



Soluble Lutein (Lutemax2020[®]) Prevents Retinal Damage in Streptozotocin (STZ)-induced Diabetic Rats

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Disclosure

- ❖ **Manager**, Scientific and Clinical Affairs, OmniActive Health Technologies, Inc.
- ❖ **Patents** – Nutrition 21 Inc., OmniActive Health Technologies
- ❖ **Professional Societies - Affiliations:**
 - American Diabetes Association Committee – Women’s working group & Women and Diabetes
 - American Heart Association – Speaker’s Bureau/Spokes Person; Council member
 - American Society of Nutritional Sciences – Abstract Reviewer/Jury
 - Academy of American Dietetic Association
 - Consultant
 - Reviewer
 - HOD/PID , Research and Development - committee member
 - Evidence Analyst/Evidence Analysis Committee
 - American College of Nutrition – Council Member

Global Diabetes Prevalence Is Projected to Increase 242% Between 2000 and 2030

2000: 14.2 M
2010: 17.5 M
+23%

2000: 26.5 M
2010: 32.8 M
+24%

2000: 84.5 M
2010: 132.3 M
+57%

2000: 9.4 M
2010: 14.2 M
+50%

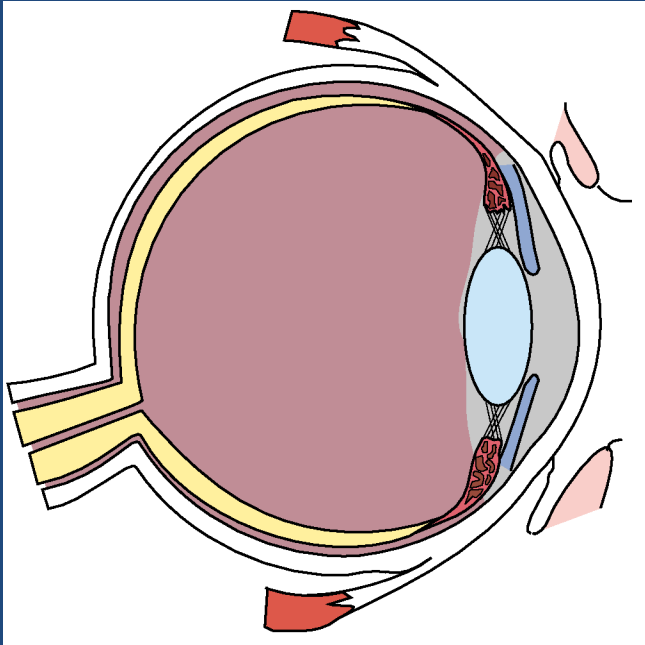
2000: 15.6 M
2010: 22.5 M
+44%

2000: 1.04 M
2010: 1.33 M
+28%

Global data
2000: 151 million patients
2010: 221 million patients
2030: 366 million patients

Amos AF, et al. *Diabet Med.* 1997;14:S7-S85.
Wild S, et al. *Diabetes Care.* 2004;27:1047-1053.

Diabetic Retinopathy



- Diabetic retinopathy is the most common cause of new cases of blindness among adults 20-74 years of age.
- Each year, between 12,000 to 24,000 people lose their sight because of diabetes.
- During the first two decades of disease, nearly all patients with type 1 diabetes and over 60% of patients with type 2 diabetes have retinopathy

What is Diabetic Retinopathy?

- Diabetic retinopathy is the result of damage to the tiny blood vessels that nourish the retina. They leak blood and other fluids that cause swelling of retinal tissue and clouding of vision.
- Fluid can leak into the macula, the area of the retina which is responsible for clear central vision. Although small, the macula is the part of the retina that allows us to see colors and fine detail.
- The fluid causes the macula to swell, resulting in blurred vision. The condition usually affects both eyes.
- The longer a person has diabetes, the more likely they will develop diabetic retinopathy. If left untreated, diabetic retinopathy can cause blindness.

Natural History of Diabetic Retinopathy



- Mild nonproliferative diabetic retinopathy (NPDR)
- Moderate NPDR
- Severe NPDR
- Very Severe NPDR
- Proliferative diabetic retinopathy (PDR)

Diabetic Retinopathy and Sight Threatening Conditions : Global Prevalence

35 studies
N=22,896 with
diabetes from US,
Australia, Europe,
and Asia

52% female
44.4% Caucasian
30.9% Asian
13.9% Hispanic
8.9% African
American

Mean age: 58.1 yrs
Median diabetes
duration: 7.9 yrs
Median A1C: 8.0%

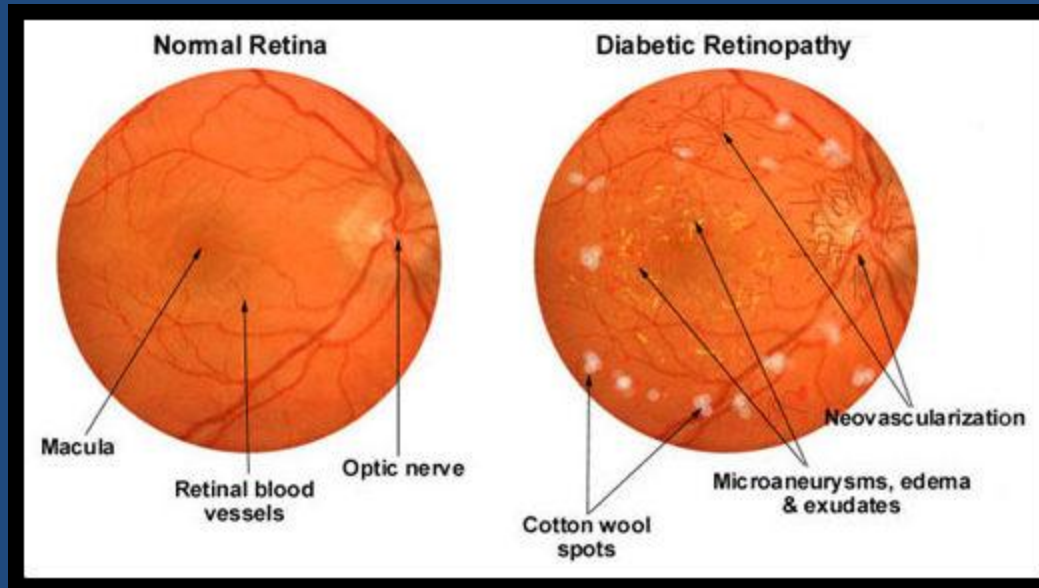
Diabetic Retinopathy (DR): 34.6% • 92.6 million

