

Ophthalmology Times
Research Scholar
Honoree Program

The Proteome of Proliferative Vitreoretinopathy

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November 5th, 2020

FINANCIAL DISCLOSURES:

None

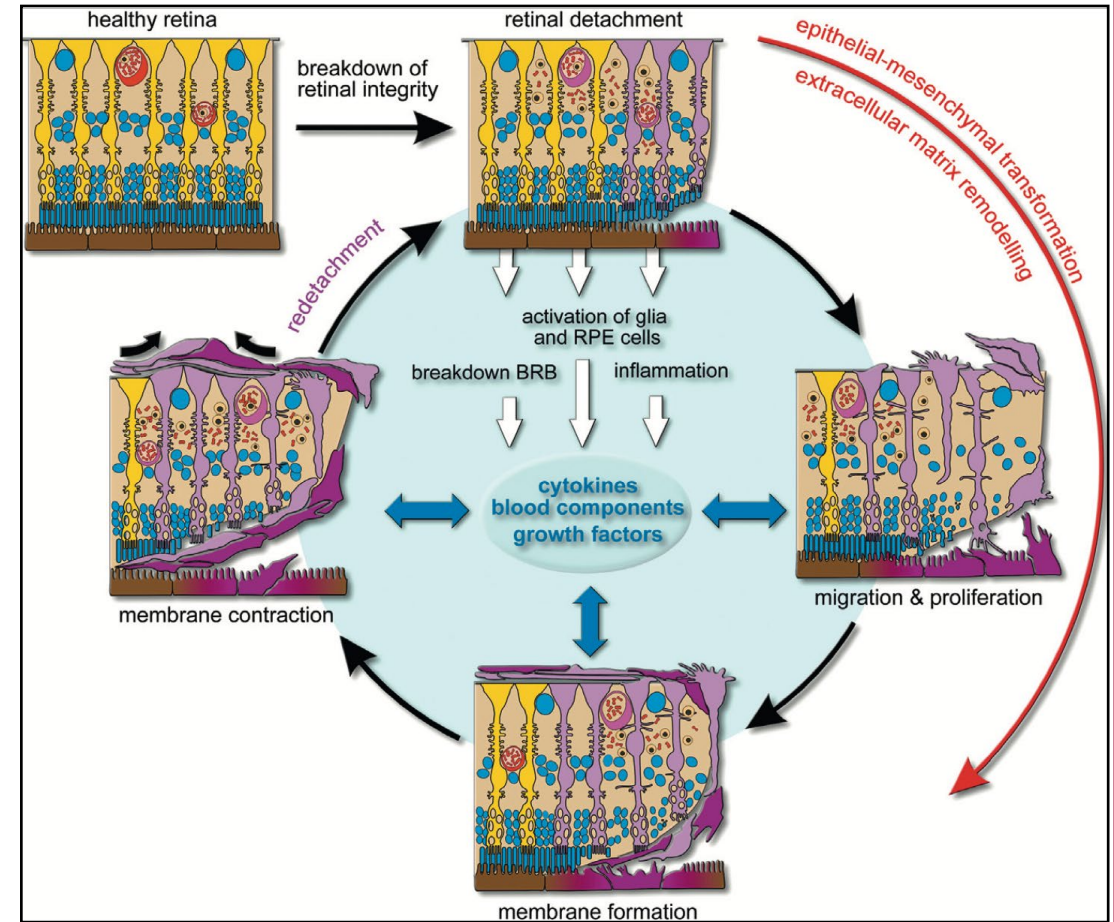
MY ROLE IN THIS RESEARCH:

Please answer which of the following portions of the research you participated in:

- Conception and design of the work/project
- Acquisition of data
- Analysis and interpretation of data
- Creation and/or critical review of the presentation

