UV RADIATION, DNA DAMAGE, MUTATIONS AND SKIN CANCER

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1. Introduction

About UV radiation, ozone and life

More than blue light, UV radiation is scattered in the earth's atmosphere: going from a wavelength (\( \lambda \)) of 400 down to 340 nm, the scattering goes up almost 2 fold (Rayleigh scattering \( \propto \lambda^{-4} \)). Although we do not see it, the sky is more violet-ultraviolet than it is blue. Blocking the UV radiation from the direction of the solar disc - e.g. by a small parasol - would still leave a substantial part of the UV radiation, i.e. the part reaches us through scattering from the blue sky (and possibly by reflection from sand or snow). UV radiation can initiate a great variety of photochemical reactions. We are all familiar with examples such as “photochemical smog”, photodegradation of plastics and bleaching of pigments in paints. Although high-energy UV radiation from the sun may have contributed to the early synthesis of organic molecules in the primitive anoxic atmosphere (wavelengths below 200 nm are absorbed by CH\(_4\), H\(_2\)O and NH\(_3\)), it needed to be blocked out in early evolution because of its very detrimental effects on highly evolved organic molecules such as proteins and DNA, essential building blocks of living organisms. Most of the sun’s harmful UV radiation could pass through the earth’s primordial anoxic atmosphere, and life could not sustain itself on the earth’s bare surface. Early life on earth must have evolved shielded from the UV radiation by barriers, e.g., in oceans below a layer of dissolved organic compounds\(^1\) or very deep near hot vents and/or in the earth's crust, and/or a few millimeters deep in soil\(^2\). By a very fortunate evolutionary event plant-like organisms started to produce oxygen from photosynthesis in substantial amounts over 2 billion years ago, and this oxygen provided protection against UV radiation from the sun.

Up in the stratosphere, oxygen (O\(_2\)) is bombarded by high-energy UV radiation, absorbs this radiation, splits up (in O) and recombines with oxygen to form ozone (O\(_3\)). This stratospheric layer of ozone is spread over a wide range in altitude (from 10 to 50 km), but it is extremely rarified and would amount to a sheath of only about 3 mm thick if it were compressed at ground level conditions. This modest amount of ozone shields off most of the harmful UV radiation in the UVB band that is not absorbed by oxygen. Life on earth has thus generated its own “stratospheric sunscreen”. However, the UVB radiation is only partially absorbed, and the fraction that reaches ground level is still capable of damaging and killing unprotected cells. To cope with this residual UV...
radiation organisms at the earth’s surface have acquired certain adaptive features: e.g., UV-absorbing surface layers, repair of damaged cells or replacing damaged or killed cells entirely. Because of the high absorption in organic material, UV radiation does not penetrate any deeper than the skin, and this organ clearly shows all of the mentioned adaptive features. Despite these adaptations, solar UV radiation still affects human health, but the full extent of these effects remain largely unknown. Any increase in ambient UVB radiation due to loss of stratospheric ozone can therefore be expected to have important public health impacts.

**About DNA, genes and cancer**

Basic cancer research has shown that cancer is a disease stemming from disturbances in signaling pathways that control the cell cycle and differentiation. The most persistent disturbance is introduced by synthesis of dysfunctional signaling proteins or by a complete lack of synthesis of such proteins from miscoding or lost genes. Two types of genes are directly relevant to carcinogenesis: the oncogene (dominant) whose protein actively contributes to the cancerous progression, and the tumor suppressor gene (recessive) whose protein should counter such an uncontrolled progression. A combination of such genes need to be affected in order for a cell to become cancerous. Such altered genes are passed on to daughter cells, thus propagating the problem of controlling cell growth. From the above it is immediately obvious that the ubiquitous solar UV radiation can damage the DNA of genes in exposed skin cells. Thus solar UV radiation poses a continuous threat to the genomic integrity of skin cells. The fact that healthy humans do not readily develop skin cancer attests to an impressively adequate adaptation of the human skin, it has several lines of defence ranging from increasing UV absorption to protect germinative basal cells, to DNA repair or removal of damages or transformed cells.

**2. UV radiation, DNA damage, repair and mutation**

**UV absorption and DNA damage**

Typical UV absorbing features in organic molecules are conjugated bonds: alternating single and double bonds, absorbing generally radiation of wavelengths between 200 and 250 nm, and in a ring between 250 and 300 nm (see reference 3). (Feynman et al. give an elegantly simplified, quantummechanical introductory analysis of energy states of double bonds). Absorption maxima at longer wavelengths (300 - 450 nm) are found in some molecules with three (e.g., riboflavin) or four rings (e.g., porphyrines), and in long-chain repeats (e.g., carotenoids) of conjugated bonds. The collective protein fraction from cells shows a maximum absorption around 280 nm, whereas the DNA fraction shows a maximum around 260 nm. Major absorbers in the protein fraction are the tryptophan and tyrosine amino acids. In the DNA all nucleic acids are aromatic and contribute to the absorption maximum. DNA appears to contribute appreciably to the total absorption of UVC (200 - 280nm) radiation by a cell. Although absorption by DNA in the UVB around 300 nm is far less than in the UVC (10 to 100 fold lower), sun exposure causes significant levels of DNA damage.