

Gene Section

Mini Review

GPR68 (G protein-coupled receptor 68)

Yan Xu

Department of Obstetrics and Gynecology, Indiana University School of Medicine, 975 W. Walnut St
IB355A, Indianapolis, IN 46202, USA (YX)

Published in Atlas Database: December 2008

Online updated version : <http://AtlasGeneticsOncology.org/Genes/GPR68ID40745ch14q32.html>
DOI: 10.4267/2042/44611

This work is licensed under a Creative Commons Attribution-Noncommercial-No Derivative Works 2.0 France Licence.
© 2009 Atlas of Genetics and Cytogenetics in Oncology and Haematology

Identity

Other names: GPR12A; MGC111379; MGC156983; OGR-1; OGR1

HGNC (Hugo): GPR68

Location: 14q32.12

Note: GPR68 (OGR1) is a G protein-coupled receptor (GPCR), which share high homology with other three GPCRs (TDAG8, G2A and GPR4). OGR1, as well as TDAG8, G2A and GPR4, has been shown to be proton-sensing GPCRs. In particular, OGR1 has been shown to be a proton-sensing receptor in bone. OGR1 is expressed in osteoclasts and osteoblasts, where it mediates acid-induced signaling pathways via G(q/11) protein, phospholipase C, IP(3) formation, and subsequent Ca²⁺ release from thapsigargin-sensitive stores. Acidic pH has been shown to induce cyclooxygenase-2 (COX-2) induction and prostaglandin E2 (PGE2) production, resulting in stimulation of bone calcium release and osteoclastogenesis. OGR1 family receptors can also mediate effects of several phospholipids. However, whether the lipid regulation is specific to these receptors is still under debate.

DNA/RNA

Note

GPR68 (OGR1) is a proton sensing receptor. Its physiological role need to be further investigated.

Description

The open reading frame of GPR68 is encoded by a single exon (1095 bp) located at chromosome 14q31.

Transcription

GPR68 transcripts of ~3.0 kb in human.

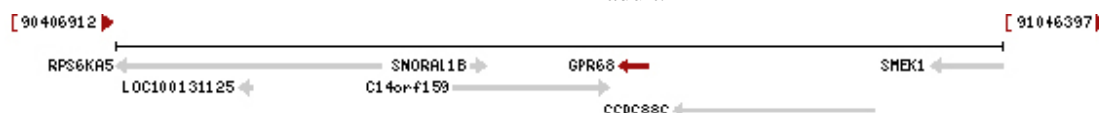
Protein

Description

Size: 365 amino acids.

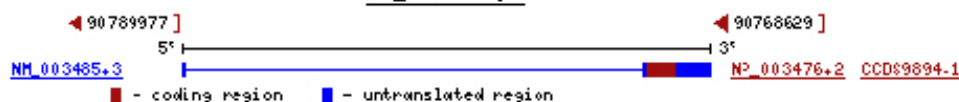
Expression

GPR68 is expressed in blood; bone; brain; connective tissue; embryonic tissue; eye; heart, intestine; lung; pancreas; placenta; peripheral blood leukocyte, prostate; skin; stomach; thymus; uterus; chondrosarcoma; leukemia; normal; pancreatic cancer; small intestine, soft tissue/muscle tissue tumor; spleen, stomach tumor; testis, uterine tumor; embryo; fetus; adult.



Picture from Entrez Gene.

NC_000014.7



Picture from Entrez Gene.

Localisation

Cell membrane.

Function

Osteoclastogenesis.

Homology

OGR1, GPR4, G2A, and TDAG8 share 40% to 50% homology with each other and seem to form a family of GPCRs. GPCRs form homo- and hetero-dimers or -oligomers. Although GPR4 and OGR1 share more than 50% homology, GPR4 forms strong homo- and hetero-dimers with LPA and S1P receptors, but OGR1 forms very weak homo-dimer and relatively weak hetero-dimers with other receptors.

Implicated in

Prostate cancer

Note

Down regulated in metastatic prostate cancer.

Oncogenesis

OGR1 is down regulated in metastatic prostate cancer tissues and over-expression OGR1 in prostate cancer cells suppresses tumor metastasis. Thus, OGR1 has been considered as a tumor metastasis suppressor genes for prostate cancer (Singh et al., 2007).

