ERCC6 Gene

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1. Normal Function

The *ERCC6* gene provides instructions for making a protein called Cockayne syndrome B (CSB). This protein is involved in repairing damaged DNA and appears to assist with gene transcription, which is the first step in protein production.

DNA can be damaged by ultraviolet (UV) rays from the sun and by toxic chemicals, radiation, and unstable molecules called free radicals. If left uncorrected, DNA damage accumulates, which causes cells to malfunction and can lead to cell death. Although DNA damage occurs frequently, cells are usually able to fix it before it can cause problems. Cells have several mechanisms to correct DNA damage; one such mechanism involves the CSB protein. This protein specializes in repairing damaged DNA within active genes (those genes undergoing gene transcription). When DNA in active genes is damaged, the enzyme that carries out gene transcription (RNA polymerase) gets stuck, and the process stalls. Researchers think that the CSB protein helps remove RNA polymerase from the damaged site, so the DNA can be repaired. The CSB protein may also assist in restarting gene transcription after the damage is corrected.

2. Health Conditions Related to Genetic Changes

2.1 Cockayne Syndrome

More than 60 *ERCC6* gene mutations that cause Cockayne syndrome have been identified. This rare condition includes a variety of features, including an abnormally small head size (microcephaly), very slow growth resulting in short stature, delayed development, and an increased sensitivity to sunlight (photosensitivity).

Many of the *ERCC6* gene mutations that cause Cockayne syndrome lead to the production of an abnormally short version of the CSB protein that cannot function properly. Other mutations change single building blocks (amino acids) in the CSB protein, which also results in a malfunctioning protein.

The mechanism by which *ERCC6* gene mutations lead to Cockayne syndrome is not well understood. The altered CSB protein probably hinders DNA repair and may be unable to assist with gene transcription. As a result, damaged DNA is not fixed, which disrupts gene transcription and prevents the normal production of proteins. These abnormalities impair cell function and eventually lead to the death of cells in many organs and tissues. Faulty DNA repair underlies photosensitivity in affected individuals, and researchers suspect that it also contributes to the other features of Cockayne syndrome. It is unclear how *ERCC6* gene mutations cause all of the varied features of this condition.

2.2 UV-sensitive Syndrome

At least one mutation in the *ERCC6* gene can cause UV-sensitive syndrome, a condition characterized by unusual sensitivity to UV rays from the sun. People with UV-sensitive syndrome sunburn easily and have freckled skin or other changes in skin coloring (pigmentation). The known mutation, which is written as Arg77Ter or R77X, replaces the amino acid arginine with a premature stop signal at position 77 in the CSB protein. If any protein is produced, it is abnormally short and quickly broken down. Without this protein, skin cells cannot repair DNA damage caused by UV rays, and transcription of damaged genes is blocked. However, it is unclear how a loss of the CSB protein causes UV-sensitive syndrome. Additionally, it is unknown why the Arg77Ter mutation causes photosensitivity without the other features of Cockayne syndrome (described above).

2.3 Age-related macular degeneration

3. Other Names for This Gene

- ARMD5
- CKN2
- COFS
- CSB
- ERCC6_HUMAN
- excision repair cross-complementation group 6
- RAD26
- Rad26 (yeast) homolog

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