

# PROK2 Gene

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## 1. Normal Function

The *PROK2* gene provides instructions for making a protein called prokineticin 2. This protein interacts with another protein called prokineticin receptor 2 (produced from the *PROKR2* gene). On the cell surface, prokineticin 2 attaches (binds) 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.

## 2. Health Conditions Related to Genetic Changes

### 2.1. Kallmann syndrome

At least 16 mutations in the *PROK2* gene have been identified in people with 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 *PROK2* and *PROKR2* genes together account for about 9 percent of all cases of Kallmann syndrome.

Most of the *PROK2* gene mutations that cause Kallmann syndrome change single protein building blocks (amino acids) in prokineticin 2. These mutations disrupt the protein's activity, affecting its ability to bind to its receptor to send signals normally. Studies suggest that 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 *PROK2*, and these genetic changes may contribute to the varied features of the condition.

## 3. Other Names for This Gene

- BV8

- KAL4
- MIT1
- PK2
- PROK2\_HUMAN
- Protein Bv8 homolog

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