An update on somatostatin receptor signaling in native systems and new insights on their pathophysiology

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Abstract

The peptide somatostatin (SRIF) has important physiological effects, mostly inhibitory, which have formed the basis for the clinical use of SRIF compounds. SRIF binding to its 5 guanine nucleotide-binding proteins-coupled receptors leads to the modulation of multiple transduction pathways. However, our current understanding of signaling exerted by receptors endogenously expressed in different cells/tissues reflects a rather complicated picture. On the other hand, the complexity of SRIF receptor signaling in pathologies, including pituitary and nervous system diseases, may be studied not only as alternative intervention points for the modulation of SRIF function but also to exploit new chemical space for drug-like molecules.

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Abbreviations: $[Ca^{2+}]_i$, intracellular Ca^{2+} concentration; A β , amyloid- β peptide; AD, Alzheimer's disease; CaMKII, Ca^{2+} /calmodulin-dependent protein kinase II; cdk, cyclin-dependent protein kinase; DEP/PTP, density-enhanced protein-tyrosine phosphatase; ERK, extracellular signal-regulated protein kinases; G proteins, guanine nucleotide-binding proteins; GH, growth hormone; GIP, GPCR-interacting proteins; GPCR, G protein-coupled receptors; GRK, GPCR protein kinases; GSK, glycogen synthase protein kinase; IKK, inhibitor κ B protein kinase; ILK, integrin-linked protein kinase; IP₃, inositol trisphosphate; MAP kinases, mitogen-activated protein kinases; PDK, phosphoinositide-dependent kinase; PI3 kinase, phosphatidylinositol 3 protein kinase; PKA, cAMP-dependent protein kinase; PKC, phospholipase C-dependent protein kinase; PKG, cGMP-dependent protein kinase; PP, serine/threonine phosphatases; RGS, regulators of G-protein signaling; r-PTP, receptor-like tyrosine phosphatase; SAPK/JNK, stress-activated protein kinase/c-Jun NH₂-terminal protein kinase; SHP, SH2 domain-containing cytosolic tyrosine phosphatase; SRIF, somatostatin or somatotropin release inhibiting factor; sst₁₋₅, somatostatin receptor 1 to 5.

Contents

1.	Introduction	323
2.	Somatostatin receptor signaling in native systems	323
2.1.	Adenylyl cyclase pathway	324
2.2.	Guanylyl cyclase/nitric oxide pathway	324
2.3.	Phospholipase C pathway	325
2.4.	Ca^{2+} modulation	325
2.5.	K^+ channels	326
2.6.	Phospholipase A ₂ pathway	327
2.7.	Na ⁺ /H ⁺ exchanger	327
2.8.	Phosphoprotein phosphatase pathway	327
2.9.	Mitogen-activated protein kinase pathway	328

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