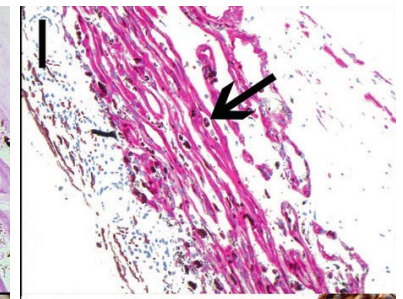
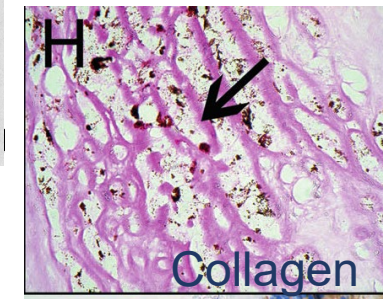
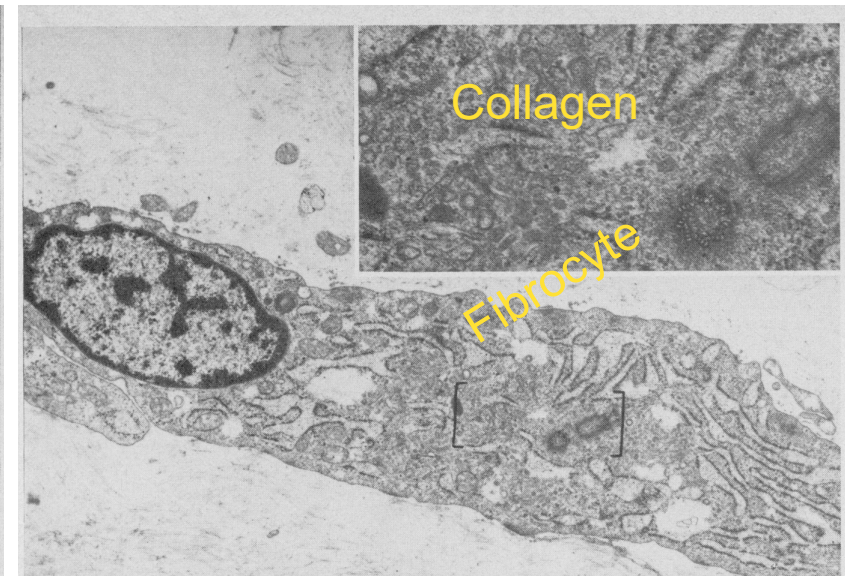
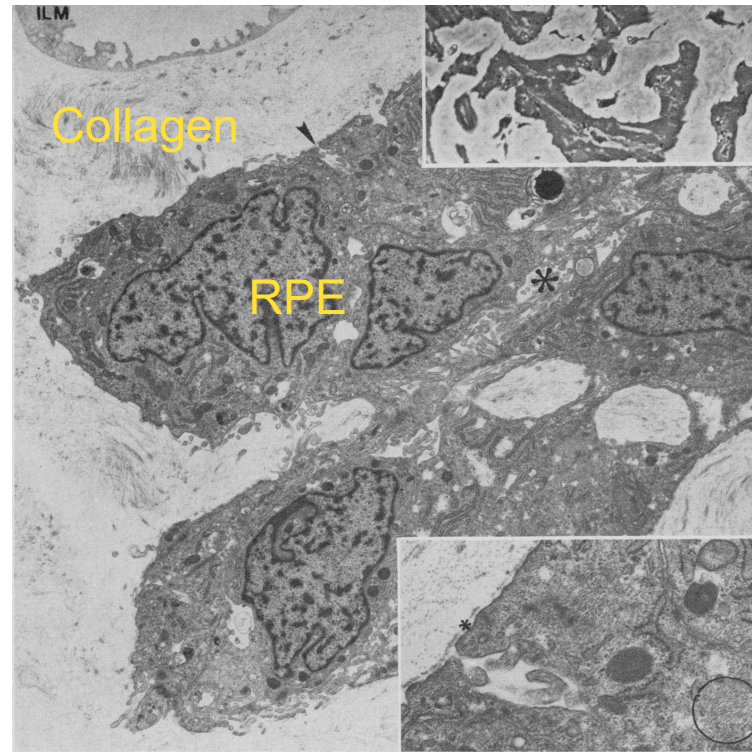
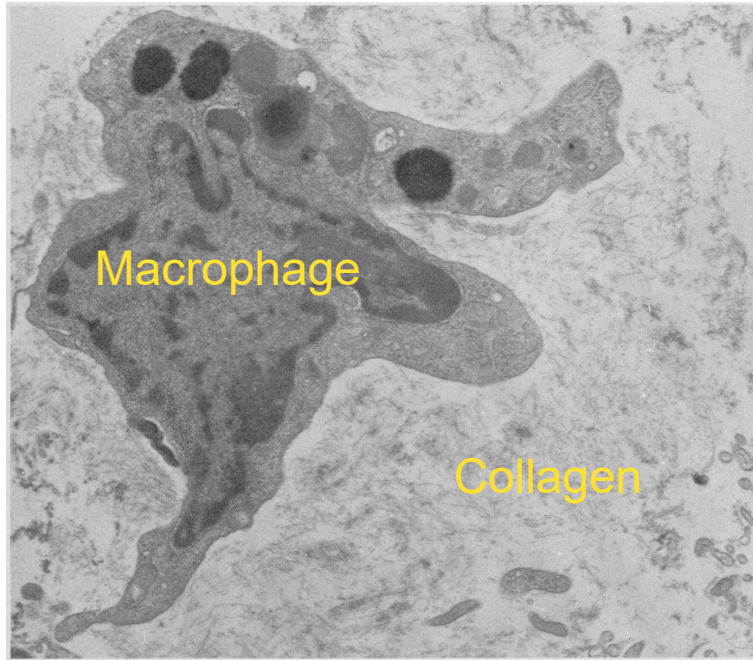
Proliferative vitreoretinopathy (PVR)

