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Opinion Article

# Insights of Nucleotide Excision Repair, Genome Stability and Human Disease

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## DESCRIPTION

Ultraviolet (UV) radiation is one of the most common environmental health hazards, causing the most toxic effects on most organisms. UV radiation can lead to harmful effects such as skin aging, eye damage and skin cancer due to the production of cellular reactive oxygen species and direct DNA damage. Damaged DNA, if not properly repaired, can become the source of mutation and interfere with many cellular mechanisms, such as replication, transcription, and the cell cycle. Since most UV-damaged DNA can be effectively repaired by the Nucleotide Excision Repair (NER), a UV-induced DNA damage repair system, many UV-induced properties are closely related to NER. Therefore, understanding the function of NER genes will explain the cause of the various UV-induced symptoms. Furthermore, awareness of the wide variety of effects of unrepaired DNA damage on damaged DNA repair systems and other cellular mechanisms will lead to a better understanding of UV-induced symptoms and the development of various prevention and treatment methods for UV damage. For this purpose, one needs to know the NER-related human genetic disorders to discuss here.

Nucleotide Excision Repair (NER) of DNA-lesions is the most versatile DNA repair procedure involved in gene management, cell and organism care. Interpretation of the stepwise mechanism of NER is a rare case in which patients present with genetically predisposed genetic disorders, such as Xeroderma Pigmentosum (XP), Trichothiodystrophy (TTD) and Cocaine Syndromes (CS). Cells from these patients contain different ranges of impaired ability to repair UV-induced DNA lesions (cyclobutane pyrimidine dimers, 6-4 pyrimidine-pyrimidone photo products) in transcribed DNA strands or inactive DNA.

Xeroderma Pigmentosum (XP) is a hereditary condition characterized by extreme sun exposure that poses a very high risk for skin cancer and other medical problems. People with XP are very sensitive to Ultraviolet (UV) radiation from the sun. These include UV type A and UV type B. Exposure to even the smallest amount of UV radiation can cause severe sunburn and blisters, which begin at a very young age. Sensitivity to UV radiation causes small scars to grow, as well as light skin pigmentation. They may also have very dry skin. The risk of developing squamous cell and basal cell skin cancers and melanoma is high.

In general, each cell contains 2 copies of each gene: 1 inherited from the mother and 1 inherited from the father. XP follows the autosomal recessive inheritance model, in which case a mutation in two copies of the gene is mandatory for an individual to be affected. Both parents must provide genetic mutation to influence children. A person who has only 1 copy of a genetic mutation is called a "carrier". When both parents are carriers of regressive mutation in the same gene, children have a 25% chance of inheriting and inheriting 2 mutations.

Trichothiodystrophy (TTD), a rare hereditary condition that affects many parts of the body. The hallmark of this condition is brittle hair, which is very rare and easily broken. Tests show that the hair is deficient in sulfur, an element that usually gives strength to the hair. The signs and symptoms of Trichothiodystrophy vary widely. In mild cases there may be only hair. More severe cases can also lead to delayed development, significant intellectual disability and recurrent infections; severely affected individuals can only survive in infancy or childhood.

In most cases of the photosensitive form of trichothiodystrophy there are mutations in one of the three genes: *ERCC2*, *ERCC3* or *GTF2H5*. Proteins produced from these genes work together as part of a group of proteins called the common Transcription Factor IIH (TFIIH) complex. This complex is involved in the repair of DNA damage, which can be caused by UV radiation from the sun. The TFIIH complex also plays an important role in genetic transcription, which is the first step in protein production.

Cockayne Syndrome (CS) is a rare disease that causes short stature, premature aging (progeria), severe photosensitivity and moderate to severe learning delays. The syndrome is characterized by failure to develop in the newborn, even a very small head (microcephaly) and the development of a weakened nervous system. Other symptoms may include hearing loss, dental

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caries, vision problems and bone abnormalities.

There are three subtypes according to the severity of the disease and the onset of symptoms:

Cockayne Syndrome is caused by mutations in the *ERCC8* (CSA) or *ERCC6* (CSB) genes. Inheritance autosomal recessive. Type 2 is the most severe and affected individuals are usually unable to spend childhood. People with type 3 live to middle age. There is no cure yet. Treatment may be helpful and may include educational programs required for developmental delay, physical therapy, and gastrostomy tube placement; Medications for spasticity and tremor as needed; Use of sunscreens and sunglasses; Treatment of hearing loss and cataracts; and other types of treatments as needed.