Proliferative DR: 6.96% • 17.2 million

Diabetic Macular Edema: 6.81% • 20.6 million

Vision-Threatening DR: 10.2% • 28.4 million

Normal Retina and Diabetic Retinopathy

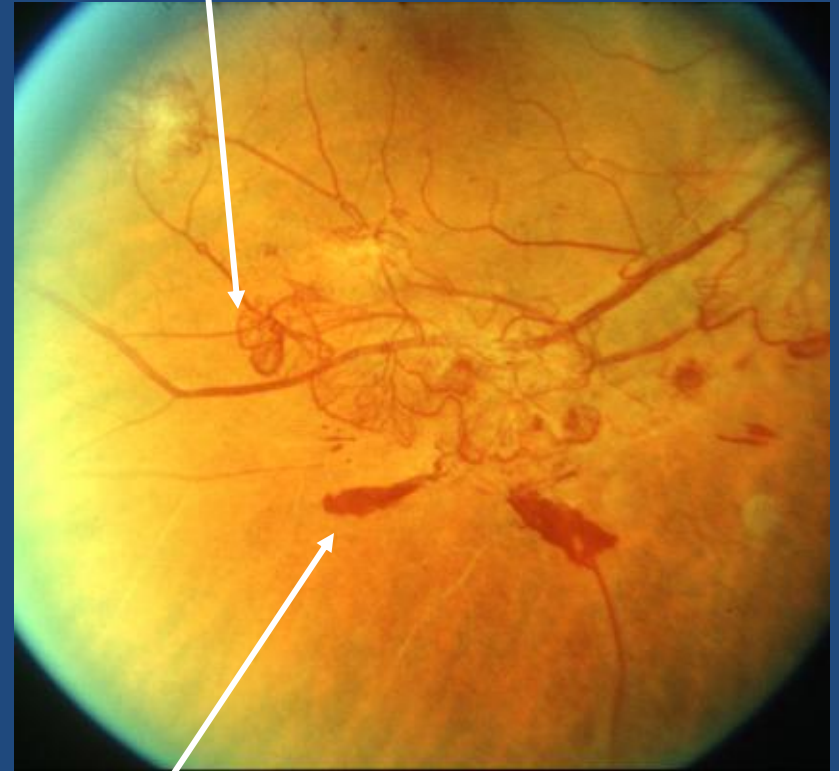
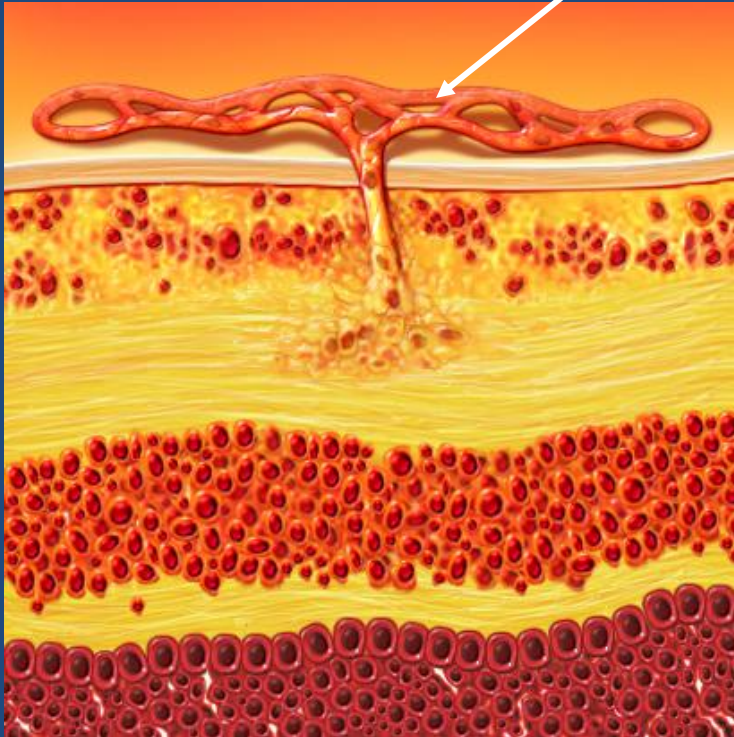


Symptoms

- Seeing spots or floaters in your field of vision
- Blurred vision
- Having a dark or empty spot in the center of your vision
- Difficulty seeing well at night

