RFXAP gene

regulatory factor X associated protein

Normal Function

The *RFXAP* gene provides instructions for making a protein called RFX associated protein (RFXAP). It primarily helps control the activity (transcription) of genes called major histocompatibility complex (MHC) class II genes. Transcription is the first step in the production of proteins, and RFXAP is critical for the production of specialized immune proteins called MHC class II proteins from these genes.

The RFXAP protein is part of a group of proteins called the regulatory factor X (RFX) complex. This complex attaches to a specific region of DNA involved in the regulation of MHC class II gene activity. The RFXAP protein helps the complex attach to the correct region of DNA. The RFX complex attracts other necessary proteins to this region and helps turn on MHC class II gene transcription, allowing production of MHC class II proteins.

MHC class II proteins are found on the surface of several types of immune cells, including white blood cells (lymphocytes) that are involved in immune reactions. These proteins play an important role in the body's immune response to foreign invaders, such as bacteria, viruses, and fungi. To help the body recognize and fight infections, MHC class II proteins bind to fragments of proteins (peptides) from foreign invaders so that other specialized immune system cells can interact with them. When these immune system cells recognize the peptides as harmful, they trigger the lymphocytes and other immune cells to launch immune responses to get rid of the foreign invaders.

The RFX complex also appears to play a role in the transcription of MHC class I genes, which provide instructions for making immune system proteins called MHC class I proteins. Like MHC class II proteins, MHC class I proteins attach to peptides from foreign invaders and present them to specific immune system cells. These cells then attack the foreign invaders to rid them from the body. While the RFX complex is able to help control MHC class I gene activity, it is not the primary regulator of these genes. Other proteins play a more prominent role in their transcription.

Health Conditions Related to Genetic Changes

Bare lymphocyte syndrome type II

At least seven mutations in the *RFXAP* gene have been found to cause an immune system disorder called bare lymphocyte syndrome type II (BLS II). BLS II is a type of combined immunodeficiency (CID), in which affected individuals have virtually no immune protection from foreign invaders. Consequently, individuals with BLS II have persistent infections in the respiratory, gastrointestinal, and urinary tracts, which can be life-threatening.

Mutations in the *RFXAP* gene lead to production of an abnormally short RFXAP protein that likely does not function properly, if any protein is produced at all. These changes impair binding of the RFX complex to DNA, which prevents transcription of MHC class II proteins. Consequently, lymphocytes lack any MHC class II proteins on their surface, and the body has difficulty getting rid of bacteria, viruses, and fungi, leading to the persistent infections characteristic of BLS II.

Other disorders

At least one mutation in the *RFXAP* gene has been found to cause bare lymphocyte syndrome type III (BLS III). This type of bare lymphocyte syndrome is characterized by absence of MHC class II proteins and a reduced amount of MHC class I proteins on the surface of lymphocytes. However, it is unclear if BLS III is a distinct diagnosis. Some doctors consider such cases to be BLS II (described above). Both types of BLS cause persistent, life-threatening infections.

The *RFXAP* gene mutation involved in BLS III likely impairs the function of the RFX complex, preventing transcription of MHC class II genes and reducing the activity of MHC class I genes. Without the important immune system proteins produced from these genes, the body is less able to fight infections. It is unclear why certain *RFXAP* gene mutations impair production of MHC class I proteins and others do not.

Other Names for This Gene

- regulatory factor X-associated protein
- RFX DNA-binding complex 36 kDa subunit
- RFX-associated protein

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of RFXAP (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=5994[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28RFXAP%5BTIAB%5D%29+OR+%28regulatory+factor+X+associated+protein%5BTIAB%5D%29%29+OR+%28%28RFX+DNA-binding+complex+36+kDa+subunit%5BTIAB%5D%29+OR+%2

8RFX-associated+protein%5BTIAB%5D%29+OR+%28regulatory+factor+X-associated+protein%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- REGULATORY FACTOR X-ASSOCIATED PROTEIN; RFXAP (https://omim.org/entry/601861)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/5994)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=RFXAP[gene])

References

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Genomic Location

The *RFXAP* gene is found on chromosome 13 (https://medlineplus.gov/genetics/chromosome/13/).

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