Nationwide Children's
When your child needs a hospital, everything matters.

The Ohio State University

A New Path for Inherited Retinal Disease Gene Therapy

Ohio Ophthalmological Society

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FOUNDATION FIGHTING BLINDNESS
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Research to Prevent Blindness
New Chair Challenge Grant

NIH
National Eye Institute
K08 EY036957
NEI Loan Repayment Program
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Path to K Award

Ohio Lions Eye Research Foundation, Inc.
Research Today . . .
Vision Tomorrow

Knights Templar Eye Foundation, Inc.
Career Starter Grant

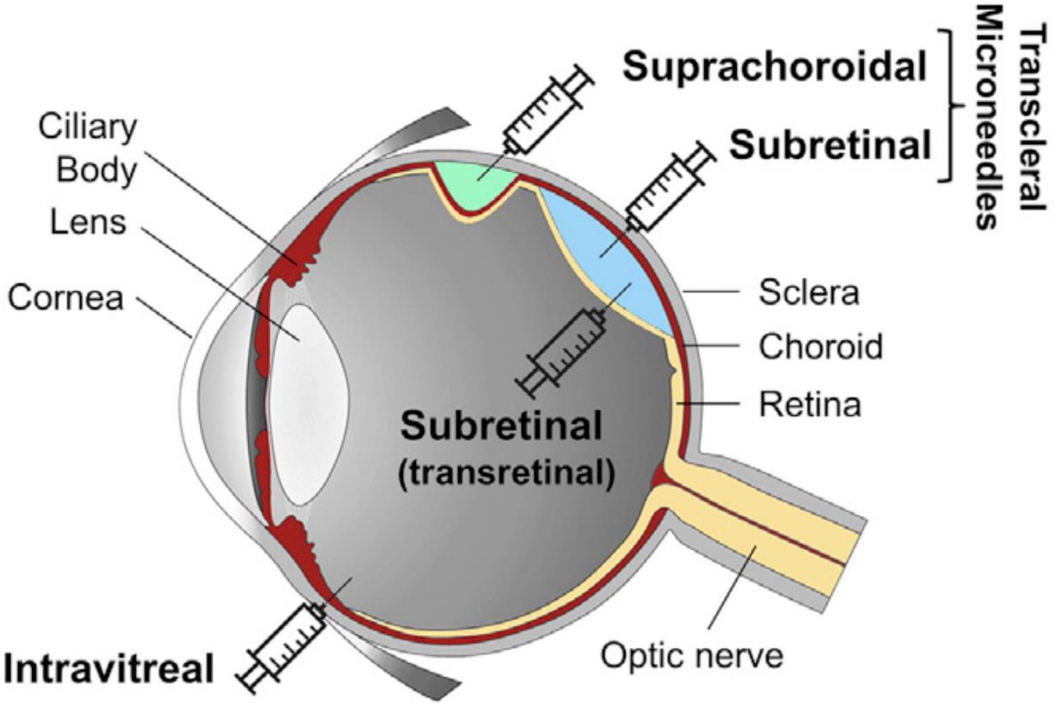
- Consultant – Insmed, Eyepoint, Harrow
- Grant Support – Biomarin research at Nationwide Children's funding for intravitreal enzyme replacement therapy
- Patent – Alycone Therapeutics

Inherited Retinal Degeneration Basics

- 400,000 patients in the US
- 5.5 million patients globally
- Usually bilateral eye disease
- Often progressive
- Over 220 different retinal degenerations
- Reactive inflammation component
- Can be associated with systemic diseases (e.g. if a ciliopathy)