Proliferative Diabetic Retinopathy

Neovascularization



Hemorrhage

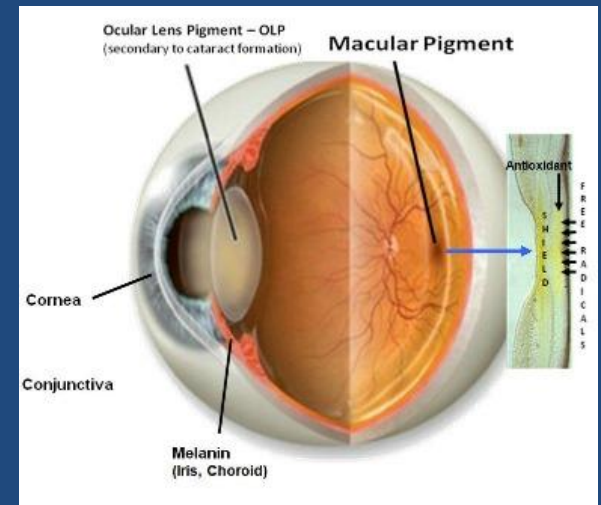
Factors Contributing to Diabetic Retinopathy

- Hyperglycemia
- Hypertension
- Inflammatory dyslipidemia
- Oxidative stress
- Apoptosis
- Release and suppression of growth factors
- Hormonal influences
- Up regulation of inflammatory cytokines
- Blood-retinal barrier [BRB] breakdown and hypoxia

Of the >600 carotenoids found in nature

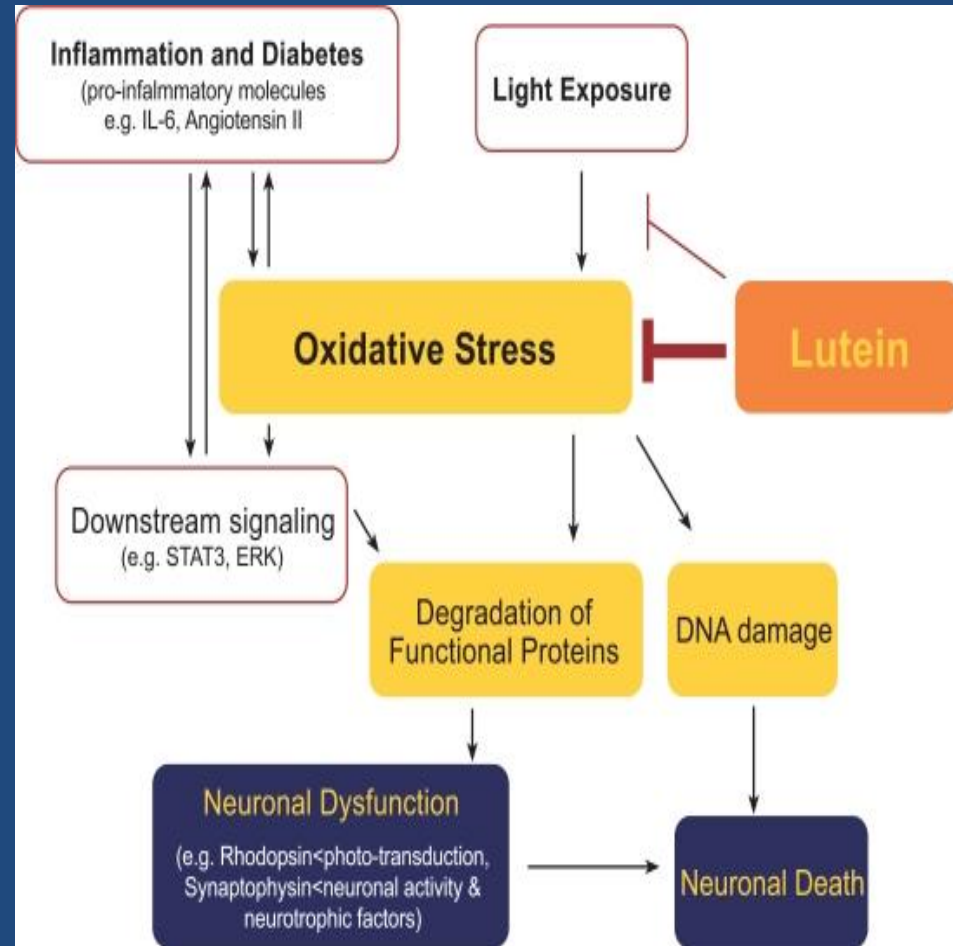
3 are found in the eye

Lutein & Zeaxanthin Isomers



Lutein and Retina

- Lutein is a xanthophyll and one of 600 known naturally occurring carotenoids.
- Lutein is synthesized only by plants and like other xanthophyll's is found in high quantities in green leafy vegetables and fruits.
- The human retina accumulates lutein.
- It serves as a photo-protectant for retina from the damaging effects of free radicals produced by blue light.
- Lutein suppresses oxidative stress in tissue.
- Lutein can also prevent free radicals from combining with retinal collagen and strengthen the structure of retinal collagen.



Lutein: Eye Health

Summary of Scientific Evidence

- Estimated 70 clinical studies
- Approximately 10000 human subjects assessed
 - AMD, Cataract and healthy population
 - Men and women
 - Younger and older
 - From various locations (U.S. and overseas)
- Lutein alone or in conjunction with zeaxanthin
 - 6-40mg/day of lutein
- Study duration
 - Single intake (acute lab studies) to 5 years with daily intake (intervention studies)
- Outcome measures
 - MPOD; Plasma/Serum and buccal mucosal cells lutein ; visual acuity, foveal and glare sensitivity, visual field area , luminous and chromatic sensitivity ; visual fatigue

