



Photobiomodulation Therapy for Eye Disease

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Disclosures

Thank you to the Organizers



Service on Scientific and Medical Advisory Panel

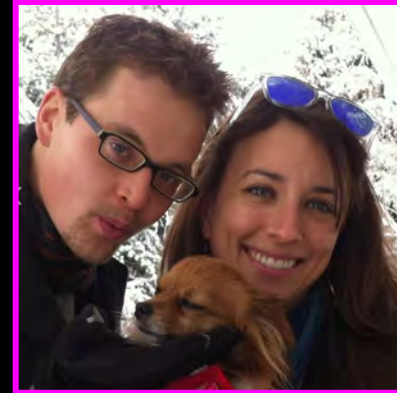




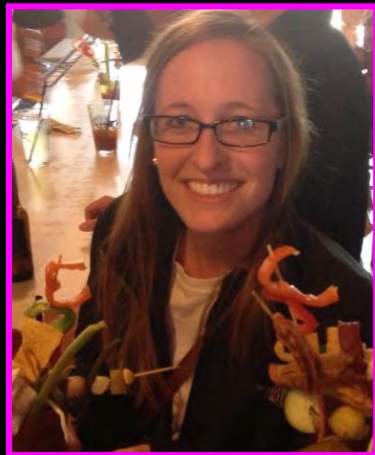
Raiders of the Red Light



Elizabeth Liedhegner



Heather Schmitt



Hannah Nonarath



Alex Hall



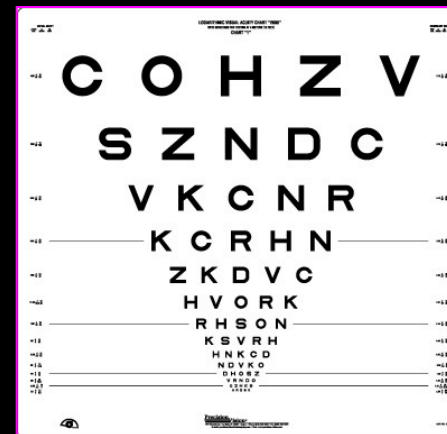
Betsy Abroe



Sandeep Gopalakrishnan

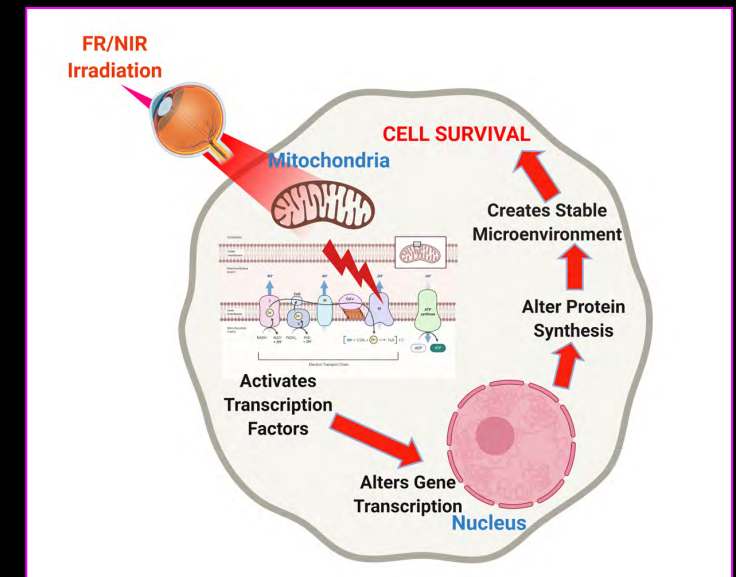
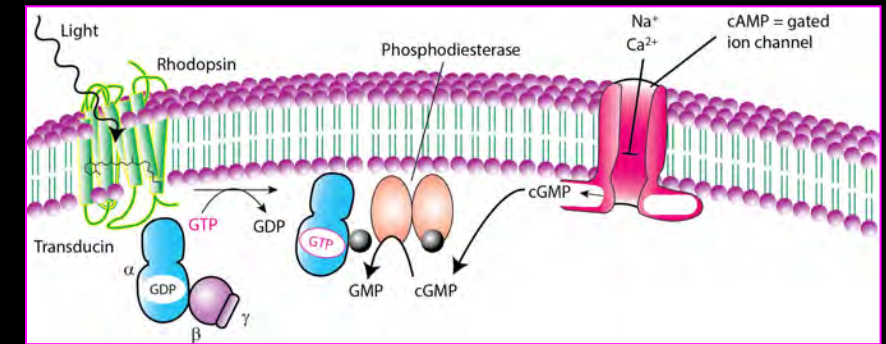
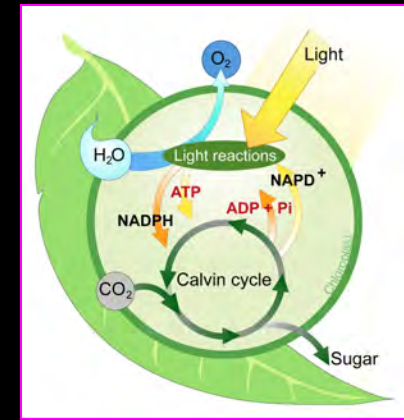
PBMt – From Growing Plants in Space to Treating Eye Disease on Earth

- Astronauts observed wound healing*
- Improved healing of Chemo/Rad Induced Mucositis*
- Protection against loss of vision in animal models of retinal disease*
- Protection against loss of vision in clinical studies*

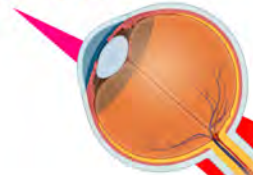


What is Photobiomodulation and How Does it Work

- *Photobiomodulation* is the process by which a chain of biochemical reactions is triggered by exposure to light
- Photons must be absorbed by *photoacceptor* molecule
- *Photosynthesis in Plants*
- *Phototransduction in Vision*
- *Mitochondrial Stimulation and Cell Protection*



