Natriuretic peptide

Overview: Natriuretic peptide receptors (provisional nomenclature) are homodimeric, catalytic receptors with a single TM domain and guanylyl cyclase (EC 4.6.1.2) activity on the intracellular domain of the protein sequence. Isoforms are activated by the peptide hormones α-atrial natriuretic peptide (ANP, ENSG00000175206), brain natriuretic peptide (BNP, ENSG00000120937) and type C-natriuretic peptide (CNP, ENSG00000163273). Another family member is GUCY2C, the receptor for guanylin (ENSG00000113389) and uroguanylin (ENSG00000044012). Family members have conserved catalytic and regulatory domains, but divergent ligand-binding domains. NPR3 has an extracellular binding domain homologous to that of NPR1 and 2, but with a truncated intracellular domain which appears to couple, *via* the $G_{i/o}$ family of G-proteins, to activation of phospholipase C, inwardly-rectifying potassium channels and inhibition of adenylyl cyclase activity (Murthy and Makhlouf, 1999; Ahluwalia & Hobbs, 2005); NPR3 also binds and removes natriuretic peptides from the circulation, and consequently has been termed the 'clearance receptor'.

Nomenclature	NPR1	NPR2	NPR3	GUCY2C
Other names	GC-A, ANP_A receptor, NPR-A, GUCY2A	GC-B, ANP_B receptor, NPR-B, GUCY2B	ANPRC, NPR-C,	GC-C, guanylin receptor, STaR
Ensembl ID	ENSG00000169418	ENSG00000159899	ENSG00000113389	ENSG00000070019
Potency order	ANP ≥ BNP >> CNP	CNP >> ANP ≥BNP	ANP > CNP > BNP	Uroguanylin > guanylin
Selective agonists	ANP, BNP, sANP (Olson *et al.*, 1996)	CNP	$cANF^{4–23}$ (Maack *et al.*, 1987)	*Escherichia coli* heat-stable enterotoxin (ST_a), linaclotide (Harris and Crowell, 2007)
Selective antagonists	A71915 (9.2–9.5, Delporte *et al.*, 1991), [Asu7,23′]-β-$ANP^{7–28}$ (7.5, Kambayashi *et al.*, 1989), anantin (Wyss *et al.*, 1991)	Monoclonal antibody 3G12 (Drewett *et al.*, 1995)	AP811 (9.3, Veale *et al.*, 2000), M372049 (Hobbs *et al.*, 2004)	–
Probes	[^{125}I]-ANP	[^{125}I]-CNP	[^{125}I]-ANP	[^{125}I]-ST_a

The polysaccharide obtained from fermentation of *Aureobasidium* species, HS142-1, acts as an antagonist for NPR1 and NPR2 receptors (Morishita *et al.*, 1991).

Orphan receptors GC-D, GC-E (RetGC-1, ENSG00000132518), GC-F (RetGC-2, ENSG00000101890) and GC-G (ENSG00000080218) have been cloned from various mammals. GC-G exhibits structural similarity to the natriuretic peptide receptors (Schulz *et al.*, 1998).

Abbreviations: **A71915**, ([Arg^6,Cha^8]$ANP^{6–15}$-d-Tic-Arg-Cys-NH_2; **anantin**, cyclo(Gly-Phe-Ile-Gly-Trp-Gly-Asn-β-Asp)-Ile-Phe-Gly-His-Tyr-Ser-Gly-Asp-Phe; **AP811**, (s)-N^2-([4-{(2-naphthalenylcarbonyl)amino}phenyl]acetyl)-l-arginyl-l-isoleucyl-l-α-aspartyl-*N*-(2-methylbutyl)-l-argininamide; **[Asu7,23′]-β-ANP(7–28)**, an antiparallel dimer linked by 7-23′ and 7′-23 disulphide bonds (Asu, l-α-aminosuberic acid); **$cANF^{4–23}$**, des[Gln^{18},Ser^{19},Gly^{20},Leu^{21},Gly^{22}]$ANP^{4–23}$-NH_2; **HS142-1**, *Aureobasidium*-derived polysaccharide; **M372049**, (structure not known); **sANP**, [G9T, R11S, G16R]ANP

Further Reading

Ahluwalia A, Hobbs AJ (2005). Endothelium-derived C-type natriuretic peptide: more than just a hyperpolarizing factor. *Trends Pharmacol Sci* **26**: 162–167.

Carrillo-Jimenez R, Borzak S, Hennekens CH (2007). Brain natriuretic peptide: clinical and research challenges. *J Cardiovasc Pharmacol Ther* **12**: 85–88.

Cataliotti A, Chen HH, James KD, Burnett JC, Jr. (2007). Oral brain natriuretic peptide: a novel strategy for chronic protein therapy for cardiovascular disease. *Trends Cardiovasc Med* **17**: 10–14.

Del Ry S, Passino C, Emdin M, Giannessi D (2006). C-type natriuretic peptide and heart failure. *Pharmacol Res* **54**: 326–333.

Doust JA, Pietrzak E, Dobson A, Glasziou P (2005). How well does B-type natriuretic peptide predict death and cardiac events in patients with heart failure: systematic review. *BMJ* **330**: 625–662.

Dries DL (2007). Relevance of molecular forms of brain natriuretic peptide for natriuretic peptide research. *Hypertension* **49**: 971–973.

Gardner DG, Chen S, Glenn DJ, Grigsby CL (2007). Molecular biology of the natriuretic peptide system: implications for physiology and hypertension. *Hypertension* **49**: 419–426.

Moe GW (2006). B-type natriuretic peptide in heart failure. *Curr Opin Cardiol* **21**: 208–214.

Potter LR, Abbey-Hosch S, Dickey DM (2006). Natriuretic peptides, their receptors, and cyclic guanosine monophosphate-dependent signaling functions. *Endocr Rev* **27**: 47–72.

Rademaker MT, Richards AM (2005). Cardiac natriuretic peptides for cardiac health. *Clin Sci* **108**: 23–36.

Sandow SL, Tare M (2007). C-type natriuretic peptide: a new endothelium-derived hyperpolarizing factor? *Trends Pharmacol Sci* **28**: 61–67.

Scotland RS, Ahluwalia A, Hobbs AJ (2005). C-type natriuretic peptide in vascular physiology and disease. *Pharmacol Ther* **105**: 85–93.

References:

Delporte C *et al.* (1991). *Eur J Pharmacol* **207**: 81–88.

Drewett JG *et al.* (1995). *J Biol Chem* **270**: 4668–4674.

Harris LA, Crowell MD (2007). *Curr Opin Mol Ther* **9**: 403–410.

Hobbs A *et al.* (2004). *Circulation* **110**: 1231–1235.

Kambayashi Y *et al.* (1989). *FEBS Lett* **248**: 28–34.

Maack T *et al.* (1987). *Science* **238**: 675–678.

Morishita Y *et al*. (1991). *Biochem Biophys Res Commun* **176**: 949–957.
Murthy KS, Makhlouf GM (1999). *J Biol Chem* **274**: 17587–17592.
Olson LJ *et al*. (1996). *Mol Pharmacol* **50**: 430–435.
Schulz S *et al*. (1998). *J Biol Chem* **273**: 1032–1037.
Veale CA *et al*. (2000). *Bioorg Med Chem Lett* **10**: 1949–1952.
Wyss DF *et al*. (1991). *J Antibiot (Tokyo)* **44**: 172–180.