NCF2 gene

neutrophil cytosolic factor 2

Normal Function

The *NCF2* gene provides instructions for making a protein called neutrophil cytosolic factor 2 (also known as p67-phox). This protein is one part (subunit) of a group of proteins that forms an enzyme complex called NADPH oxidase, which plays an essential role in the immune system. Specifically, NADPH oxidase is primarily active in immune system cells called phagocytes. These cells catch and destroy foreign invaders such as bacteria and fungi. NADPH oxidase is also thought to regulate the activity of immune cells called neutrophils. These cells play a role in adjusting the inflammatory response to optimize healing and reduce injury to the body.

The presence of foreign invaders stimulates phagocytes and triggers the assembly of NADPH oxidase. This enzyme participates in a chemical reaction that converts oxygen to a toxic molecule called superoxide. Superoxide is used to generate several other compounds, including hydrogen peroxide (a strong disinfectant) and hypochlorous acid (the active ingredient in bleach). These highly reactive, toxic substances are known as reactive oxygen species. Phagocytes use these substances to kill foreign invaders, preventing them from reproducing in the body and causing illness.

Health Conditions Related to Genetic Changes

Chronic granulomatous disease

More than 50 mutations in the *NCF2* gene have been found to cause chronic granulomatous disease. People with this disorder are at increased risk of developing recurrent episodes of infection and inflammation due to a weakened immune system. Mutations in the *NCF2* gene cause less than 5 percent of all cases of this condition. These mutations change single protein building blocks (amino acids) in the neutrophil cytosolic factor 2 protein, which cause the protein to be abnormally short and nonfunctional or alter its 3-dimensional structure. All of these mutations decrease the function of the neutrophil cytosolic factor 2 protein or prevent its production. Without this protein, NADPH oxidase cannot assemble or function properly. As a result, phagocytes are unable to produce reactive oxygen species to kill foreign invaders and neutrophil activity is not regulated. A lack of NADPH oxidase leaves affected individuals vulnerable to many types of infection and excessive inflammation.

Systemic lupus erythematosus

Studies suggest that certain normal variations in the *NCF2* gene can increase the risk of a condition called systemic lupus erythematosus. This condition is one of a group of related diseases known as autoimmune disorders, which occur when the immune system malfunctions and attacks the body's tissues and organs. The variants associated with increased risk of systemic lupus erythematosus change single DNA building blocks (nucleotides) in the *NCF2* gene. These changes are thought to result in the production of a neutrophil cytosolic factor 2 protein with an altered function that impairs the function of NADPH oxidase. As a result, fewer reactive oxygen species are produced when foreign invaders trigger an immune reaction. This lack of reactive oxygen species causes the body to overcompensate by activating more immune cells and producing more immune proteins. The overactive immune reaction increases the risk that the immune cells will attack the body's tissues and organs, causing systemic lupus erythematosus. Researchers believe that a combination of genetic and environmental factors play a role in development of this complex condition.

Other Names for This Gene

- NADPH oxidase activator 2
- NCF-2
- NCF2_HUMAN
- neutrophil cytosol factor 2
- NOXA2
- P67-PHOX
- P67PHOX

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of NCF2 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=4688[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28NCF2%5BTIAB%5D%29+OR+%28p67phox%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- NEUTROPHIL CYTOSOLIC FACTOR 2; NCF2 (https://omim.org/entry/608515)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/4688)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=NCF2[gene])

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Genomic Location

The *NCF2* gene is found on chromosome 1 (https://medlineplus.gov/genetics/chromosome/1/).

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