Current Gene Therapy Delivery Approaches

- Intravitreal
- Suprachoroidal
- Subretinal



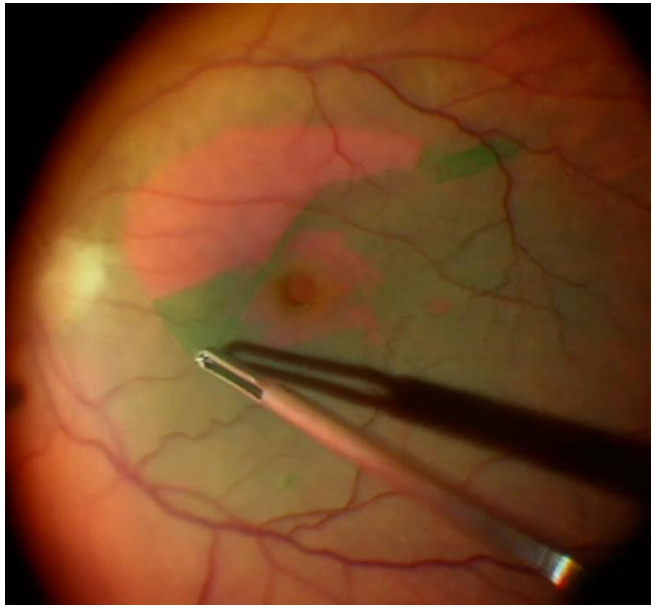
Two Fundamental Questions

1) How do we achieve efficient AAV transduction without traumatically detaching the retina?

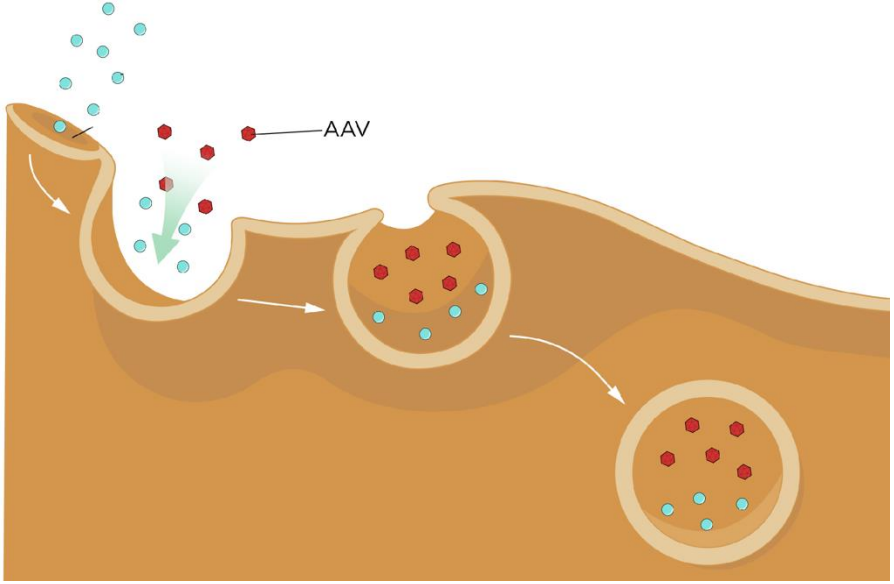
2) How do we prevent intraocular inflammation?

Expose attached and prepared retina to AAV for only 30 minutes, then remove all residual AAV so there is no remaining extracellular vector to incite immune response.

Remove the Barrier to the Retina – the Inner Limiting Membrane



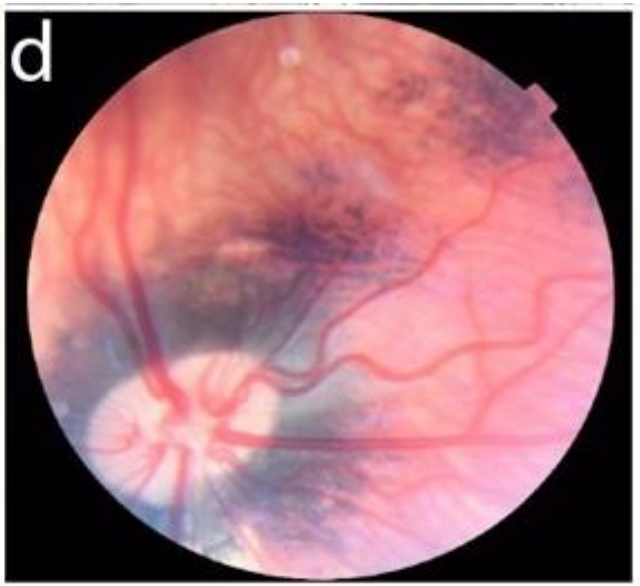
Add **Insulin** to the AAV gene therapy to induce cellular uptake of extracelluar material.



