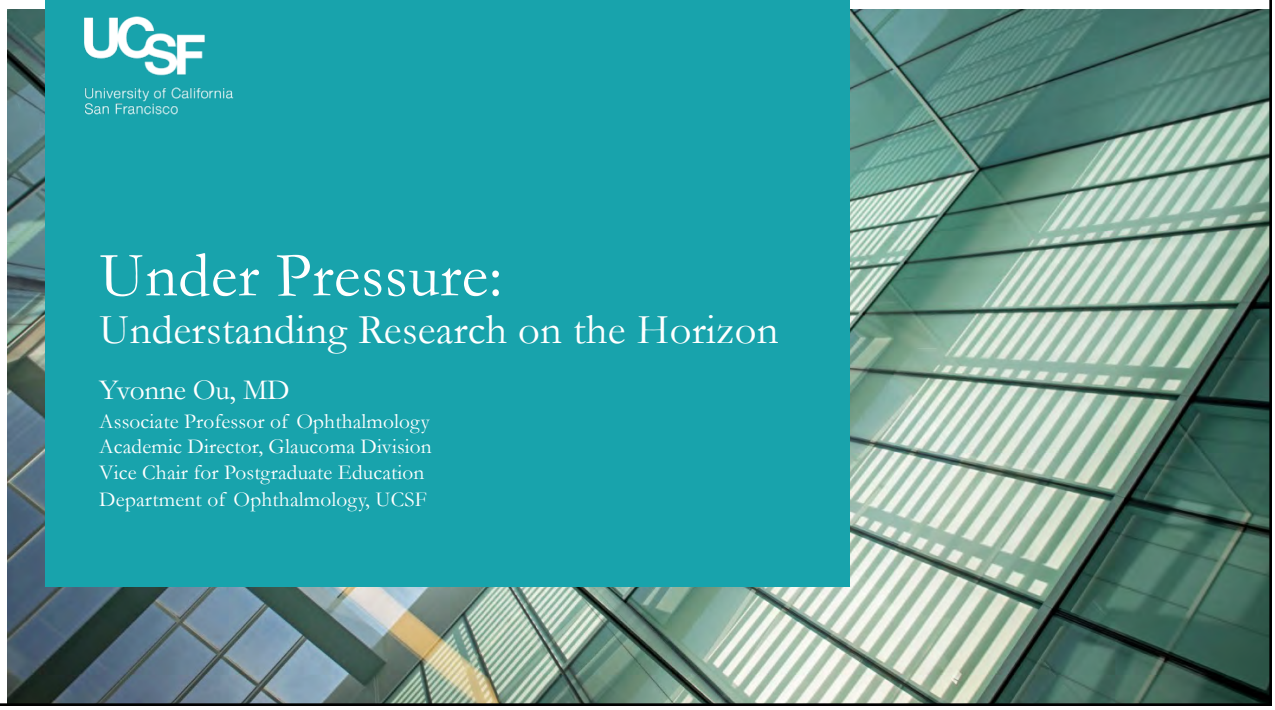

University of California
San Francisco

Under Pressure:
Understanding Research on the Horizon

Yvonne Ou, MD
Associate Professor of Ophthalmology
Academic Director, Glaucoma Division
Vice Chair for Postgraduate Education
Department of Ophthalmology, UCSF