- Complicates 8-10% of rhegmatogenous retinal detachments
 - Leading reason for failure of RD repair
- Breakdown of the blood-retinal barrier and tissue hypoxia
 - Mitogens and chemotactic factors → cell proliferation and EMT
- Migration of RPE and glial cells onto the retinal surface



Ryan's Retina, 2017

Extracellular matrix (ECM) in PVR



Department of Eye Pathology Laboratory,
The Johns Hopkins Hospital, 600 N Wolfe St,
Baltimore, MD 21205 (Dr Green).

material, and maturation of
epiretinal membrane. Also unc

Eye (2020) 34:246–250

Medical therapy for PVR

operative fluid gas exchange, and photocoagulation, periocular and subconjunctival 5-fluorouracil appears to improve the prognosis for longterm retinal reattachment following the development of proliferative vitreoretinopathy. [Key words: 5-fluorouracil, antimetabolites, massive periretinal proliferation, massive periretinal retraction, massive vitreous retraction, proliferative vitreoretinopathy, retinal detachment, scleral buckle, vitrectomy.] Ophthalmology 91:122-130, 1984

Consistently successful therapy for proliferative vitreoretinopathy (PVR) remains an elusive goal, despite multiple technical and surgical innovations within the retinal detachment, proliferative vitreoretinopathy its forms accounted for nearly 60% of all surgical failures in the treatment of rhegmatogenous retinal detachment. Where men

Adjunctive Daunorubicin in the Treatment of Proliferative Vitreoretinopathy: Results of a Multicenter Clinical Trial

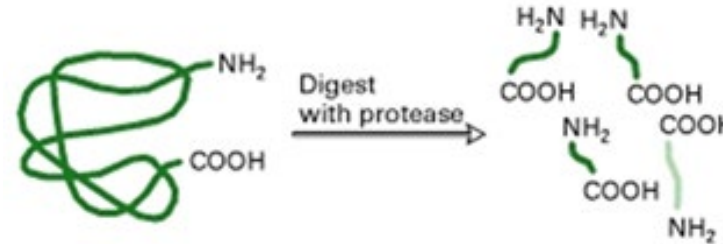
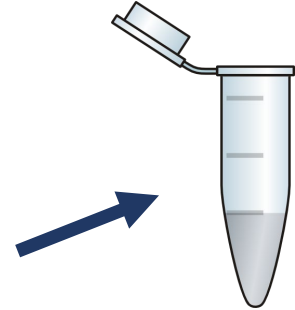
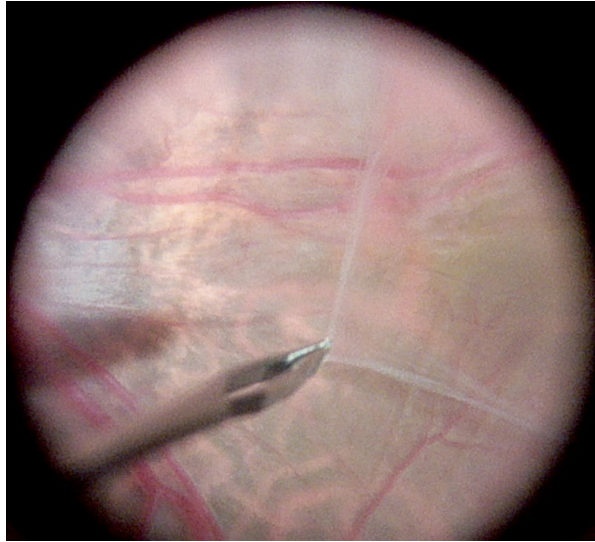
AMERICAN JOURNAL OF OPHTHALMOLOGY
OCTOBER 1998

