FANCG Gene

Subjects: Genetics & Heredity
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FA complementation group G

genes

1. Normal Function

The *FANCG* 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 FANCG 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 FANCG) 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, attracts 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 50 mutations in the *FANCG* 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. About 10 percent of all cases of Fanconi anemia are caused by mutations in the *FANCG* gene. When Fanconi anemia results from mutations in this gene, it is often associated with a more severe shortage of blood cells than when the condition is caused by mutations in other genes.

Most mutations in the *FANCG* gene that cause Fanconi anemia lead to absent or reduced protein function. Individuals who have mutations that lead to no protein production typically have more severe signs or symptoms

than people who have mutations that allow for some FANCG protein production. Due to a decrease in FANCG protein function, the FA core complex cannot function and the entire FA pathway is disrupted. 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

- FAG
- FANCG_HUMAN
- Fanconi anemia complementation group G
- Fanconi anemia, complementation group G
- XRCC9

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