EXT2 Gene

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exostosin glycosyltransferase 2

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1. Normal Function

The *EXT2* gene provides instructions for producing a protein called exostosin-2. This protein is found in a cell structure called the Golgi apparatus, which modifies newly produced enzymes and other proteins. In the Golgi apparatus, exostosin-2 attaches (binds) to another protein, exostosin-1, to form a complex that modifies a protein called heparan sulfate so it can be used in the body. Heparan sulfate is involved in regulating a variety of body processes including the formation of blood vessels (angiogenesis) and blood clotting. It also has a role in the spread (metastasis) of cancer cells.

2. Health Conditions Related to Genetic Changes

2.1 Hereditary Multiple Osteochondromas

About 220 mutations in the *EXT2* gene have been identified in people with hereditary multiple osteochondromas type 2, a condition in which people develop multiple benign (noncancerous) bone tumors called osteochondromas. Most of these mutations prevent any functional exostosin-2 protein from being made, and are called "loss-of-function" mutations. The loss of exostosin-2 protein function prevents it from forming a complex with the exostosin-1 protein and modifying heparan sulfate. It is unclear how this impairment leads to the development of multiple osteochondromas.

2.2 Potocki-Shaffer Syndrome

A genetic change resulting in the deletion of the *EXT2* gene causes a condition called Potocki-Shaffer syndrome. People with this condition have multiple osteochondromas (described above) and enlarged openings in two bones that make up much of the top and sides of the skull (enlarged parietal foramina). Other signs and symptoms seen in some people with Potocki-Shaffer syndrome include intellectual disability, developmental delay, distinctive facial features, vision problems, and defects in the heart, kidneys, and urinary tract.

Potocki-Shaffer syndrome (sometimes referred to as proximal 11p deletion syndrome) is caused by a deletion of genetic material from the short (p) arm of chromosome 11. In people with this condition, a loss of the *EXT2* gene within this region is responsible for multiple osteochondromas. The deletion likely leads to a reduction of exostosin-2 protein and the inability to process heparan sulfate correctly. Although heparan sulfate is involved in many body processes, it is unclear how the lack of this protein causes multiple osteochondromas. The loss of additional genes in the deleted region likely contributes to the other features of Potocki-Shaffer syndrome. Specifically, loss of the *ALX4* gene results in enlarged parietal foramina, and deletion of the *PHF21A* gene causes intellectual disability and distinctive facial features.

2.3 Other Disorders

At least two mutations in the *EXT2* gene have been found in a family with seizures-scoliosis-macrocephaly syndrome. In individuals with this condition, seizures typically begin in early childhood. Affected individuals also have an abnormal curvature of the spine (scoliosis), an unusually large head (macrocephaly), intellectual disability, and weak muscle tone (hypotonia). The *EXT2* gene mutations associated with seizures-scoliosis-macrocephaly syndrome change single protein building blocks (amino acids) in the exostosin-2 protein. These changes reduce the amount of functional exostosin-2 protein, which likely disrupts normal modification of heparan sulfate. It is unclear how this disruption leads to the varied signs and symptoms of the condition. Individuals with seizures-scoliosis-macrocephaly syndrome do not appear to develop osteochondromas (described above).

3. Other Names for This Gene

- exostoses (multiple) 2
- exostosin 2
- EXT2_HUMAN
- Glucuronosyl-N-acetylglucosaminyl-proteoglycan 4-alpha-N- acetylglucosaminyltransferase
- N-acetylglucosaminyl-proteoglycan 4-beta-glucuronosyltransferase
- SOTV

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