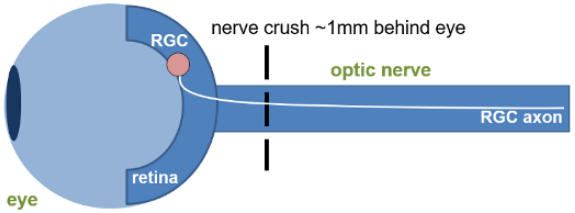
About the Model

Crush injury to the optic nerve severs the retinal ganglion cell (RGC) axons leading to the gradual death of RGC neurons in the retina. The model studies neuronal outcomes following injury including survival, apoptosis, regeneration, and associated biomarkers.



Molecular Readouts Illustrate Model Induction

Multidimensional observations strengthen the interpretation: in addition to in-life measurements, immunocytochemistry monitors therapeutic effect, immunoassays track biomarkers, and qRT-PCR provides information on retinal gene expression. The table below summarizes markers tracked in this model.

Protein/Gene	Significance
pcJun	neuronal injury
TUJI	RGC marker
Atf3	regeneration associated genes
Sprr1a	
Ddit3 (Chop)	pro-apoptotic transcription factor
Gfap	Reactive astrocyte marker

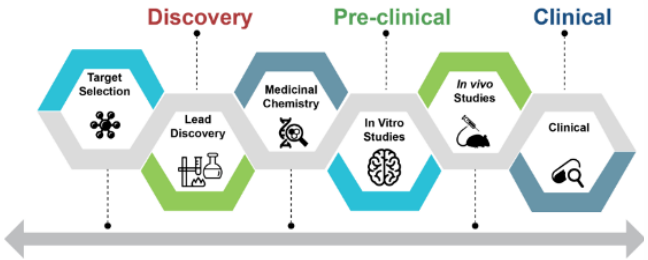
About the GD³ Ocular Center of Excellence

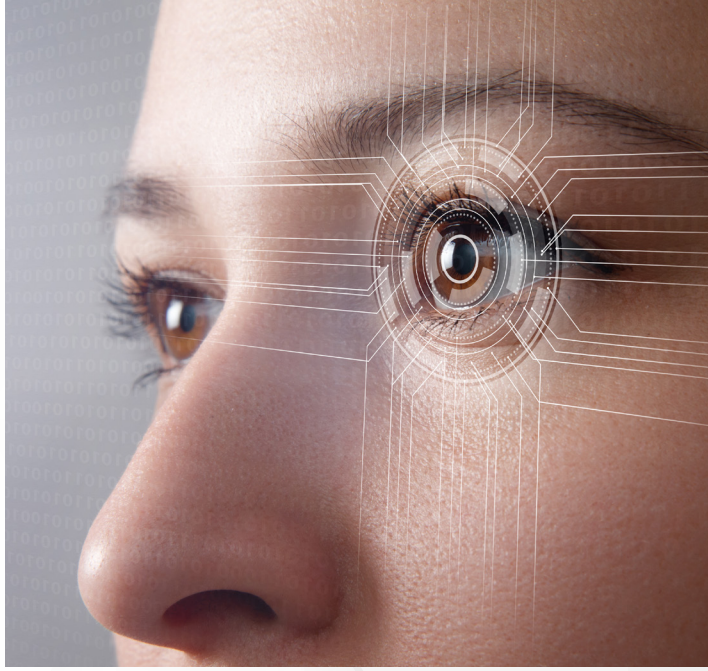
The **GD³ Ocular Center of Excellence** was founded to accelerate the development of much-needed medicines in ophthalmology by providing animal models of ocular disease and a state-of-the-art pharmacokinetics testing infrastructure. Our team has established themselves as leaders in the ocular field and will provide expert guidance on your ophthalmology programs.

About GD³

Genesis Drug Discovery & Development (GD³) is a fully integrated CRO focused on providing services to support preclinical and clinical drug discovery and development.

Scan the QR code to book a consultation with our ocular team:





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Optic Nerve Crush Efficacy Model

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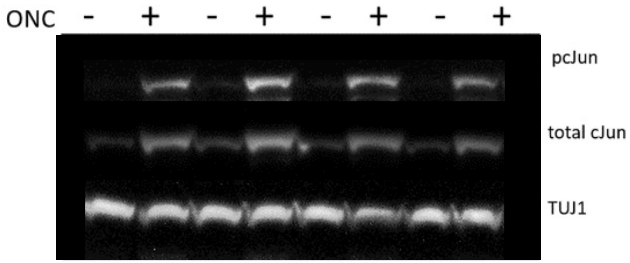
In-vivo Mouse Model for Glaucoma, Traumatic Optic Neuropathies, CNS Injury and Neurodegenerative Diseases

The **GD³ Ocular Center of Excellence** is proud to offer efficacy models in which physiological readouts coupled with cellular and biochemical measurements provide a comprehensive snapshot of your treatment's therapeutic potential.

