RNF10 role in synaptic plasticity

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RNF10 is a synaptonuclear messenger involved in the NMDA receptors (NMDAR) signaling cascade. RNF10 binds to the C-terminal region of the GluN2A subunit of the NMDAR and its translocation from the synapse to the nucleus translates synaptic NMDAR activation into gene expression changes. RNF10 is crucial in the physiology of the neurons, being involved in Long Term Potentiation (LTP) dependent modulation of dendritic spine morphology and in shaping of the dendrite's architecture in hippocampal neurons. In addition to its synaptonuclear role, RNF10 works as an E3 ubiquitin ligase. It is involved in the initial ribosome quality control (iRQC) in protein translation, by ubiquitinating the 40S ribosomal subunit in cell lines. Our study explored for the first time the role of RNF10 as an ubiquitin ligase in primary hippocampal neurons. Surface Sensing of Translation (SUnSET) experiments and general ubiquitin analyses were conducted to assess RNF10's impact on protein translation in synaptic plasticity events, a higly demanded process for protein translation. These experiments showed that RNF10 may modulate general ubiquitination levels in rat primary hippocampal neurons and may have an effect in protein regulation. Reviewing other members of the RNF family, we observe that RNF10's function as an E3 ubiquitin ligase could align the roles of RNF20 and RNF40, which are known to regulate gene expression through histone ubiquitination. This led us to hypothesize that RNF10, after shuttling from the synapse to the nucleus, could similarly influence epigenetic mechanisms. To investigate this, we performed biochemistry experiments to asses histone ubiquitination levels in RNF10 knockout (KO) mice compared to wild-type controls. In summary, RNF10 impacts neuronal ubiquitination and protein regulation, and its relationship with NMDAR in synapses suggests it could be a key target to study in pathologies such as Alzheimer's Disease (AD) due to its effect disrupting the synapses.