**FR/NIR
Irradiation**



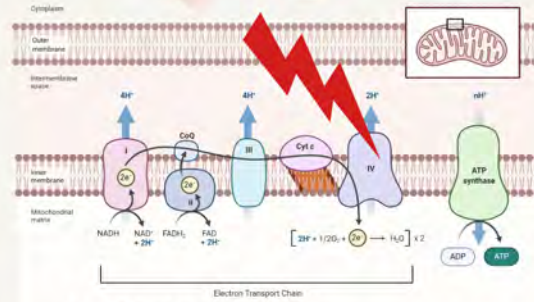
Mitochondria



CELL SURVIVAL

**Creates Stable
Microenvironment**

**Alter Protein
Synthesis**



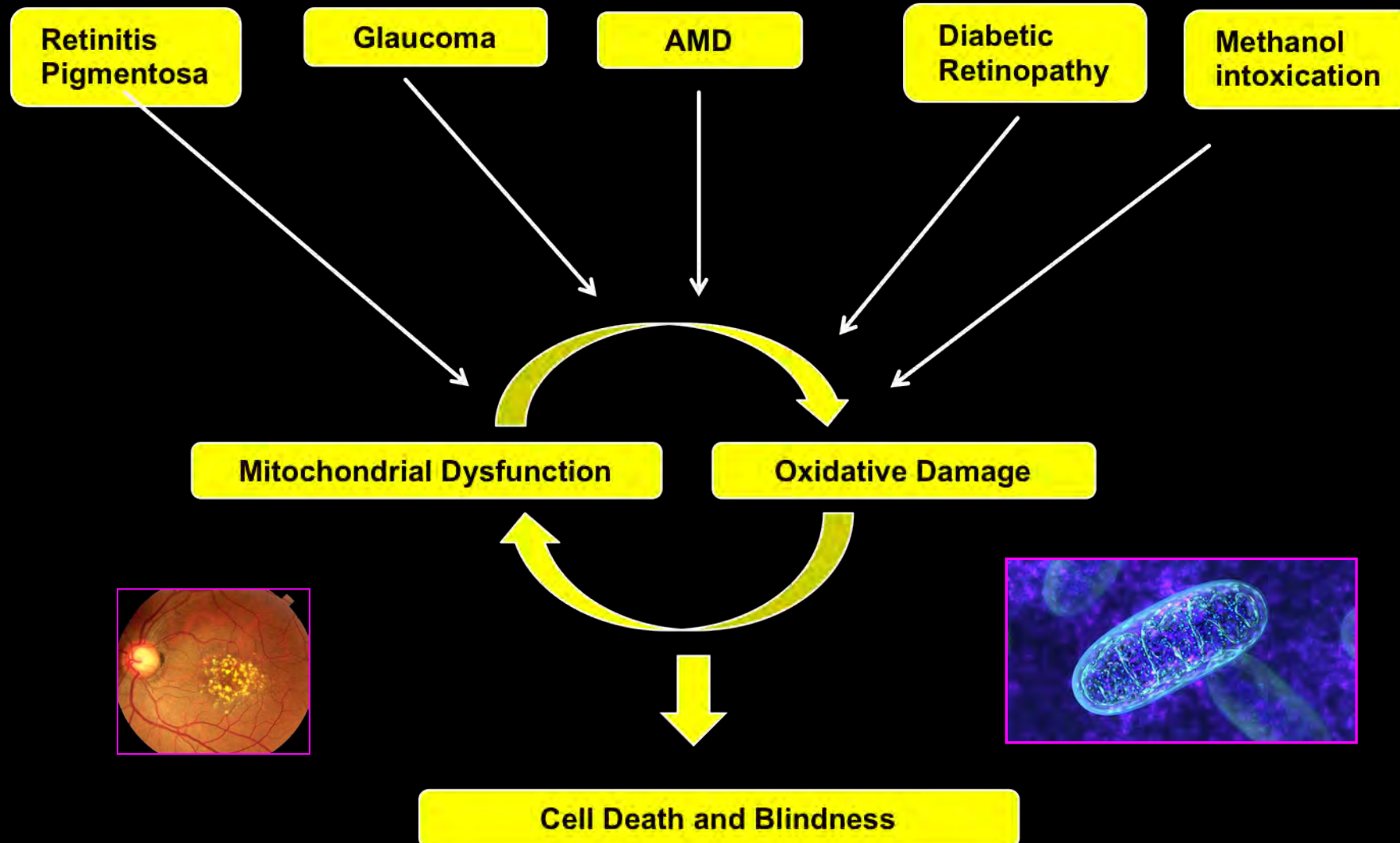
**Activates
Transcription
Factors**

**Alters Gene
Transcription**

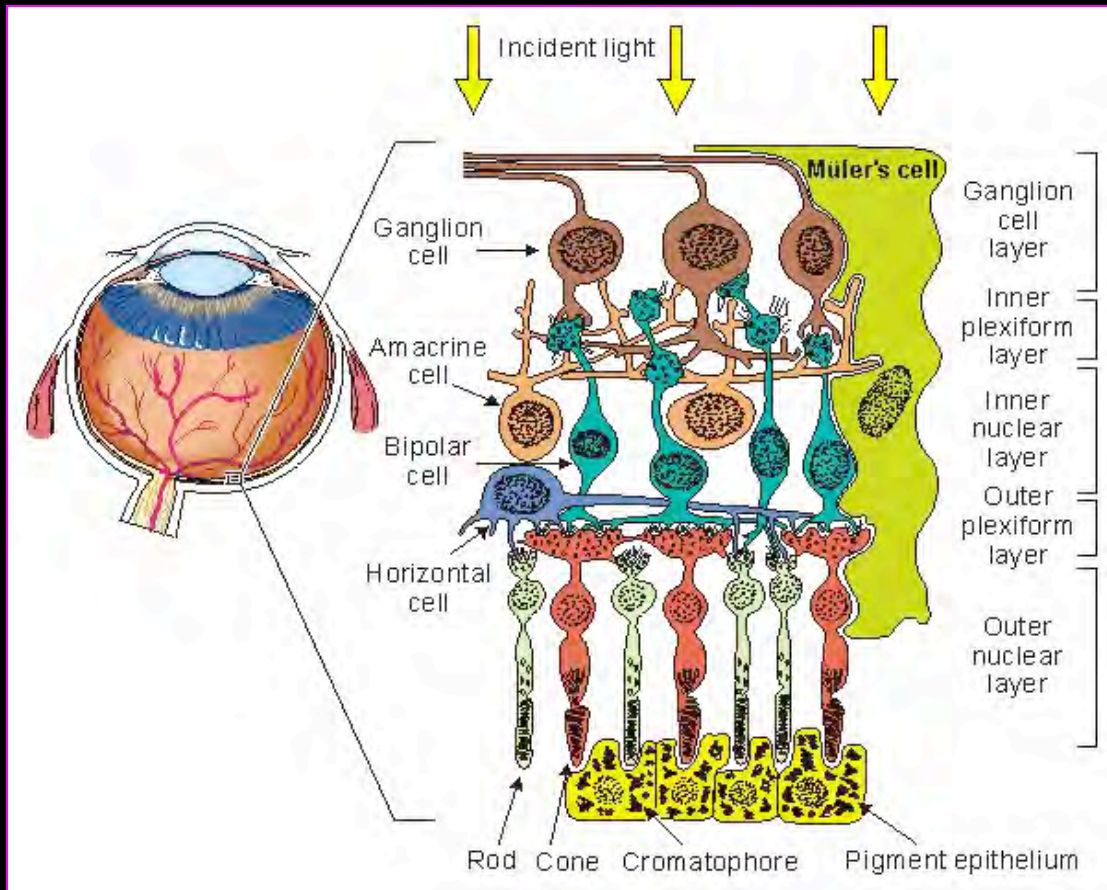
Nucleus



Mitochondrial Dysfunction Plays a Key Role in Retinal Injury and Disease

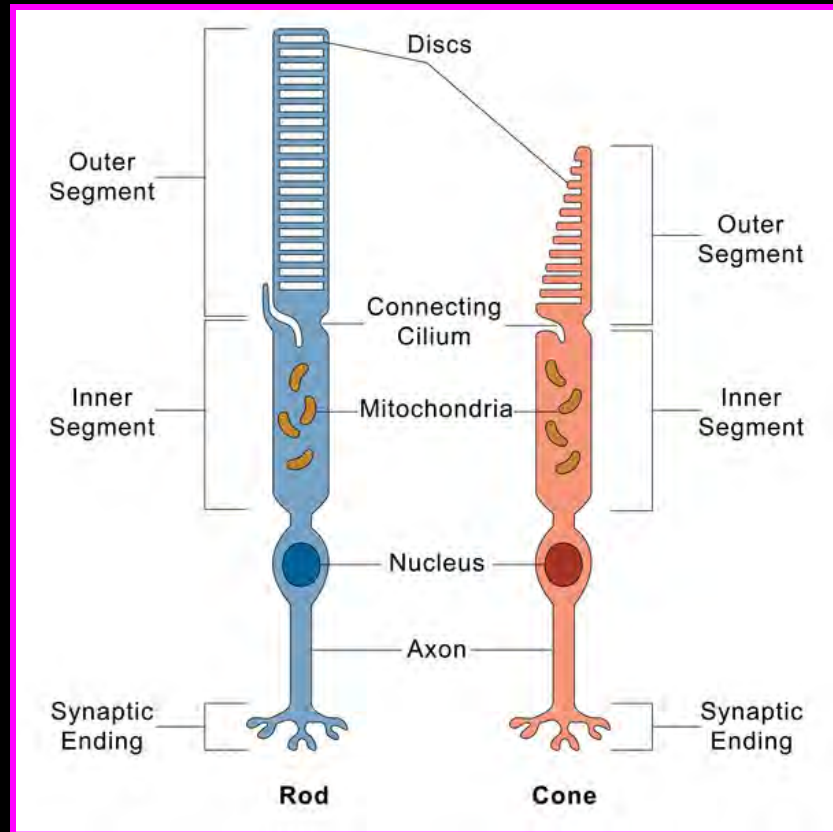
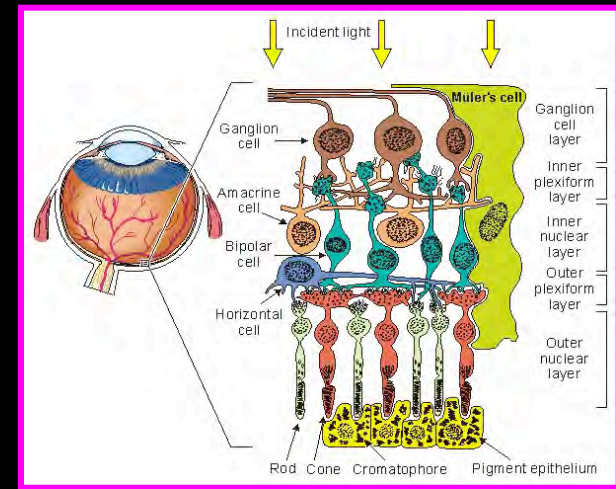


Retinal Cell Function



- Photoreceptors - transduce light signal to electrical signal
- Bipolar Cells – connect photoreceptors to ganglion cells
- Amacrine Cells – process motion and contrast
- Horizontal Cells – process light conditions
- Ganglion Cells – encode light information from action potentials to be processed and reconstructed by the visual cortex

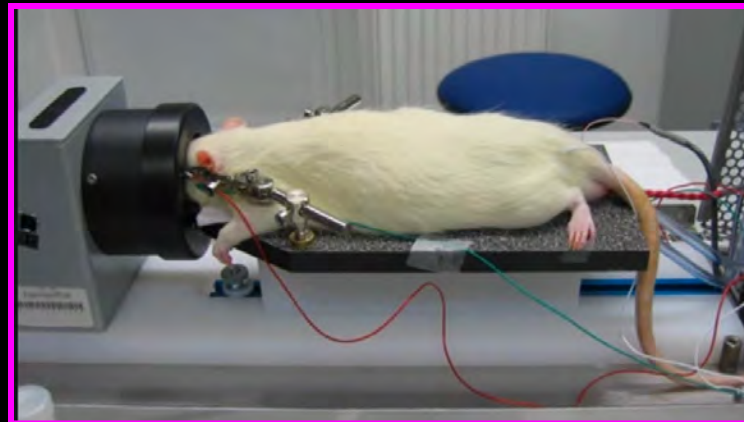
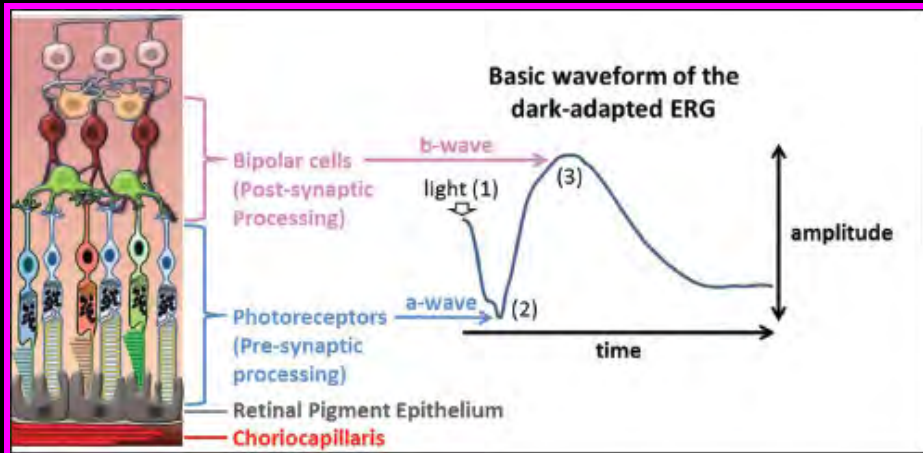
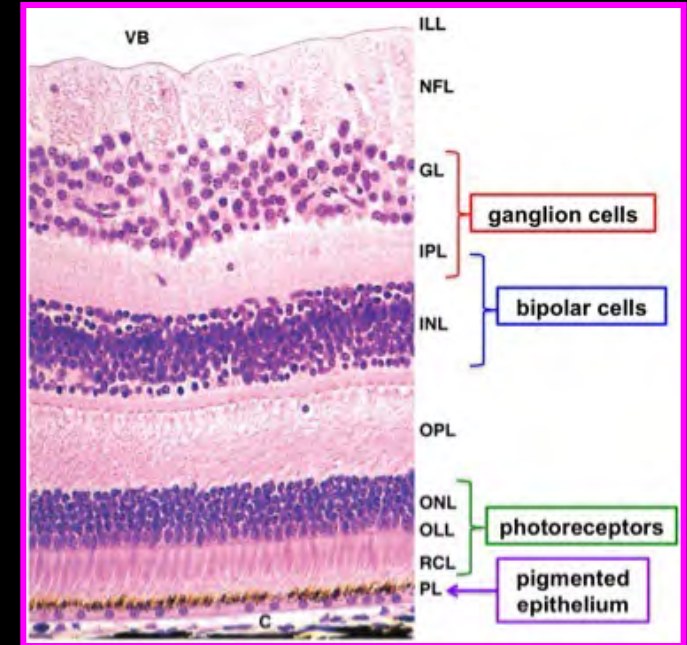
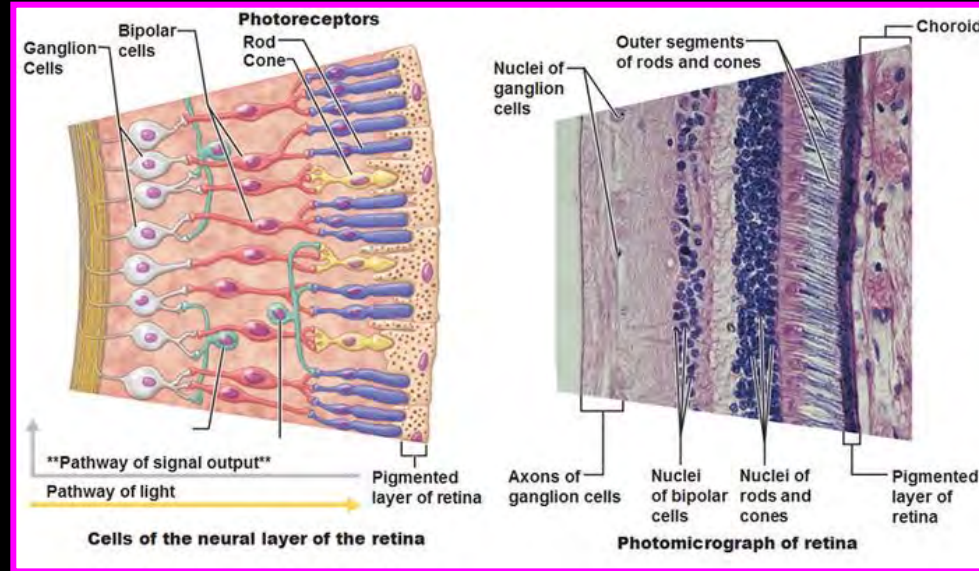
Photoreceptors are Vulnerable to Metabolic Inhibition and Oxidative Stress



- Most metabolically active cells in body - dark current
- Inner Segment - packed with mitochondria
- Outer segments contain high concentrations of PUFAs subject to lipid peroxidation

