

NKX2-1 gene

NK2 homeobox 1

Normal Function

The *NKX2-1* gene provides instructions for making a protein called homeobox protein Nkx-2.1, which is a member of the homeobox protein family. Homeobox proteins direct the formation of body structures during early embryonic development. Homeobox protein Nkx-2.1 is particularly involved in the development and function of the brain, lungs, and thyroid gland. The thyroid is a butterfly shaped gland in the lower neck that makes hormones to help regulate a wide variety of critical body functions, including growth and brain development.

Homeobox protein Nkx-2.1 functions as a transcription factor, which means it attaches to DNA and controls the activity (expression) of other genes. In the brain, homeobox protein Nkx-2.1 regulates genes that play a role in the development and movement (migration) of specialized nerve cells (neurons), called interneurons, to their proper location. Interneurons relay signals between other neurons. In the lungs, homeobox protein Nkx-2.1 controls development of lung structures and regulates the expression of surfactant genes, which provide instructions for producing surfactant proteins. Together with certain fats, these proteins form surfactant, which lines the lung tissue and makes breathing easy. In the thyroid gland, homeobox protein Nkx-2.1 controls genes that are critical in the production of thyroid hormones.

Health Conditions Related to Genetic Changes

Brain-lung-thyroid syndrome

At least 100 mutations in the *NKX2-1* gene have been found to cause brain-lung-thyroid syndrome, which encompasses a group of conditions that affect the brain, lungs, and thyroid gland. About half of affected individuals have problems with all three organs, while others have problems with one or two of them. The most common features of this syndrome are benign hereditary chorea, which involves involuntary jerking movements (chorea) of the face, torso, and limbs and other uncontrolled movements; severe breathing difficulty (respiratory distress syndrome); and reduced thyroid gland function (hypothyroidism).

Many of the *NKX2-1* gene mutations involved in brain-lung-thyroid syndrome result in an abnormally short homeobox protein Nkx-2.1 that cannot function normally. Other

mutations change single protein building blocks (amino acids) in the protein, impairing its ability to attach to DNA. Still others delete the whole *NKX2-1* gene. A shortage of functional homeobox protein Nkx-2.1 alters the expression of genes important for the normal development and functioning of the brain, lungs, and thyroid. The production of surfactant proteins is reduced, leading to breathing difficulty; expression of genes involved in the production of thyroid hormones is impaired, accounting for hypothyroidism; and brain development is impaired, likely due to improper interneuron formation or migration, which may underlie the movement abnormalities characteristic of brain-lung-thyroid syndrome.

Other Names for This Gene

- BCH
- BHC
- homeobox protein NK-2 homolog A
- homeobox protein Nkx-2.1 isoform 1
- homeobox protein Nkx-2.1 isoform 2
- NK-2
- NK-2 homolog A
- NKX2.1
- NKX2A
- NMTC1
- T/EBP
- TEBP
- thyroid nuclear factor 1
- thyroid transcription factor 1
- thyroid-specific enhancer-binding protein
- TITF1
- TTF-1
- TTF1

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of NKX2-1 ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=7080\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=7080[geneid]))

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28NKX2-1%5BTIAB%5D%29+OR+%28NK2+homeobox+1%5BTIAB%5D%29%29+AND+%28%28Genes%5B>

MH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- NK2 HOMEBOX 1; NKX2-1 (<https://omim.org/entry/600635>)

Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/7080>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=NKX2-1\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=NKX2-1[gene]))

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Genomic Location

The *NKX2-1* gene is found on chromosome 14 (<https://medlineplus.gov/genetics/chromosome/14/>).

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