FANCA Gene

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Contributor: Vivi Li

FA complementation group A

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1. Normal Function

The *FANCA* gene provides instructions for making a protein that is involved in a cell process known as the Fanconi anemia (FA) pathway. The FA pathway is turned on (activated) when the process of making new copies of DNA, called DNA replication, is blocked due to DNA damage. The FA pathway is particularly responsive to a certain type of DNA damage known as interstrand cross-links (ICLs). ICLs occur when two DNA building blocks (nucleotides) on opposite strands of DNA are abnormally attached or linked together, which stops the process of DNA replication. ICLs can be caused by a buildup of toxic substances produced in the body or by treatment with certain cancer therapy drugs.

The FANCA protein is one of a group of proteins known as the FA core complex. The FA core complex is composed of eight FA proteins (including FANCA) and two proteins called Fanconi anemia-associated proteins (FAAPs). This complex activates two proteins, called FANCD2 and FANCI, by attaching a single molecule called ubiquitin to each of them (a process called monoubiquitination). The activation of these two proteins, which attach (bind) together to form the ID protein complex, attract DNA repair proteins to the area of DNA damage so the error can be corrected and DNA replication can continue.

2. Health Conditions Related to Genetic Changes

2.1 Fanconi Anemia

More than 450 mutations in the *FANCA* gene have been found to cause Fanconi anemia, a disorder characterized by a decrease in bone marrow function, an increased cancer risk, and physical abnormalities. Mutations in the *FANCA* gene are responsible for 60 to 70 percent of all cases of Fanconi anemia. These mutations change single DNA building blocks (nucleotides) or insert or delete pieces of DNA in the *FANCA* gene. Some mutations allow production of a FANCA protein that has some residual function; other mutations prevent the production of any FANCA protein. Mutations that prevent all protein production usually lead to a shortage of blood cells at an earlier age and increase the risk of developing cancer of the blood-forming cells (leukemia) as compared to mutations that allow for some FANCA protein production.

Mutations in the *FANCA* gene lead to a nonfunctional FA core complex, which disrupts the entire FA pathway. As a result, DNA damage is not repaired efficiently and ICLs build up over time. The ICLs stall DNA replication, ultimately resulting in either abnormal cell death due to an inability make new DNA molecules or uncontrolled cell growth due to a lack of DNA repair processes. Cells that divide quickly, such as bone marrow cells and cells of the developing fetus, are particularly affected. The death of these cells results in the decrease in blood cells and the physical abnormalities characteristic of Fanconi anemia. When the buildup of errors in DNA leads to uncontrolled cell growth, affected individuals can develop leukemia or other cancers.

3. Other Names for This Gene

- FA
- FAA
- FACA
- FANCA_HUMAN

- Fanconi anemia complementation group A
- Fanconi anemia, complementation group A

References

1. de Winter JP, Joenje H. The genetic and molecular basis of Fanconi anemia.Mutat Res. 2009 Jul 31;668(1-2):11-9. doi: 10.1016/j.mrfmmm.2008.11.004.
2. Deakyne JS, Mazin AV. Fanconi anemia: at the crossroads of DNA repair.Biochemistry (Mosc). 2011 Jan;76(1):36-48. Review.
3. Kee Y, D'Andrea AD. Expanded roles of the Fanconi anemia pathway in preservinggenomic stability. Genes Dev. 2010 Aug 15;24(16):1680-94. doi:10.1101/gad.1955310. Review.
4. Taniguchi T, D'Andrea AD. Molecular pathogenesis of Fanconi anemia: recentprogress. Blood. 2006 Jun 1;107(11):4223-33.