PROKR2 gene

prokineticin receptor 2

Normal Function

The *PROKR2* gene provides instructions for making a protein called prokineticin receptor 2. This receptor interacts with a protein called prokineticin 2 (produced from the *PROK2* gene). On the cell surface, prokineticin 2 attaches to the receptor like a key in a lock. When the two proteins are connected, they trigger a series of chemical signals within the cell that regulate various cell functions. Prokineticin 2 and its receptor are produced in many organs and tissues, including the small intestine, certain regions of the brain, and several hormone-producing (endocrine) tissues.

Prokineticin 2 and its receptor play a role in the development of a group of nerve cells that are specialized to process smells (olfactory neurons). These neurons move (migrate) from the developing nose to a structure in the front of the brain called the olfactory bulb, which is critical for the perception of odors. Prokineticin 2 and its receptor are also involved in the migration of nerve cells that produce gonadotropin-releasing hormone (GnRH). GnRH controls the production of several hormones that direct sexual development before birth and during puberty. These hormones are also important for the normal function of the ovaries in women and the testes in men.

Several additional functions of prokineticin 2 and its receptor have been discovered. These proteins help stimulate the movement of food through the intestine and are likely involved in the formation of new blood vessels (angiogenesis). They also play a role in coordinating daily (circadian) rhythms, such as the sleep-wake cycle and regular changes in body temperature. Prokineticin 2 and its receptor are active in a region of the brain called the suprachiasmatic nucleus (SCN), which acts as an internal clock that controls circadian rhythms.

Health Conditions Related to Genetic Changes

Kallmann syndrome

At least 30 mutations in the *PROKR2* gene can cause Kallmann syndrome, a disorder characterized by the combination of hypogonadotropic hypogonadism (a condition affecting the production of hormones that direct sexual development) and an impaired sense of smell. Researchers estimate that mutations in the *PROKR2* and *PROK2* genes together account for about 9 percent of all cases of Kallmann syndrome.

Most of the *PROKR2* gene mutations that cause Kallmann syndrome change single protein building blocks (amino acids) in prokineticin receptor 2. These mutations disrupt the function of the receptor, affecting its ability to trigger chemical signals within cells. A loss of this signaling disrupts the migration and survival of olfactory neurons and GnRH-producing neurons in the developing brain. If olfactory nerve cells do not extend to the olfactory bulb, a person's sense of smell will be impaired or absent. Misplacement or premature loss of GnRH-producing neurons prevents the production of sex hormones, which interferes with normal sexual development and causes puberty to be delayed or absent.

Because the features and severity of Kallmann syndrome vary among individuals, researchers believe that additional genetic and environmental factors may be involved. Some affected individuals have mutations in one of several other genes in addition to *PROKR2*, and these genetic changes may contribute to the varied features of the condition.

Combined pituitary hormone deficiency

MedlinePlus Genetics provides information about Combined pituitary hormone deficiency

Septo-optic dysplasia

MedlinePlus Genetics provides information about Septo-optic dysplasia

Other disorders

A few mutations in the *PROKR2* gene have been identified in people with only one of the two major features of Kallmann syndrome (described above): hypogonadotropic hypogonadism or an impaired sense of smell. When hypogonadotropic hypogonadism occurs with a normal ability to smell, it is called normosmic isolated hypogonadotropic hypogonadism (nIHH). An impaired sense of smell without hypogonadotropic hypogonadism is called isolated congenital anosmia (ICA). Like the *PROKR2* gene mutations that cause Kallmann syndrome, the mutations associated with these conditions impair the function of prokineticin receptor 2, preventing it from transmitting signals properly. A loss of this signaling can disrupt the migration of GnRH-producing nerve cells or olfactory neurons in the developing brain. It is unclear why some mutations in this gene cause both hypogonadotropic hypogonadism and an impaired sense of smell in people with Kallmann syndrome, and only one of these features in people with nIHH or ICA.

Other Names for This Gene

- G protein-coupled receptor 73-like 1
- GPR73b
- GPR73L1
- GPRg2

- KAL3
- PK-R2
- PKR2
- PKR2_HUMAN

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of PROKR2 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=128674[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28PROKR2%5BTIAB%5D%29+OR+%28prokineticin+receptor+2%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- PROKINETICIN RECEPTOR 2; PROKR2 (https://omim.org/entry/607123)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/128674)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=PROKR2[gene])

References

- Dode C, Rondard P. PROK2/PROKR2 Signaling and Kallmann Syndrome. FrontEndocrinol (Lausanne). 2013 Apr 12;4:19. doi: 10.3389/fendo.2013.00019. eCollection 2013. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/23596439) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3624607/)
- Dode C, Teixeira L, Levilliers J, Fouveaut C, Bouchard P, Kottler ML,Lespinasse J, Lienhardt-Roussie A, Mathieu M, Moerman A, Morgan G, Murat A,Toublanc JE, Wolczynski S, Delpech M, Petit C, Young J, Hardelin JP. Kallmannsyndrome: mutations in the genes encoding prokineticin-2 and prokineticinreceptor-2. PLoS Genet. 2006 Oct 20;2(10):e175. doi:10.1371/journal.pgen.0020175. Epub 2006 Sep 1. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17054399) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1617130/)
- Matsumoto S, Yamazaki C, Masumoto KH, Nagano M, Naito M, Soga T, Hiyama H,

Matsumoto M, Takasaki J, Kamohara M, Matsuo A, Ishii H, Kobori M, Katoh M, Matsushime H, Furuichi K, Shigeyoshi Y. Abnormal development of the olfactorybulb and reproductive system in mice lacking prokineticin receptor PKR2. ProcNatl Acad Sci U S A. 2006 Mar 14;103(11):4140-5. doi: 10.1073/pnas.0508881103.Epub 2006 Mar 2. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/16537498) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1449660/)

- Moya-Plana A, Villanueva C, Laccourreye O, Bonfils P, de Roux N. PROKR2 andPROK2 mutations cause isolated congenital anosmia without gonadotropicdeficiency. Eur J Endocrinol. 2012 Dec 10;168(1):31-7. doi: 10.1530/EJE-12-0578.Print 2013 Jan. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/23082007)
- Ng KL, Li JD, Cheng MY, Leslie FM, Lee AG, Zhou QY. Dependence of olfactorybulb neurogenesis on prokineticin 2 signaling. Science. 2005 Jun24;308(5730):1923-7. doi: 10.1126/science.1112103. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/15976302)
- Prosser HM, Bradley A, Chesham JE, Ebling FJ, Hastings MH, Maywood ES. Prokineticin receptor 2 (Prokr2) is essential for the regulation of circadianbehavior by the suprachiasmatic nuclei. Proc Natl Acad Sci U S A. 2007 Jan9;104(2):648-53. doi: 10.1073/pnas.0606884104. Epub 2007 Jan 3. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17202262) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1761911/)
- Sarfati J, Dode C, Young J. Kallmann syndrome caused by mutations in the PROK2and PROKR2 genes: pathophysiology and genotype-phenotype correlations. Front HormRes. 2010;39:121-132. doi: 10.1159/000312698. Epub 2010 Apr 8. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/20389090)

Genomic Location

The *PROKR2* gene is found on chromosome 20 (https://medlineplus.gov/genetics/chromosome/20/).

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