DNA Damage By Sun

The effects of the sun can be seen within minutes on some people as freckles appear, skin tone darkens and (perhaps) redness begins to spread. However, what these visible changes within the epidermis of the skin are caused by, is much less obvious. The damaging effects of ultraviolet (UV) radiation exposure - produced by the sun - on the DNA within our cells is the cause of many undesirable side effects. These include cell death, mutagenesis, photoaging (the appearance of premature aging of the skin) and cancer (1). UVA and UVB – with UVA penetrating more deeply than UVB – are the types of UV radiation responsible for these consequences (2).

One prominent form of damage caused by these types of UV radiation includes the formation of Pyrimidine Dimers. These lesions are the result of irreversible changes to the structure of the bases due to the formation of a covalent bond between adjacent bases (3) – specifically Thymine and Cytosine, the pyrimidines [see Fig.1.]. Once the DNA sequence has been changed, any gene expression/protein synthesis associated with this may also be affected and DNA replication is blocked. If the dimers formed coincidentally still pair correctly with their complementary bases, the damaged DNA will not affect the cell. However, if the latter does not happen, non-functional proteins may be produced and mutations within Tumour-suppressor (TS) genes and/or proteins involved with cell replication may occur. A specific example of this occurs when the ‘signature mutation’ of a Cytosine (CC) dimer is formed and is mis-paired with adenine. This mutation is the most common cause for the p53 TS gene to not function (3).

These specific mutations are important because, if left untreated, may lead to the formation of cancerous tumours.

However, the body does have a method for ‘reversing’ the damage done. Within the nucleus, ‘photochemical cleaving’ of the affected bases can occur (4). This is where DNA photolyase, using energy from photons, acts on the newly formed covalent bond to break it and return the bases to their original, individual state - effectively undoing the work of the UV radiation(4).

A less direct form of DNA damage includes the absorption of UV radiation by chromophores (an example is Melanin). These exist within the skin and - if UVA photons have been absorbed - produce Free Oxygen Radicals (4). The free radicals are produced at a rapid rate so increase vastly in number in only a short period of time. This makes them more likely to cause damage for example they may cause lipid damage/peroxidation. This directly affects the membrane which inevitably leads to cell damage and, eventually, death via apoptosis. Proteins and bases can also be oxidised by free radical interference and crosslinks between DNA bases across separate strands may occur. This mutation can lead to cancer formation and/or photoaging through impaired function of TS genes.

The body has developed a resolution for the latter issue. Damaged bases can be removed and replaced with unaffected ones by a process of several enzyme actions known as ‘Base-Excision repair’ (see Fig.2.)(4). Firstly, the E-coli enzyme AlkA is used to ‘flip’ the impacted base out of the sequence. This action presents the base in a position to fit to the enzyme’s active site, and the base can then be ‘cut’ from the sequence. An AP endonuclease then

examines the hole left by the E-coli enzyme. It identifies if the hole is ‘apurinic’ or ‘apyrimidic’ and the DNA polymerase 1 enzyme can then insert the respective nucleotide.

UV radiation can also have a more indirect effect on DNA. The result of damage from UV radiation is often repaired once recognised by the body, but can frequently be incomplete (4). Often, further damage can be created by the body’s attempts to correct any of these mutations. An example of this, is the incorrect pairing of bases after a mutated nucleotide has been ‘cleaved’ (4). The form of cancer known as ‘Lynch Syndrome’ originates from such an error. Generally, if the bases have not been paired with their complementary bases, specific proteins will recognise this and correct the issue. However, due to an accumulation of mutations and errors throughout the genome, the proteins do not recognise or change the base that is wrongly paired and the mutation is expressed (4). This results in the person developing the cancer.

However, despite the damage our bodies can incur from sunlight, the benefits of Vitamin D production outweigh many of the negatives and indeed is essential for life. UVB is the type of radiation required to induce its production in our bodies and UVB can only be absorbed by our bodies through direct exposure to sunlight (6). To name only a few of the essential properties, Vitamin D has a direct role in; supporting the immune system; increasing absorption of calcium into the intestines; and reducing the risk of Type 2 Diabetes by negatively effecting insulin secretion and glucose tolerance(6). For pregnant women, a healthy level of vitamin D has been said to lead to the likelihood of healthier pregnancy and to decrease the risk of developing harmful conditions and/or requiring an emergency caesarean(6). Even when disregarding the benefits, a lack of vitamin D can actively be harmful, as deficiencies can cause illnesses such as Osteoporosis, CVD, Alzheimer’s Disease and may increase the severity of Asthma(6).

Despite the damage excessive UV radiation exposure can cause to the DNA within our bodies, restricting humans to no sunlight is potentially just as harmful. There is not necessarily damage done to our DNA every time we are exposed to it - and even when there is, it’s often reversible. Visible change we see due to sunlight - e.g. tanning - is even considered desirable to some. Therefore exposure to sunlight can lead to DNA damage through UV radiation but sunlight and UV radiation are also essential for vitamin production.