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UV-specific DNA repair recombinant fusion enzyme: a new stable pharmacologically active principle suitable for photoprotection.

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BACKGROUND: UV radiation can produce mutations in skin cells and correlates strongly with the onset of actinic keratoses and basal and squamous cell carcinomas. Xeroderma pigmentosum (XP) is a heritable disease characterized by an extreme sensitivity of skin to UV radiation. Recently, studies in cultured cells as well as in XP patients have demonstrated that the recombinant T4 endonuclease V UV-specific endonuclease could enhance repair of UV-induced photoproducts. OBJECTIVE: We aimed to obtain a stable UV-specific DNA recombinant endonuclease, pharmacologically active in mammalian cells so as to be used in treatment and prophylaxis of sun damage. METHODS: The UV-specific DNA endonuclease gene obtained from Micrococcus luteus, was fused to a leader peptide and expressed (alphaUveA), refolded and purified. A construction under the control of an eukaryotic promoter was used to transfect XP fibroblasts deficient in DNA damage repair. Transformed cells were UV irradiated and cell survival was assessed. RESULTS: alphaUveA was obtained as a highly active UV-specific repair enzyme stable for at least 2 years. XP fibroblasts transfected with alphaUveA gene increased the resistance to UV radiation and, in consequence, cell survival. CONCLUSION: alphaUveA is stable and pharmacologically active in human cells. The topical administration of this long-term stable new active principle could help diminish the risks of skin cancer after sun exposure.