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"Interaction of Membrane Cholesterol with G Protein-Coupled Receptors: Novel Insights in Health & Disease"

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*Refreshments begin at 2:00 PM

Abstract

G protein-coupled receptors (GPCRs) are the largest class of molecules involved in signal transduction across membranes, and represent major drug targets in all clinical areas. The serotonin$_{1A}$ receptor is an important neurotransmitter receptor of the GPCR superfamily and is implicated in the generation and modulation of various cognitive, behavioral and developmental functions. We previously demonstrated that membrane cholesterol is necessary for ligand binding, and G-protein coupling of serotonin$_{1A}$ receptors. Interestingly, recently reported crystal structures of GPCRs have shown structural evidence of cholesterol binding site(s). In this context, we reported the presence of cholesterol recognition/interaction amino acid consensus (CRAC) motifs in the serotonin$_{1A}$ receptor. We also showed that the receptor is more stable and compact in the presence of membrane cholesterol. Our recent results utilizing coarse-grain molecular dynamics simulations to analyze the molecular nature of receptor-cholesterol interaction offer interesting insight in cholesterol binding site(s) in the receptor and oligomerization of the receptor. We showed utilizing homo-FRET that the serotonin$_{1A}$ receptor is constitutively oligomerized in live cells, with the possibility of higher order oligomers of the receptor. Progress in deciphering molecular details of the nature of GPCR-cholesterol interaction in the membrane would lead to better insight into our overall understanding of GPCR function in health and disease.

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