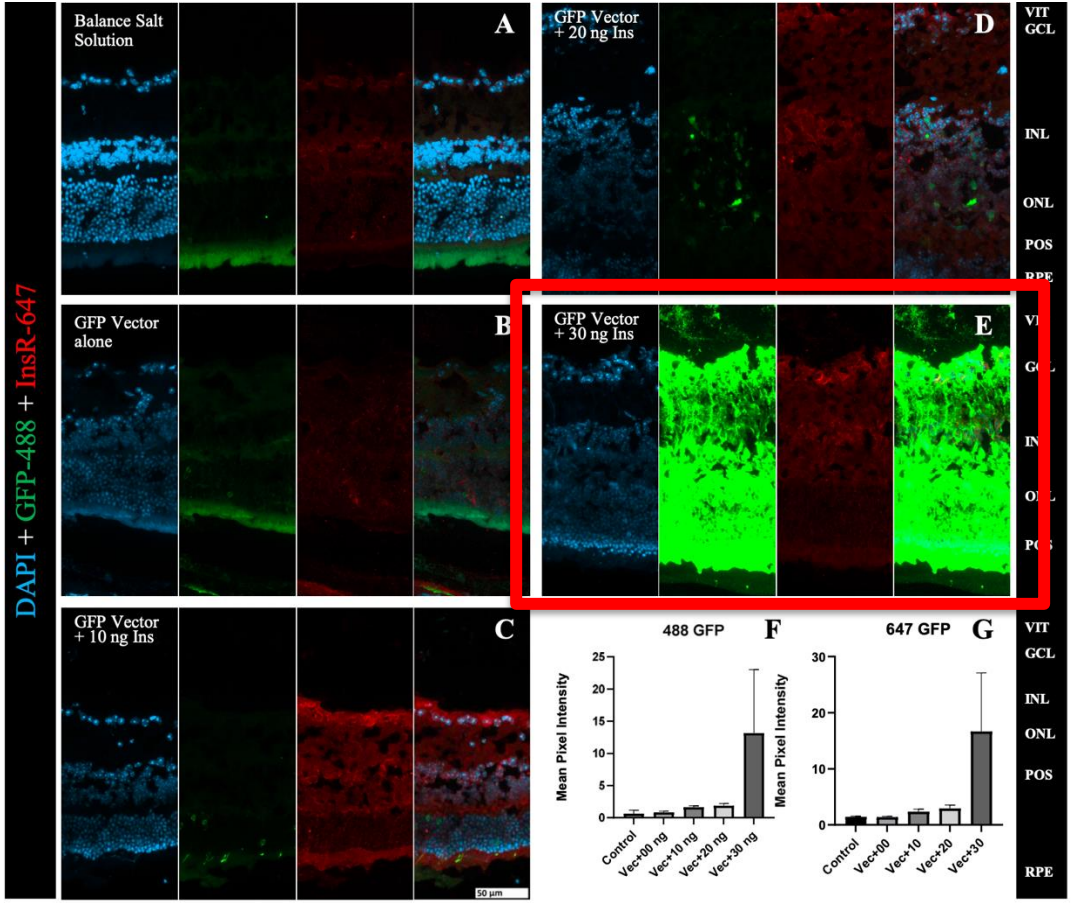
Gene Agnostic Approach

Let's Build and Operating Room

And Build a Veterinary Eye Clinic



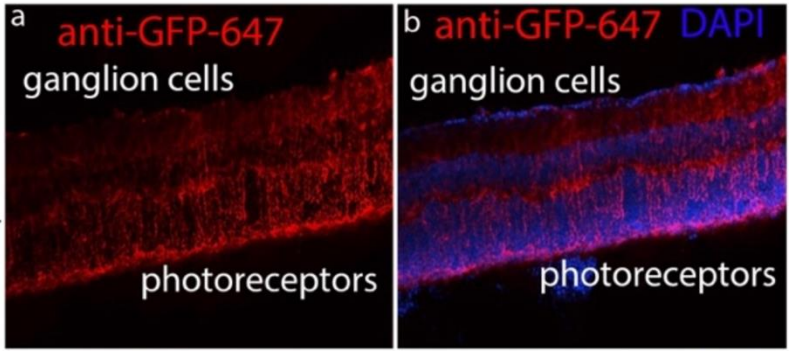
Insulin produces a robust dose response of increased AAV transduction throughout retina in intravitreal mouse injections.