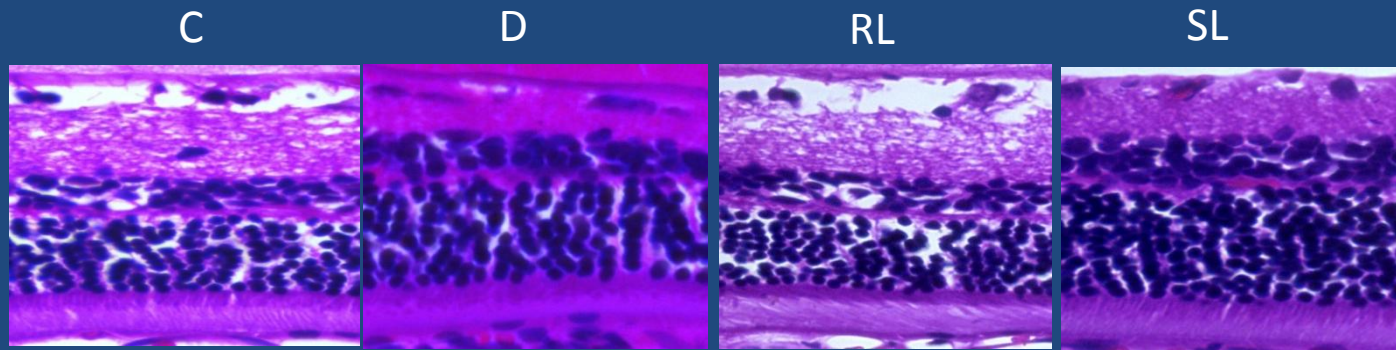
Objectives

- To investigate the protective effects of Lutein in streptozotocin-induced (STZ) diabetic rat retina.

Study design: Treatments

Groups	Number of animals	Diet
Control	6	AIN 93
Diabetic (D)	9	AIN 93
Diabetic +SL	8	AIN 93 with Lutemax [®] 2020 Ultra 0.5 %
Diabetic +RL	6	AIN 93 with lutein 0.5 %

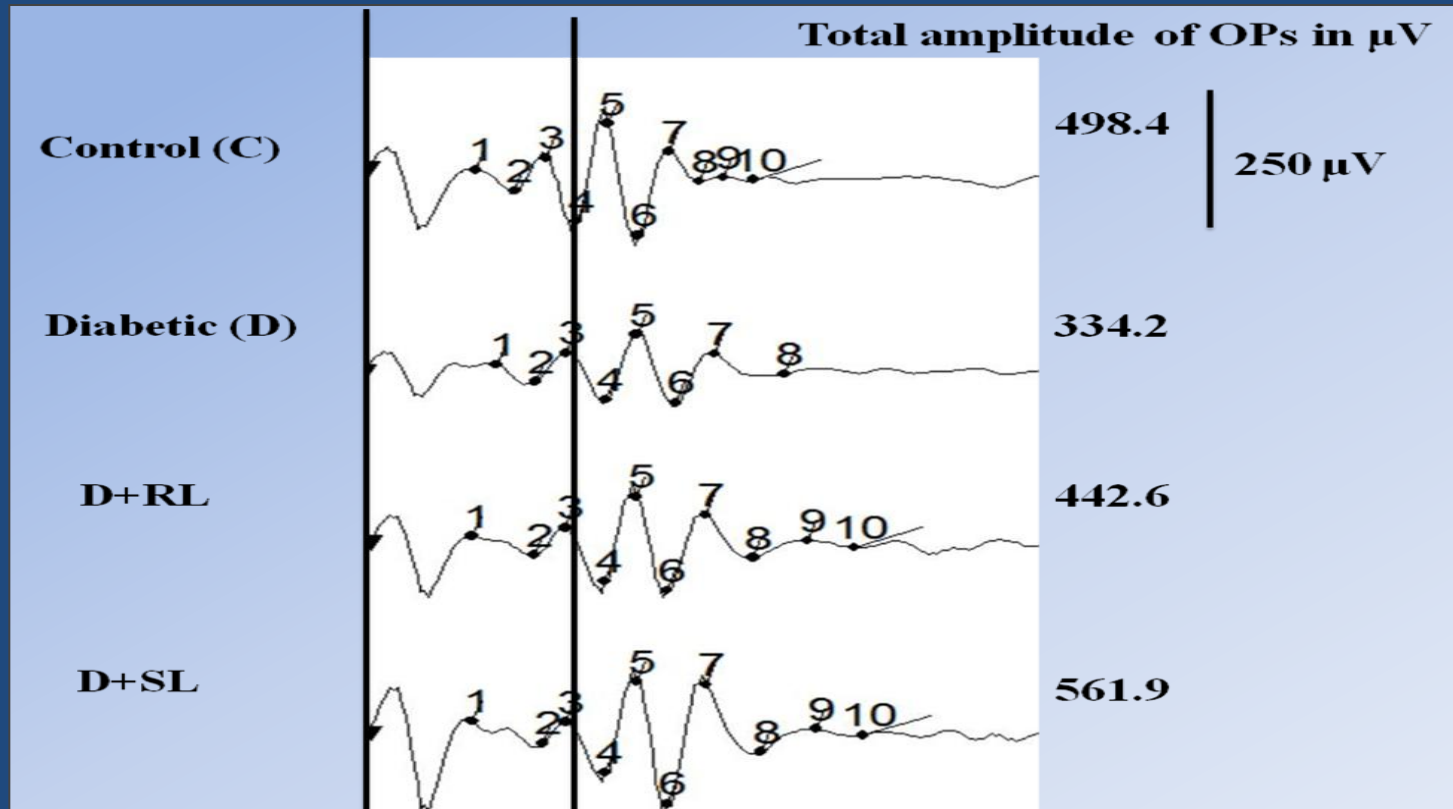
Diabetes induced gross structural alterations (Retinal layers' Thickness)