Financial disclosures: none

Promising research on the horizon…

Rewiring in the retina	Axon regeneration	Stem cells
		

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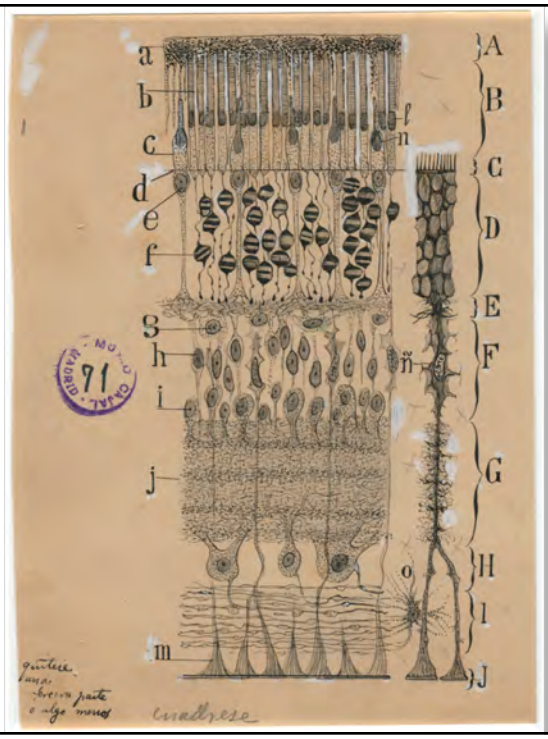

The Beautiful Brain:
The Drawings of Santiago Ramon y Cajal

Cells in the retina of the eye, 1904
Ink and pencil on paper
No. 27

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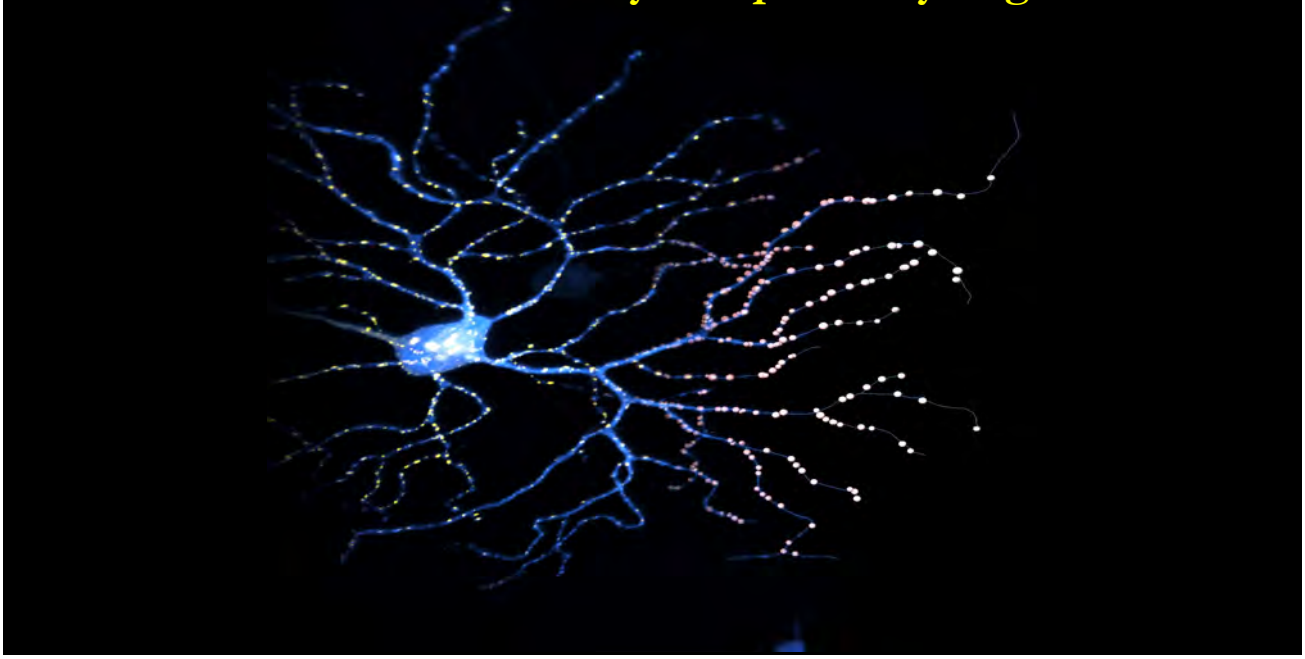
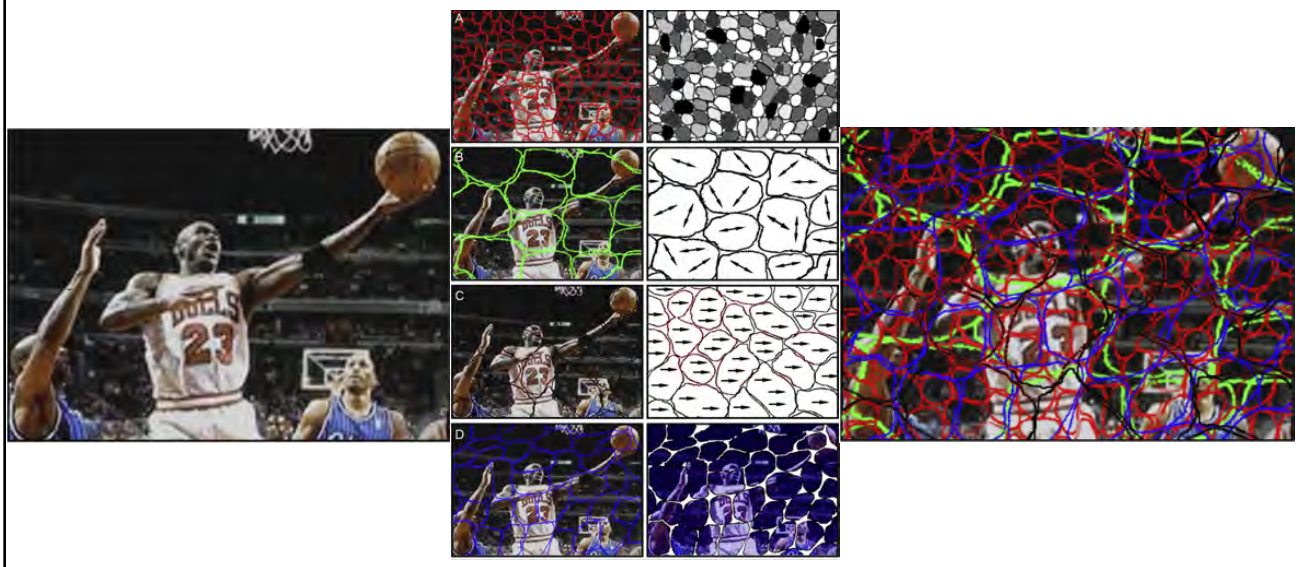
Retinal circuit connectivity and plasticity in glaucoma