Slow-Release Dexamethasone in Proliferative Vitreoretinopathy

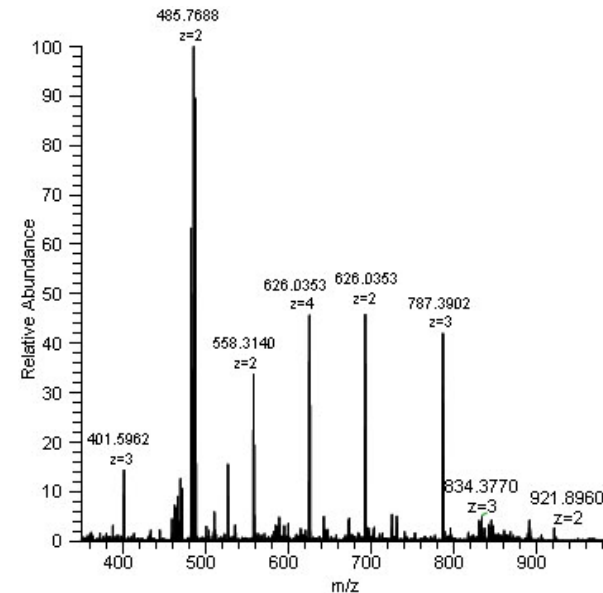
Ophthalmology Volume 124, Number 6, June 2017

- A deeper understanding of the molecular pathogenesis of PVR is needed in order to inform the development of novel targeted molecular therapies

Mass Spectrometry



- Measures mass-to-charge ratio of molecules present in a sample
- Known cleavage sites allow for peptide identification and relative quantification



