

## RFX5 gene

regulatory factor X5

### Normal Function

The *RFX5* gene provides instructions for making a protein that 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 RFX5 is critical for the production of specialized immune proteins called MHC class II proteins from these genes.

The RFX5 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 RFX5 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 *RFX5* 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 *RFX5* gene lead to production of an abnormally short RFX5 protein that likely does not function properly. 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 Names for This Gene

- DNA-binding protein RFX5
- regulatory factor X 5
- regulatory factor X, 5 (influences HLA class II expression)

## Additional Information & Resources

### Tests Listed in the Genetic Testing Registry

- Tests of RFX5 ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=5993\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=5993[geneid]))

## Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28RFX5%5BTIAB%5D%29+OR+%28regulatory+factor+X%5BTIAB%5D%29%29+OR+%28%28DNA-binding+protein+RFX5%5BTIAB%5D%29+OR+%28regulatory+factor+X%5BTIAB%5D%29+OR+%28regulatory+factor+X,+%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+2880+days%22%5Bdp%5D>)

## Catalog of Genes and Diseases from OMIM

- REGULATORY FACTOR X, 5; RFX5 (<https://omim.org/entry/601863>)

## Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/5993>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=RFX5\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=RFX5[gene]))

## References

- Burd AL, Ingraham RH, Goldrick SE, Kroe RR, Crute JJ, Grygon CA. Assembly of major histocompatibility complex (MHC) class II transcription factors: association and promoter recognition of RFX proteins. *Biochemistry*. 2004 Oct 12; 43(40):12750-60. doi: 10.1021/bi030262o. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/15461447>)
- Garvie CW, Boss JM. Assembly of the RFX complex on the MHCII promoter: role of RFXAP and RFXB in relieving autoinhibition of RFX5. *Biochim Biophys Acta*. 2008 Dec; 1779(12):797-804. doi: 10.1016/j.bbagra.2008.07.012. Epub 2008 Aug 6. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/18723135>)
- Gobin SJ, Peijnenburg A, van Eggermond M, van Zutphen M, van den Berg R, vanden Elsen PJ. The RFX complex is crucial for the constitutive and CIITA-mediated transactivation of MHC class I and beta2-microglobulin genes. *Immunity*. 1998 Oct; 9(4):531-41. doi: 10.1016/s1074-7613(00)80636-6. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/9806639>)
- Villard J, Reith W, Barras E, Gos A, Morris MA, Antonarakis SE, Van den Elsen PJ, Mach B. Analysis of mutations and chromosomal localisation of the gene encoding RFX5, a novel transcription factor affected in major histocompatibility complex class II deficiency. *Hum Mutat*. 1997; 10(6):430-5. doi:10.1002/(SICI)1098-1004(1997)10:63.0.CO;2-H. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/9401005>)

## Genomic Location

The *RFX5* gene is found on chromosome 1 (<https://medlineplus.gov/genetics/chromosome/1/>).

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