PTPN11 Gene

Subjects: Genetics & Heredity
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protein tyrosine phosphatase, non-receptor type 11

genes

1. Normal Function

The *PTPN11* gene provides instructions for making a protein called SHP-2. This protein helps regulate the RAS/MAPK signaling pathway. This pathway is involved in several important cell functions, including the growth and division of cells (proliferation), the process by which cells mature to carry out specific functions (differentiation), cell movement (migration), and the self-destruction of cells (apoptosis). During embryonic development, the SHP-2 protein is critical in the development of the heart, blood cells, bones, and several other tissues.

The *PTPN11* gene belongs to a class of genes known as oncogenes. When mutated, oncogenes have the potential to cause normal cells to become cancerous.

2. Health Conditions Related to Genetic Changes

2.1. Noonan syndrome

More than 90 mutations causing Noonan syndrome have been identified in the *PTPN11* gene. This condition is characterized by mildly unusual facial characteristics, short stature, heart defects, bleeding problems, skeletal malformations, and many other signs and symptoms. Most of the *PTPN11* gene mutations replace single amino acids used to make the SHP-2 protein. The resulting protein is either continuously turned on (active) or has prolonged activation, rather than promptly switching on and off in response to other cellular proteins. This increase in protein activity disrupts the regulation of the RAS/MAPK signaling pathway that controls cell functions such as proliferation. This misregulation can result in the heart defects, growth problems, skeletal abnormalities, and other features of Noonan syndrome.

Rarely, a person with Noonan syndrome caused by *PTPN11* gene mutations will also develop juvenile myelomonocytic leukemia, which is a type of blood cancer that typically affects children or adolescents.

2.2. Noonan syndrome with multiple lentigines

At least 11 mutations in the *PTPN11* gene have been found to cause Noonan syndrome with multiple lentigines (formerly called LEOPARD syndrome). This condition is characterized by multiple brown skin spots (lentigines), heart defects, short stature, a sunken or protruding chest, and distinctive facial features. Two mutations that account for approximately 65 percent of cases of Noonan syndrome with multiple lentigines caused by *PTPN11* gene mutations change single protein building blocks (amino acids) in the SHP-2 protein: One mutation replaces the amino acid tyrosine with the amino acid cysteine at position 279 (written Tyr279Cys or Y279C) and the other mutation replaces the amino acid threonine with the amino acid methionine at position 468 (written as Thr468Met or T468M).

All known *PTPN11* gene changes that cause Noonan syndrome with multiple lentigines are believed to disrupt the SHP-2 protein's normal function. This decrease in protein function impairs the activation of the RAS/MAPK signaling pathway that controls cell functions such as growth and division. This misregulation can result in the various features of Noonan syndrome with multiple lentigines.

Although the *PTPN11* gene is an oncogene, a reduction in this protein's function does not seem to increase cancer risk in people with Noonan syndrome with multiple lentigines.

2.3. Cancers

Gene mutations can be acquired during a person's lifetime and are present only in certain cells. This type of mutation is called a somatic mutation, and it is not inherited. Somatic mutations in the *PTPN11* gene can increase the risk of developing juvenile myelomonocytic leukemia. These mutations cause the SHP-2 protein to be continuously active. Overactivity of the SHP-2 protein disrupts the regulation of pathways that control the production of immature blood cells. As a result, certain white blood cells are overproduced, leading to this type of leukemia. Somatic mutations in the *PTPN11* gene are found in about 35 percent of people with juvenile myelomonocytic leukemia.

Some studies indicate that somatic mutations in the *PTPN11* gene are also associated with other blood disorders including chronic myelomonocytic leukemia, myelodysplastic syndrome, nonsyndromic acute myeloid leukemia, and acute lymphocytic leukemia. In rare cases, somatic *PTPN11* gene mutations are found in cancers of the lung, colon, brain, thyroid, and in a type of skin cancer called melanoma.

2.4. Other disorders

Mutations in the *PTPN11* gene can cause a condition called metachondromatosis. This condition is characterized by multiple benign (noncancerous) bone tumors called osteochondromas on the bones of the hands and feet. People with this condition also develop enchondromas, which are benign growths of cartilage. In people with metachondromatosis, the growths form at the ends of the long bones or the sides of the hip bones. The growths characteristic of metachondromatosis typically develop during childhood and for reasons that are not understood, usually disappear over time.

3. Other Names for This Gene

- BPTP3
- protein tyrosine phosphatase, non-receptor type 11 (Noonan syndrome 1)
- protein-tyrosine phosphatase 2C
- PTN11_HUMAN
- PTP-1D
- PTP2C
- SH protein-tyrosine phosphatase
- SH-PTP2
- SH-PTP3
- SHP2
- SHP2 phosphatase

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