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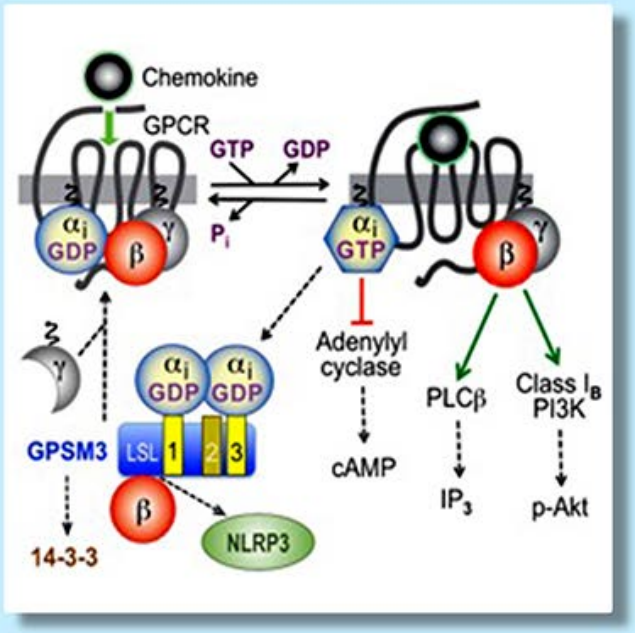

Model for GPSM3 Function in Regulating GPCRs

G-protein Signaling Modulator-3 Regulates Monocyte Survival

G protein signaling modulator 3 (GPSM3), a GoLoco family protein that regulates G protein coupling receptors (GPCRs), is highly expressed in immune cells, particularly monocytes. A single nucleotide polymorphism (SNP) at the GPSM3 gene locus was associated with a decreased incidence of autoimmunity in humans. Furthermore, Gpsm3-/- mice are protected from disease in two preclinical mouse models of rheumatoid arthritis, but the underlying mechanism of protection is currently unknown. Our published and preliminary data suggest that Gpsm3 expression levels impacts monocyte survival, which could explain why Gpsm3-/- mice fail to develop inflammatory disease. To directly test the impact of Gpsm3 on monocyte survival *ex vivo*, monocytes were differentiated from the bone marrow of wild type and Gpsm3-/- mice and treated with one of four chemokines (CCL2, CX3CL1, chemerin, and CXCL12) under apoptotic stress. Monocyte survival versus apoptosis was then measured. Preliminary results suggested that CX3CL1, chemerin and CXCL12 all protect against apoptosis in wild type monocytes, but fail to protect the Gpsm3-/- monocytes. Future directions involve identifying potential monocyte subpopulations with greater dependence on Gpsm3 for survival. Overall, Gpsm3 is critical to the development of monocyte inflammatory responses in both healthy and diseased states, and could impact future development of novel therapeutic targets for the treatment of arthritis in humans.