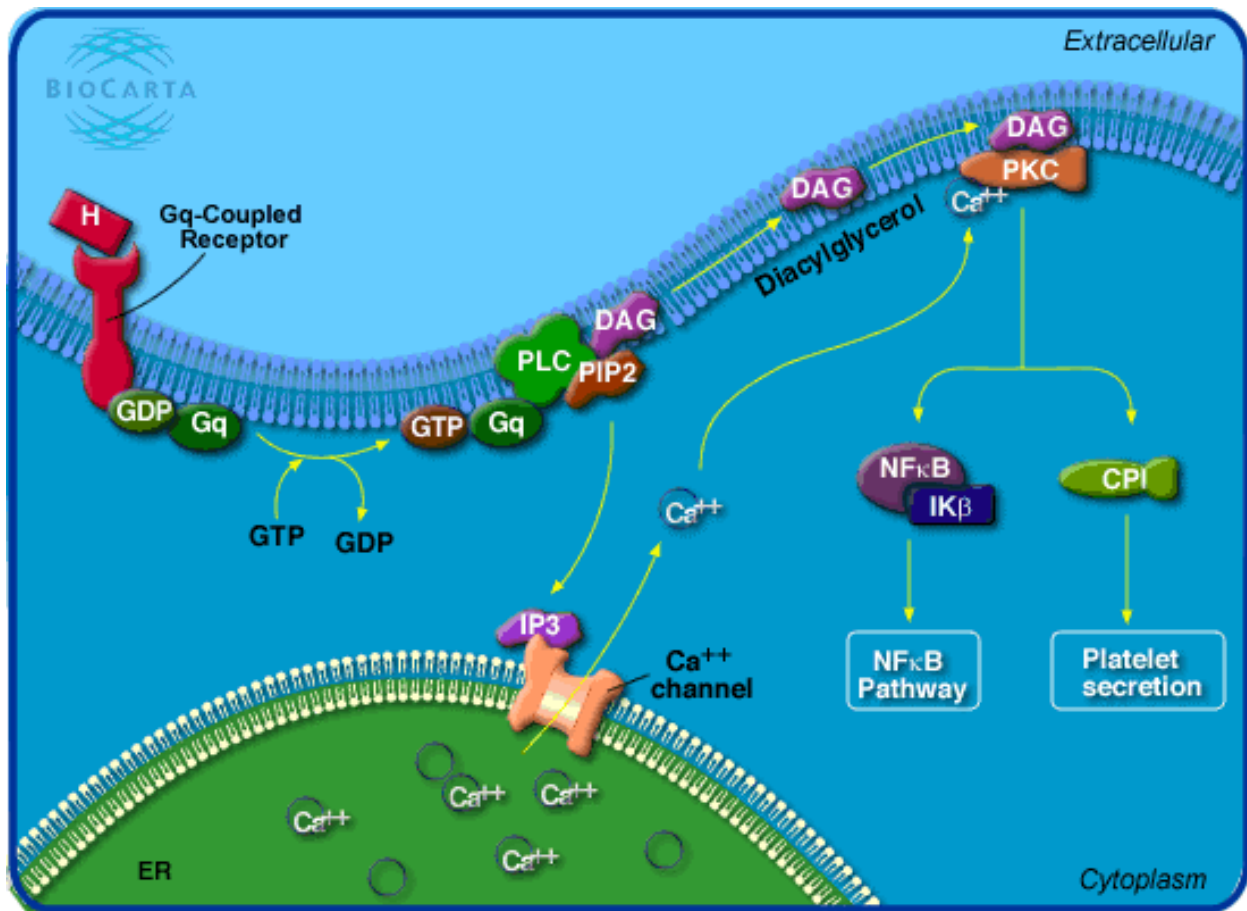


## PKC, Calcium & NFkB



G-protein coupled receptors (GPCRs) transduce a variety of signals from the extracellular environment across the plasma membrane. One of the common signaling systems utilized by GPCRs activates protein kinase C (PKC), a ubiquitous family of serine/threonine protein kinases. The pathway leading to PKC activation starts with a class of GPCRs that interact with and activate Gq G-proteins when the receptor has agonist ligand bound. GPCRs that act through Gq include some muscarinic acetylcholine receptors, many peptide receptors, and the 5-HT<sub>2</sub> serotonin receptors. Activated Gq with GTP bound activates its downstream target phospholipase C (PLC) to hydrolyze the membrane lipid PIP<sub>2</sub>, producing IP<sub>3</sub> and diacylglycerol (DAG). IP<sub>3</sub> is water-soluble and diffuses through the cytoplasm to the ER, where it binds to and opens a calcium channel, releasing calcium stores from inside the ER into the cytoplasm. Calcium alters many cellular processes, in part by binding to regulatory proteins such as calmodulin and calcineurin. The interaction of both DAG and calcium with PKC activates its kinase activity and the phosphorylation of many different protein targets alters their activity. The involvement of PKC in cellular proliferation and the cell cycle is indicated by the activity of tumor promoters like phorbol esters as PKC activators.