Glucagon, glucagon-like peptide and secretin

Overview: The glucagon family of receptors (nomenclature as agreed by NC-IUPHAR Subcommittee on the Glucagon receptor family, see Mayo *et al*., 2003) are activated by the endogenous peptide (27–44 aa) hormones glucagon, glucagon-like peptide 1 (GLP-1), glucagon-like peptide 2 (GLP-2), glucose-dependent insulinotropic polypeptide (also known as gastric inhibitory polypeptide or GIP, ENSG00000159224), growth hormone-releasing hormone (GHRH, ENSG00000118702) and secretin (ENSG00000070031). One common precursor (ENSG00000115263) generates glucagon, GLP-1 and GLP-2 peptides (Irwin, 2001).

Nomenclature	Glucagon	GLP-1	GLP-2
Ensembl ID	ENSG00000141558	ENSG00000112164	ENSG00000065325
Principal transduction	G_s	G_s	G_s
Selective agonists	Glucagon	GLP-1-(7-37) (Dillon *et al*., 1993); GLP-1-(7-36)amide (Thorens *et al*., 1993), exendin-3 (Raufman *et al*., 1991), exendin-4 (Thorens *et al*., 1993)	GLP-2
Selective antagonists	L168049 (Cascieri *et al*., 1999), des-His[1]-[Glu[9]]glucagon amide (Post *et al*., 1993), BAY27-9955 (Petersen and Sullivan, 2001), xNNC92-1687 (Madsen *et al*., 1998)	Exendin-(9-39) (Thorens *et al*., 1993), T0632 (Tibaduiza *et al*., 2001)	–
Probes	[^{125}I]-glucagon	[^{125}I]-GLP-1-(7-36) amide, [^{125}I]-exendin, [^{125}I]-exendin-(9-39), [^{125}I]-GLP-1-(7-37)	–

Nomenclature	GIP	GHRH	Secretin
Ensembl ID	ENSG00000010310	ENSG00000106128	ENSG00000080293
Principal transduction	G_s	G_s	G_s
Selective agonists	GIP	BIM28011 (Coy *et al*., 1996)	Secretin
Selective antagonists	[Pro[3]]GIP	JV-1-36 (Schally and Varga, 1999), JV-1-38 (Schally and Varga, 1999)	[$(CH_2NH)^{4,5}$]secretin (Kim *et al*., 1993)
Probes	[^{125}I]-GIP	[^{125}I]-GHRH	[^{125}I]-(Tyr[10])secretin

The glucagon receptor has been reported to interact with receptor activity modifying proteins (RAMPs), specifically RAMP2, in heterologous expression systems (Christopoulos *et al*., 2003), although the physiological significance of this has yet to be established.

Abbreviations: **BAY27-9955**, (+)-3,5-diiospropyl-2-(1-hydroxyethyl)-6-propyl-4′-fluoro-1,1′-biphenyl; **BIM28011**, [D-Ala[2],Ala[8,9,15,27],D-Arg[29]]hGHRH-(1–29)NH_2; **JV-1-36**, [PhAc-Tyr[1],D-Arg[2],Phe(4-Cl)[6],Arg[9],Abu[15],Nle[27],D-Arg[28],Har[29]]hGHRH(1–29)NH_2; **JV-1-38**, [PhAc-Tyr[1],D-Arg[2],Phe(4-Cl)[6],Har[9],Tyr(Me)[10],Abu[15],Nle[27],D-Arg[28],Har[29]]hGHRH(1–29)NH_2; **L168049**, 2-(4-pyridyl)-5-(4-chlorophenyl)-3-(5-bromo-2-propyloxyphenyl)pyrrole; **NNC92-1687**, 2-(benzimidazol-2-ylthio)-1-(3,4-dihydroxyphenyl)-1-ethanone; **T0632**, sodium (*S*)-3-(1-[2-fluorophenyl]-2,3-dihydro-3-[{3-isoquinolinyl}-carbonyl]amino-6-methoxy-2-oxo-1*H*-indole)propanoate

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