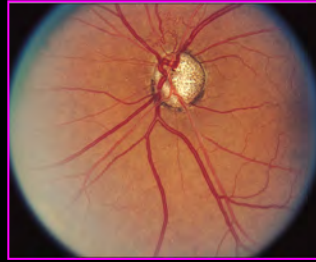
How to Study Retinal Disease

- Retinal Metabolism
- Retinal Function
- Retinal Microscopic Anatomy



PBMt in Experimental and Clinical Eye Disease

Methanol Toxicity



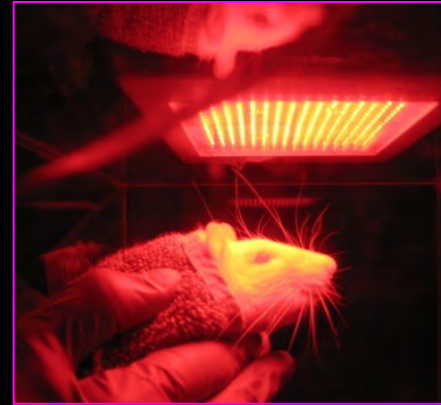
Retinitis Pigmentosa



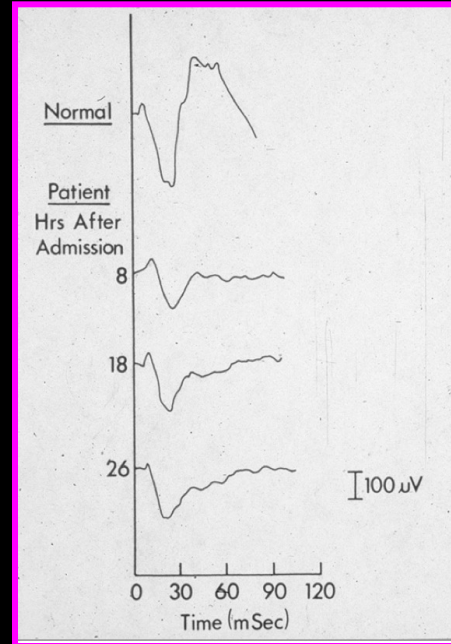
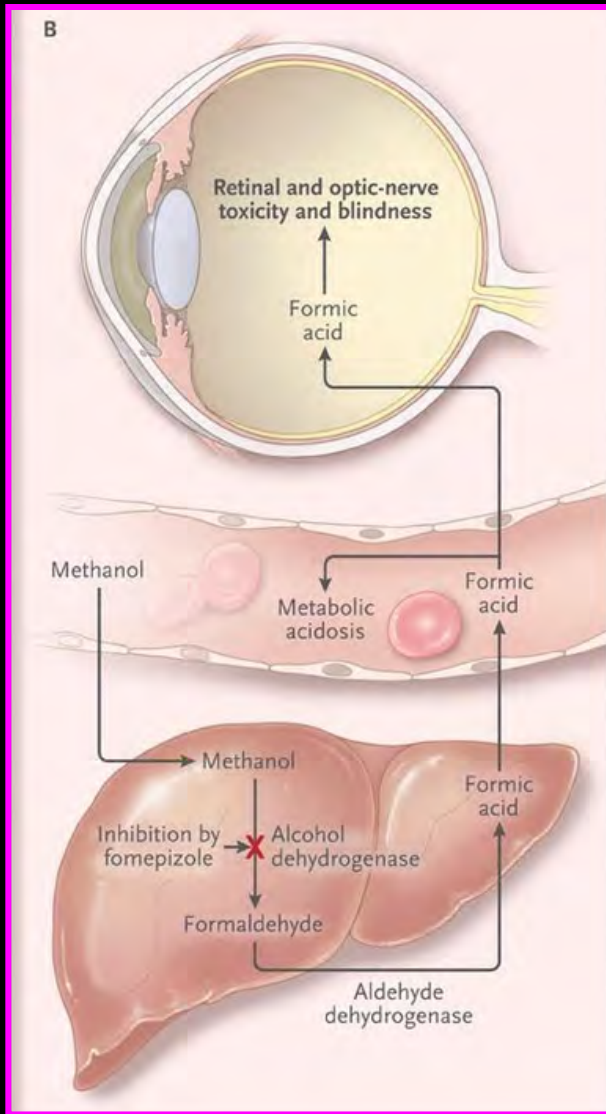
Diabetic Retinopathy



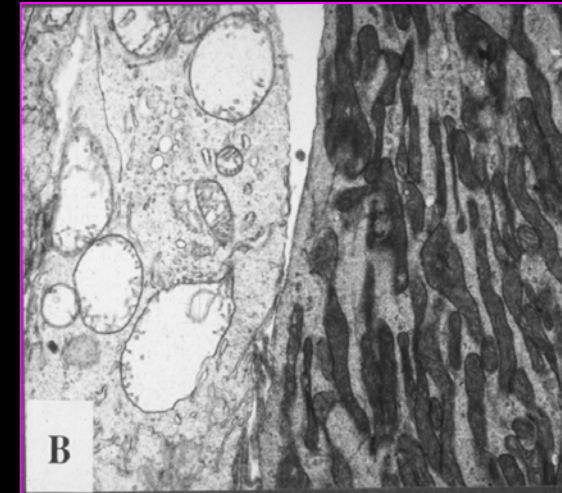
Age-Related Macular Degeneration (AMD)



Methanol Intoxication Produces Blindness



Retinal Dysfunction



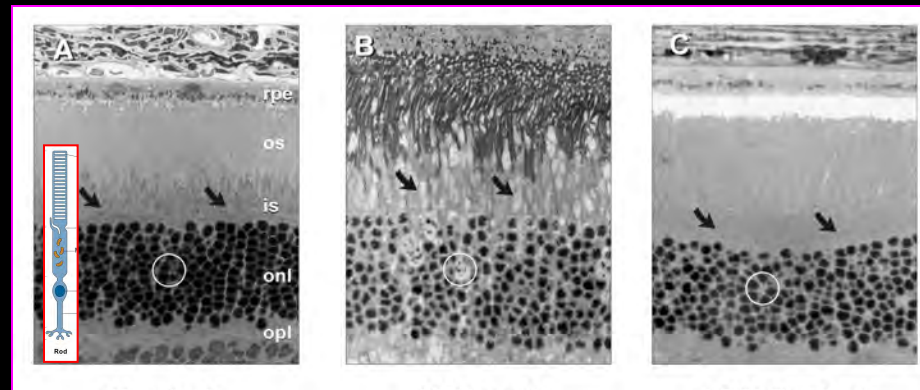
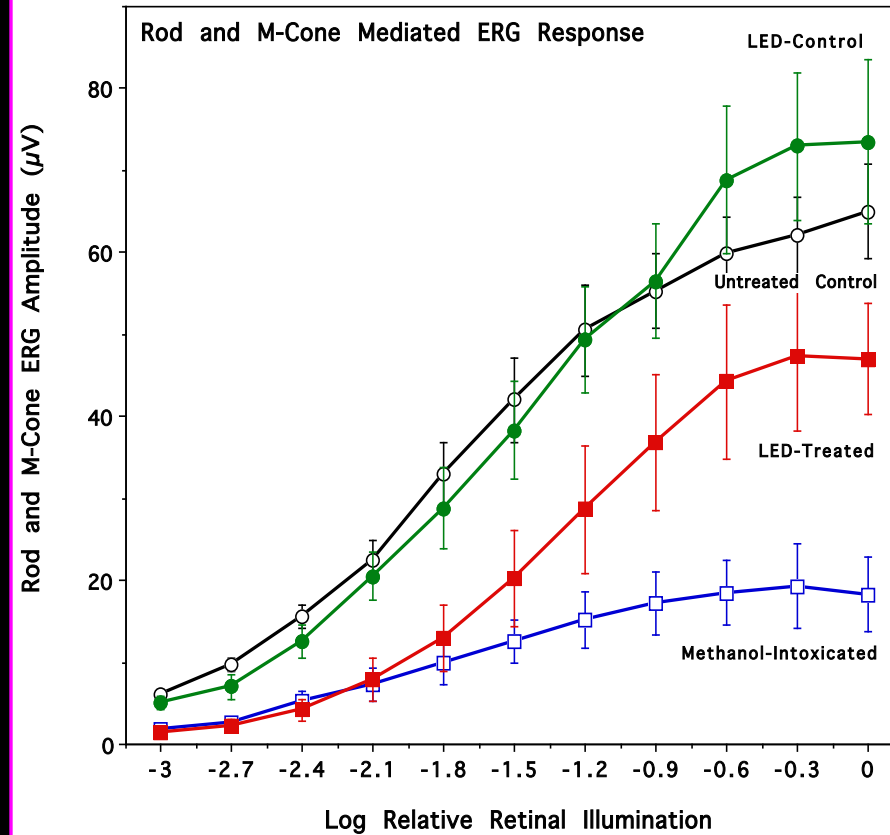
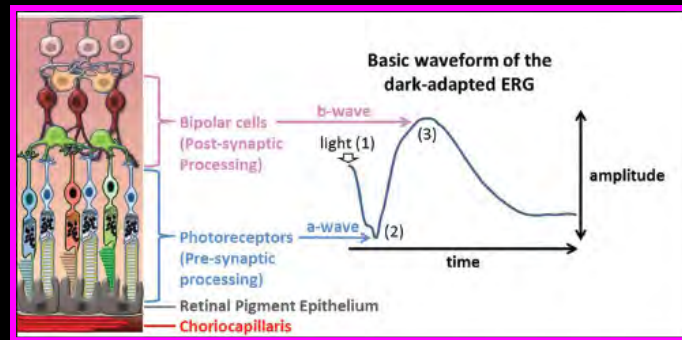
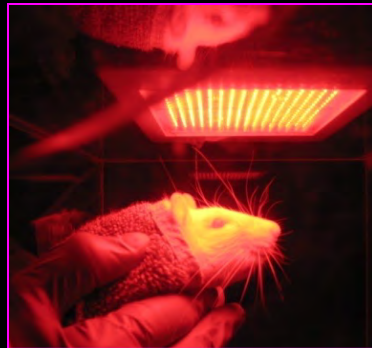
Photoreceptor Mitochondrial Disruption



Optic Nerve Atrophy

PBMt Attenuates Methanol Induced-Retinal Toxicity

670 nm Treatment
 At 5 hr, 25hr, 50 hr
 25 mW/cm² – 160 sec
 4 joules/cm²



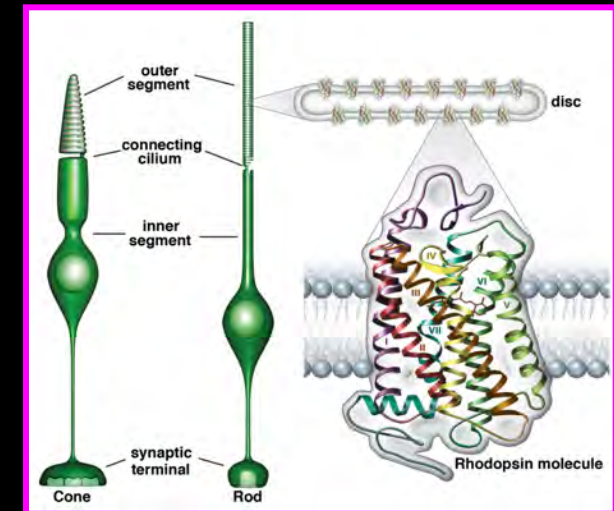
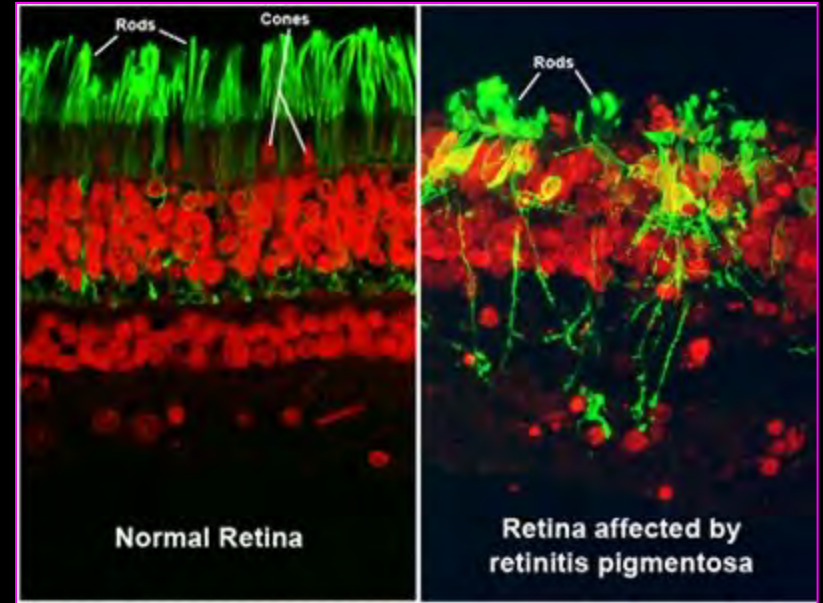
Sham

