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Cv-pdg Facilitates Repair of UVB-Induced DNA Damage in Skin

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More than one million cases of non-melanoma skin cancer, largely caused by sun exposure, are diagnosed in the United States yearly. Further, individuals affected with Xeroderma Pigmentosum are more than 2000-fold more cancer prone than the general population due to inherited deficiencies in enzymes responsible for DNA damage repair. Human cells possess only one mechanism (Nucleotide Excision Repair, NER) for the repair of UV-induced DNA damage. However, certain prokaryotes and viruses produce DNA glycosylases (pdgs) with the ability to repair DNA photo-damage through Base Excision Repair (BER). The bacteriophage T4 DNA glycosylase (T4-pdg) has been shown by other laboratories to be deliverable to human skin and to enhance repair of DNA photo-damage. A homologue of T4-pdg, identified in chlorella virus and termed cv-pdg, has been shown by our laboratory to be more stable, to possess higher catalytic efficiency, and to have a broader substrate specificity than T4-pdg, making cv-pdg potentially even more effective at enhancing repair of UV-induced DNA damage. Here we show effective delivery of a nuclear-targeted cv-pdg enzyme to basal and suprabasal keratinocytes in a model of repair proficient human skin (Mattek, Epiderm FT). The delivered cv-pdg enzyme was capable of rapidly enhancing repair of TT dimers following skin exposure to UVB. Characterization of the biological response of the skin and cultured cells to UVB-induced damage and treatment with cv-pdg will be discussed. The delivery of cv-pdg to skin represents one proactive strategy to treat and prevent human disease resulting from inefficient repair of UV-induced DNA damage.