Metabolic Biomarkers of Early Retinal Oxidative Stress

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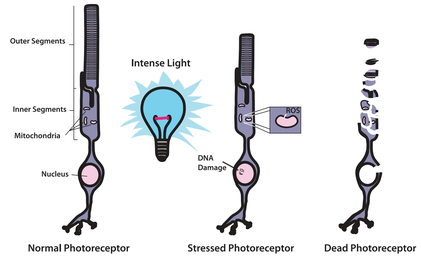
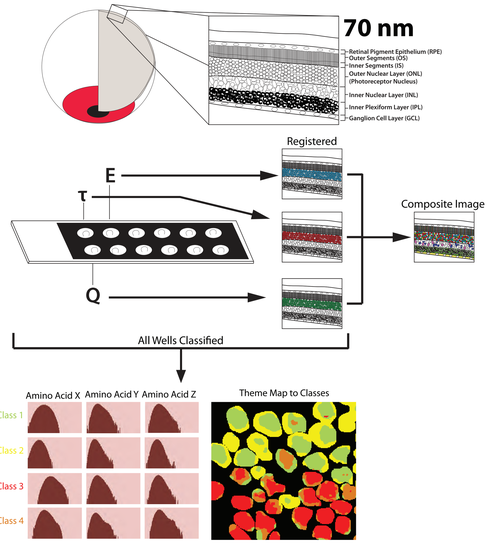
Oxidative Stress Causes the Retina to Degenerate

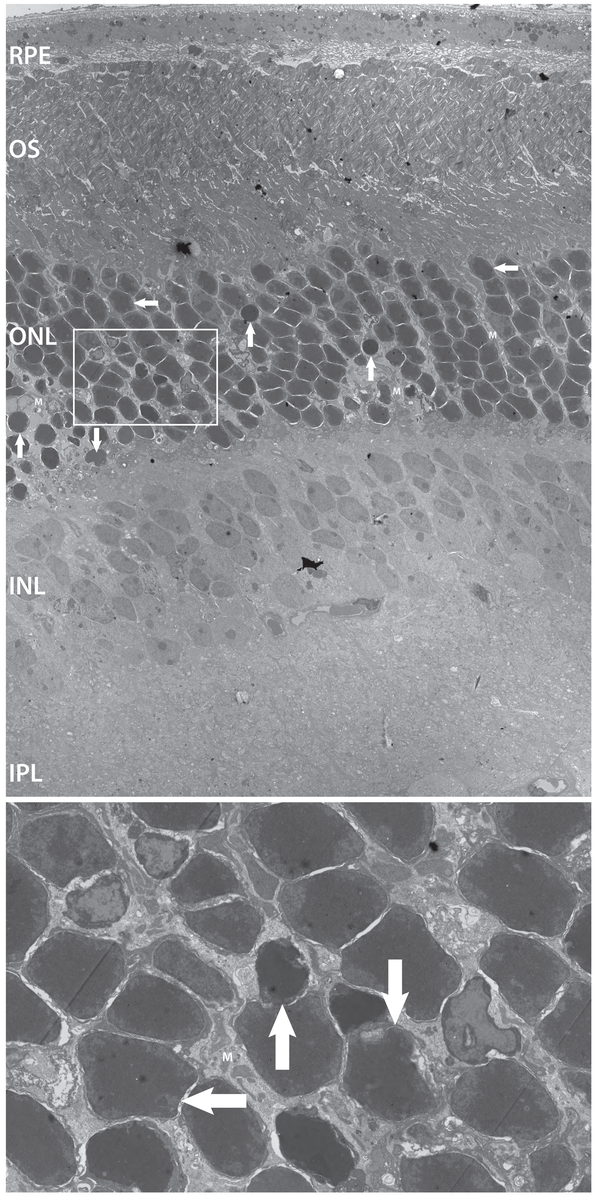
Photoreceptors are vulnerable to oxidants produced from smoking, exposure to intense lights, and the aging process. This study shows how prolonged, bright light alters the metabolic function of photoreceptors. We explore metabolic function by measuring changes in metabolite content. We hope these analyses will reveal (a) the mechanisms by which photoreceptors die, and (b) potential strategies to target photoreceptor survival.