Solubilization



Proteolysis

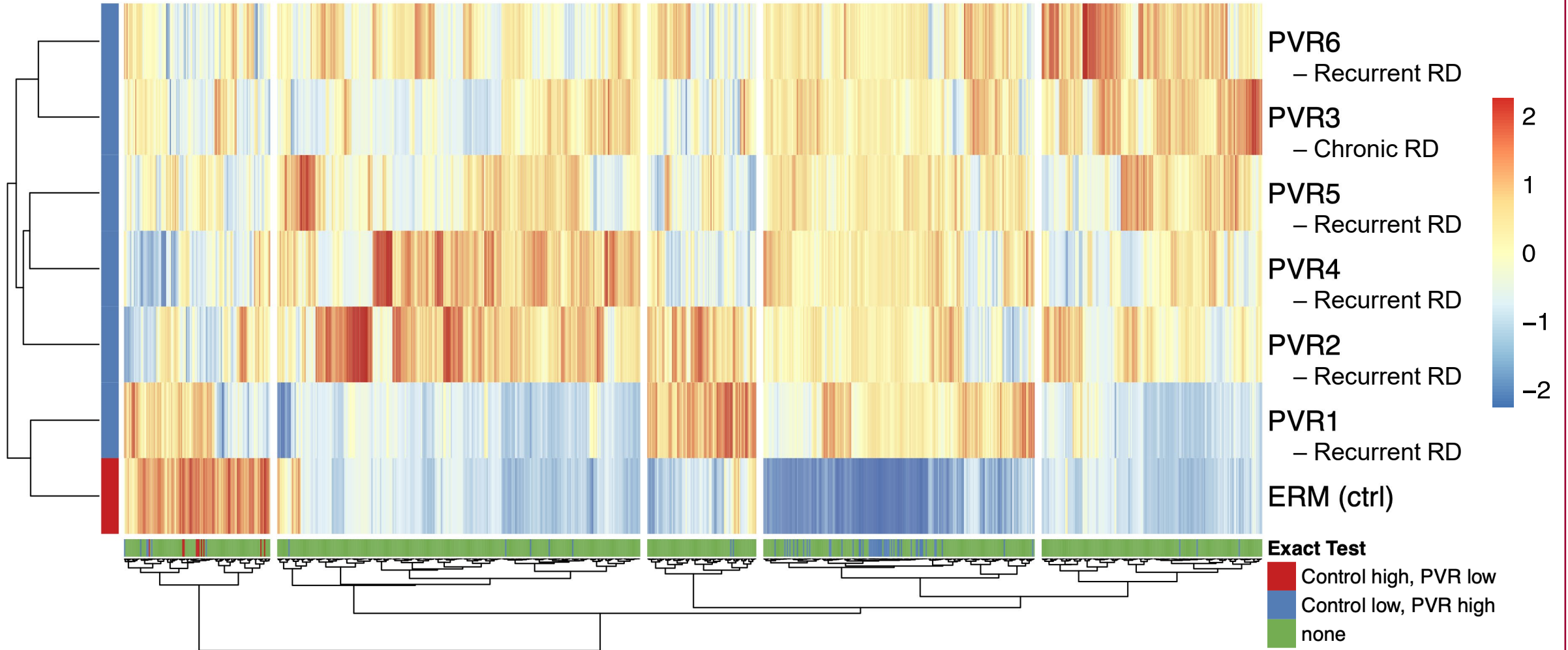


LC/MS



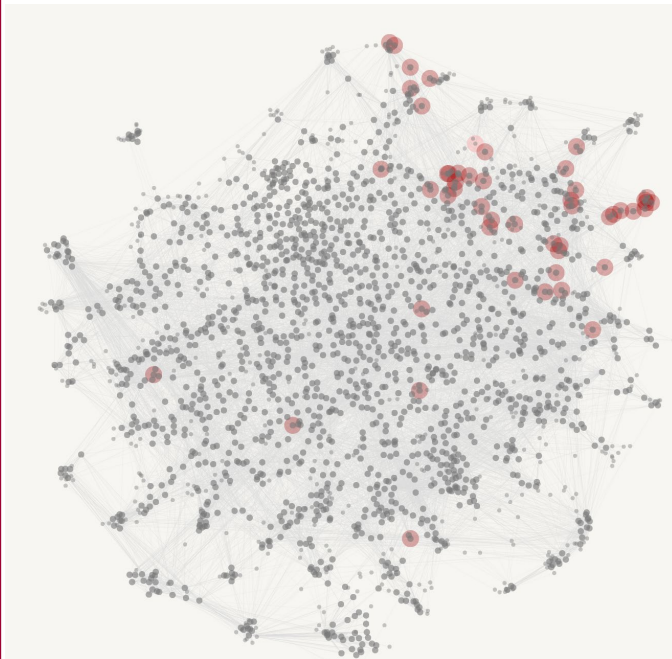
Database Search

Heatmap



Gene Ontology (GO) Pathway Analysis

GO-term	Description	Enrichment score	Pathway size	False discovery
GO:0030198	extracellular matrix organization	0.833808	296	2.16E-05
GO:0043062	extracellular structure organization	0.789592	339	2.16E-05

