Soluble guanylyl cyclase (E.C. 4.6.1.2)

Overview: Soluble guanylyl cyclase [GTP diphosphate-lyase (cyclizing)] is a heterodimer comprising α and β chains, both of which have two subtypes in man (predominantly $\alpha1\beta1$; see Zabel *et al*., 1998). A heme group is associated with the β chain and is the target for the endogenous ligand nitric oxide (NO•), and, potentially, carbon monoxide (Friebe *et al*., 1996). The enzyme converts guanosine-5′-triphosphate (GTP) to the intracellular second messenger 3′,5′-guanosine monophosphate (cGMP).

Nomenclature	Soluble guanylyl cyclase
Preferred abbreviation	sGC
Ensembl ID	$\alpha1$ ENSG00000164116; $\alpha2$ ENSG00000152402; $\beta1$ ENSG00000061918; $\beta2$ ENSG00000123201
Selective activators	NO•, YC1 (Friebe *et al*., 1996), BAY412272 (Stasch *et al*., 2001), BAY582667 (Stasch *et al*., 2002)
Selective inhibitors	ODQ (7.5; Garthwaite *et al*., 1995)

ODQ also shows activity at other heme-containing proteins (Feelisch *et al*., 1999), while YC1 may also inhibit cGMP-hydrolysing phosphodiesterases (Friebe *et al*., 1998; Galle *et al*., 1999).

Abbreviations: **BAY412272**, 5-cyclopropyl-2-[1-(2-fluoro-benzyl)-1*H*-pyrazolo[3,4-*b*]pyridin-3-yl]-pyrimidin-4-ylamine); **BAY582667**, 4-([4-carboxybutyl][2-{(4-phenethylbenzyl)oxy}phenethyl]amino)methyl(benzoic)acid; **ODQ**, 1*H*-[1,2,4]oxadiazolo[4,3-*a*]quinoxalin-1-one; **YC1**, 3-(5′-hydroxymethyl-2′-furyl)-1-benzylindazole HMR1766

Further Reading

Cary SP, Winger JA, Derbyshire ER, Marletta MA (2006). Nitric oxide signaling: no longer simply on or off. *Trends Biochem Sci* **31**: 231–239.
Cerra MC, Pellegrino D (2007). Cardiovascular cGMP-generating systems in physiological and pathological conditions. *Curr Med Chem* **14**: 585–599.
Doggrell SA (2005). Clinical potential of nitric oxide-independent soluble guanylate cyclase activators. *Curr Opin Investig Drugs* **6**: 874–878.
Evgenov OV, Pacher P, Schmidt PM, Hasko G, Schmidt HH, Stasch JP (2006). NO-independent stimulators and activators of soluble guanylate cyclase: discovery and therapeutic potential. *Nat Rev Drug Discov* **5**: 755–768.
Jackson EB, Mukhopadhyay S, Tulis DA (2007). Pharmacologic modulators of soluble guanylate cyclase/cyclic guanosine monophosphate in the vascular system – from bench top to bedside. *Curr Vasc Pharmacol* **5**: 1–14.
Moncada S, Higgs EA (2006). Nitric oxide and the vascular endothelium. *Handb Exp Pharmacol* **176**: 213–254.
Poulos TL (2006). Soluble guanylate cyclase. *Curr Opin Struct Biol* **16**: 736–743.
Pyriochou A, Papapetropoulos A (2005). Soluble guanylyl cyclase: more secrets revealed. *Cell Signal* **17**: 407–413.

References

Feelisch M *et al*. (1999). *Mol Pharmacol* **56**: 243–253.
Friebe A *et al*. (1996). *EMBO J* **15**: 6863–6868.
Friebe A *et al*. (1998). *Mol Pharmacol* **54**: 962–967.
Galle J *et al*. (1999). *Br J Pharmacol* **127**: 195–203.
Garthwaite J *et al*. (1995). *Mol Pharmacol* **48**: 184–188.
Stasch JP *et al*. (2001). *Nature* **410**: 212–215.
Stasch JP *et al*. (2002). *Br J Pharmacol* **136**: 773–783.
Zabel U *et al*. (1998). *Biochem J* **335**: 51–57.