

RANBP2 Gene

Subjects: Genetics & Heredity

Contributor: Karina Chen

RAN binding protein 2

Keywords: genes

1. Normal Function

The *RANBP2* gene provides instructions for making a protein that typically associates with a protein complex known as the nuclear pore. The nuclear pore is embedded within the membrane that surrounds the cell's nucleus (called the nuclear envelope), forming a channel that allows transport of molecules in and out of the nucleus. The RANBP2 protein is attached to the nuclear pore outside of the nucleus, where it helps regulate the transport of proteins and other molecules through the nuclear pore and also helps modify proteins coming into or out of the nucleus.

When found elsewhere in the cell, the RANBP2 protein plays multiple roles during cell division, including breaking down and forming the nuclear envelope and dividing chromosomes. The RANBP2 protein is thought to associate with cell structures called microtubules, which form scaffolding within the cell to help cells maintain their shape. In conjunction with microtubules, the RANBP2 protein helps transport materials within cells.

In nerve cells in the brain, the RANBP2 protein is likely involved in the regulation of energy and the maintenance of the protective barrier that allows only certain substances to pass between blood vessels and the brain (the blood-brain barrier).

2. Health Conditions Related to Genetic Changes

2.1. Acute necrotizing encephalopathy type 1

At least three mutations in the *RANBP2* gene have been found to increase the risk of developing acute necrotizing encephalopathy type 1. This condition, also known as susceptibility to infection-induced acute encephalopathy 3 or IIAE3, is a rare type of brain disease (encephalopathy) that occurs following a viral infection such as the flu. These mutations change single protein building blocks (amino acids) in the RANBP2 protein, resulting in the production of a protein that cannot function normally either due to altered shape or because it cannot get to the nuclear pore where it is needed.

These *RANBP2* gene mutations do not cause health problems on their own; it is unclear how they are involved in the process by which a viral infection triggers neurological damage. While individuals with acute necrotizing encephalopathy type 1 frequently have damage to and often lose their blood-brain barrier, the influence of *RANBP2* gene mutations is unknown. Researchers suspect that individuals who develop acute necrotizing encephalopathy type 1 produce too many immune system proteins called cytokines in response to the infection. The excess cytokines lead to prolonged inflammation, although the role of the altered RANBP2 protein in this process is unknown. Inflammation is a normal immune system response to injury and foreign invaders (such as viruses). However, excessive inflammation can damage many of the body's tissues. Additionally, certain cytokines can be toxic to nerve cells when present in large amounts. It is suspected that the combination of the altered RANBP2 protein and the abnormal immune response play a role in individuals' susceptibility to recurrent episodes of acute necrotizing encephalopathy type 1. In people with acute necrotizing encephalopathy type 1, the virus is not found in nerve cells in the brain or spinal cord (central nervous system), so it is likely that the immune reaction, rather than the infection itself, accounts for the neurological signs and symptoms.

2.2. Cancers

Genetic abnormalities that involve the *RANBP2* gene can cause an abnormal growth called an inflammatory myofibroblastic tumor. This type of tumor can be noncancerous (benign) or cancerous (malignant) and can be found in tissues throughout the body. The genetic changes that cause this tumor are somatic, which means that they are acquired during a person's lifetime and are present only in certain cells. These genetic abnormalities result in a rearrangement (translocation) within chromosome 2 that fuses part of the *RANBP2* gene with another gene known as *ALK*. The fusion of these two genes results in production of an abnormal protein that promotes uncontrolled cell growth, which can lead to the formation of a tumor.

3. Other Names for This Gene

- 358 kDa nucleoporin
- ADANE
- ANE1
- E3 SUMO-protein ligase RanBP2
- IIAE3
- nuclear pore complex protein Nup358
- nucleoporin 358
- nucleoporin Nup358
- NUP358
- P270
- ran-binding protein 2
- transformation-related protein 2
- TRP1
- TRP2

References

1. Chen ST, Lee JC. An inflammatory myofibroblastic tumor in liver with ALK and RANBP2 gene rearrangement: combination of distinct morphologic, immunohistochemical, and genetic features. *Hum Pathol*. 2008 Dec;39(12):1854-8. doi: 10.1016/j.humpath.2008.04.016.
 2. Li J, Yin WH, Takeuchi K, Guan H, Huang YH, Chan JK. Inflammatory myofibroblastic tumor with RANBP2 and ALK gene rearrangement: a report of two cases and literature review. *Diagn Pathol*. 2013 Sep 13;8:147. doi:10.1186/1746-1596-8-147. Review.
 3. Neilson DE, Adams MD, Orr CM, Schelling DK, Eiben RM, Kerr DS, Anderson J, Bassuk AG, Bye AM, Childs AM, Clarke A, Crow YJ, Di Rocco M, Dohna-Schwake C, Dueckers G, Fasano AE, Gika AD, Giannis D, Gorman MP, Grattan-Smith PJ, Hackenberg A, Kuster A, Lentschig MG, Lopez-Laso E, Marco EJ, Mastroianni S, Perrier J, Schmitt-Mechelke T, Servidei S, Skardoutsou A, Uldall P, van der Knaap MS, Goglin KC, Tefft DL, Aubin C, de Jager P, Hafler D, Warman ML. Infection-triggered familial or recurrent cases of acute necrotizing encephalopathy caused by mutations in a component of the nuclear pore, RANBP2. *Am J Hum Genet*. 2009 Jan;84(1):44-51. doi: 10.1016/j.ajhg.2008.12.009.
 4. Neilson DE. The interplay of infection and genetics in acute necrotizing encephalopathy. *Curr Opin Pediatr*. 2010 Dec;22(6):751-7. doi:10.1097/MOP.0b013e3283402bfe. Review.
 5. Sell K, Storch K, Hahn G, Lee-Kirsch MA, Ramantani G, Jackson S, Neilson D, von der Hagen M, Hehr U, Smitka M. Variable clinical course in acute necrotizing encephalopathy and identification of a novel RANBP2 mutation. *Brain Dev*. 2016 Sep;38(8):777-80. doi: 10.1016/j.braindev.2016.02.007.
-

