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Lipofuscin granules of the retinal pigment epithelium: Source of free radicals and auto-fluorescence

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Lipofuscin granules (LGs) accumulate in the cells of retinal pigment epithelium (RPE) with age, particularly in patients with hereditary diseases. These granules are heterogeneous, being composed of mixtures of proteins and lipids, including more than 21 different fluorescent compounds. Studies of LGs structure and fluorescence by means of atomic force and near-field microscopy, as well as time-of-flight secondary ion mass spectrometry show that bisretinoids and its oxidation products are present in the interior, but not at the surface layer (lipid membrane) of LGs. Bisretinoids and their photo-oxidation and photo-degradation products represent the main source of LGs fluorescence and exhibit phototoxic properties. *In vitro* experiments have shown that bisretinoid photo-oxidation and photo-degradation products are able to damage lipid membranes and cell structures even in the absence of light. Photosensitization of LGs with blue light can generate reactive oxygen species, which can damage the RPE. Defined differences in fluorescence properties between chloroform extracts obtained from cadaver eyes with and without signs of pathology hold promise for the future development of fundus auto-fluorescence imaging. The lecture reviews the recent advances in knowledge of the composition, origin and possible deleterious effects of RPE cell lipofuscin granules.

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