How the retina surveys the world



Masland RH Neuron 2012;76(2):266-80.

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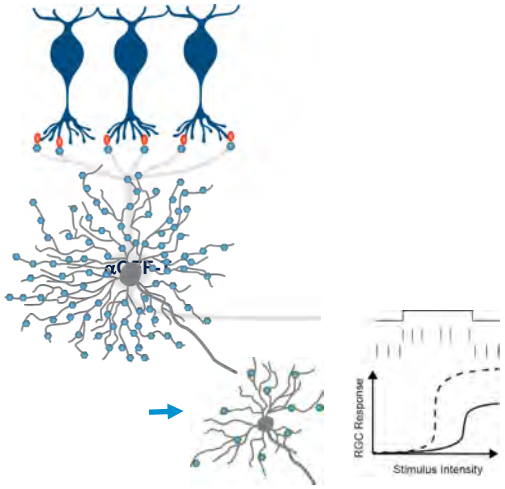
Who's lost first?
αOFF-transient RGCs are selectively vulnerable



1. αOFF-transient RGCs die
2. Dendritic and receptive field size shrink
3. Early postsynaptic component loss

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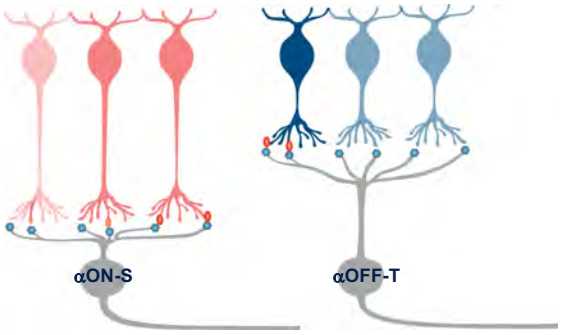
Are there specific retinal microcircuits that are more vulnerable vs. resilient in glaucoma?

