



PHOTOBIOLOGY AND PHOTOPROTECTION

## OLTIPRAZ ATTENUATES UV INDUCED CELLULAR SENESCENCE THROUGH NUCLEAR LAMINS AND CELL CYCLE MODULATION IN DERMAL FIBROBLASTS

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**Introduction:** Cellular senescence, a complex biological process that causes cells to limit their rates of proliferation, is accelerated by various factors. Photo-oxidative stress has been implicated in the deleterious effects of chronic exposure to sunlight leading to skin aging. Oltipraz (OPZ), a potent NRF-2 activator, is originally identified as an anti-schistosomiasis and anti-liver cirrhosis agent. Recent studies suggest that OPZ can be used as an anti-aging agent for Hutchinson-Gilford progeria syndrome (HGPS), which caused by constitutive production of progerin, a mutant form of the nuclear architectural protein lamin A.

**Objective:** This study aims to investigate the protective properties of Oltipraz in skin photo aging.

**Materials and Methods:** Dermal fibroblasts were pre-treated with OPZ for 24h and then exposed to UV radiation. Cell growth was determined by WST-8 assay and Ki67 staining. SA-beta-gal staining were use to indicate senescent cells. Expression of extra cellular matrix (ECM) and senescence-associated secretory phenotypes (SASP) were evaluated by Q-PCR and ELISA. Nuclear lamins and DNA damages were explored by immunofluorescence. Cell cycle was analyzed by FACS and Western blot.

**Results:** OPZ efficiently prevents fibroblasts from UV damage, thereby postponing photo aging. OPZ can maintain cell proliferation and diminish the accumulation of SA-beta-gal+ senescent cells. Meanwhile OPZ maintains ECM synthesis and reduces SASPs expression. Similar to HGPS model, OPZ restore expression of Lamin B1 and ameliorates the levels of progerin and DNA damage (gammaH2AX staining). Moreover OPZ abrogates S-phase arrest by modulating a set of cell cycle checkpoints.

**Conclusions:** Together, these findings indicate that OPZ attenuates photo aging by modulating nuclear lamins and cell cycle. OPZ is a promising therapeutic avenue for photo aging.

