ANOS1 Gene

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Contributor: Vicky Zhou

anosmin 1

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1. Normal Function

The *ANOS1* gene, also known as *KAL1*, provides instructions for making a protein called anosmin-1. This protein is involved in development before birth. Anosmin-1 is found in the extracellular matrix, which is the intricate lattice of proteins and other molecules that forms in the spaces between cells. Anosmin-1 is active in many parts of the developing embryo, including the respiratory tract, kidneys, digestive system, and certain regions of the brain.

Researchers are working to determine the functions of anosmin-1. They have discovered that, in the developing brain, this protein is involved in the movement (migration) of nerve cells and the outgrowth of axons, which are specialized extensions of nerve cells that transmit nerve impulses. The protein also plays a role in regulating contact between nerve cells (cell adhesion).

Anosmin-1 appears to help control the growth and migration of a group of nerve cells that are specialized to process the sense of smell (olfactory neurons). These nerve cells originate in the developing nose and then migrate together to a structure in the front of the brain called the olfactory bulb, which is critical for the perception of odors. Studies suggest that anosmin-1 is also involved in the migration of neurons that produce a hormone called gonadotropin-releasing hormone (GnRH). Like olfactory neurons, GnRH-producing neurons migrate from the developing nose to the front of the brain. GnRH controls the production of several hormones that direct sexual development before birth and during puberty. These hormones are important for the normal function of the ovaries in women and testes in men.

2. Health Conditions Related to Genetic Changes

Kallmann syndrome

More than 140 mutations in the *ANOS1* 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. This condition can also affect other body systems, and its features vary among affected individuals. Researchers estimate that mutations in the *ANOS1* gene account for 5 to 10 percent of all cases of Kallmann syndrome.

The *ANOS1* gene mutations that cause Kallmann syndrome delete part or all of the gene, change single protein building blocks (amino acids) in anosmin-1, or alter the size of the protein. All of these mutations disrupt the normal production or function of anosmin-1 during embryonic development. Researchers suspect that the missing or altered protein is unable to direct the migration of olfactory nerve cells and GnRH-producing nerve cells to their usual locations in the developing brain. If olfactory nerve cells do not extend to the olfactory bulb, a person's sense of smell will be impaired. Misplacement of GnRH-producing neurons prevents the production of sex hormones, which interferes with normal sexual development and causes puberty to be delayed or absent.

It is unclear how *ANOS1* gene mutations lead to other possible signs and symptoms of Kallmann syndrome, including a failure of one kidney to develop (unilateral renal agenesis), hearing loss, and mirror movements of the hands (bimanual synkinesia). Because these features vary among individuals, researchers suspect that other genetic and environmental factors may be involved. Some affected individuals have mutations in one of several other genes in addition to *ANOS1*, and these genetic changes may contribute to the varied features of the condition.

3. Other Names for This Gene

- adhesion molecule-like X-linked
- ADMLX
- anosmin-1
- HHA
- KAL
- KAL1
- KALIG-1
- Kallmann syndrome 1 protein
- Kallmann syndrome protein
- KALM_HUMAN
- KMS
- WFDC19

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