Avenues for translation

Electrophysiology

Psychophysics

Advanced imaging



ON vs. OFF

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Assessment of visual function in glaucoma patients is challenging

- Visual Field tests are subjective, uncomfortable, and use bulky, expensive equipment, and *difficult for patients to do*!

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ERG is not currently used in visual function assessment for glaucoma patients

- Handheld ERG may overcome traditional ERG obstacles:
  - Small
  - Portable
  - Does not require dilation or invasive electrodes

Image from *Webvision: The Organization of the Retina and Visual System*

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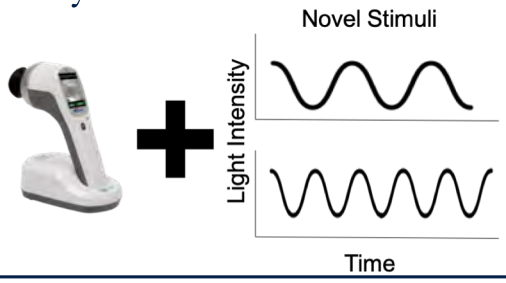
Lab to clinic: Can a new handheld ERG device be used to objectively detect relative changes to ON- and OFF-pathways?



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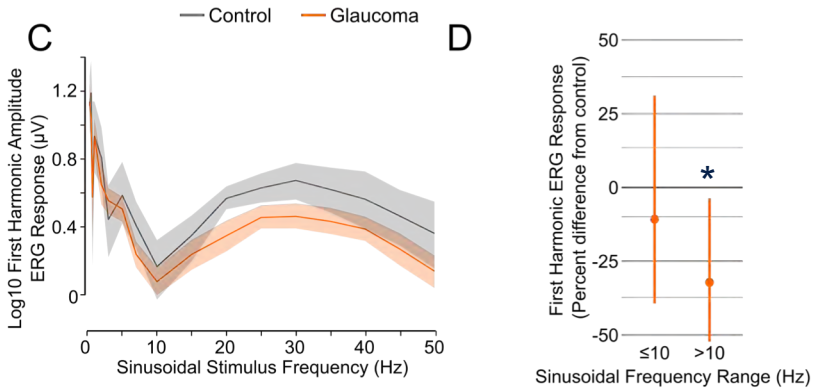
Higher sinusoidal stimuli frequencies were associated with lower ERG amplitudes



Kong AW et al. *Ophthalmology Science* 2021

* P = 0.03 adjusting for age, sex, hypertension, diabetes, and dilation

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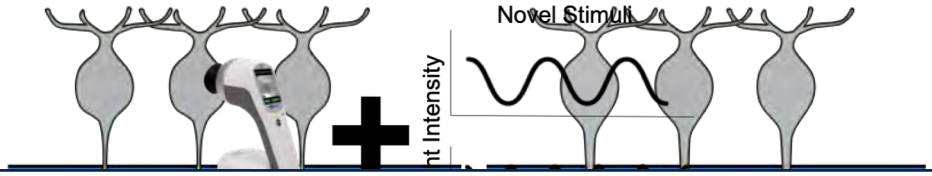
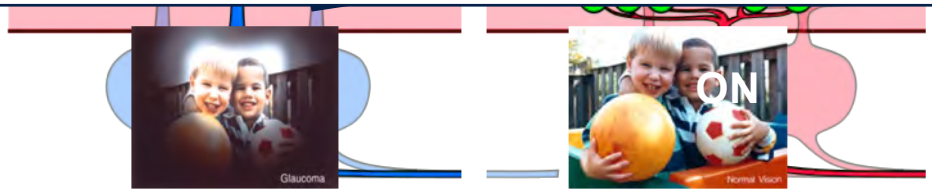


Handheld ERG using a sinusoidal stimulus may provide an *objective* assessment that demonstrates greater OFF-pathway impact in glaucoma



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Courtesy of James Blaha, Ben Backus, Bertil Damato, Mike Deiner, Manish Gupta and my patient

