NPHS1 Gene

Subjects: Genetics & Heredity
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NPHS1, nephrin

genes

1. Introduction

The *NPHS1* gene provides instructions for making a protein called nephrin. Nephrin is primarily found in the kidneys, which are organs that filter waste products from the blood and remove them in urine. Specifically, nephrin is found in cells called podocytes, which are located in specialized kidney structures called glomeruli. Nephrin is located at the cell surface in the area between two podocytes called the slit diaphragm. The slit diaphragm is known as a filtration barrier because it captures proteins in blood so that they remain in the body while allowing other molecules like sugars and salts to be excreted in urine. Nephrin proteins on one cell interact with nephrin proteins on adjacent podocytes, forming a zipper-like structure. This structure allows the passage of small molecules through the slit diaphragm while preventing larger molecules like proteins from passing through. Nephrin proteins are essential for forming the slit diaphragm, anchoring the slit diaphragm to podocytes, and filtering blood.

Nephrin is also involved in cell signaling. It relays signals from outside the cell to inside the cell. Additionally, nephrin proteins on the surface of adjacent cells send and receive signals, allowing podocytes to communicate with one another.

2. Health Conditions Related to Genetic Changes

2.1. Congenital nephrotic syndrome

At least 250 mutations in the *NPHS1* gene have been found to cause congenital nephrotic syndrome. This condition is a kidney disorder that begins in infancy and typically leads to irreversible kidney failure (end-stage renal disease) by early childhood.

NPHS1 gene mutations account for all cases of congenital nephrotic syndrome of the Finnish type. This form of the condition is found in people of Finnish ancestry. Two specific mutations, both of which result in an abnormally short, nonfunctional nephrin protein, account for nearly all cases. The first mutation, known as $Finn_{major}$, is written as L41fsX90 and is responsible for 78 percent of cases. The second mutation, known as $Finn_{minor}$, is written as R1109X and is responsible for 16 percent of cases.

NPHS1 gene mutations can also cause congenital nephrotic syndrome in non-Finnish individuals. Most of these mutations result in an abnormal nephrin protein that is trapped inside the cell and cannot get to the podocyte cell surface. A shortage of functional nephrin at the podocyte cell surface impairs the formation of normal slit diaphragms. Without a functional slit diaphragm, molecules pass through the kidneys abnormally and are excreted in urine. The filtering ability of the kidneys worsens from birth, eventually leading to end-stage renal disease.

3. Other Names for This Gene

- CNF
- nephrin
- nephrin precursor
- nephrosis 1, congenital, Finnish type (nephrin)
- NPHN
- NPHS1 nephrin
- renal glomerulus-specific cell adhesion receptor

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