Photosensitization of Lipofuscin from Human Skin Keratinocytes by Visible Light and Malignant Transformation

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INTRODUCTION: Lipofuscin is an autofluorescent pigment that accumulates progressively during the aging of cells in post-mitotic period in various tissues, including the skin, which is the outermost tissue of the body and more exposed to visible light. Photosensitization of lipofuscin induces photooxidatives processes through the generation of reactive oxygen species (ROS), which can damage DNA and generate mutations. We hypothesize that photosensitization of lipofuscin by visible light can generate mutations in DNA, which possibly lead to malignant transformation. **OBJECTIVES:** Show that photosensitized lipofuscin by visible light could generate a skin tumor, breaking the paradigm that visible light is safety to the health. **METHODOLOGY:** Lipofuscinogenesis was induced in HaCat cells through oxidative damage in lysosomes by photosensitization of 1,9-dimethyl methylene blue (10 nM) with red light (λ= 633 nm, 11 $J.cm^{-2}$). After 48h, photosensitization of lipofuscin was made exposuring cells to blue light (λ= 466 nm, 100 $J.cm^{-2}$).**RESULTS AND DISCUSSION:** Photosensitization of DMMB allowed lipofuscinogenesis, after 48h. Perinuclear accumulation of lipofuscin was observed by transmission electronic microscopy. FLIM analysis showed lipofuscin granules with a homogenous lifeftime of 2 ns. FACS analysis showed increases of acid vacuoles accompanied by lipofuscinogenesis and cell size. Exposure of lipofuscin-loaded cells to blue light significantly decreased the cellular viability. Generation of singlet oxygen, responsible for the lesion 8-oxo-7,8-dihydro-guanine in DNA, was higher in lipofuscin-loaded cells compared to control cells, setting a proper condition to tranversions mutations (G·C→T·A). Damage and lesions on DNA is being presently investigated. **CONCLUSION:** Photosensitization of lipofuscin by visible light is cytotoxic to HaCat cells, generating higher levels of ROS that can damage DNA and mutates DNA.

Keywords: lipofuscin, lysosomes, mutations, visible light
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