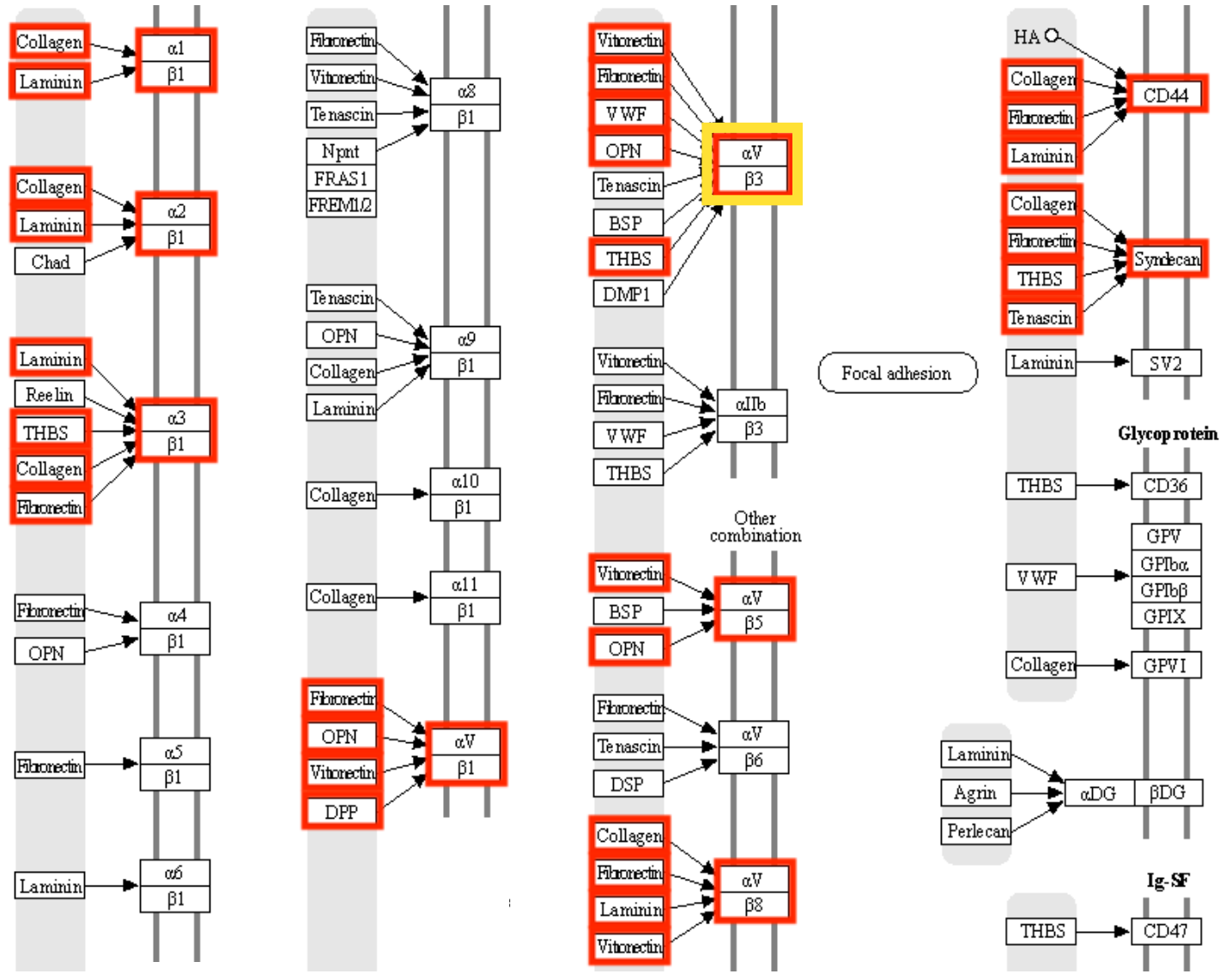


HSPG2	Heparan sulfate
FN1	Fibronectin
TNC	Tenascin
COL12A1	Type XII collagen α chain
GFAP	Glial fibrillary acid protein
LAMA5	Laminin subunit α -5
LAMC1	Laminin subunit γ -1
FBN1	Fibrillin-1
COL6A3	Type VI collagen α chain
LAMB2	Laminin subunit β -2

