

# NCF2 Gene

Subjects: **Genetics & Heredity**

Contributor: Lily Guo

neutrophil cytosolic factor 2

genes

## 1. Introduction

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.

## 2. Health Conditions Related to Genetic Changes

### 2.1. 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.

## 2.2. Autoimmune disorders

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.

## 3. Other Names for This Gene

- NADPH oxidase activator 2
- NCF-2
- NCF2\_HUMAN
- neutrophil cytosol factor 2
- NOXA2
- P67-PHOX
- P67PHOX

## References

1. Cunningham Graham DS, Morris DL, Bhangale TR, Criswell LA, Syvänen AC, Rönnblom L, Behrens TW, Graham RR, Vyse TJ. Association of NCF2, IKZF1, IRF8, IFIH1, and TYK2 with systemic lupus erythematosus. *PLoS Genet.* 2011 Oct;7(10):e1002341. doi: 10.1371/journal.pgen.1002341.
2. Jacob CO, Eisenstein M, Dinauer MC, Ming W, Liu Q, John S, Quismorio FP Jr, Reiff A, Myones BL, Kaufman KM, McCurdy D, Harley JB, Silverman E, Kimberly RP, Vyse TJ, Gaffney PM, Moser KL, Klein-Gitelman M, Wagner-Weiner L, Langefeld CD, Armstrong DL, Zidovetzki R. Lupus-associated causal mutation in neutrophil cytosolic factor 2 (NCF2) brings unique insights to the

structure and function of NADPH oxidase. *Proc Natl Acad Sci U S A.* 2012 Jan 10;109(2):E59-67. doi:10.1073/pnas.1113251108.

3. Kannengiesser C, Gérard B, El Benna J, Henri D, Krovíarski Y, Chollet-Martin S, Gougerot-Pocidalo MA, Elbim C, Grandchamp B. Molecular epidemiology of chronic granulomatous disease in a series of 80 kindreds: identification of 31 novel mutations. *Hum Mutat.* 2008 Sep;29(9):E132-49. doi: 10.1002/humu.20820.

4. Roos D, Kuhns DB, Maddalena A, Bustamante J, Kannengiesser C, de Boer M, van Leeuwen K, Köker MY, Wolach B, Roesler J, Malech HL, Holland SM, Gallin JI, Stasia MJ. Hematologically important mutations: the autosomal recessive forms of chronic granulomatous disease (second update). *Blood Cells Mol Dis.* 2010 Apr 15;44(4):291-9. doi: 10.1016/j.bcmd.2010.01.009.

5. Stasia MJ, Li XJ. Genetics and immunopathology of chronic granulomatous disease. *Semin Immunopathol.* 2008 Jul;30(3):209-35. doi:10.1007/s00281-008-0121-8.

6. Sumimoto H. Structure, regulation and evolution of Nox-family NADPH oxidases that produce reactive oxygen species. *FEBS J.* 2008 Jul;275(13):3249-77. doi:10.1111/j.1742-4658.2008.06488.x. 2008 Aug;275(15):3984.

Retrieved from <https://encyclopedia.pub/entry/history/show/13736>