NDP gene

norrin cystine knot growth factor NDP

Normal Function

The *NDP* gene provides instructions for making a protein called norrin. Norrin participates in chemical signaling pathways that affect the way cells and tissues develop. Studies suggest that norrin may play a role in Wnt signaling, which is important for cell division (proliferation), attachment of cells to one another (adhesion), cell movement (migration), and many other cellular activities.

Norrin is one of many proteins, or ligands, that can attach (bind) to other proteins called frizzled receptors. These receptors are embedded in the outer membranes of cells. Norrin binds with the receptor frizzled-4 (produced from the *FZD4* gene). The two proteins fit together like a key in a lock. When a ligand binds to a frizzled receptor, it initiates a multi-step process that regulates the activity of certain genes.

The norrin protein and frizzled-4 participate in developmental processes that are believed to be crucial for normal development of the eye and other body systems. In particular, norrin seems to play critical roles in the specialization of cells in the retina (the light-sensitive tissue that lines the back of the eye) and the formation of blood vessels in the retina and in the inner ear.

Health Conditions Related to Genetic Changes

Familial exudative vitreoretinopathy

Several *NDP* gene variants (also called mutations) have been found to cause the eye disorder familial exudative vitreoretinopathy. This disorder affects the retina and can cause vision loss that worsens over time.These variants change single protein building blocks (amino acids) in the norrin protein, altering the normal folding of norrin or preventing it from binding to frizzled-4. The defective norrin disrupts chemical signaling in the developing eye, which interferes with the formation of blood vessels at the edges of the retina. The resulting abnormal blood supply to this tissue leads to retinal damage and vision loss in some people with familial exudative vitreoretinopathy.

Norrie disease

Several variants in the *NDP* gene have been identified in people with Norrie disease.

Norrie disease is an inherited eye disorder that leads to blindness in male infants at birth or soon after birth. The *NDP* gene variants that cause this condition affect the ability of the norrin protein to bind with frizzled-4, interfering with the specialization of retinal cells. As a result, immature retinal cells accumulate in the back of the eyes. The variants also affect the formation of the blood vessels that carry blood to the eye. Without these vessels. some of the tissues of the eye eventually break down.

Norrin is also expressed in other systems of the body, and the effects of the disorder can be widespread and include intellectual disabilities, seizures, behavioral problems, and delayed development. The specific abnormalities and their severity depend on the type and location of the *NDP* gene variant. Variants that delete portions of the *NDP* gene prevent the production of norrin and result in severe problems that affect many body systems in addition to the eyes. Variants that delete or change single amino acids usually result in less widespread effects.

Other retinal dystrophies

NDP gene variants may cause other disorders that affect the retina. One of these disorders is called Coats disease. This disorder causes leakage of blood vessels in the retina and retinal detachment, a condition in which layers of the retina separate. This condition can result in vision loss.

Persistent hyperplastic primary vitreous (PHPV) is another retinal disorder that may be caused by *NDP* gene variants. In PHPV, a remnant of a blood vessel found in the eye before birth remains as a fibrous white stalk between the back of the eye and the lens. Persistent hyperplastic primary vitreous can cause vision loss through retinal detachment, cloudiness of the lens (cataract), or increased pressure inside the eye (glaucoma) that can damage the optic nerve.

In addition, *NDP* gene variants may influence the course of a retinal disorder that affects some premature infants. Retinopathy of prematurity is a condition in which abnormal blood vessels appear in the retina and can cause retinal detachment. Babies with retinopathy of prematurity may experience improvement of the condition over time, but some *NDP* gene variants have been associated with a worsening of the condition.

Other Names for This Gene

- ND
- NDP_HUMAN
- Norrie disease (pseudoglioma)
- norrin

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of NDP (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=4693[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28NDP%5BTIAB%5D%29+OR+%28Norrie+disease%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%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

- NORRIN CYSTINE KNOT GROWTH FACTOR NDP; NDP (https://omim.org/entry/300658)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/4693)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=NDP[gene])

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Genomic Location

The *NDP* gene is found on the X chromosome (https://medlineplus.gov/genetics/chromosome/x/).

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