

Interaction Partners and Signaling of Nogo

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Reticulons (RTNs) gained increasing attention in the recent years due to their involvement and crucial role especially in neurodegenerative diseases. RTNs are endomembrane bound proteins with a uniquely conserved C-terminal Reticulon homology domain (RHD), via which they anchor themselves to membrane compartments, in particular endoplasmic reticulum (ER).

Amongst reticulons, myelin associated RTN-4/Nogo proteins are well characterized members of the RTN protein family, shown to impair axonal regeneration after brain insult and to restrict neuronal plasticity in the intact adult mammalian nervous system. In addition to its role in the injured mammalian CNS, Nogo-A acts as a regulator of neuronal growth and plasticity in the intact CNS. On the other hand, despite the data accumulated from *in vivo* studies, confined to the minor fraction of Nogo residing on the cell membrane, the intracellular biological function of Nogo *in neurons* remained elusive, leaving the function and significance in cellular and molecular mechanisms largely unknown. Sourcing from the studies with non-neuronal cells, however, current literature suggest localization for Nogo to the endomembrane system, and roles in regulation of membrane curvature, and a function in membrane trafficking and in endo-/exocytosis pathways.

To further investigate these hypotheses and to unravel possible molecular mechanisms of Nogo function in neurons, we aimed to identify interaction partners of Nogo.

For this purpose, we performed pull-down assays using NiR, the N-terminal domain of Nogo-A and Nogo-B. Purified recombinant Nogo domain fusion protein NiR was used as bait to interact with proteins from mouse brain preparations. The pull-down products were analyzed by Mass Spectrometry (MS). This approach identified a set of proteins, majority of which had been classified as signal transduction, cytoskeleton dynamics related, and synaptic-vesicle and vesicle trafficking (endocytosis/exocytosis) associated. Identification of these novel putative Nogo interaction partners belonging to such pathways, provide support to the notion that Nogo proteins are critical in these cellular mechanisms.

Currently, in-detail biochemical/molecular characterization of Nogo interaction with those selected proteins from putative potential interactors are being investigated and physiological relevance of these interactions is addressed.

With the body of knowledge obtained, we aim to shed light on the functional role and physiological significance of Nogo interactions in neurons, and to narrow the gap of knowledge of how does Nogo function at a cellular level, most likely via the associated subcellular structures like endoplasmic reticulum, and related cellular mechanisms, such as endocytosis and exocytosis.