Intoxicated

PBM-Treated

Inherited Retinal Diseases - Retinitis Pigmentosa

- RP is a group of inherited retinal disorders characterized by progressive loss of photoreceptors leading to retinal degeneration and atrophy
- Affects 1:4000
- Common cause: mutations in proteins involved in phototransduction
- Point mutation in codon 23 of rhodopsin gene (P23H) - autosomal dominant RP
- P23H rodent model of RP - same mutation as human disease
- Unfolded protein response leading to mitochondrial dysfunction and apoptotic photoreceptor cell death



PBMt Preserves Mitochondrial Redox State and is Retinoprotective in a Rodent Model of Retinitis Pigmentosa



Treatment Protocol

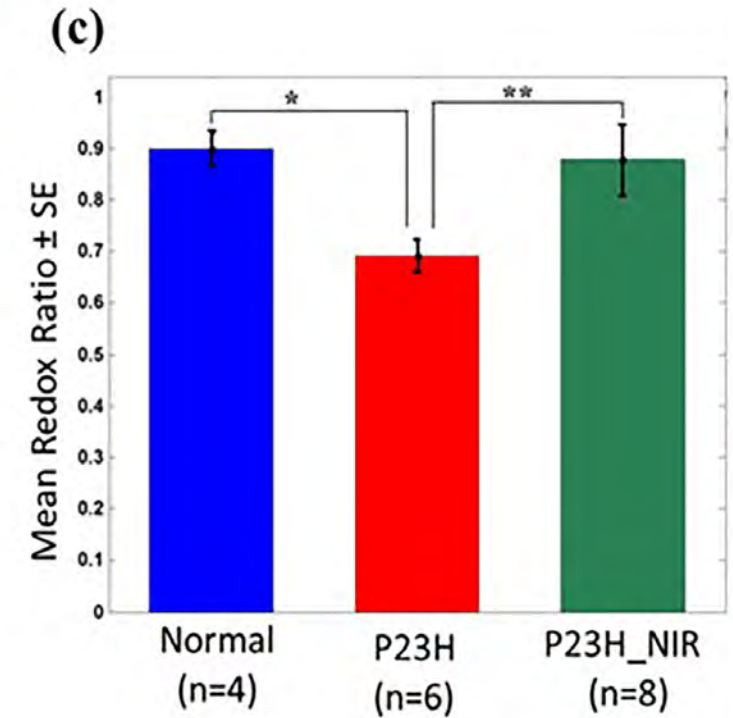
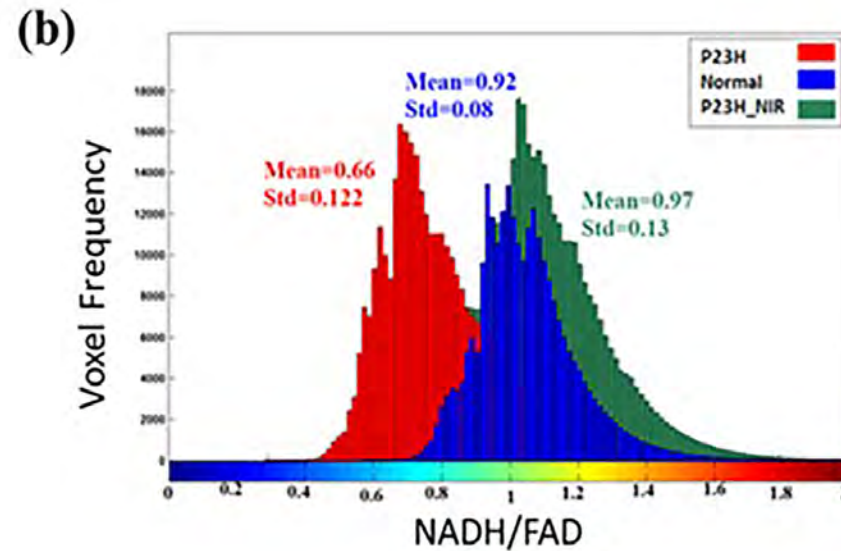
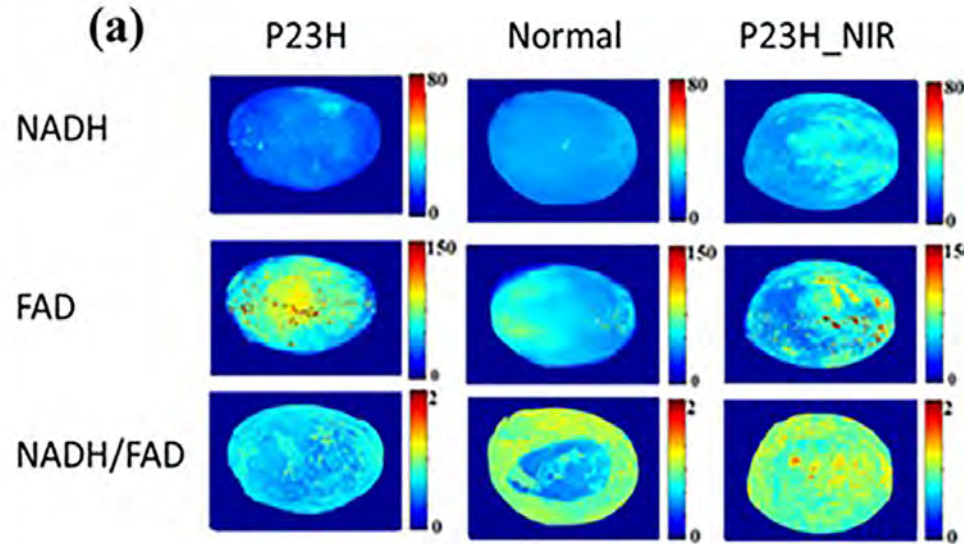
Critical Period
From p10 - p25
830nm LED Array
180 sec
25mW/cm² 4.5 J/cm²



Outcomes at P30

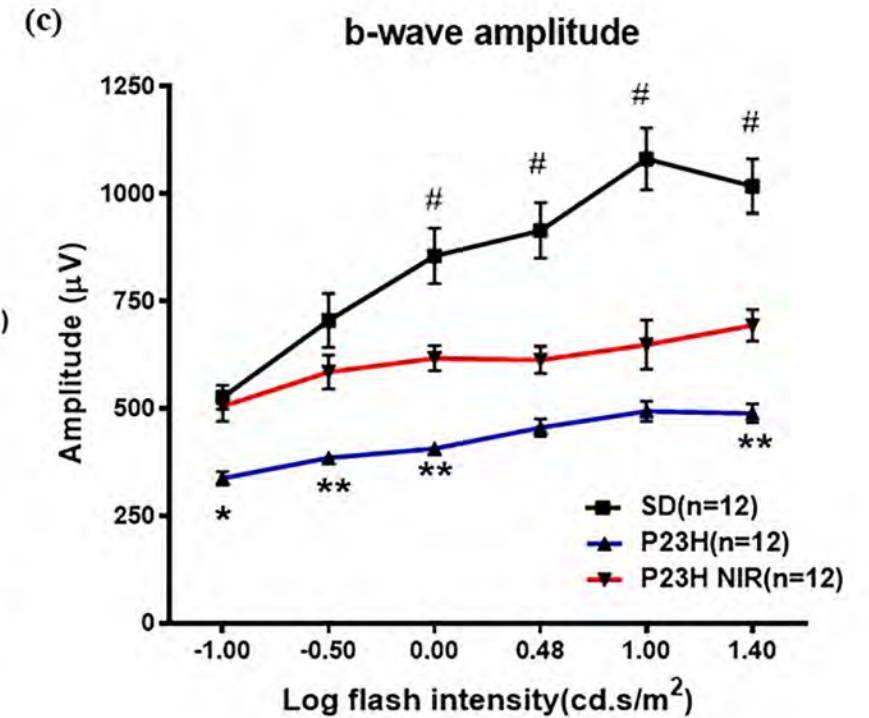
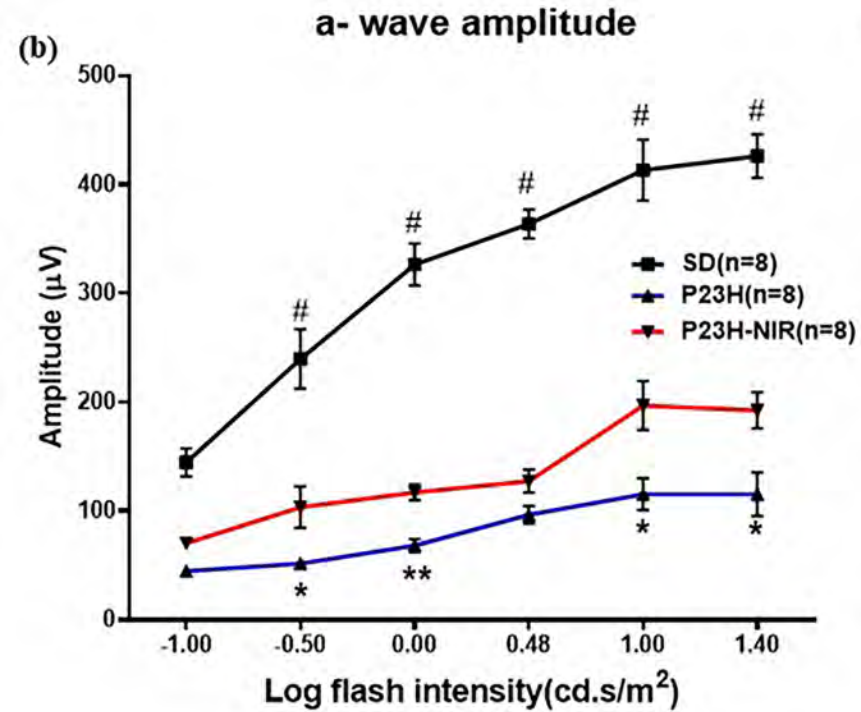
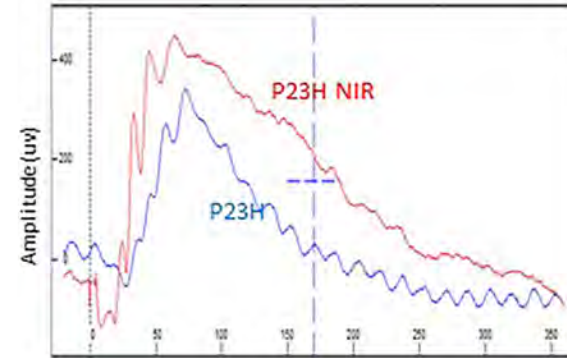
Retinal Metabolic State
Retinal Function
Retinal Morphology