The **optic nerve crush** model can test agents treating **glaucoma, traumatic optic neuropathies, neurodegeneration, and CNS injury and inflammation**. If your organization is working to treat any of these debilitating diseases, we encourage you to examine our capabilities.

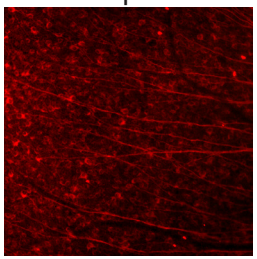
Activation of Signaling Pathways

Western blot of retinal tissue three days following optic nerve crush (ONC) compared to uninjured control: upregulation of injury marker, pcJun, demonstrates activation of signaling pathways important for neuronal outcome following ONC.

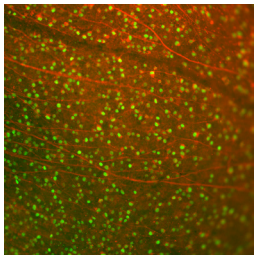


pcJun and total cJun - Injury markers
TUJI - RGC specific loading control

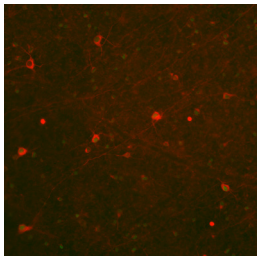
Uninjured



5 Days Post ONC



3 Weeks Post ONC



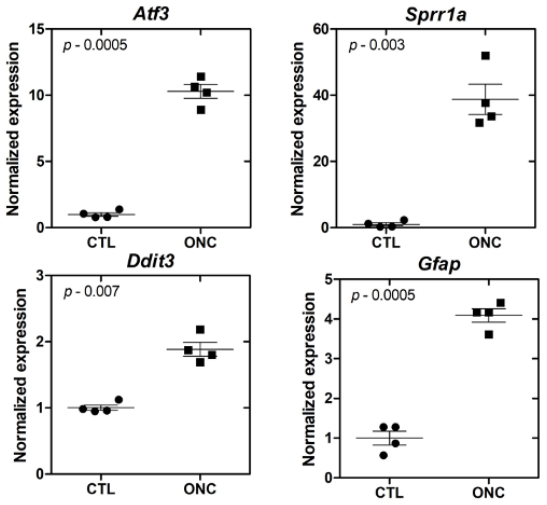
Whole mount retinas immunostained for **TUJ1** and **pcJun**

Upregulation of Injury Markers

Immunostained whole mount retinas following optic nerve crush (ONC): upregulation of injury marker, pcJun, demonstrates activation of injury signaling pathways resulting in retinal ganglion cell (RGC) death following ONC. Loss of pcJun and TUJI signal three weeks after ONC demonstrates a reduction in the number of surviving RGCs in the weeks following axotomy.

Robust Transcriptional Response

qRT-PCR of *Atf3*, *Sprr1a*, *Ddit3 (Chop)*, and *Gfap* from retinal RNA four days after optic nerve crush (ONC) compared to uninjured contralateral control (CTL): upregulation of regeneration-associated genes *Atf3* and *Sprr1a*, pro-apoptotic transcription factor *Ddit3 (Chop)*, and reactive astrocyte marker *Gfap* demonstrates a robust response to injury following ONC. Relative gene expression was calculated using the $\Delta\Delta C_T$ method relative to *Gapdh* and normalized to expression levels in CTL samples.



References

1. Dual leucine zipper kinase-dependent PERK activation contributes to neuronal degeneration following insult. Larhammar et al. eLife 2017; 6:e20725.
2. Longitudinal Morphological and Functional Assessment of RGC Neurodegeneration After Optic Nerve Crush in Mouse. Li et al. Front. Cell. Neurosci. 2020; 14 (109).
3. An Optic Nerve Crush Injury Murine Model to Study Retinal Ganglion Cell Survival. Tang et al. J. Vis. Exp. 2011; (50): 2685.