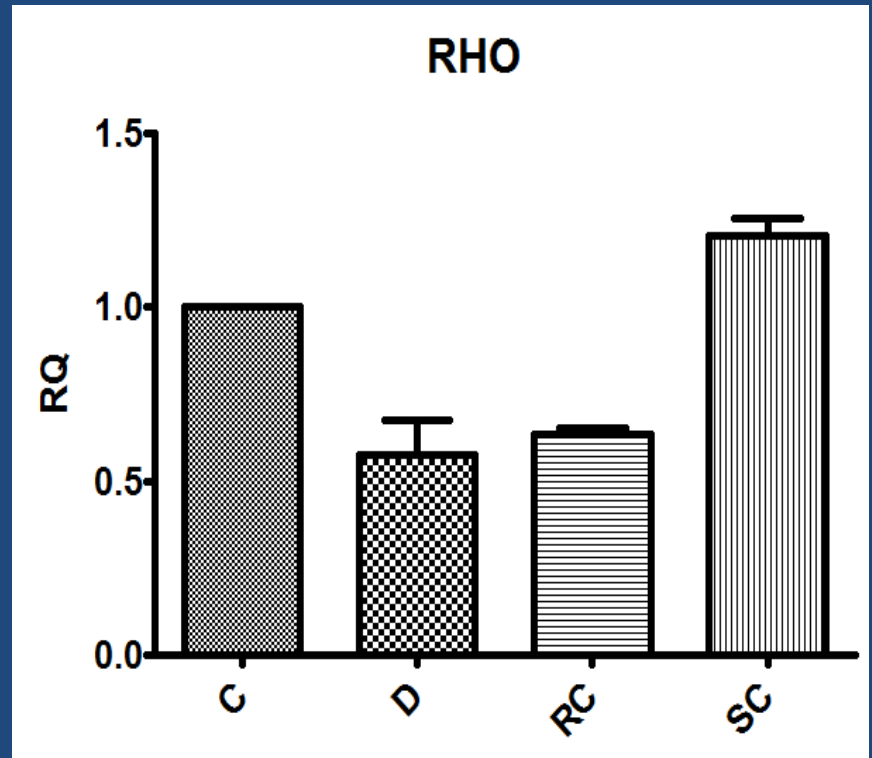
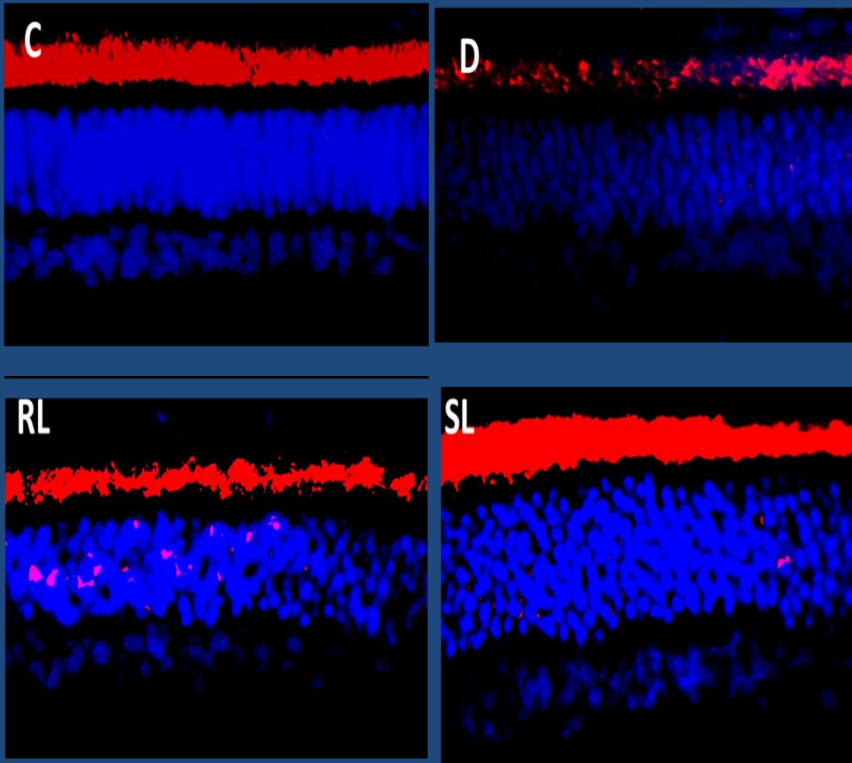
Retinal layers	Total retinal thickness	GCL+IPL	INL	OPL	ONL	PRL
C	121.74	46.813	10.767	5.024	25.697	19.426
D	58.848	12.508	9.257	0.791	23.052	12.184
RL	89.409	31.518	12.117	1.41	23.181	12.600
SL	112.714	40.877	16.074	4.718	31.196	23.072

Outer Nuclear Layer (ONL); Outer Plexiform Layer (OPL); Inner Nuclear Layer (INL); Inner Plexiform Layer (IPL); Layer of Ganglion cells (GCL)

