

# RUB

## SEMINAR ANNOUNCEMENT

### TUESDAY, 24.10.2017 16:15 h ZEMOS

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#### "Mimicking Neuroligin-2 (NL-2) Functions in β-Cells as a Novel Approach for Antidiabetic Therapy"

Both pancreatic  $\beta$ -cell membrane and presynaptic active zones of neurons are the assembly sites of similar protein complexes mediating regulated secretion of bioactive molecules. These synapse-inducing proteins include neuroligins and their binding partners: neurexins. Similar to other synaptic adhesion molecules, these proteins participate in trans-cellular protein-protein interactions across the synaptic cleft. It was shown that  $\beta$ -cells express both neuroligins and neurexins on their plasma membrane. It was also found that insulin secretion and the proliferation rate of  $\beta$ -cells increased when  $\beta$ -cells were co-cultured with cells overexpressing neuroligins. Building on these results, we propose that neuroligin-derived molecules arranged in clusters can enhance  $\beta$ -cell functions, thereby increasing glucose-stimulated insulin secretion and functional maturity, as well as protecting  $\beta$ -cells in stress conditions. To test this hypothesis, several peptides were derived from crystal structures of different neuroligins and neurexins using molecular modelling methods. These peptides were conjugated with nanoscale composite particles. One of the compounds (polyamine based nanoparticles covered by NL-2 derived peptide) enhanced  $\beta$ -cell functions in terms of glucose-stimulated insulin secretion and protects them under stress conditions. Recruiting the  $\beta$ -cells' "neuron-like" secretory machinery as a target for diabetes treatment use has never been reported before. Such nanoscale composites might therefore provide a unique starting point for designing a novel class of antidiabetic therapeutic agents that possess a unique mechanism of action.

Guests are very welcome!