神戸大学グローバルCOEプログラム「次世代シグナル伝達医学の教育研究国際拠点」

第29回グローバルCOE学術講演会

日時：2010年9月9日(木)17:00～

場所：外来診療棟 6F 大講義室

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UVB and UVA radiation reactions of DNA in cells and human skin: photoproduct formation and repair

The photo-induced formation of base damage to DNA is strongly implicated in the etiology of most of skin cancers as the result of exposure to solar radiation and/or UVA photons provided by lamps in tan booths. It is now assumed that the UVB component of solar light is mostly responsible for the formation of bipyrimidine photoproducts within cellular DNA. Indirect support for the major biological role played by the latter photoproducts is provided by the observation of CC to TT tandem mutations that are considered as a molecular signature of the deleterious effects of UVB photons in targeted genes such as p53. Three main classes of photoproducts including *cis-syn* cyclobutadipyrimidines (P<>Ps), pyrimidine (6-4) pyrimidone adducts (64-PPs) and related Dewar valence isomers (DewPPs) may be generated at each of the four main bipyrimidine sites (TT,TC,CT and CC sequences) giving rise to a total of 12 possible tandem lesions. A sensitive HPLC-tandem mass spectrometry analysis allows the unambiguous and accurate measurement of several bipyrimidine photoproducts at a dose of UVB radiation as low as 0.2 $kJ.m^{-2}$. Thus, cyclobutadithymine (T<>T) and a lesser extent 6-4-TC and T<>C are detected as the main UVB photoproducts in the DNA of human fibroblasts, keratinocytes and skin. An interesting observation deals with the UVA-induced formation of T<>T, and to a lesser extent of T<>C, in the DNA of cells and human skin. The specific formation of Pyr<>Pyr, at the exclusion of 64-TT, may be accounted for by a triplet energy transfer mechanism that is likely to involve still unknown endogenous photosensitizer(s). UVA photons are also able to photo-oxidize cellular DNA. This was established using a modified comet assay that allows the detection of strand breaks, oxidized pyrimidine bases and modified purine residues respectively. Thus, singlet oxygen that is generated by a type II photosensitization mechanism was found to be the main contributor to UVA-mediated oxidatively generated DNA damage including 8-oxo-7,8-dihydroguanine. Relevant information on the DNA repair of bipyrimidine photoproducts in cells and human skin was gained from HPLC-MS/MS measurements.

For more information

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