Framework for Metabolic Profiling

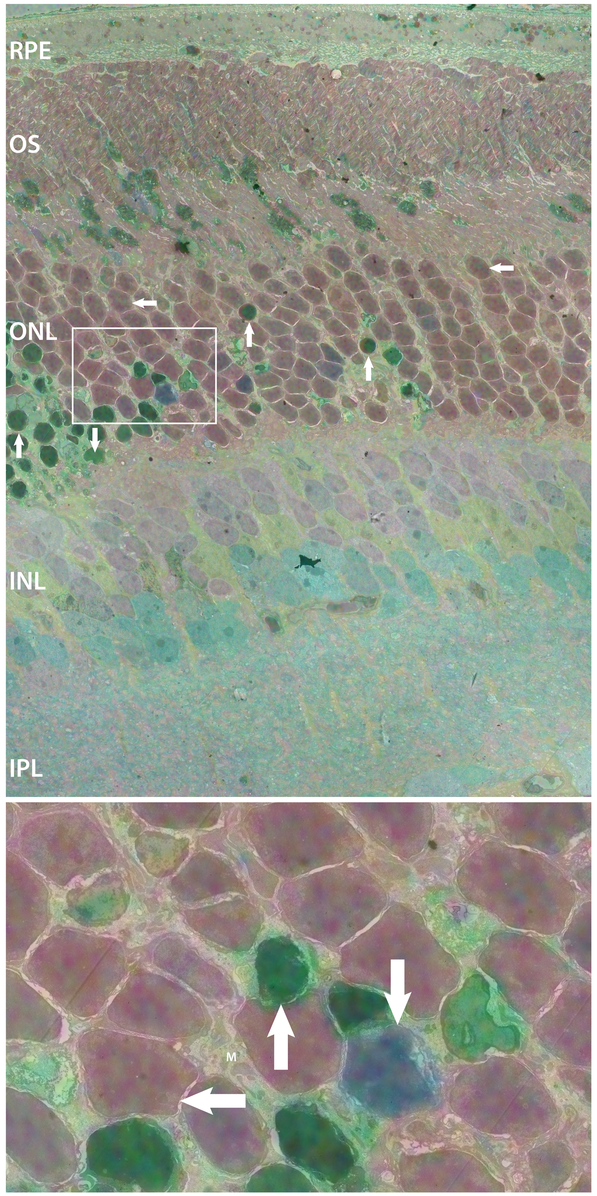


Oxidative Stress Induces Diverse Morphological Changes in Photoreceptors



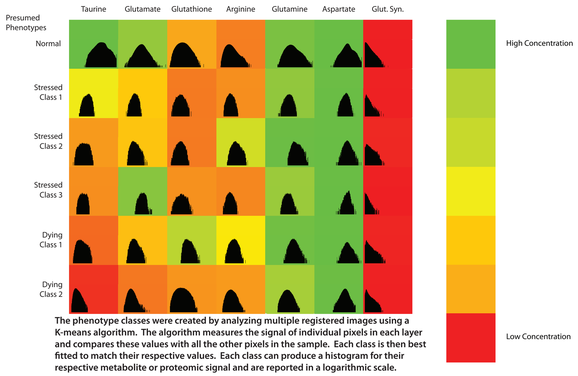
Electron microscopy of albino BALB/c mouse retina exposed to 24 hours light damage, sacrificed immediately. Top figure shows mosaic of EM of nearly 500 tiles. Arrows pointing up, down, and left are photoreceptors that have condensed chromatin, formed vacuoles, and normal photoreceptors respectively. The outlined box is enlarged in the figure below. One can see various levels of morphological damage. Müller glia cells (M) are becoming hypertrophic in areas of cell loss.

Stressed Photoreceptors Display dynamic Levels of Metabolites



Taurine (red) Glutamine (green) Glutamate (blue) composite overlaid on electron microscopy. RGB has an opacity of 50%. Arrows pointing up signify cells that are absent of taurine and glutamate. Arrows pointing down are absent of taurine and spike in glutamate. Arrows pointing left signify cells that are normal photoreceptor signatures .

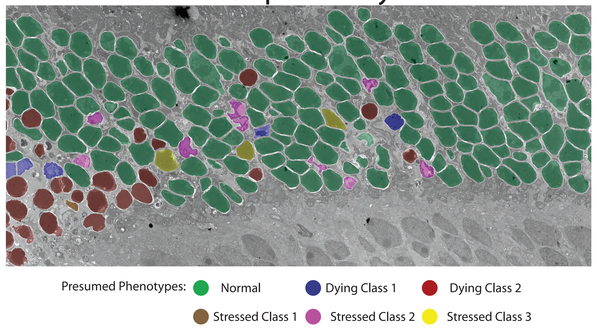
Clustering Identifies Metabolic Signatures within the photoreceptor population



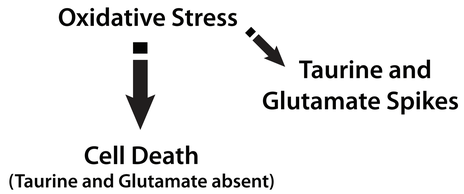
The phenotype classes were created by analyzing multiple registered images using a K-means algorithm. The algorithm measures the signal of individual pixels in each layer and compares these values with all the other pixels in the sample. Each class is then best fitted to match their respective values. Each class can produce a histogram for their respective metabolite or proteomic signal and are reported in a logarithmic scale.

Metabolic Signatures Correlate with Distinct Photoreceptor Stress Levels.

Refined Theme Map Overlay



Conclusions:



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