References

An S, Tsai C, Goetzl EJ. Cloning, sequencing and tissue distribution of two related G protein-coupled receptor candidates expressed prominently in human lung tissue. *FEBS Lett.* 1995 Nov 13;375(1-2):121-4

Xu Y, Casey G. Identification of human OGR1, a novel G protein-coupled receptor that maps to chromosome 14. *Genomics.* 1996 Jul 15;35(2):397-402

Ludwig MG, Vanek M, Guerini D, Gasser JA, Jones CE, Junker U, Hofstetter H, Wolf RM, Seuwen K. Proton-sensing G-protein-coupled receptors. *Nature.* 2003 Sep 4;425(6953):93-8

Kostenis E. Novel clusters of receptors for sphingosine-1-phosphate, sphingosylphosphorylcholine, and (lyso)-phosphatidic acid: new receptors for "old" ligands. *J Cell Biochem.* 2004 Aug 1;92(5):923-36

Im DS. Two ligands for a GPCR, proton vs lysolipid. *Acta Pharmacol Sin.* 2005 Dec;26(12):1435-41

Mogi C, Tomura H, Tobo M, Wang JQ, Damirin A, Kon J, et al. Sphingosylphosphorylcholine antagonizes proton-sensing ovarian cancer G-protein-coupled receptor 1 (OGR1)-mediated inositol phosphate production and cAMP accumulation. *J Pharmacol Sci.* 2005 Oct;99(2):160-7

Radu CG, Nijagal A, McLaughlin J, Wang L, Witte ON. Differential proton sensitivity of related G protein-coupled receptors T cell death-associated gene 8 and G2A expressed in immune cells. *Proc Natl Acad Sci U S A.* 2005 Feb 1;102(5):1632-7

Tomura H, Mogi C, Sato K, Okajima F. Proton-sensing and lysolipid-sensitive G-protein-coupled receptors: a novel type of multi-functional receptors. *Cell Signal.* 2005 Dec;17(12):1466-76

Tomura H, Wang JQ, Komachi M, Damirin A, Mogi C, et al. Prostaglandin I(2) production and cAMP accumulation in response to acidic extracellular pH through OGR1 in human aortic smooth muscle cells. *J Biol Chem.* 2005 Oct 14;280(41):34458-64

Afrasiabi E, Blom T, Ekokoski E, Tuominen RK, Törnquist K. Sphingosylphosphorylcholine enhances calcium entry in thyroid FRO cells by a mechanism dependent on protein kinase C. *Cell Signal.* 2006 Oct;18(10):1671-8

Seuwen K, Ludwig MG, Wolf RM. Receptors for protons or lipid messengers or both? *J Recept Signal Transduct Res.* 2006;26(5-6):599-610

Yang M, Mailhot G, Birnbaum MJ, MacKay CA, Mason-Savas A, Odgren PR. Expression of and role for ovarian cancer G-protein-coupled receptor 1 (OGR1) during osteoclastogenesis. *J Biol Chem.* 2006 Aug 18;281(33):23598-605

Zaslavsky A, Singh LS, Tan H, Ding H, Liang Z, Xu Y. Homo- and hetero-dimerization of LPA/S1P receptors, OGR1 and GPR4. *Biochim Biophys Acta.* 2006 Oct;1761(10):1200-12

Huang CW, Tzeng JN, Chen YJ, Tsai WF, Chen CC, Sun WH. Nociceptors of dorsal root ganglion express proton-sensing G-protein-coupled receptors. *Mol Cell Neurosci.* 2007 Oct;36(2):195-210

Iwai K, Koike M, Ohshima S, Miyatake K, Uchiyama Y, Saeki Y, Ishii M. RGS18 acts as a negative regulator of osteoclastogenesis by modulating the acid-sensing OGR1/NFAT signaling pathway. *J Bone Miner Res.* 2007 Oct;22(10):1612-20

Meyer zu Heringdorf D, Jakobs KH. Lysophospholipid receptors: signalling, pharmacology and regulation by lysophospholipid metabolism. *Biochim Biophys Acta.* 2007 Apr;1768(4):923-40

Singh LS, Berk M, Oates R, Zhao Z, Tan H, Jiang Y, et al. Ovarian cancer G protein-coupled receptor 1, a new metastasis suppressor gene in prostate cancer. *J Natl Cancer Inst.* 2007 Sep 5;99(17):1313-27

Huang WC, Swietach P, Vaughan-Jones RD, Ansoorge O, Glitsch MD. Extracellular acidification elicits spatially and temporally distinct Ca²⁺ signals. *Curr Biol.* 2008 May 20;18(10):781-5

Pereverzev A, Komarova SV, Korcok J, Armstrong S, Tremblay GB, Dixon SJ, Sims SM. Extracellular acidification enhances osteoclast survival through an NFAT-independent, protein kinase C-dependent pathway. *Bone.* 2008 Jan;42(1):150-61

Tomura H, Wang JQ, Liu JP, Komachi M, Damirin A, et al. Cyclooxygenase-2 expression and prostaglandin E2 production in response to acidic pH through OGR1 in a human osteoblastic cell line. *J Bone Miner Res.* 2008 Jul;23(7):1129-39

Frick KK, Krieger NS, Nehrke K, Bushinsky DA. Metabolic acidosis increases intracellular calcium in bone cells through activation of the proton receptor OGR1. *J Bone Miner Res.* 2009 Feb;24(2):305-13

This article should be referenced as such:

Xu Y. GPR68 (G protein-coupled receptor 68). *Atlas Genet Cytogenet Oncol Haematol.* 2009; 13(11):845-846.