Electroretinograph: A measure of retinal function

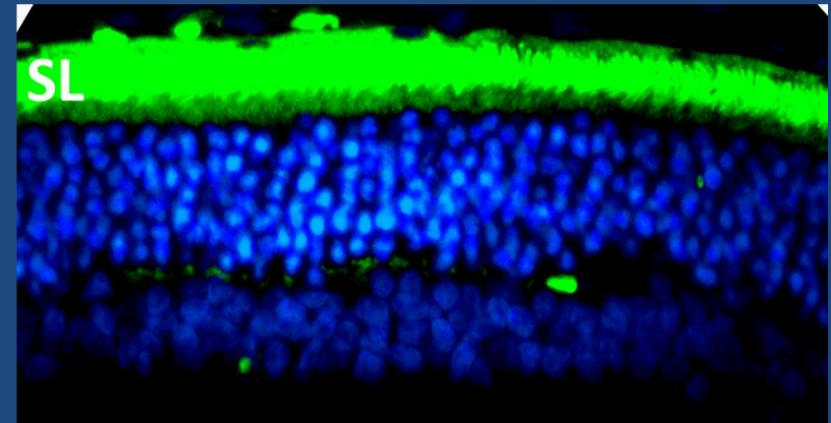
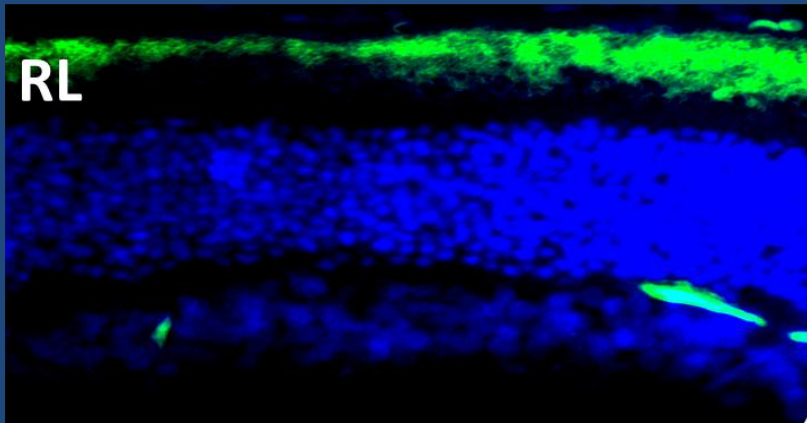
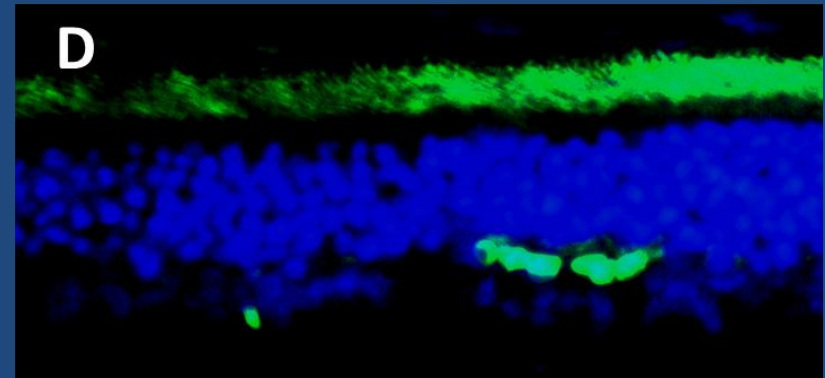
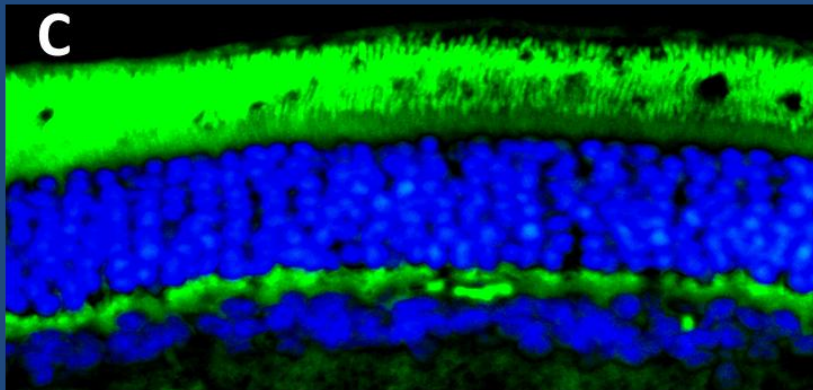


Rhodopsin (RHO)



