

## Gene Section

### Mini Review

# APLNR (apelin receptor)

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### Identity

**Other names:** AGTRL1; APJ; APJR; FLJ90771; HG11; MGC45246

**HGNC (Hugo):** APLNR

**Location:** 11q12.1

### DNA/RNA

#### Description

1 exon.

#### Transcription

3.8 kb mRNA; 1140 bp open reading frame.

### Protein

#### Description

380 amino acids.

#### Expression

Blood vessels, hypothalamus, heart, stomach, colon, endocrine pancreas, bone, skeletal muscle, spleen.

### Localisation

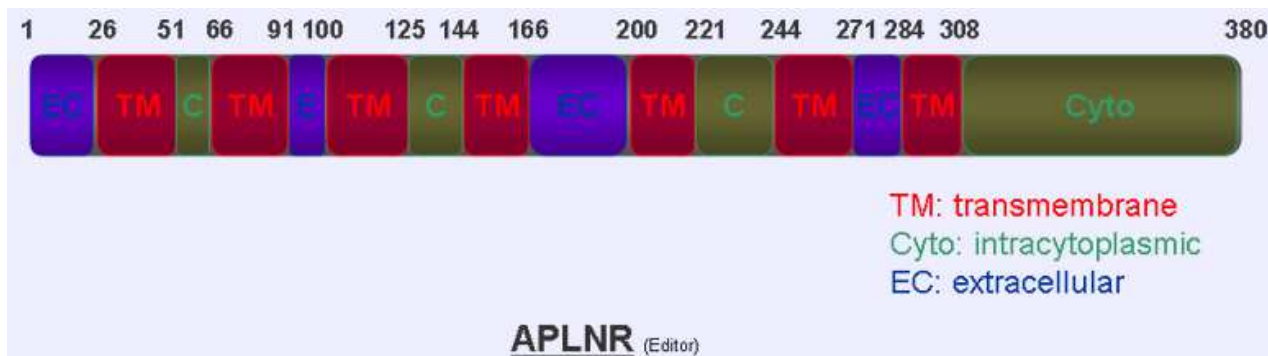
Plasma membrane.

### Function

The apelin receptor APJ belongs to the family of G protein-coupled receptors (O'Dowd et al., 1993; Devic et al., 1996; Devic et al., 1999; Scott et al., 2007) and is coupled to a Gi/o protein (Masri et al., 2006). Its activation leads to the regulation of various intracellular effectors with the following consequences: adenylylcyclase inhibition (Masri et al., 2006; Habata et al., 1999), increase of intracellular calcium (Choe et al., 2000) and activation of extracellular signal-regulated kinases (ERKs), PI-3K, Akt or p70S6 kinase (S6K1) (Masri et al., 2006; Masri et al., 2004).

Expression of apelin receptors by the endothelial cell (Devic et al., 1996; Devic et al., 1999) is associated with two effects :

- 1) NO release leading to vessel vasodilatation (Tatemoto et al., 2001) and peripheral hypotension (Lee et al., 2000);
- 2) cell proliferation and migration (Masri et al., 2004; Kasai et al., 2004) linked to angiogenesis (Cox et al., 2006).



The expression in the central nervous system is high in hypothalamus (De Mota et al., 2000; O'Carroll et al., 2000) where receptor activation leads to the decrease of vasopressin release (De Mota et al., 2004). Activation of apelin receptors expressed by cardiomyocytes results in a strong inotropic effect (Szokodi et al., 2002). In stomach, apelin receptors are expressed by enterochromaffin-like cells where their stimulation decreases gastrin-induced acid secretion (Lambrecht et al., 2006). Apelin receptors may regulate epithelial proliferation in the colon (Han et al., 2007). Expression of apelin receptors both in endocrine pancreas and skeletal muscle contributes to the regulation of insulin plasma levels and glucose uptake (Sorhede Winzell et al., 2005; Dray et al., 2008). Apelin signalling also increases osteoblast proliferation (Xie et al., 2007) and cytokine expression by T lymphocytes (Habata et al., 1999).