PBMt Preserves Mitochondrial Redox State

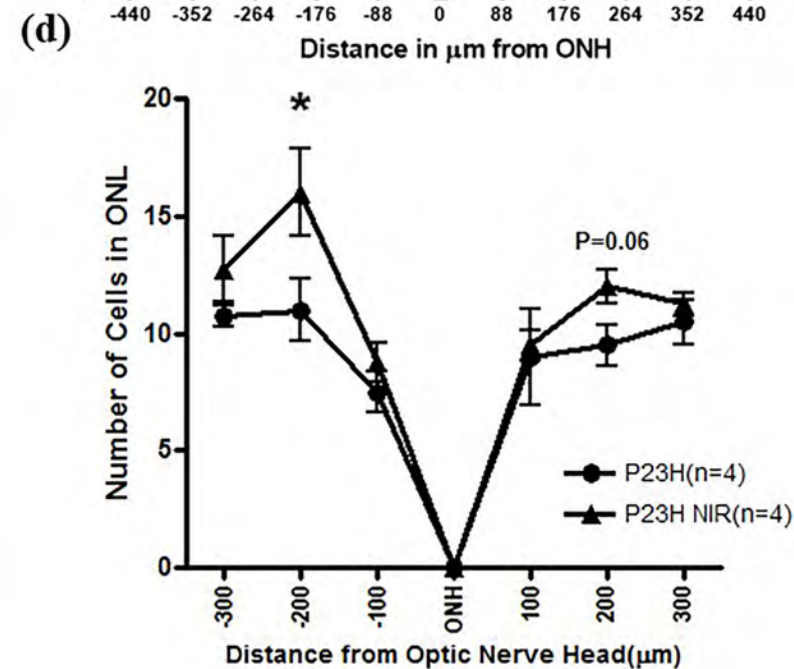
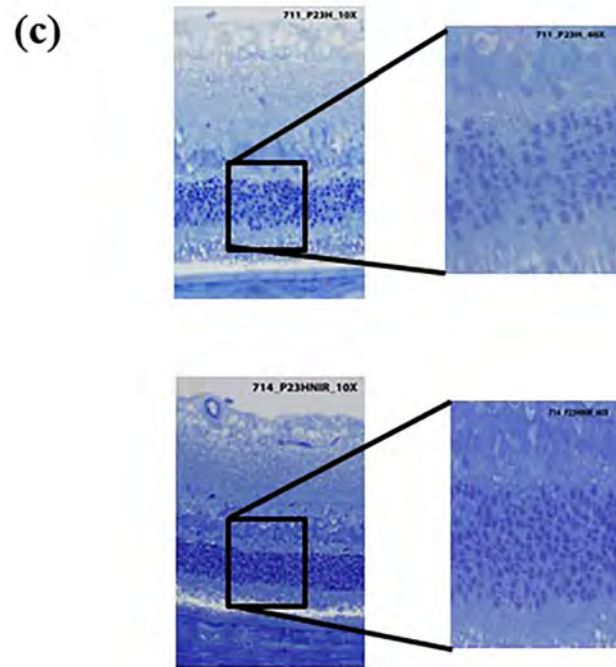
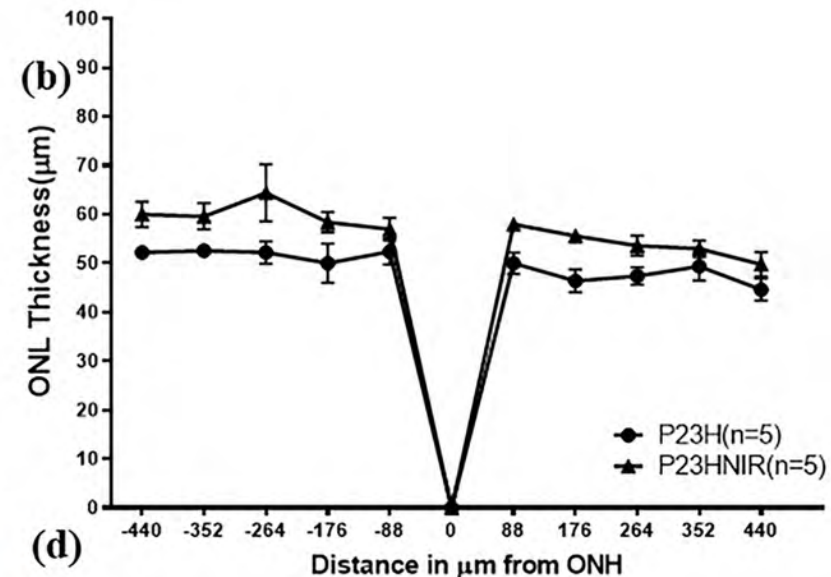
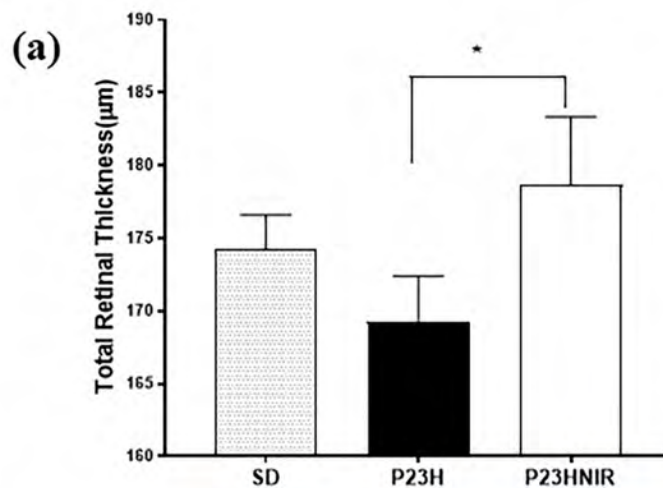


PBMt Preserves Retinal Function

(a)

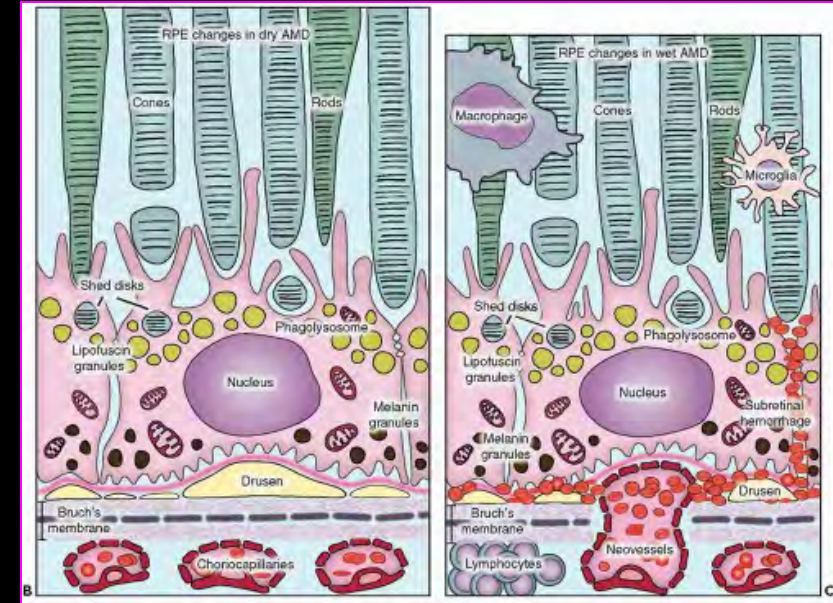
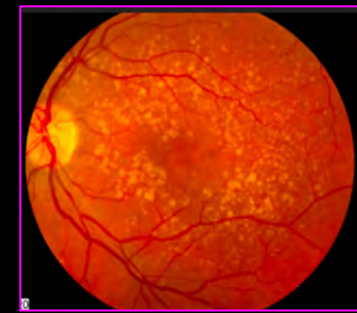


PBMt Prevents Retinal Cell Death



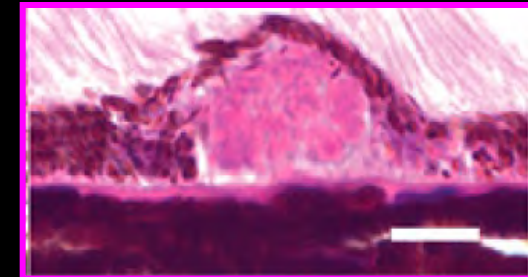
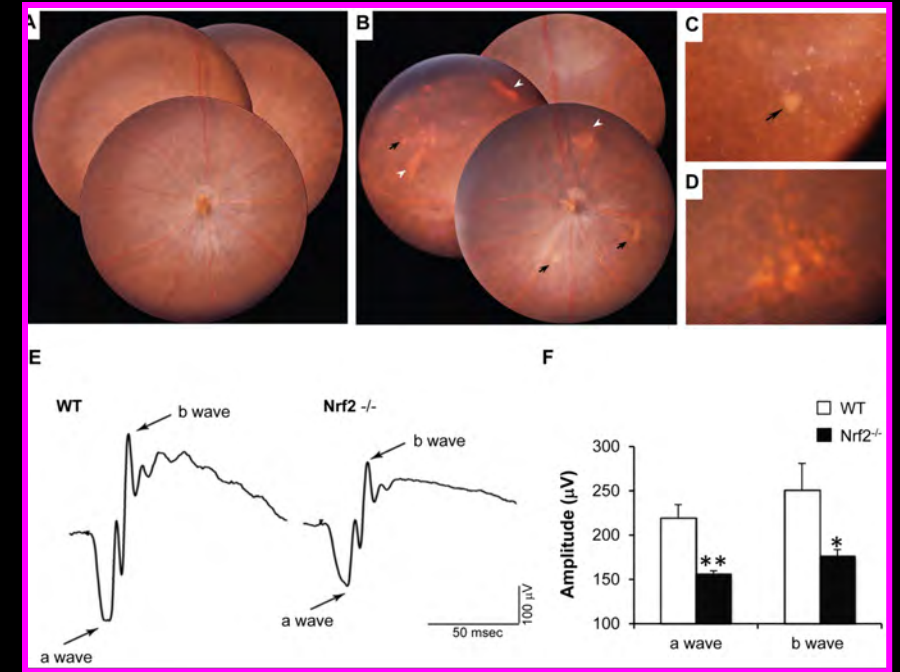
Age-Related Macular Degeneration (AMD)

- Leading cause of blindness in individuals over 65 in developed countries.
- AMD primarily affects the central retina or macula.
- It is characterized by the development of drusen, extracellular lipoprotein deposits under the retinal pigment epithelium (RPE), in the early stages of the disease, followed by the loss of photoreceptors and RPE.
- Choroidal neovascularization (CNV) develops during later stages of the disease (wet AMD)
- Dry or atrophic AMD is the most common form of AMD and there are no treatments for this form of AMD.

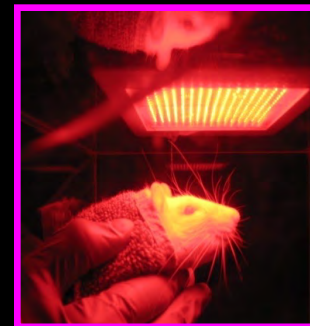


PBMt Attenuates Visual Dysfunction in a Mouse Model of AMD

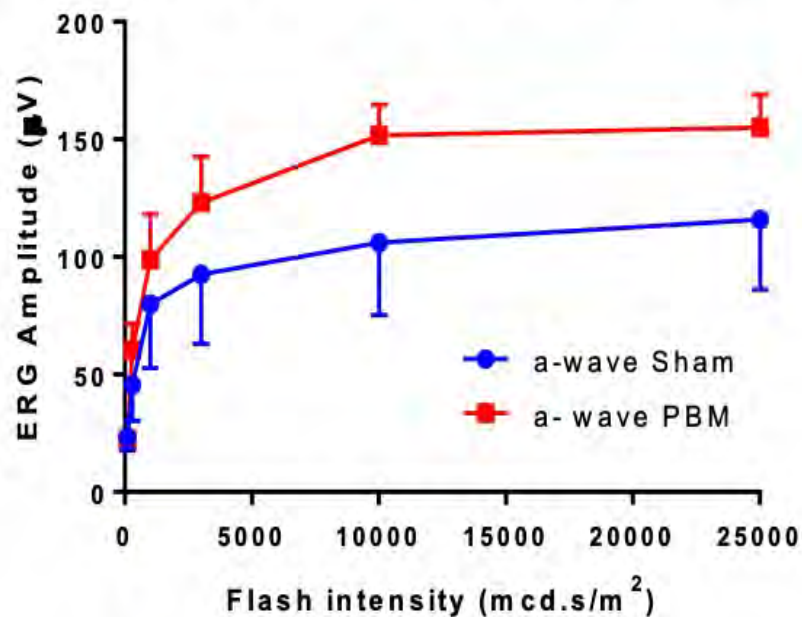
- Nrf2 knockout mouse
- Nrf2 is a transcription factor that plays a key role in retinal antioxidant and detoxification responses
- *Nrf2 ko Mouse Exhibits AMD-like pathology*
 - RPE degeneration
 - ERG reductions
 - Drusen-like deposits
- PBMt daily (4.5 J/cm²) for 12 weeks



