IMPACT, A TRANSLATIONAL REGULATOR, IS PRESENT IN GROWTH CONES AND SYNAPSIS

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Synaptogenesis and synaptic plasticity are dependent on the synthesis of new proteins. One mechanism underlying regulated translation in neurons is the phosphorylation of eukaryotic Initiation Factor 2 (eIF2), which reduces general translation but increases translation of a specific class of mRNAs, such as ATF4/CREB-2 mRNA. GCN2 is one of the four different eIF2 kinases in mammalian cells and is activated by amino acid starvation. Recently, GCN2 was implicated in the control of synaptic plasticity and memory. We previously described that IMPACT, a protein preferentially expressed in the mouse brain, is a GCN2 inhibitor. In this work we studied the subcellular distribution of IMPACT in hippocampal neurons. IMPACT is found in the cytoplasm presenting a punctate pattern, and more interesting, in axonal growth cones (GC). GC are motile structures present in neurite tips, directing the development of synapses. In GC, IMPACT is enriched in the peripheral zone and filopodia, co-localizing with F-actin. Furthermore, we detected IMPACT in GC-enriched sub-cellular fractions, confirming the above results. Synapses, like GC, need a tight regulation of protein synthesis, and IMPACT could be involved in such a control. Accordingly, we found IMPACT and GCN2 in synaptosomes, a fraction enriched in pre- and post-synaptic elements. These results suggest that IMPACT, could be involved in the control of local protein synthesis and a possible interaction of IMPACT with the actin cytoskeleton.

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