## Mutations

### Note

No mutation has been presently described.

## Implicated in

### *Malignant glioma*

### Note

On a quantitative point of view, APLNR gene expression is highly upregulated in microvascular proliferations of malignant gliomas (Kalin et al., 2007).

### *Various diseases*

### Note

On a qualitative point of view, two single nucleotide polymorphisms (SNP) have been reported. A functional SNP in an Sp1-binding site of APLNR gene is associated with susceptibility to brain infarction (Hata et al., 2007). The 212A variant of the APJ receptor gene is associated with slower heart failure progression in idiopathic dilated cardiomyopathy (Sarzani et al., 2007).

## References

O'Dowd BF, Heiber M, Chan A, Heng HH, Tsui LC, Kennedy JL, Shi X, Petronis A, George SR, Nguyen T. A human gene that shows identity with the gene encoding the angiotensin receptor is located on chromosome 11. *Gene*. 1993 Dec 22;136(1-2):355-60

Devic E, Paquereau L, Vernier P, Knibiehler B, Audigier Y. Expression of a new G protein-coupled receptor X-msr is associated with an endothelial lineage in *Xenopus laevis*. *Mech Dev*. 1996 Oct;59(2):129-40

Devic E, Rizzoti K, Bodin S, Knibiehler B, Audigier Y. Amino acid sequence and embryonic expression of *msr/apj*, the mouse homolog of *Xenopus X-msr* and human APJ. *Mech Dev*. 1999 Jun;84(1-2):199-203

Habata Y, Fujii R, Hosoya M, Fukusumi S, Kawamata Y, Hinuma S, Kitada C, Nishizawa N, Murosaki S, Kurokawa T, Onda H, Tatemoto K, Fujino M. Apelin, the natural ligand of the

orphan receptor APJ, is abundantly secreted in the colostrum. *Biochim Biophys Acta*. 1999 Oct 13;1452(1):25-35

Choe W, Albright A, Sulcove J, Jaffer S, Hesselgesser J, Lavi E, Crino P, Kolson DL. Functional expression of the seven-transmembrane HIV-1 co-receptor APJ in neural cells. *J Neurovirol*. 2000 May;6 Suppl 1:S61-9

De Mota N, Lenkei Z, Llorens-Cortès C. Cloning, pharmacological characterization and brain distribution of the rat apelin receptor. *Neuroendocrinology*. 2000 Dec;72(6):400-7

Lee DK, Cheng R, Nguyen T, Fan T, Kariyawasam AP, Liu Y, Osmond DH, George SR, O'Dowd BF. Characterization of apelin, the ligand for the APJ receptor. *J Neurochem*. 2000 Jan;74(1):34-41

O'Carroll AM, Selby TL, Palkovits M, Lolait SJ. Distribution of mRNA encoding B78/apj, the rat homologue of the human APJ receptor, and its endogenous ligand apelin in brain and peripheral tissues. *Biochim Biophys Acta*. 2000 Jun 21;1492(1):72-80

Tatemoto K, Takayama K, Zou MX, Kumaki I, Zhang W, Kumano K, Fujimiya M. The novel peptide apelin lowers blood pressure via a nitric oxide-dependent mechanism. *Regul Pept*. 2001 Jun 15;99(2-3):87-92

Szokodi I, Tavi P, Földes G, Voutilainen-Myllylä S, Ilves M, Tokola H, Pikkarainen S, Piuholta J, Rysä J, Tóth M, Ruskoaho H. Apelin, the novel endogenous ligand of the orphan receptor APJ, regulates cardiac contractility. *Circ Res*. 2002 Sep 6;91(5):434-40

De Mota N, Reaux-Le Goazigo A, El Messari S, Chartrel N, Roesch D, Dujardin C, Kordon C, Vaudry H, Moos F, Llorens-Cortès C. Apelin, a potent diuretic neuropeptide counteracting vasopressin actions through inhibition of vasopressin neuron activity and vasopressin release. *Proc Natl Acad Sci U S A*. 2004 Jul 13;101(28):10464-9