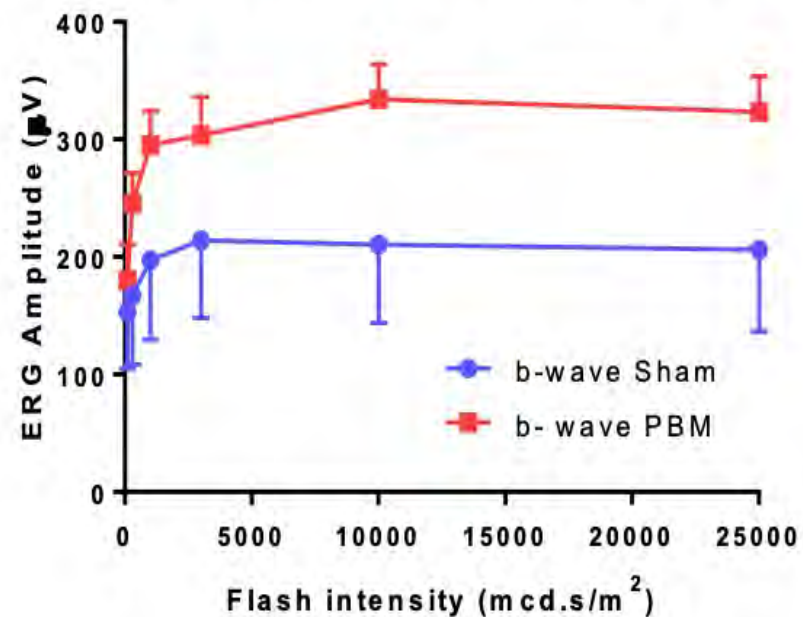
PBMt Attenuates Retinal Dysfunction a Mouse Model of Dry AMD



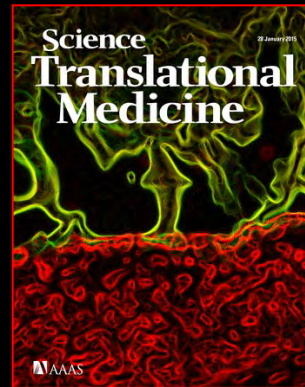
Effect of 670nm PBM on ERG a-Wave



Effect of 670nm PBM on ERG b-Wave



Between 2003-2021: Explosion of Research on PBM in Retinal Disease



Experimental Models

- *Retinitis Pigmentosa*
- *Bright Light-Induced Retinal Injury*
- *Retinopathy of Prematurity*
- *Retinal Aging*
- *Age Related Macular Degeneration*
- *Diabetic Retinopathy*

From Bench to Bedside: PBM in Retinal Disease



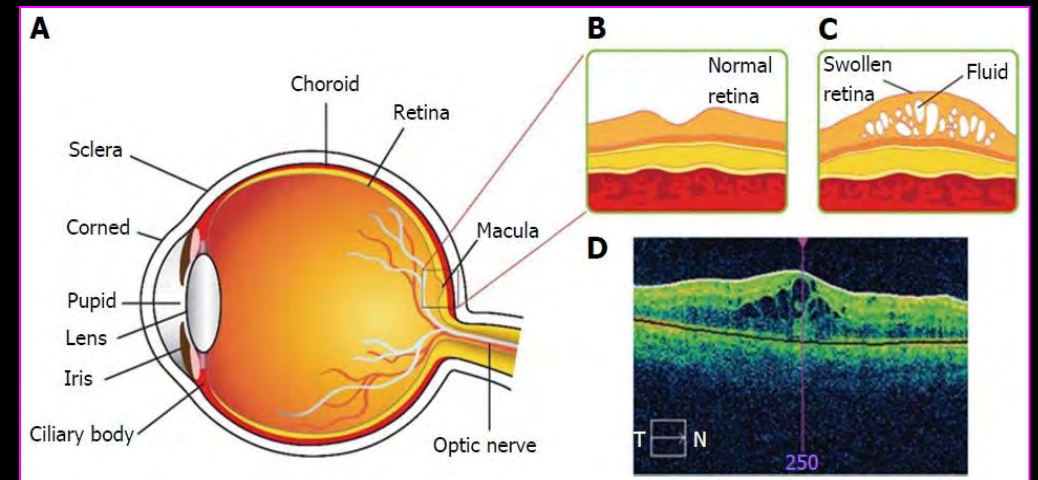
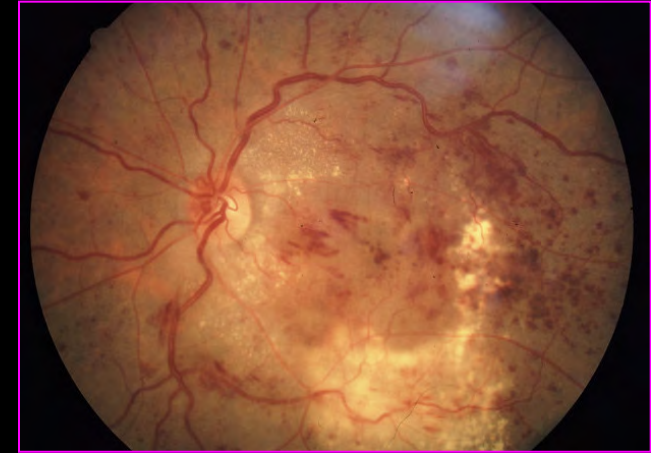
Diabetic Macular Edema
Pilot CTSI Study
DRCRnet Jaeb Center NEI Study

Dry Age -Related Macular Degeneration
LumiThera Lightsite Trials



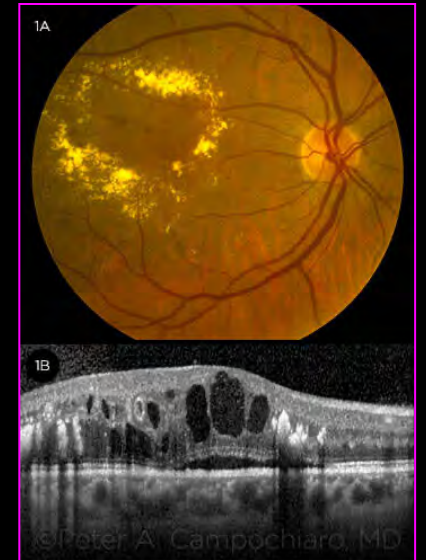
PBMt Attenuates Diabetic Macular Edema

- Diabetic retinopathy (DR) is the most common complication of diabetes.
- DR currently affects almost 100 million people worldwide and is set to become an ever-increasing health burden.
- Complex Pathophysiology involving oxidative stress, elevated VEGF and BRB breakdown.
- Resulting in extracellular fluid accumulation in macula and decreased vision.
- Treatment : Anti-VEGF injections, steroids

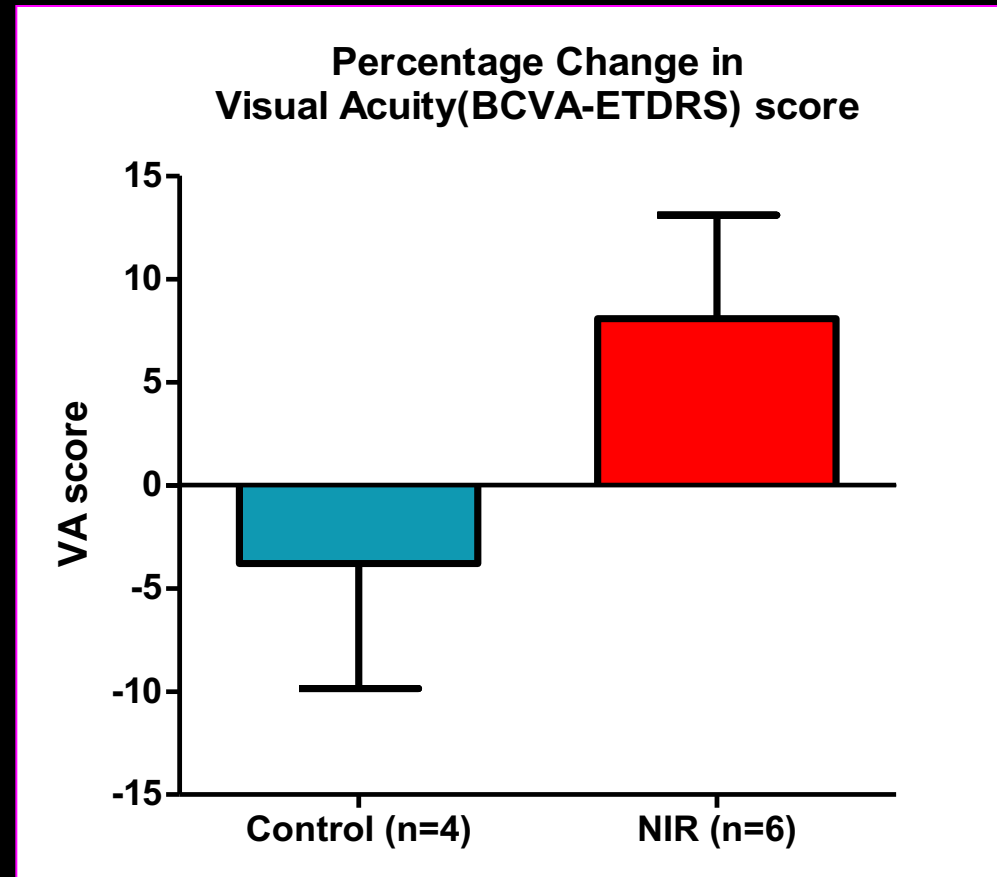
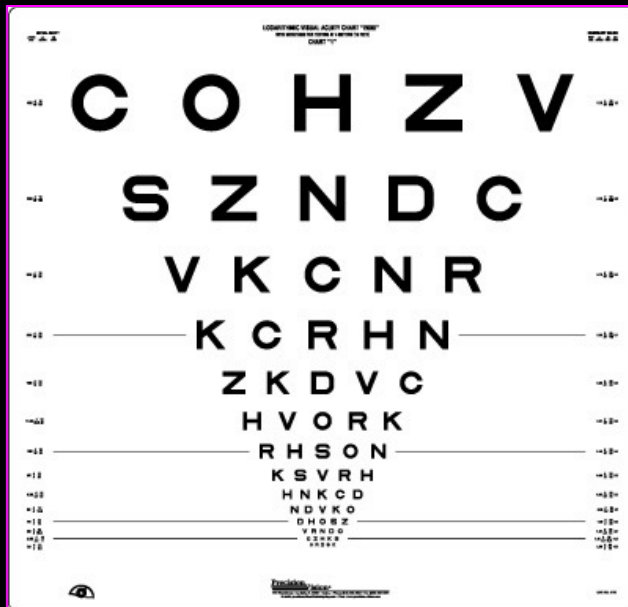