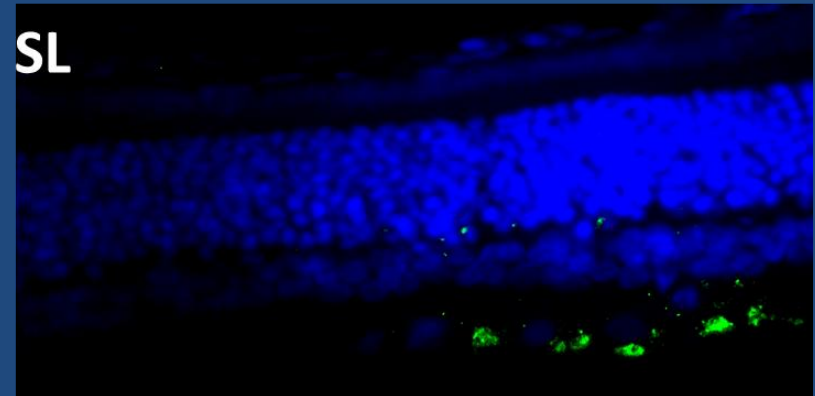
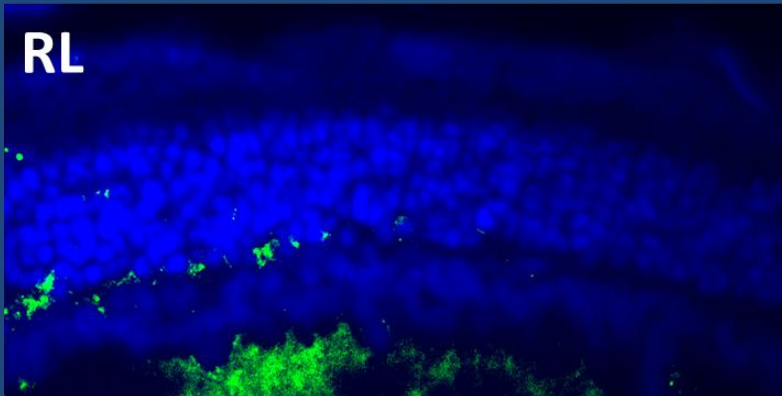
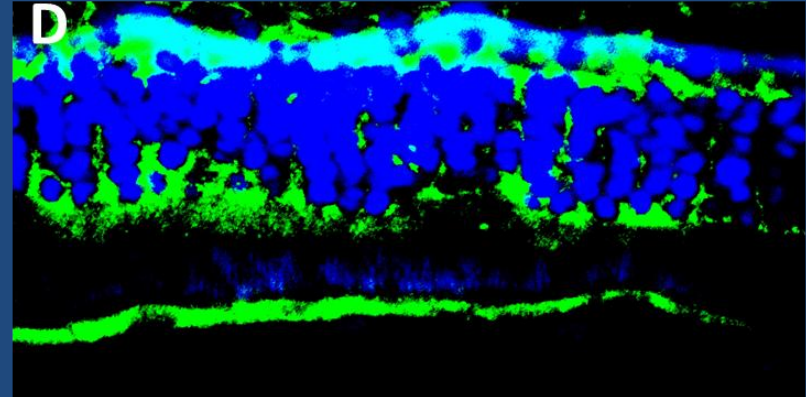
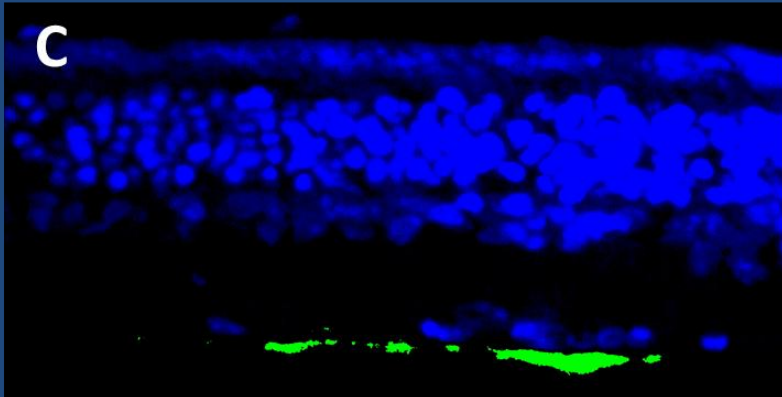
Rhodopsin, is a biological pigment in photoreceptor cells of the retina that is responsible for the first events in the perception of light.

Nerve Growth Factor (NGF)



- NGF is an important regulator of retinal development and also plays a key role in regulating survival, growth, and functional maintenance of retinal ganglion cells, photoreceptors and other retinal neurons.

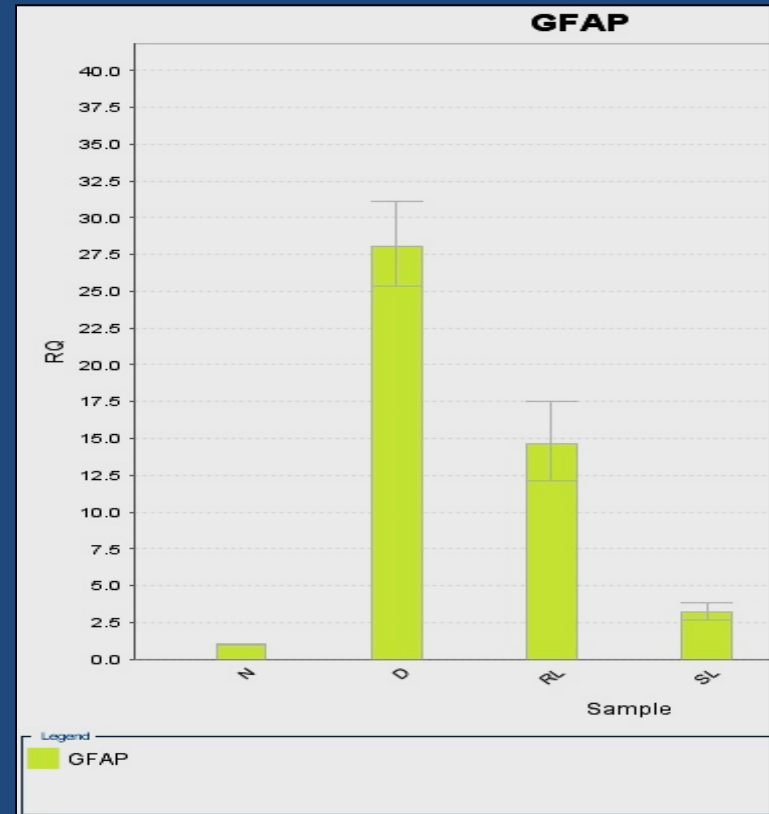
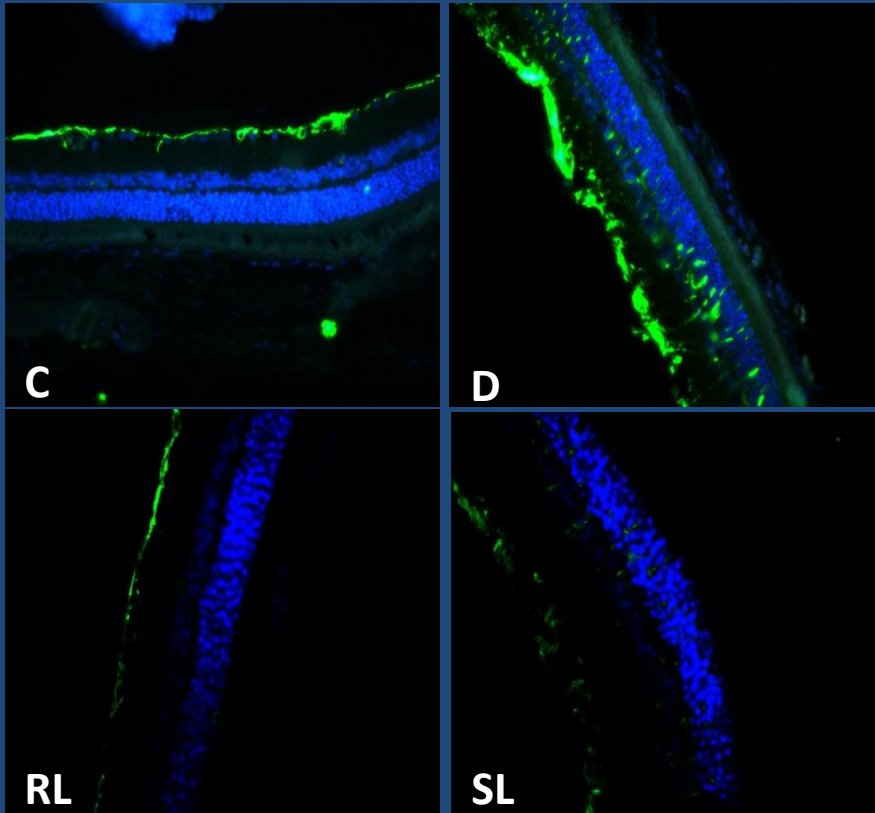
Hypoxia-Inducible Factor (HIF α)