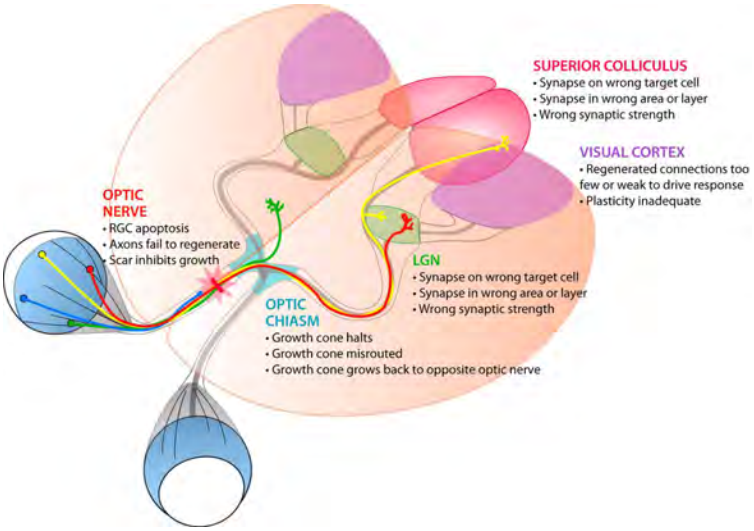
Promising research on the horizon…

Rewiring in the retina

Axon regeneration

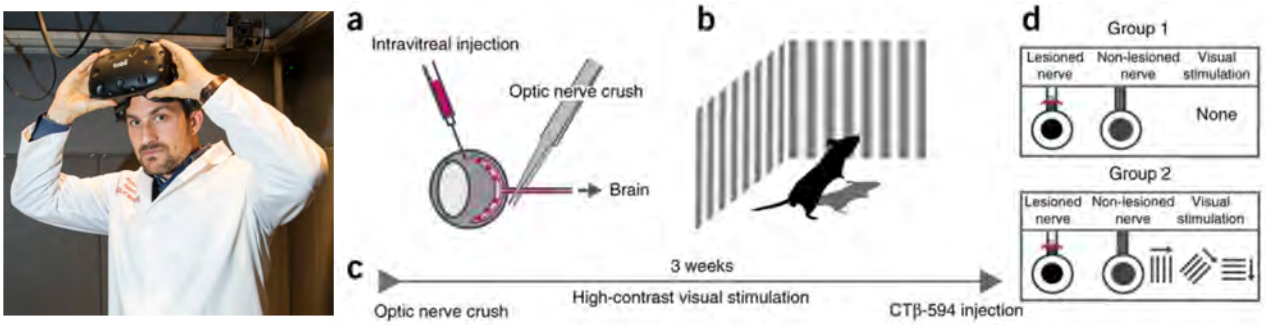
Stem cells

The challenges of axon regeneration



Michael C. Crair, and Carol A. Mason J. Neurosci. 2016;36:10707-10722

Visual stimulation triggers axon regeneration



Lim JH et al. *Nature Neuroscience* **volume19**, pages1073–1084 (2016)

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Promising research on the horizon…

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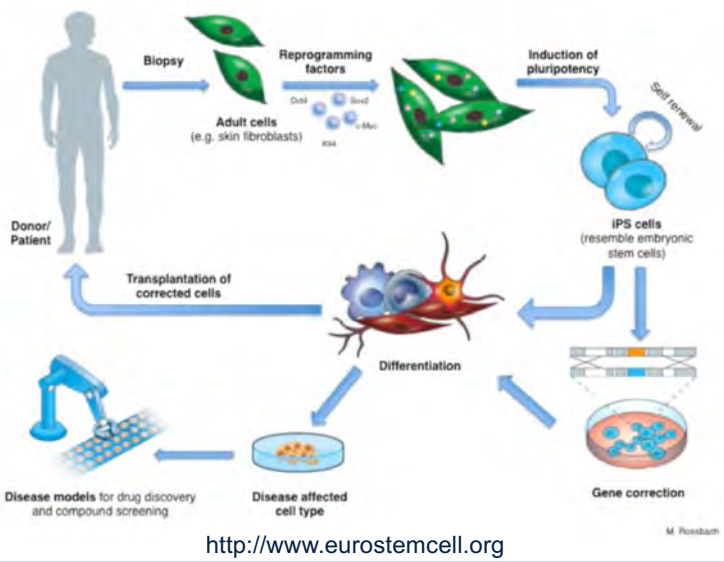
Uses of Human Pluripotent Stem Cells