670 nm PBMt as a Therapy for Diabetic Macular Edema

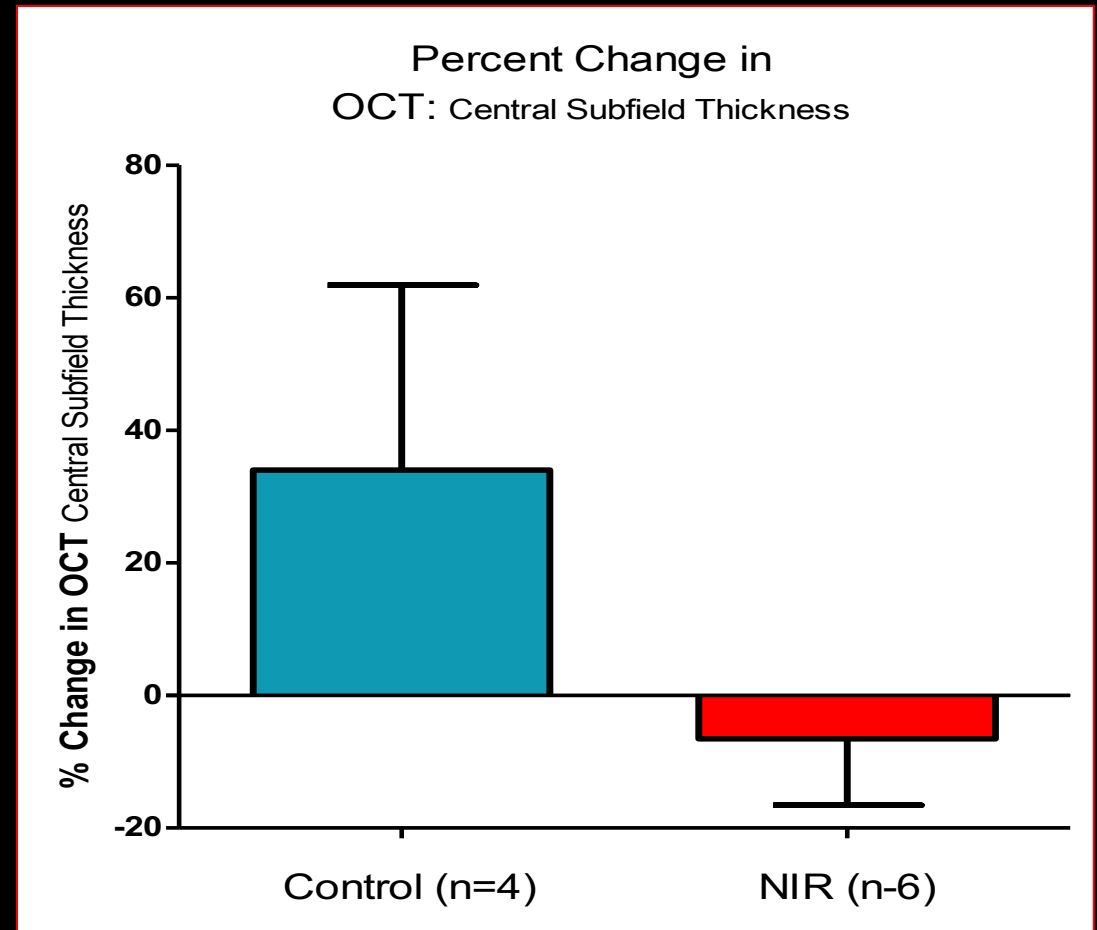
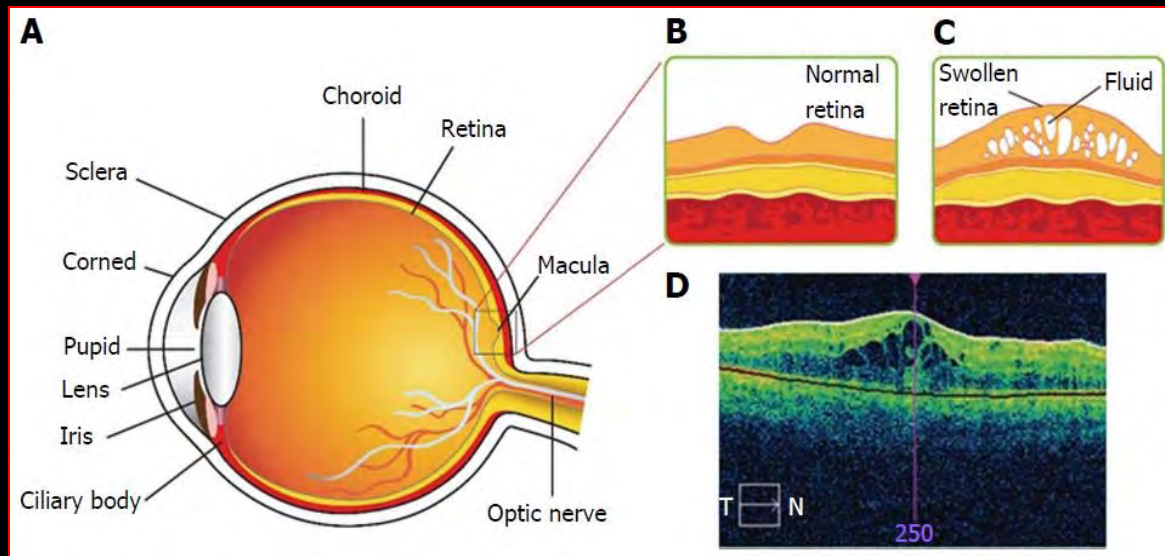
- Treatment Resistant Diabetic patients with clinically significant DME
 - Control: Standard of Care (n = 4)
 - Treated: Standard of Care plus PBM (n = 6)
- PBM Treatment Protocol:
 - LED Array given to patient for treatment
 - Treatment - 90 sec 3 x per week for 8 weeks
- Assessments at Baseline, 8 weeks and 24 weeks
 - Visual Acuity
 - OCT



670 nm PBMt Improves Visual Acuity in DME

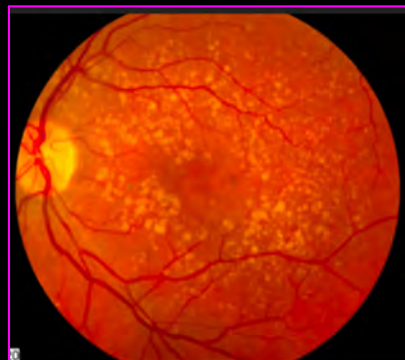
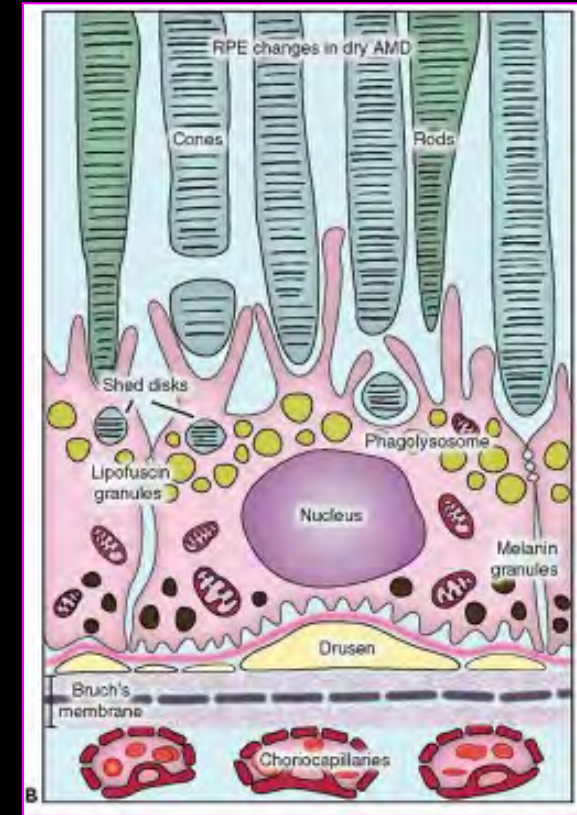


670nm PBMt Decreases Retinal Edema in DME

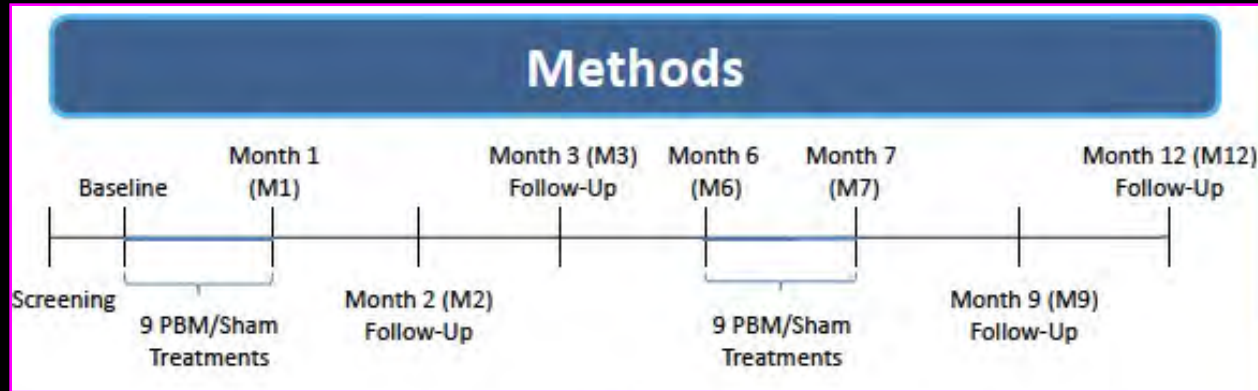


Age-Related Macular Degeneration (AMD)

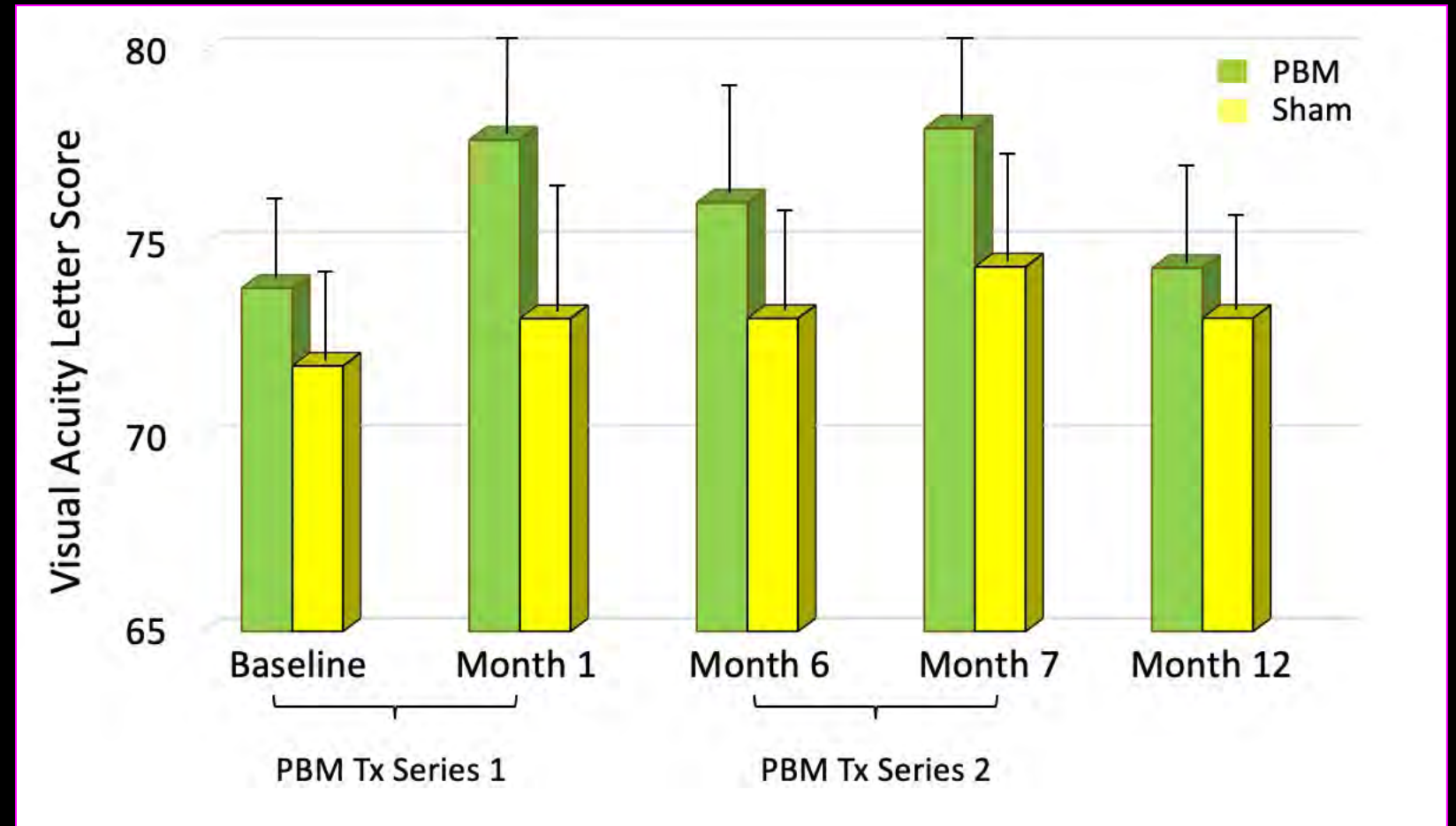
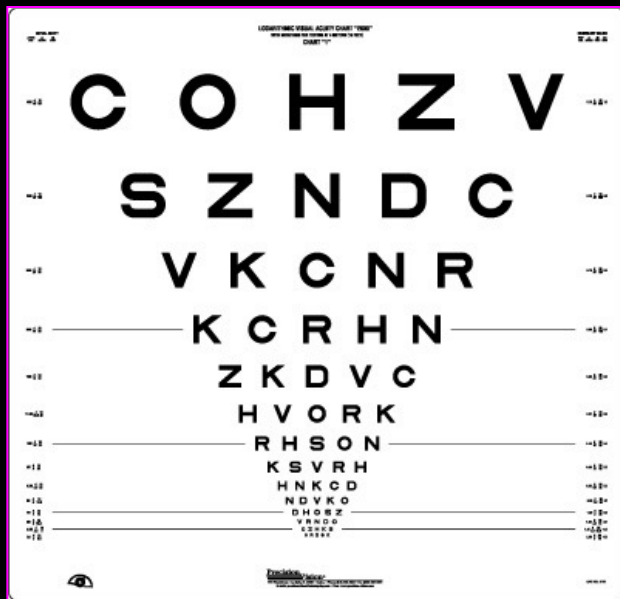
- AMD is the leading cause of blindness in individuals over 65 in developed countries.
- Dry or atrophic AMD is the most common form of AMD and there are no treatments for this form of AMD.