Hypoxia-inducible factor 1-alpha (HIF-1-alpha) is expressed at low oxygen concentrations and plays an essential role in cellular and systemic responses to hypoxia.

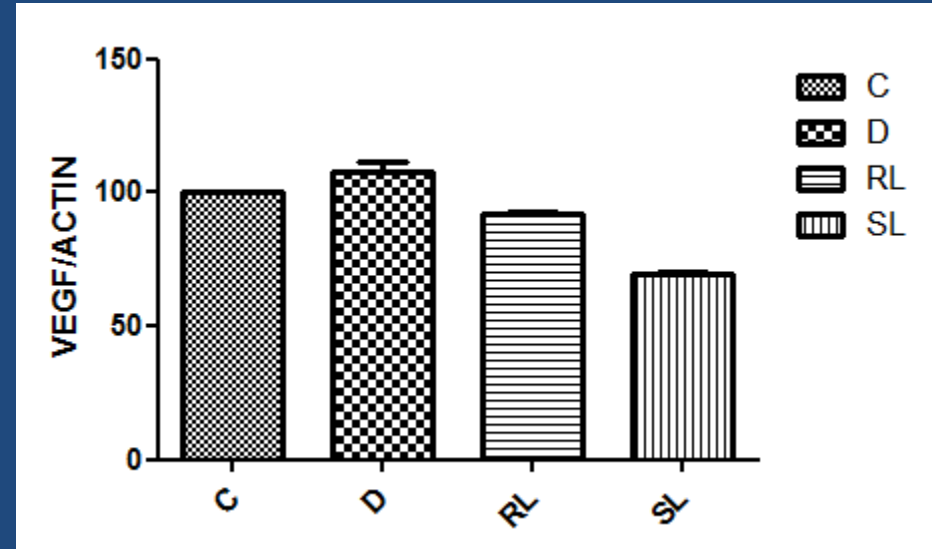
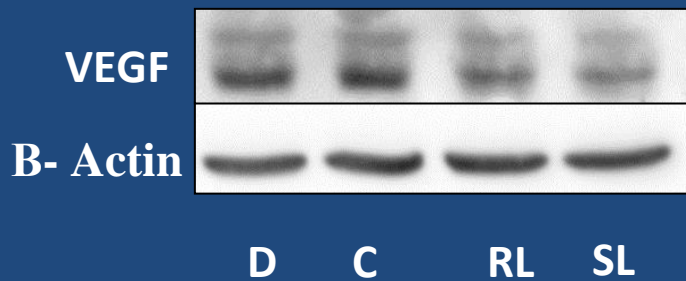
Glial acidic Fibrillary Protein (GFAP)

- GFAP is an intermediate filament present in retinal glial cells (ganglion cells) and retinal astrocytes maintains structure and function of the cell's cytoskeleton.



Glial fibrillary acidic protein (GFAP) is involved in many important central nervous system processes, including cell communication, cell strength and shape and the functioning of the blood brain barrier.

Vascular Endothelial Growth Factor (VEGF)



Vascular endothelial growth factor (VEGF) is a signal protein produced by cells that stimulates vasculogenesis and angiogenesis.

Prevention of Diabetic Retinopathy Associated Vision Loss

- Intensive glycemic control
- Tight blood pressure control
($<130/80$ mmHg)
- Comprehensive eye examinations

What we have to do?



Public health importance: maintenance of healthy eyes critical to quality of life

- Public health education regarding eye health
- Increase awareness of
 - Diabetes mellitus
 - Diabetes complications
 - Age related eye disease
 - importance of early detection
 - Importance of regular, comprehensive eye examinations
 - Nutritional impact on eye health
- Health professional education of importance of early detection and prevention
- Lutein intake may help reduce progression of DR
- In addition to significant results, we can also focus on cost savings.



Thank You