Guanine nucleotide exchange factor

Guanine nucleotide exchange factors (GEFs) are proteins or protein domains that activate monomeric GTPases by stimulating the release of guanosine diphosphate (GDP) to allow binding of guanosine triphosphate (GTP).

A variety of unrelated structural domains have been shown to exhibit guanine nucleotide exchange activity. Some GEFs can activate multiple GTPases while others are specific to a single GTPase.

Guanine nucleotide exchange factors (GEFs) play important roles in many cellular processes, including regulation of the structural plasticity of dendritic spines. A GEF protein, adenomatous polyposis coli-stimulated GEF 1 (Asef1, ARHGEF4) is highly expressed in the nervous system. However, the function of Asef1 has not been investigated in neurons.

Oh et al., present evidence showing that Asef1 negatively regulates the synaptic localization of postsynaptic density protein 95 (PSD-95) in the excitatory synapse by inhibiting Staufen-mediated synaptic localization of PSD-95. Accordingly, Asef1 expression impairs synaptic transmission in hippocampal cultured neurons. In addition, neuronal activity facilitates the dissociation of Asef1 from Staufen in a phosphoinositide 3 kinase (PI3K)-dependent manner. Taken together, our data reveal Asef1 functions as a negative regulator of synaptic localization of PSD-95 and synaptic transmission [1)].

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Oh JY, Lim CS, Yoo KS, Park HJ, Park YS, Kim EG, Lee YS, Kaang BK, Kim HK. Adenomatous polyposis coli-stimulated GEF 1 (Asef1) is a negative regulator of excitatory synaptic function. J Neurochem. 2018 Aug 20. doi: 10.1111/jnc.14570. [Epub ahead of print] PubMed PMID: 30125942.