

Design and characterization of methods and biological components to realize synthetic neurotransmission

Abstract

A major challenge in neuroscience research is to dissect the circuits that orchestrate behavior in health and disease. Proteins from a wide range of non-mammalian species, such as microbial opsins, have been successfully transplanted to specific neuronal targets to override their natural communication patterns. The goal of our work is to manipulate synaptic communication in a manner that closely incorporates the functional intricacies of synapses by preserving temporal encoding (i.e. the firing pattern of the presynaptic neuron) and connectivity (i.e. target specific synapses rather than specific neurons). Our strategy to achieve this goal builds on the use of non-mammalian transplants to create a synthetic synapse. The mode of modulation comes from pre-synaptic uptake of a synthetic neurotransmitter (SN) into synaptic vesicles by means of a genetically targeted transporter selective for SN. Upon natural vesicular release, exposure of the SN to the synaptic cleft will modify the post-synaptic potential through an orthogonal ligand gated ion channel. To achieve this goal we have functionally characterized a mixed cationic methionine-gated ion channel from *Arabidopsis thaliana*, designed a method to functionally characterize a synthetic transporter in isolated synaptic vesicles without the need for transgenic animals, identified and extracted multiple prokaryotic uptake systems that are substrate specific for methionine (Met), and established a primary/cell line co-culture system that would allow future combinatorial testing of this orthogonal transmitter-transporter-channel tripartite.

Synthetic synapses will provide a unique opportunity to manipulate synaptic communication while maintaining the electrophysiological integrity of the pre-synaptic cell. In this way information may be preserved that was generated in upstream circuits and that could be essential for concerted function and information processing.

About the Author

Catherine McKenzie completed her BSc in General Biology with an emphasis on Neuroscience at the University of California, San Diego in combination with internships at the Space and Naval Warfare Systems Outreach Division (SPAWAR) at the US Department of Defense and Scripps Institute of Oceanography as well as implementing science education outreach programs in San Diego before joining IST in September 2011. Her main research interests lie in approaching old problems in new ways by designing and building biological methods to specifically address how tangible elements of the mammalian brain translate to cognitive processes and behavioral output. During her PhD studies she has published a springer book chapter on methodology of implementing light-gated ion channels in neuroscience research. As well as being a part of the IST doctoral program, Catherine was accepted as an Associate PhD student in the Molecular Drug Targets doctorate program funded by the Austrian Science Fund in Vienna, Austria in 2015. She was awarded the golden sponge for outstanding Teacher's Assistant in 2014 at IST. She has presented her work at a range of scientific platforms including the Casual Neuroscience FENS-IBRO Summer School in Bertinoro, Italy in 2013, the Gordon Research Seminar and Conference in Synaptic Transmission in the United States in 2016 as well as at the Society for Neuroscience conference in the United States in 2017. She was an invited speaker at the March for Science in Vienna 2017 and gave a Young Scientist Invited talk at the Joint meeting of Austrian Neuroscience Excellence Network in Alpbach, Austria in 2018.