Synapse-to-nucleus signalling and activation of synaptic NMDA receptors: role in neurodegenerative diseases

F. Gardoni

DiSFeB, Dept. Pharmacological and Biomolecular Sciences, University of Milano, 20133, Milano, Italy

Multiple synapse-to-nucleus signaling pathways arise from dendritic spines and converge to the nucleus to regulate activity-dependent gene expression that is associated with long-term functional changes of synapto-dendritic input. Here, we identified Ring Finger Protein 10 (RNF10) as a novel synaptonuclear protein messenger. RNF10 is activated by specific calcium signals at the postsynaptic compartment and elicits discrete changes at the transcriptional level. RNF10 is highly enriched at the excitatory synapse where it directly associates with the GluN2A subunit of N-methyl-D-aspartate receptors (NMDARs). Activation of synaptic GluN2A-containing NMDARs and induction of Long-Term Potentiation (LTP) lead to the translocation of RNF10 from distal dendritic segments and dendritic spines to the nucleus and result in the increase of expression of newly identified RNF10 target genes. Notably, RNF10 silencing prevents the maintenance of LTP as well as LTP-dependent structural modifications of dendritic spines. Notably, preliminary results from our laboratory indicate an alteration of RNF10 expression in models of neurodegenerative diseases such as Parkinson Disease and Alzheimer's Disease.