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## Long-term multiple A2E treatment leads to melanization of ARPE19 cells

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Incomplete degradation of outer segments (OS) by retinal pigment epithelium (RPE) leads to the accumulation of storage bodies containing autofluorescent lipofuscin, which consists of a mixture of lipids and bisretinoids including A2E. A2E and its oxidation products are major components of lipofuscin and its accumulation is implicated in pathology of Age-Related Macular Degeneration (AMD). However, A2E accumulates in RPE during normal aging. In this study we developed a cell model to determine the coping mechanisms of RPE cells to A2E accumulation. To distinguish between pathologic and normal response of RPE to A2E accumulation we used fully differentiated ARPE19 cells multiply treated with low micromolar amounts of A2E. Then the A2E-treated ARPE19 cells were challenged with OS and compared with non-treated cells for lysosomal functions, degree of OS degradation and melanization. We found that fully differentiated ARPE19 cells uptake, accumulate and partially oxidize A2E under dim light conditions. A2E is stored in lysosomes and leads to an increase in lysosomal pH. Upon challenge with ROS, A2E-treated ARPE-19 cells show an increase in melanin pigment. In addition, the specific activities of the lysosomal enzymes cathepsin D and acid phosphatase are decreased in A2E treated cells. We have developed a new ARPE19 cell model where melanization was elicited as a response to chronic accumulation of RPE's natural toxin A2E. We found that although A2E treatment leads to lysosomal alkalinization and some lysosomal impairment, as has been previously reported, ARPE19 cells compensate by increased production of a special type of lysosomes - melanized lysosomes.

### Biography

Eugenia Poliakov has completed her Ph.D. in chemistry at the age of 26 years from Case Western Reserve University and Postdoctoral studies from National Eye Institute; NIH. From 2006 to present she is a Staff Scientist at Laboratory of Retinal Molecular and Cell Biology, NEI, NIH. She has published more than 20 papers in peer-reviewed journals.

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