http://www.eurostemcell.org

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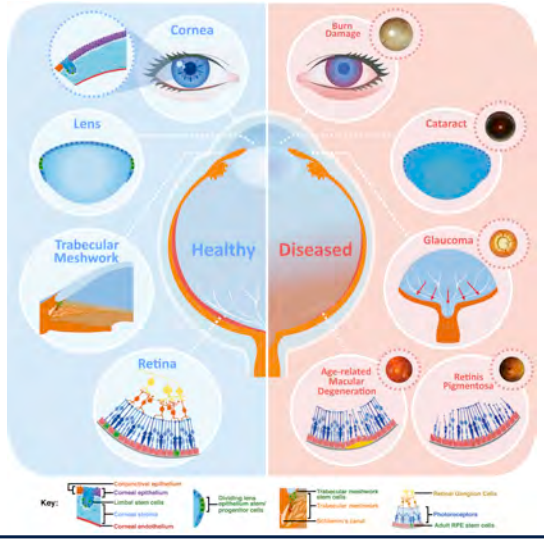
Stem cells in ocular health and disease



Cell Stem Cell 2018 22, 834-849DOI: (10.1016/j.stem.2018.05.013)

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Approaches to cure glaucoma with stem cells

- Stem cells to restore trabecular meshwork function and outflow
- Stem cells to restore retinal ganglion cell function
  - Stem cell-derived ganglion cells to model glaucoma
  - Stem cell-derived ganglion cells for high-throughput drug screening

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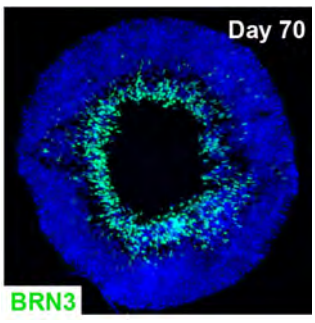
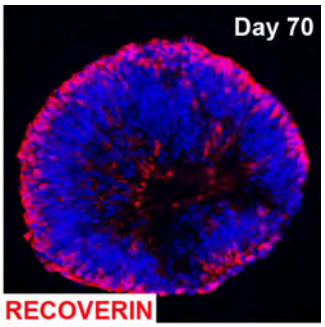
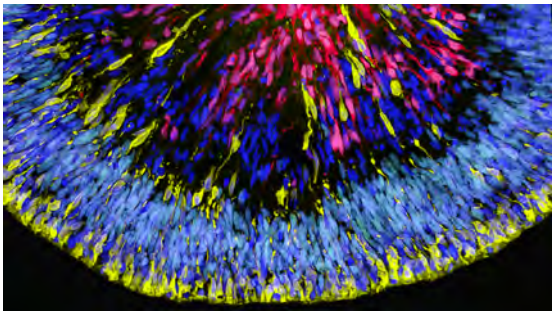
Retinal organoids recapitulate the retina



