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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 ($PI(3,5)P_2$). 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

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