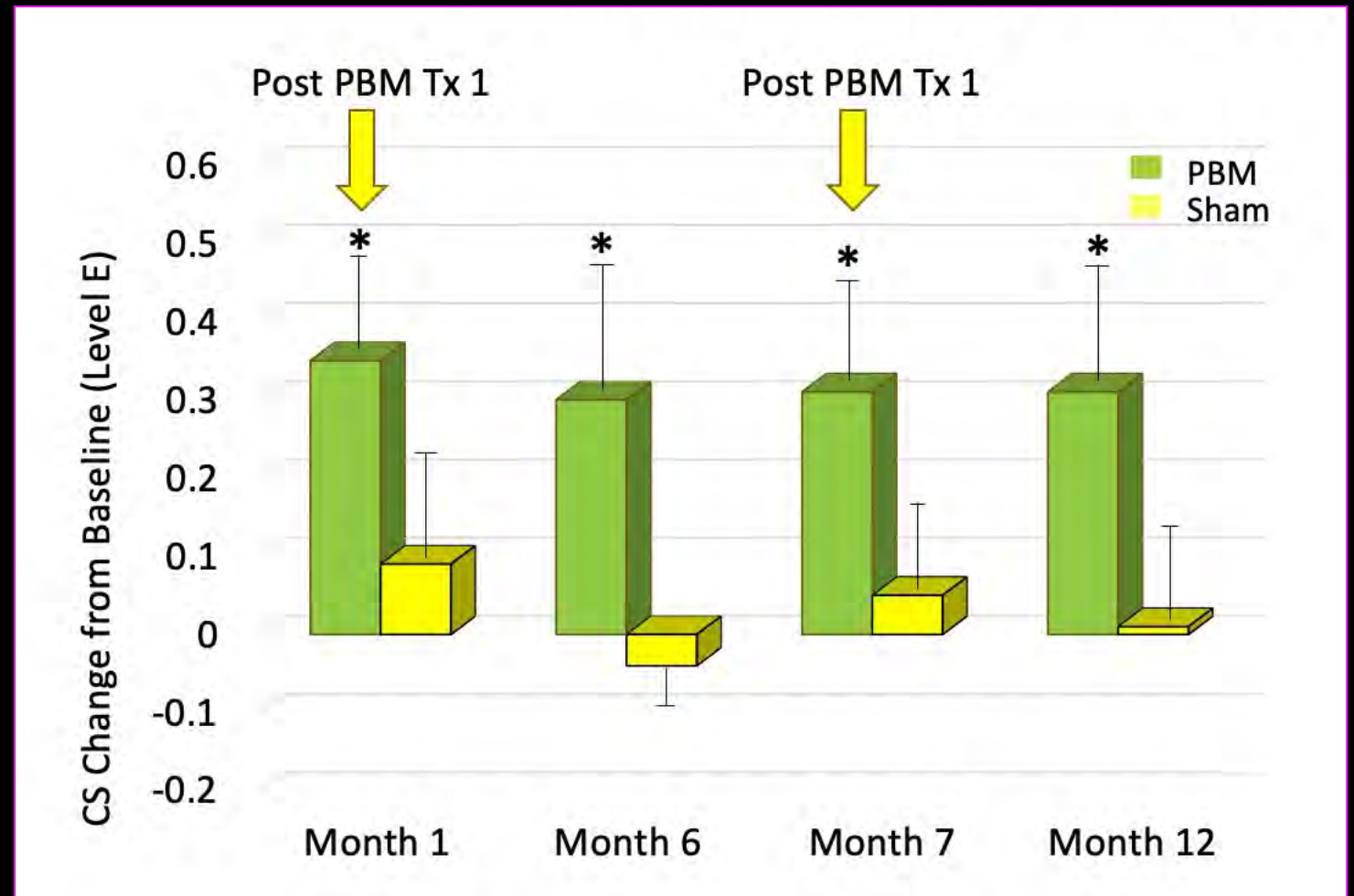
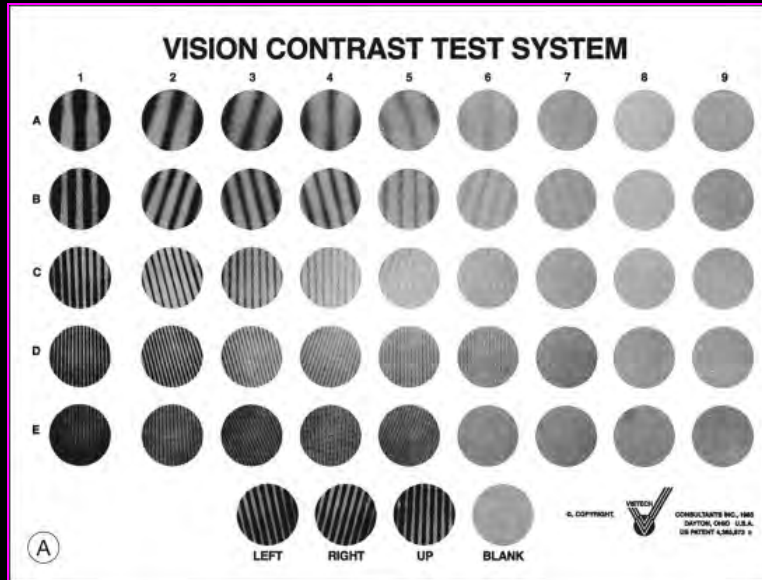
PBM Therapy Ameliorates Dry AMD



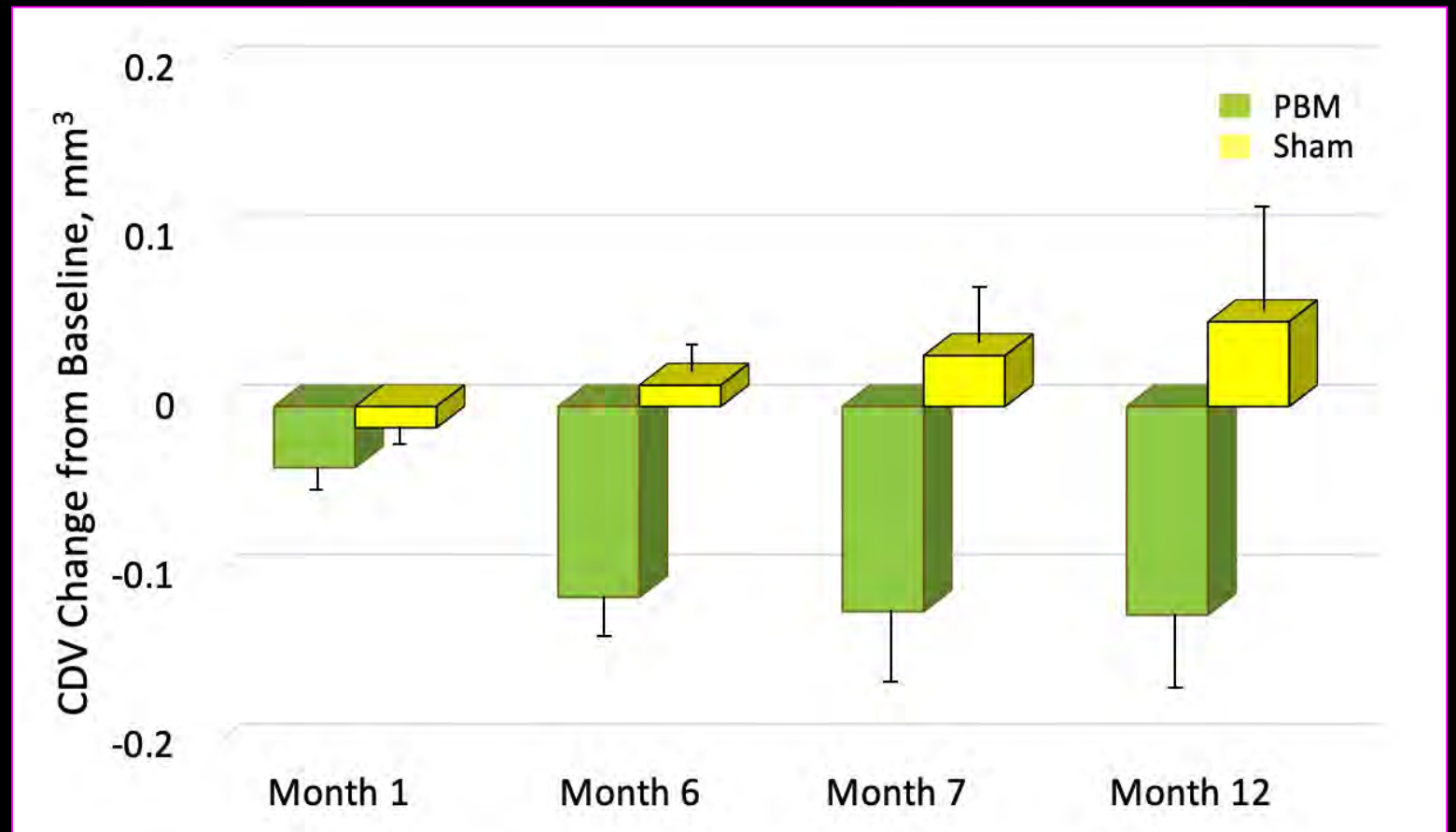
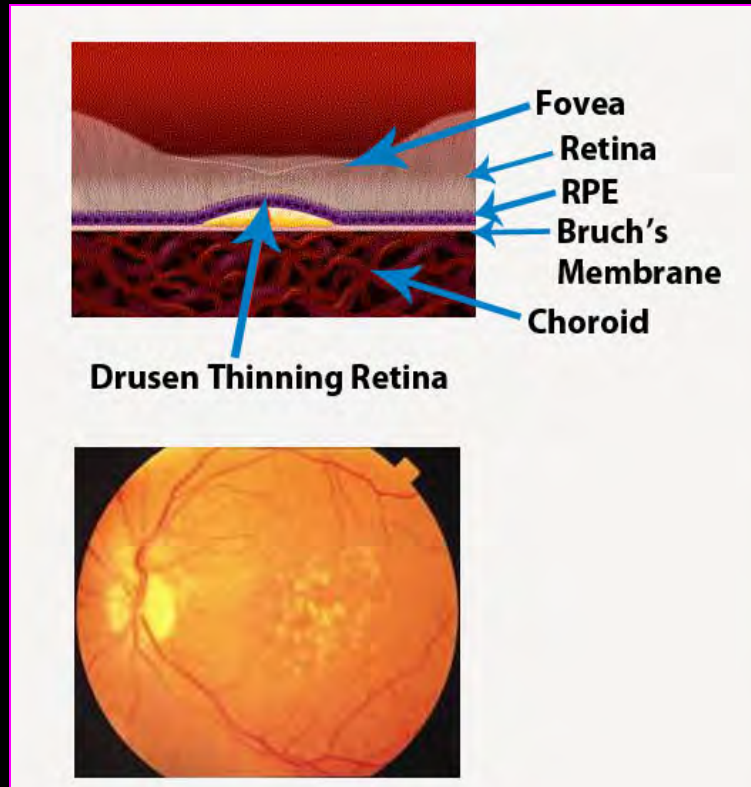
Visual Improvement Demonstrated Immediately Following PBM Therapy and at Maintenance Therapy



Improved Contrast Sensitivity Demonstrated Immediately Following PBM Therapy and at Maintenance Therapy



PBM Therapy Reduces Central Drusen Volume



Thank You!

