TNFRSF1A Gene

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Contributor: Rui Liu

TNF receptor superfamily member 1A: The TNFRSF1A gene provides instructions for making a protein called tumor necrosis factor receptor 1 (TNFR1).

genes

1. Normal Function

The *TNFRSF1A* gene provides instructions for making a protein called tumor necrosis factor receptor 1 (TNFR1). This protein is found spanning the membrane of cells, with part of the TNFR1 protein outside the cell and part of the protein inside the cell. Outside the cell, the TNFR1 protein attaches (binds) to another protein called tumor necrosis factor (TNF). The interaction of the TNF protein with the TNFR1 protein causes the TNFR1 protein to bind to two other TNFR1 proteins, forming a three-protein complex called a trimer. This trimer formation is necessary for the TNFR1 protein to be functional.

The binding of the TNF and TNFR1 proteins causes the TNFR1 protein to send signals inside the cell. Signaling from the TNFR1 protein can trigger either inflammation or self-destruction of the cell (apoptosis). Signaling within the cell initiates a pathway that turns on a protein called nuclear factor kappa B, which triggers inflammation and leads to the production of immune system proteins called cytokines. Apoptosis is initiated when the TNFR1 protein, bound to the TNF protein, is brought into the cell and starts a process known as the caspase cascade.

2. Health Conditions Related to Genetic Changes

2.1. Tumor necrosis factor receptor-associated periodic syndrome

More than 60 mutations in the *TNFRSF1A* gene have been found to cause tumor necrosis factor receptor-associated periodic syndrome (commonly known as TRAPS). Most of these mutations lead to changes in single protein building blocks (amino acids), typically involving the amino acid cysteine. Cysteines contain sulfur atoms that form connections, called disulfide bonds, with other cysteines. Disulfide bonds help a protein fold by connecting cysteines in different regions of the protein. These bonds stabilize the protein and give it the appropriate shape to carry out its particular function.

When cysteines within the TNFR1 protein are replaced with other amino acids, the disulfide bonds are not formed, and the protein is misfolded. These misfolded proteins are trapped within the cell, unable to get to the cell surface

to interact with TNF. Inside the cell, these proteins clump together and are thought to trigger alternative pathways that initiate inflammation. The clumps of protein constantly activate these alternative inflammation pathways, leading to excess inflammation in people with TRAPS. Additionally, because only one copy of the *TNFRSF1A* gene has a mutation, some normal TNFR1 proteins are produced and can bind to the TNF protein, leading to additional inflammation. It is unclear if disruption of the apoptosis pathway plays a role in the signs and symptoms of TRAPS.

Some people with mutations in the *TNFRSF1A* gene do not develop TRAPS, or they develop very mild features of the disorder. The reason for this variability is unclear, but researchers believe that other factors, such as additional genetic changes or environmental factors, may play a role in causing TRAPS.

Multiple sclerosis

3. Other Names for This Gene

- p55
- p55-R
- TNF-R
- TNF-R1
- TNF-R55
- TNFR-I
- TNFR1
- TNFR55
- TNR1A_HUMAN
- tumor necrosis factor binding protein 1
- tumor necrosis factor receptor superfamily member 1A
- tumor necrosis factor receptor superfamily, member 1A
- tumor necrosis factor receptor type 1
- tumor necrosis factor-alpha receptor

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