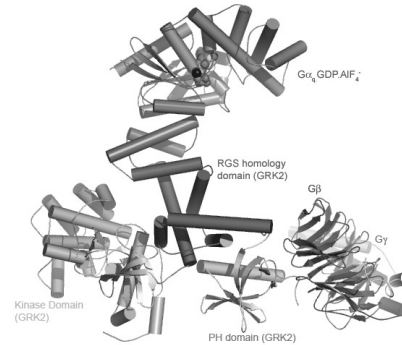


Structural Basis of Phosphorylation-Independent Desensitization of Gq-Coupled Receptors. Aruna Shankaranarayanan[‡], Valerie M. Tesmer[‡], Takeharu Kawano^{§§}, Tohru Kozasa[§] and John J. G. Tesmer[‡],
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G-protein coupled receptor kinase 2 (GRK2) desensitizes G-protein coupled receptor by phosphorylating activated receptors and sequestering activated G α and G $\beta\gamma$ subunits. Herein, we present the crystal structure of G α_q -GRK2-G $\beta\gamma$ complex that serves as a model for phosphorylation independent desensitization of GPCRs. In the structure, activated G α and G $\beta\gamma$ subunits are completely dissociated from one another and they are in an unusual orientation with respect to each other and with respect to the predicted cell membrane when compared to that of inactive G $\alpha\beta\gamma$ heterotrimer. The structure reveals that G α_q makes novel effector-like interactions with the RGS homology domain of GRK2 that also permits the binding of classic RGS proteins providing evidence for the assembly of higher order complex of GPCRs, GRK2, activated G α and G $\beta\gamma$ and RGS proteins at the cell membrane.



Reference: Snapshot of Activated G Proteins at the Membrane: The G α_q -GRK2-G $\beta\gamma$ Complex. Science 9 Dec 2005; 310: 1686-1690

Supported by: National Institute of Health, American Heart Association and American Cancer Society
We thank ALS for access to beam line 8.3.1.