A novel spine-to-nucleus signalling pathways involved in plasticity and diseases

M. DiLuca

Dept of Pharmacological and Biomolecular Sciences, University of Milan

Among the cellular mechanisms required for modifications of dendritic spines, synapse-to-nucleus communication plays a key role in the regulation of the long-term structural changes.These changes are crucial to maintain plasticity and have been indicated as early synaptic trait in neurodegenerative diseases. Emerging evidence indicates that multiple signalling pathways arising from dendritic spines converge to the nucleus regulating the expression of genes associated with changes of synapto-dendritic inputs. In the last decade, few synapto-nuclear protein messengers have been identified, and shown to play key roles in plasticity and synapse function. We recently identified Ring Finger Protein 10 (RNF10) as a new synapse-to-nucleus molecule, which responds to specific calcium signals at the postsynaptic compartment to elicit discrete changes at the transcriptional level. RNF10 is highly enriched at the excitatory synapse where it is associated to the GluN2A subunit of NMDA receptors. RNF10 is also present in the nucleus, where it is known to associate with Mesenchyme Homeobox 2 (Meox-2) transcription factor. Activation of synaptic NMDA receptors leads to RNF10 translocation from dendritic spines to the nucleus and induction of the expression of RNF10 target genes. Interestingly, modulation of RNF10 expression levels plays a fundamental role in regulating excitatory spine morphology under resting conditions as well as following activity-dependent synaptic plasticity.