TCF4 Gene

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Contributor: Rui Liu

Transcription factor 4: The TCF4 gene provides instructions for making a protein that attaches (binds) to specific regions of DNA and helps control the activity of many other genes.

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1. Normal Function

The *TCF4* gene provides instructions for making a protein that attaches (binds) to specific regions of DNA and helps control the activity of many other genes. On the basis of this action, the TCF4 protein is known as a transcription factor. The TCF4 protein is part of a group of proteins known as E-proteins. E-proteins each bind with another identical or similar protein and then bind to a specific sequence of DNA known as an E-box. E-proteins are involved in many aspects of development.

The TCF4 protein is found in the brain, muscles, lungs, and heart. This protein also appears to be active (expressed) in various tissues before birth. The TCF4 protein plays a role in the maturation of cells to carry out specific functions (cell differentiation) and the self-destruction of cells (apoptosis).

2. Health Conditions Related to Genetic Changes

2.1. Pitt-Hopkins syndrome

At least 50 mutations in the *TCF4* gene have been found to cause Pitt-Hopkins syndrome, a condition characterized by severe intellectual disability and breathing problems. Some mutations delete a few building blocks of DNA (nucleotides) within the *TCF4* gene, while other mutations delete the *TCF4* gene as well as a number of genes that surround it. Still other *TCF4* gene mutations replace single nucleotides. The type of the mutation does not appear to affect the severity of the condition.

TCF4 gene mutations disrupt the protein's ability to bind to DNA and control the activity of certain genes. These gene mutations typically do not affect the TCF4 protein's ability to bind to other proteins. The TCF4 protein's inability to bind to DNA and control the activity of certain genes, particularly those genes involved in nervous system development and function, contributes to the signs and symptoms of Pitt-Hopkins syndrome. It is also likely that the loss of the normal proteins that are attached to the nonfunctional TCF4 proteins contribute to the features of this condition.

2.2. Distal 18q deletion syndrome

The *TCF4* gene is involved in some cases of a condition called distal 18q deletion syndrome, which occurs when a piece of the long (q) arm of chromosome 18 is missing. The term "distal" means that the missing piece occurs near one end of the chromosome. Distal 18q deletion syndrome can lead to a wide variety of signs and symptoms among affected individuals, depending on which genes in this part of chromosome 18 are affected. People with this disorder whose deletions include the *TCF4* gene usually have signs and symptoms of Pitt-Hopkins syndrome (described above) in addition to other features of distal 18q deletion syndrome that are likely associated with the loss of nearby genes.

Fuchs endothelial dystrophy

3. Other Names for This Gene

- bHLHb19
- class B basic helix-loop-helix protein 19
- E2-2

- immunoglobulin transcription factor 2
- ITF-2
- ITF2
- ITF2_HUMAN
- SEF-2
- SEF2
- TCF-4

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