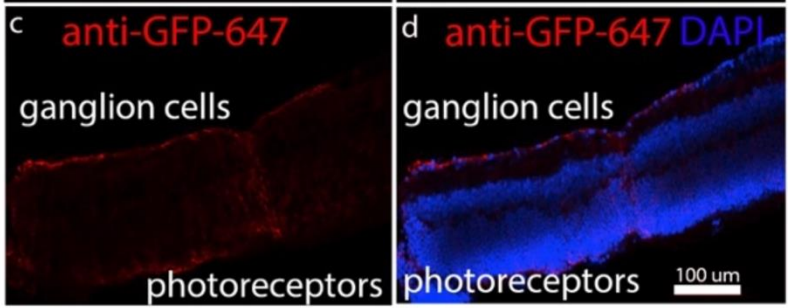
International patent filed 4/2/25 with OSU, Nationwide Children's, and Alcyone Therapeutics

Mouse Retinal Explant

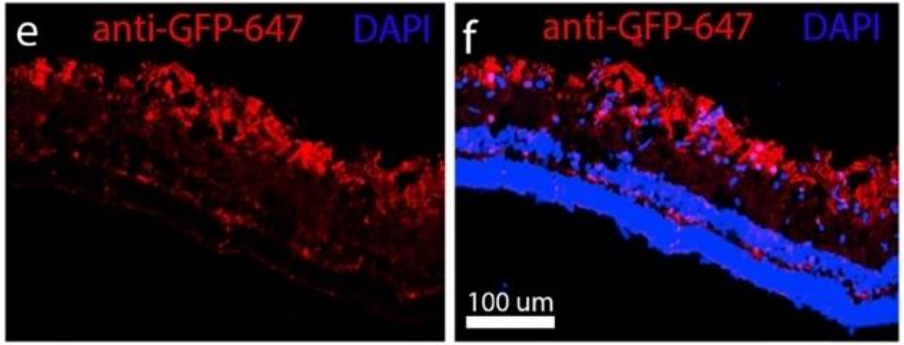
AAV + insulin



