

Poster presentation

Characterization of MRIP2 as a NO-sensitive guanylyl cyclase-associated protein

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NO-sensitive guanylyl cyclases (sGCs) are cytosolic receptors for nitric oxide (NO) catalyzing the conversion of GTP to cGMP. sGCs are obligate heterodimers composed of one α and β subunit each. The allosteric mechanism of sGC activation via NO is well understood, however, our knowledge about alternative mechanisms such as protein-protein interactions regulating activity, availability, translocation and expression of sGC is rather limited. In a search by the yeast two-hybrid system using the catalytic domain of the α_1 subunit as the bait, we have identified two structurally related proteins AGAP1 [1] and MRIP2 as novel sGC interacting proteins. MRIP2 is a multi-domain protein of 75 kDa comprising a single PH and ArfGAP domain each and two ankyrin repeats. Co-immunoprecipitation experiments using COS1 cells overexpressing both proteins demonstrated the interaction of MRIP2 with both subunits of the sGC $\alpha_1\beta_1$. Confocal microscopical analysis showed a prominent plasma membrane staining of MRIP2. This membrane association is mediated through an N-terminal myristoylation site and through binding of its PH domain to phospholipids such as phosphatidylinositol-3,5-bisphosphate (PI(3,5)P₂). We hypothesize that MRIP2 may represent an acceptor protein for sGC that mediates recruitment of cytosolic sGC to the plasma membrane or other subcellular compartments.

References

1. Meurer S, Pioch S, Wagner K, Müller-Esterl W, Gross S: **AGAP1 – a novel binding partner of NO-sensitive guanylyl cyclase.** *J Biol Chem* 2004, **279**:49346-49354.