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The Role of Protein Kinase N1 in Hippocampal Synapse Development

Abnormalities in the mechanisms that control α-Amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor (AMPAR) expression, assembly and trafficking lead to psychiatric and neurodegenerative disorders. According to our previous findings, the serine/threonine kinase Protein kinase N1 (PKN1) is a developmentally active regulator of cerebellar synaptic maturation by inhibiting AKT and the neurogenic transcription factor neurogenic differentiation factor-2 (NeuroD2). NeuroD2 is implicated in glutamatergic synaptic maturation by regulating expression levels of various synaptic proteins. Here we show how the absence of PKN1 acts on AKT phosphorylation and NeuroD2 levels in the hippocampus and the subsequent expression levels of the NeuroD2 targets and AMPAR subunit glutamate receptor 1 (GluA1). We show that PKN1 is expressed throughout the hippocampus. Postnatal and adult Pkn1 knockout (Pkn1–/–) hippocampi showed enhanced AKT phosphorylation, NeuroD2 levels, and also the AMPAR subunit GluA1 expression, particularly in area CA1. In contrast, GluA2/3 levels were not different between both genotypes. Moreover, we showed that the GluA1 content in the membrane fraction of postnatal and adult Pkn1–/– hippocampi were enhanced, while GluA2/3 levels remained unchanged. Our results point to a specific regulation of GluA1 expression and/or trafficking by the novel PKN1-AKT-NeuroD2 axis. In view of the important role of GluA1 in hippocampal development as well as the pathophysiology of several disorders, ranging from Alzheimer's, to depression and schizophrenia, our findings establish PKN1 as a target for future studies into neurological disorders related to altered AMPAR subunit expression in the hippocampus.

Biography

Motahareh Safari has compeleted her M.Sc in biotechnology at the age of 26 years at the Technical University of Graz. During her master thesis: she worked on the role of Agrin22 and Agrin15 overexpression in the synapse formation. She is currently doing her PhD in Neuroscience at the Medical University of Innsbruck in the Institute of Neurobiochemistry. The aim of her dissertation is to evaluate the role of Protein Kinase 1 (PKN1) as neuronal checkpoint in neurodevelopment and pathogenesis.