AAV no insulin

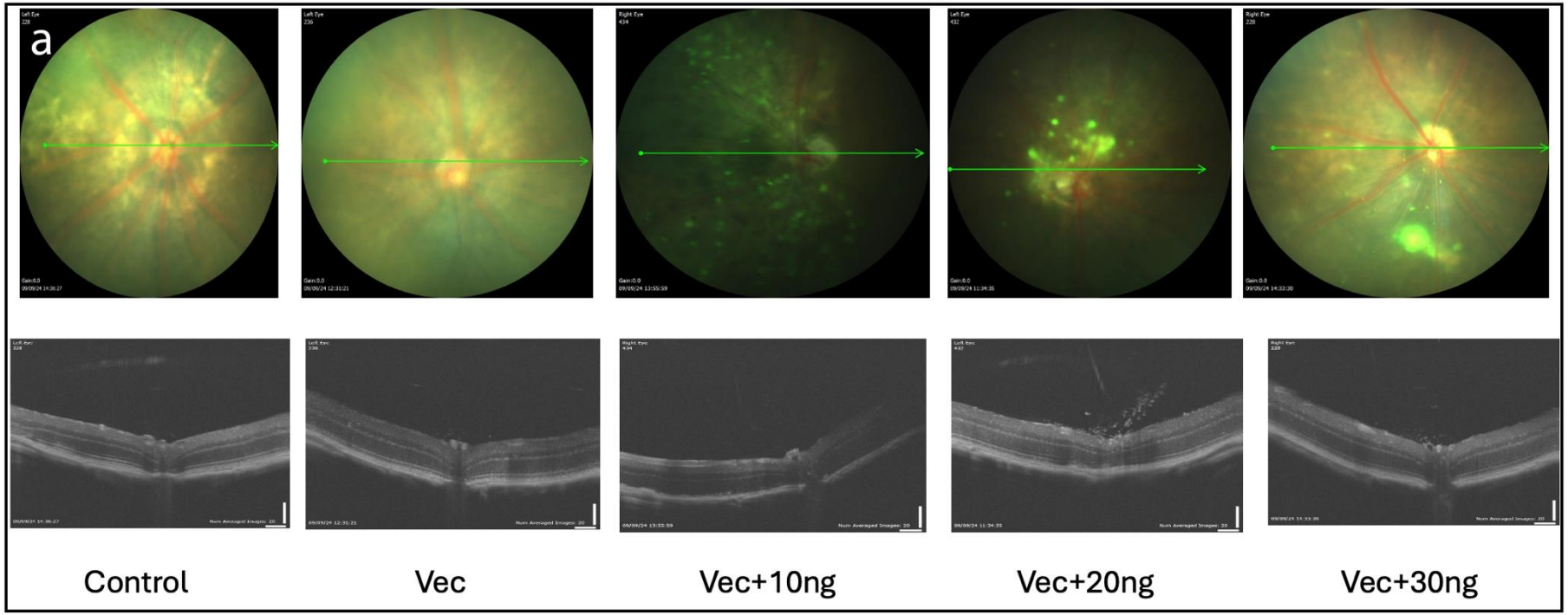


Pig Survival Surgery

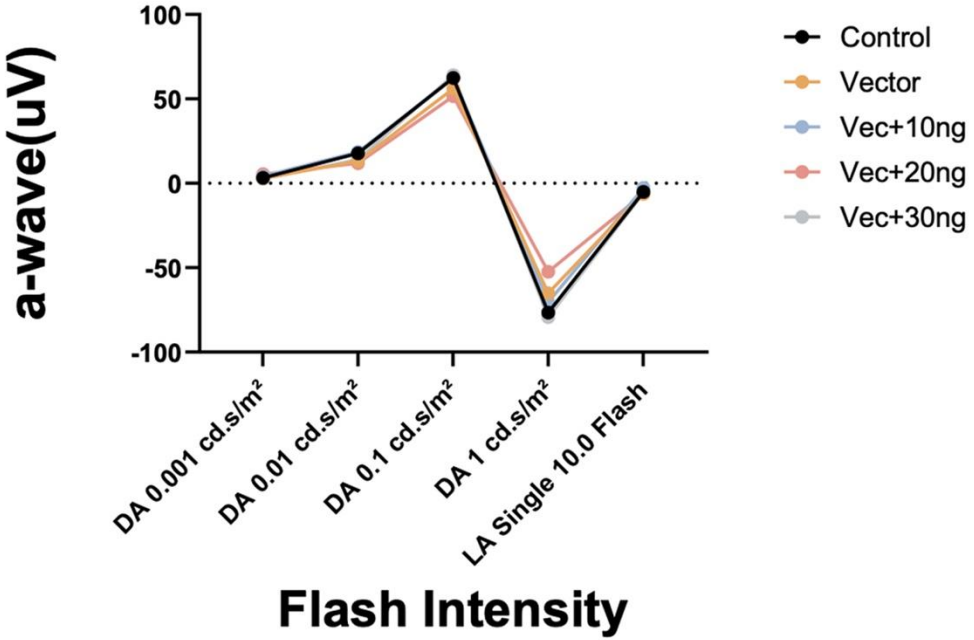


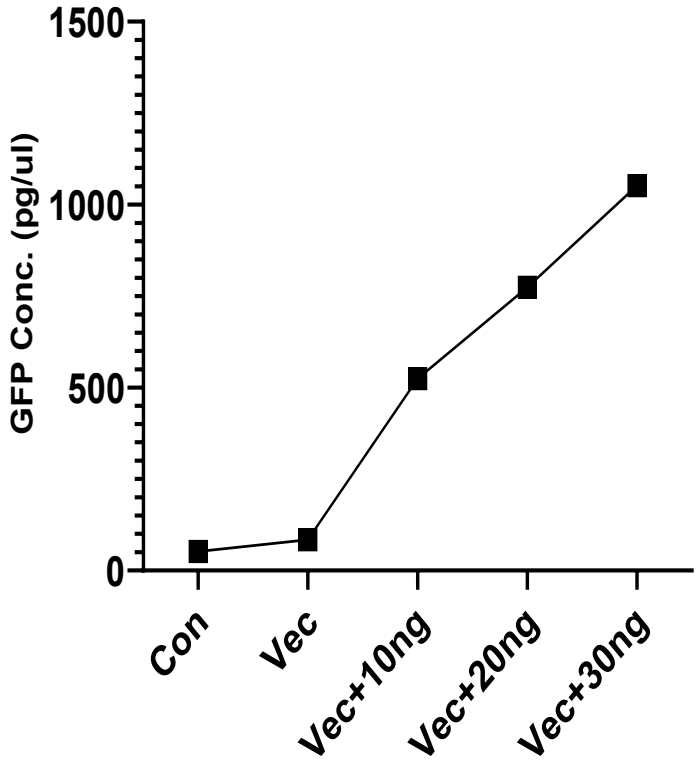
AAV + Insulin demonstrates protein expression throughout retina

