Intracellular signals employed by GHS-receptor in the regulation of pituitary growth hormone (GH) secretion

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GH is the most important anabolic hormone secreted from the pituitary somatotropes to regulate protein synthesis and adipolysis. Pituitary somatotropes secrete GH under the control of releasing hormones (GHRH and ghrelin) and inhibitory hormone (SRIF) through specific receptors (R) on the cell membrane. Ghrelin is a hormone synthesized in and released from stomach endocrine cells, and found in several regions including the hypothalamus of the brain, regulating GH secretion as well as food intake, energy consumption, and body composition. We studied effect of ghrelin and GHS-R in somatotropes aiming to find new treatment strategy for GH deficiency. Synthetic GH releasing peptides (GHRP) act on GHS-R, coupled to Gq protein, in somatotropes. GHRP activate phospholipase C (PLC)/PKC system. Activation of PLC increases production of inositol 1,4,5-triphosphate ($InsP_3$), leading to Ca^{2+} release from Ca^{2+} storage sites. Activation of PKC contributes to Ca^{2+} influx induced through modification of transmembrane voltage-gated ion channels. GHRP also activates the cAMP-PKA system to reduce inward rectifying K^+ currents, which leads to membrane depolarization and Ca^{2+} influx. Increase in intracellular Ca^{2+} ($[Ca^{2+}]_i$) activates the exocytosis process and release of GH from secretary granules. Ghrelin reduces membrane voltage-gated K^+ and Ca^{2+} currents in GH_3 cells, a rat somatotrope cell line, *via* a cGMP-dependent PKG signal pathway. Reduction in K^+ currents may contribute Ca^{2+}-influx through prolonged membrane depolarization. Reduction in Ca^{2+} currents may prevent over-loading of intracellular Ca^{2+} while constant stimulation of cells by ghrelin occurs.

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