Rescue of Nucleotide DNA Repair Deficiencies to UVB and Solar-Simulated Irradiation by Pyrimidine Dimer Glycosylases and UV Endonucleases

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UV light induces damage in DNA, resulting in skin diseases such as cancer for millions of people every year. Alternative DNA repair pathways include base excision repair (BER) and nucleotide incision repair (NIR), which E. coli and humans lack. In order to determine the biological consequences of activating BER or NIR, the enzymes cv-pdg and UVDE were expressed in repair proficient and deficient E. coli cells and challenged by UVB and solar-simulated light (SSL), which has not been addressed in previous studies. A novel approach was taken to study three aspects of the enzymes' effects. Survival curves were developed by exposing nucleotide excision repair (NER) deficient cells with the enzymes to SSL at various doses. Enzyme nicking activity was observed by incubating UVC-irradiated plasmids with the enzymes and conducting electrophoresis. In order to evaluate SOS induction, NER-deficient cells were irradiated by UVB and the intensity of LexA was observed, as incubation time increased, by western blotting. The expression of CPD and 6-4 PPs specific UVDE and CPD specific cv-pdg significantly enhanced survival in wild-type and NER-deficient cells under SSL. The percentage of nicked plasmid increased substantially in the plasmids incubated with the enzymes, and the expression of either enzyme decreased the longevity of SOS induction in NER-deficient cells. Those with Xeroderma Pigmentosum, an inherited deficiency of NER, have hypersensitivity to the sun, resulting in skin cancer at a young age. The effectiveness of the enzymes in DNA repair suggest future drug development for the prevention of skin cancer in humans.

Awards Won:
Second Award of $2,000