Kasai A, Shintani N, Oda M, Kakuda M, Hashimoto H, Matsuda T, Hinuma S, Baba A. Apelin is a novel angiogenic factor in retinal endothelial cells. *Biochem Biophys Res Commun*. 2004 Dec 10;325(2):395-400

Masri B, Morin N, Cornu M, Knibiehler B, Audigier Y. Apelin (65-77) activates p70 S6 kinase and is mitogenic for umbilical endothelial cells. *FASEB J*. 2004 Dec;18(15):1909-11

Sörhede Winzell M, Magnusson C, Ahrén B. The apj receptor is expressed in pancreatic islets and its ligand, apelin, inhibits insulin secretion in mice. *Regul Pept*. 2005 Nov;131(1-3):12-7

Cox CM, D'Agostino SL, Miller MK, Heimark RL, Krieg PA. Apelin, the ligand for the endothelial G-protein-coupled receptor, APJ, is a potent angiogenic factor required for normal vascular development of the frog embryo. *Dev Biol*. 2006 Aug 1;296(1):177-89

Lambrecht NW, Yakubov I, Zer C, Sachs G. Transcriptomes of purified gastric ECL and parietal cells: identification of a novel pathway regulating acid secretion. *Physiol Genomics*. 2006 Mar 13;25(1):153-65

Masri B, Morin N, Pedebnarde L, Knibiehler B, Audigier Y. The apelin receptor is coupled to Gi1 or Gi2 protein and is differentially desensitized by apelin fragments. *J Biol Chem*. 2006 Jul 7;281(27):18317-26

Xie H, Tang SY, Cui RR, Huang J, Ren XH, Yuan LQ, Lu Y, Yang M, Zhou HD, Wu XP, Luo XH, Liao EY. Apelin and its receptor are expressed in human osteoblasts. *Regul Pept*. 2006 May 15;134(2-3):118-25

Han S, Wang G, Qiu S, de la Motte C, Wang HQ, Gomez G, Englander EW, Greeley GH Jr. Increased colonic apelin production in rodents with experimental colitis and in humans with IBD. *Regul Pept*. 2007 Aug 16;142(3):131-7

Hata J, Matsuda K, Ninomiya T, Yonemoto K, Matsushita T, Ohnishi Y, Saito S, Kitazono T, Ibayashi S, Iida M, Kiyohara Y, Nakamura Y, Kubo M. Functional SNP in an Sp1-binding site of AGTRL1 gene is associated with susceptibility to brain infarction. *Hum Mol Genet.* 2007 Mar 15;16(6):630-9

Kälin RE, Kretz MP, Meyer AM, Kispert A, Heppner FL, Brändli AW. Paracrine and autocrine mechanisms of apelin signaling govern embryonic and tumor angiogenesis. *Dev Biol.* 2007 May 15;305(2):599-614

Sarzani R, Forleo C, Pietrucci F, Capestro A, Soura E, Guida P, Sorrentino S, Iacoviello M, Romito R, Dessi-Fulgheri P, Pitzalis M, Rappelli A. The 212A variant of the APJ receptor gene for the endogenous inotrope apelin is associated with slower heart failure progression in idiopathic dilated cardiomyopathy. *J Card Fail.* 2007 Sep;13(7):521-9

Scott IC, Masri B, D'Amico LA, Jin SW, Jungblut B, Wehman AM, Baier H, Audigier Y, Stainier DY. The G protein-coupled receptor agtr1b regulates early development of myocardial progenitors. *Dev Cell.* 2007 Mar;12(3):403-13

Dray C, Knauf C, Daviaud D, Waget A, Boucher J, Buléon M, Cani PD, Attané C, Guigné C, Carpéné C, Burcelin R, Castan-Laurell I, Valet P. Apelin stimulates glucose utilization in normal and obese insulin-resistant mice. *Cell Metab.* 2008 Nov;8(5):437-45

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