Retinal Ganglion Cells Found in Inner Layers of Retinal Organoids



Photoreceptor Cells Found in Outer Layers of Retinal Organoids



RGCs / **Progenitors** / **Photoreceptors**

Fligor et al., Scientific Reports, 2018

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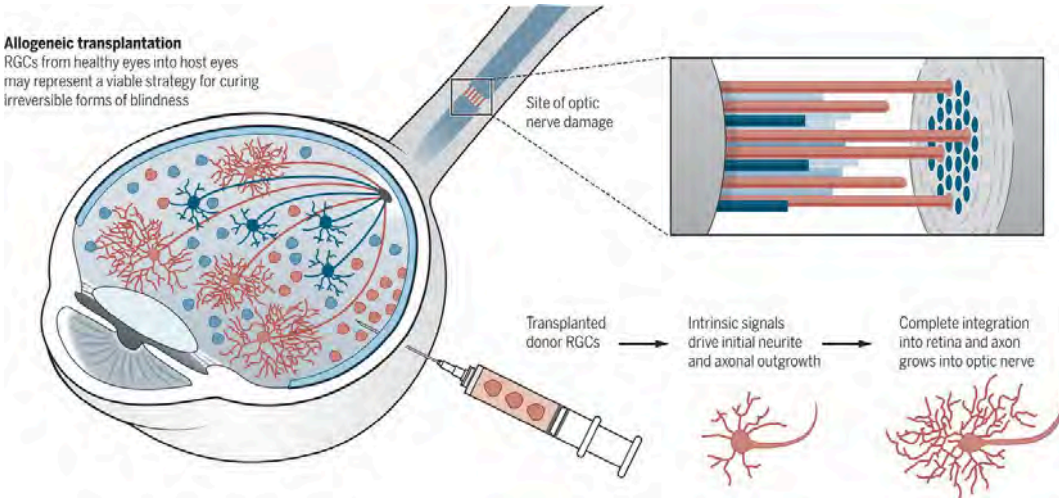
RGC transplantation to restore vision



Bireswar Laha et al. Science 2017;356:1031-1034

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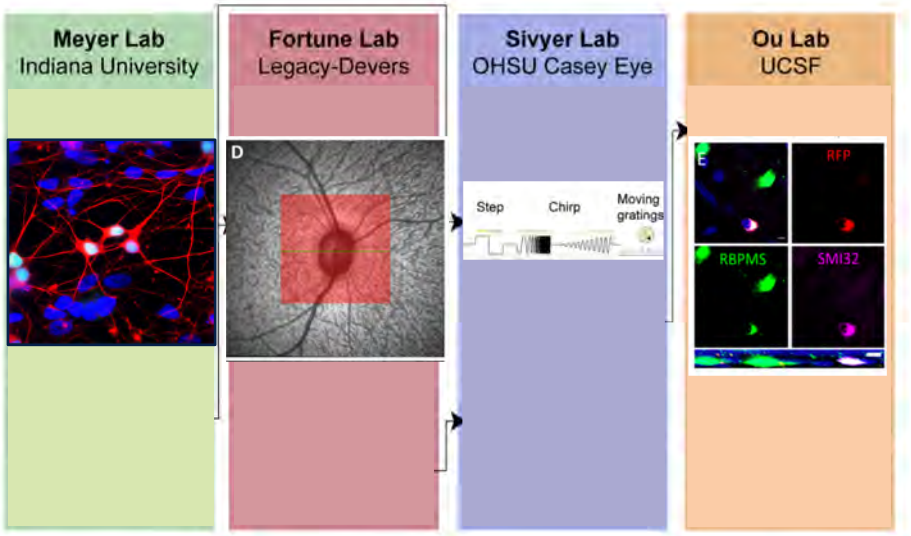
The Goal: Transplant donor RGCs into a monkey glaucoma model and rescue visual function

The Team



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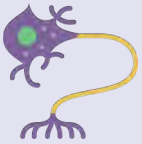
Promising research on the horizon…

Rewiring in the retina	Axon regeneration	Stem cells
		

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Thank you!

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Tonatiuh Garcia Ruiz
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Manuel Cardoña

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Erik Ullian (UCSF)
Felice Dunn & Scott Harris (UCSF)
Aparna Lakkaraju & Li Xuan Tan (UCSF)
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Brad Fortune (Devers)
Ben Sivyer (OHSU)

NEI P30 Vision Core
Yien-Ming Kuo
Suling Wang
Jimmy Pham
Eric Lam

R01 EY028148
K12 EY031372

National Eye Institute, National Institutes of Health | BrightFocus Foundation, Cure in Mind. Cure in Sight. | The E. Matilda Ziegler Foundation for the Blind, Inc | Research to Prevent Blindness, The Catalyst for Eye Research | Glaucoma Research Foundation