

# Biochemistry of nutrition

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### Cellular Responses to DNA Damage:

The cellular responses to DNA damage involve three mechanisms, namely; reversal of DNA damage, excision of DNA damage and tolerance to DNA damage. The reversal of DNA damage is mediated through various processes such as enzymatic photoreactivation, repair of spore photoproduct, and ligation of DNA strand breaks. The excision of DNA damage involves base excision repair, mismatch repair, and nucleotide excision repair. The DNA repair mechanisms which do not involve processes that remove primary damage are referred to as tolerance mechanisms to DNA damage.

Permanent mutations in genome are often a result of many DNA damage tolerance mechanisms. The mechanisms included in DNA tolerance are replicative bypass of template damage with gap formation and translesion DNA synthesis. (Friedberg et al 1995). This paper attempts to throw light on DNA repair by direct repair mechanisms.

### DNA Repair by Direct Repair Mechanisms:

#### Photoreactivation of DNA:

The major source of base damage upon exposure to UV radiation at wavelengths near absorption maximum of DNA is the production of photoproducts such as cyclobutane pyrimidine dimers and 6-4 pyrimidine-pyrimidones [(6-4) lesions]. The photoproducts mediate DNA damage by posing serious threats to viability and functional integrity of cells by interfering with vital processes including DNA replication and transcription. The reversal of DNA damage through photoreactivation is a mechanism that involves the repair of photoproducts. The light dependent process reverses

DNA damage through monomerization of cis-syn-cyclobutyl pyrimidine dimers. Furthermore, the trans-syn-cyclobutyl pyrimidine is also repaired through light dependent repair process. The process involves the formation of a DNA complex with photoreactivating enzyme. The complex absorbs light (> 300nm) which causes the repair of the damaging photoproducts after which the native DNA is restored after the release of photoreactivating enzyme. (Friedberg et al 1995).

#### Repair of Spore Photoproduct:

The depletion of one or more nutrients results in sporulation in *Bacillus subtilis*. A spore product called thymine-thymine adduct is formed when *Bacillus subtilis* is exposed to UV radiation at ~240nm. The repair of spore photoproduct occurs during early germination and is mediated through SP-specific repair process. Furthermore, spore photoproducts are also repaired through nucleotide excision repair system. (Friedberg et al 1995).

#### O6-Methylguanine Repair:

The formation of O6-Methylguanine occurs as a result of damage caused in the presence of alkylating agents such as N-methyl-N'-nitrosoguanidine. The repair of O6-Methylguanine is of prime importance because it is highly mutagenic. (Turksen 2012). The repair process involves direct enzymatic demethylation and the enzymes involved are methyl transferases. (Friedberg et al 1995).

#### Ligation of DNA Strand Breaks:

A major source of DNA damage is the production of basic fractures which are a result of damaging effects of agents such as X-rays and peroxides. The repair of DNA strand breaks are mediated through repair mechanisms

involving DNA ligase enzyme. A phosphodiester bond is formed by the enzyme between the 5' phosphate group and the 3' OH group which results in the formation of native DNA. The repair process is an energy dependent reaction. (Turksen 2012).

#### Disorders Associated With DNA Repair Deficiency:

A deficiency in genome repair increases the susceptibility of the individual to a number of disorders including Alzheimer's disease, Bloom syndrome, Fanconi anemia, Down syndrome, Gardner syndrome, Huntington disease, multiple sclerosis, Parkinson disease, Progeria, and Usher syndrome.

(Genetic Susceptibility to Cancer 1998).

#### References:

Friedberg, Errol C, Graham C. Walker, and Wolfram Siede. Dna Repair and Mutagenesis. Washington, D. C: ASM Press, 1995. Print.

Turksen, Kursad. Adult and Embryonic Stem Cells. New York: Humana Press, 2012. Internet resource.

Genetic Susceptibility to Cancer. New York, NY: Published for the International Commission on Radiological Protection by Pergamon, 1998. Print.