ERCC8 gene

ERCC excision repair 8, CSA ubiquitin ligase complex subunit

Normal Function

The *ERCC8* gene provides instructions for making a protein called Cockayne syndrome A (CSA), which is involved in repairing damaged DNA. DNA can be damaged by ultraviolet (UV) rays from the sun and by toxic chemicals, radiation, and unstable molecules called free radicals. The damage caused by these agents can block vital cell activities such as gene transcription, which is the first step in protein production. 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 CSA protein. This protein specializes in repairing damaged DNA within active genes (those genes undergoing gene transcription). However, its specific role in this process is unclear. The CSA protein interacts with other proteins, probably to identify areas of damaged DNA.

Health Conditions Related to Genetic Changes

Cockayne syndrome

Researchers have identified more than 30 *ERCC8* gene mutations that can cause Cockayne syndrome. 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).

Some of the *ERCC8* gene mutations result in the production of an abnormally short version of the CSA protein that cannot function properly. Other mutations change one of the building blocks (amino acids) used to make the CSA protein, which also results in a malfunctioning protein.

The mechanism by which *ERCC8* gene mutations lead to Cockayne syndrome is not well understood. The altered CSA protein probably disrupts DNA repair. 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 *ERCC8* gene mutations cause all of the varied features of this condition.

UV-sensitive syndrome

At least one mutation in the *ERCC8* 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 replaces the amino acid tryptophan with the amino acid cysteine at position 361 in the CSA protein (written as Trp361Cys or W361C). Although the effect of this change on the function of the protein is unknown, it somehow prevents cells from repairing DNA damage caused by UV rays, and transcription of damaged genes is blocked. It is unclear exactly how an abnormal CSA protein causes the signs and symptoms of UV-sensitive syndrome. Additionally, it is unknown why the Trp361Cys mutation causes photosensitivity without the other features of Cockayne syndrome (described above).

Other Names for This Gene

- CKN1
- Cockayne syndrome 1 (classical)
- Cockayne syndrome 1 protein
- Cockayne syndrome, type A
- CSA
- ERCC8_HUMAN
- excision repair cross-complementation group 8
- excision repair cross-complementing rodent repair deficiency, complementation group 8

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of ERCC8 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=1161[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28ERCC8%5BTIAB%5D%29+OR+%28CKN1%5BTIAB%5D%29%29+OR+%28%28CSA%5BTI%5D%29+AND+%28Cockayne%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D)

Catalog of Genes and Diseases from OMIM

- ERCC EXCISION REPAIR 8, CSA UBIQUITIN LIGASE COMPLEX SUBUNIT; ERCC8 (https://omim.org/entry/609412)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/1161)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=ERCC8[gene])

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Genomic Location

The *ERCC8* gene is found on chromosome 5 (https://medlineplus.gov/genetics/chromosome/5/).

Last updated June 1, 2016