Murine intravitreal AAV injections with insulin did not produce inflammation or retinal edema

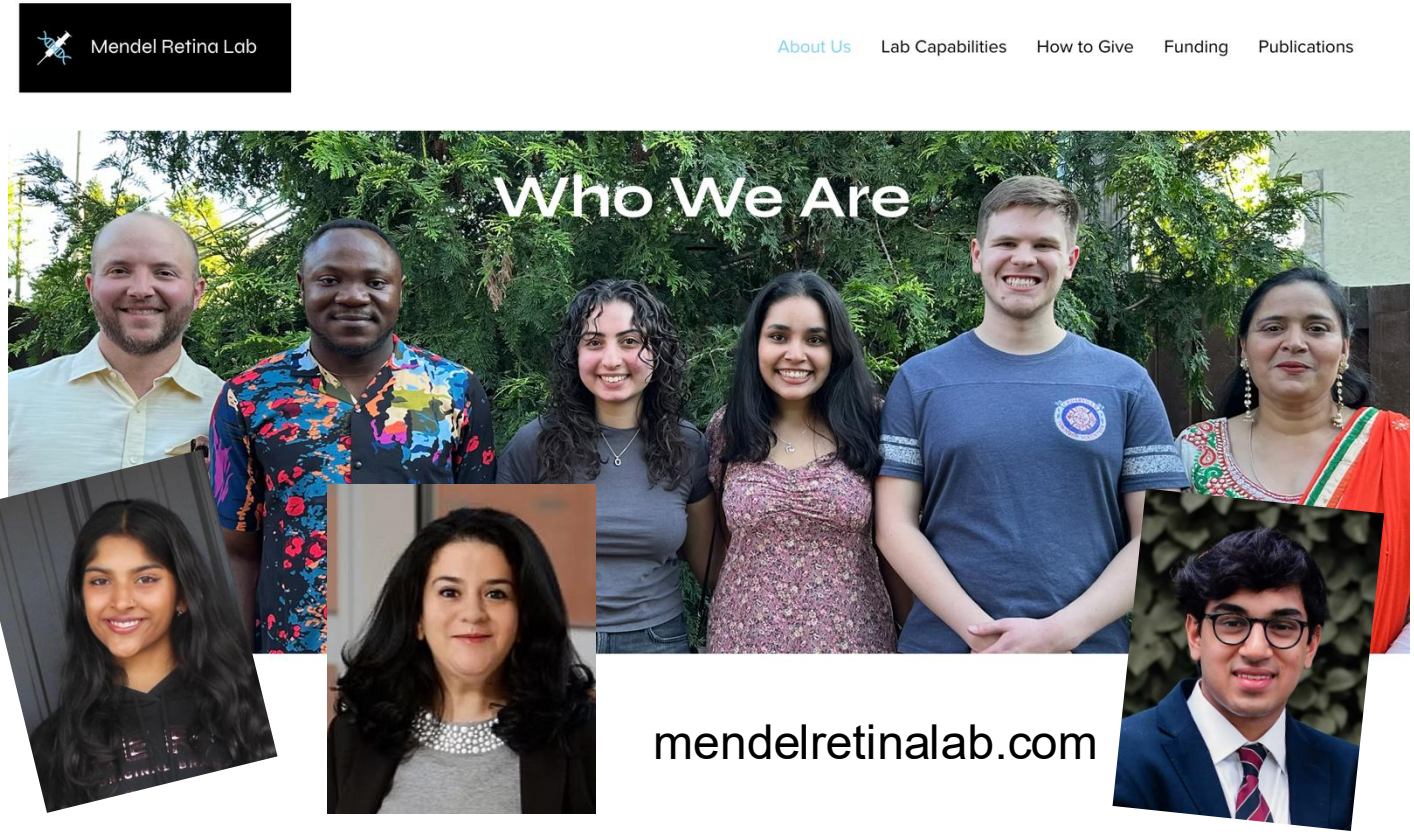


Murine intravitreal AAV injections with insulin did not degrade retinal function by ERG





ELISA showed enhanced GFP protein expression of mice retinal lysates after one month following intravitreal dose response insulin assisted AAV vector encoding GFP.



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Collaborators:
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