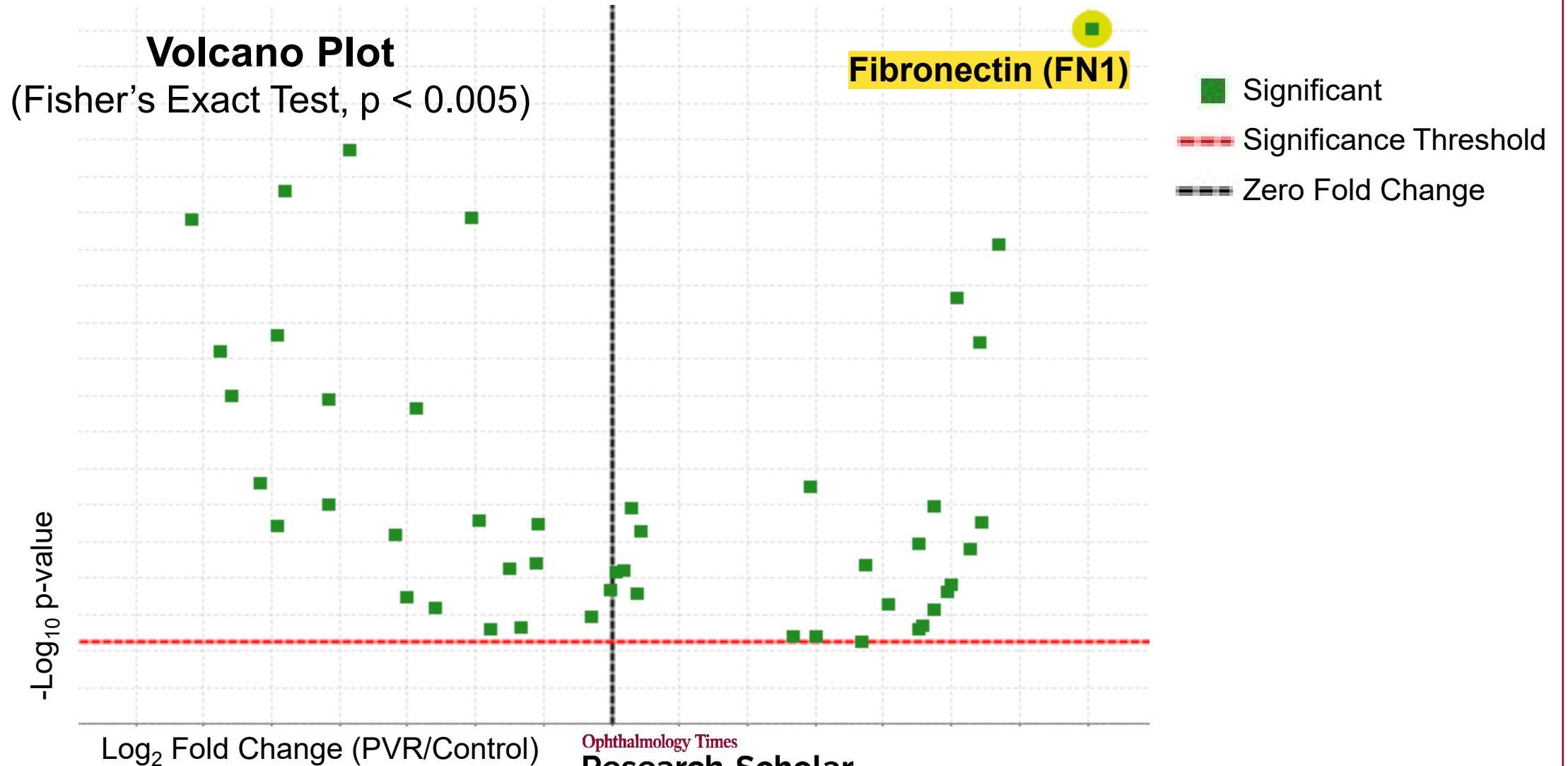
ANXA2	Annexin A2
TGFBI	Transforming growth factor- β
LAMA2	Laminin subunit α -2
COL14A1	Type XIV collagen α -1 chain
COL1A2	Type I collagen α -2 chain
COL18A1	Type XVIII chain α -1 chain
COL1A1	Type I collagen α -1 chain
POSTN	Periostin
NID1	Nidogen-1
NID2	Nidogen-2

Integrin Expression Profile

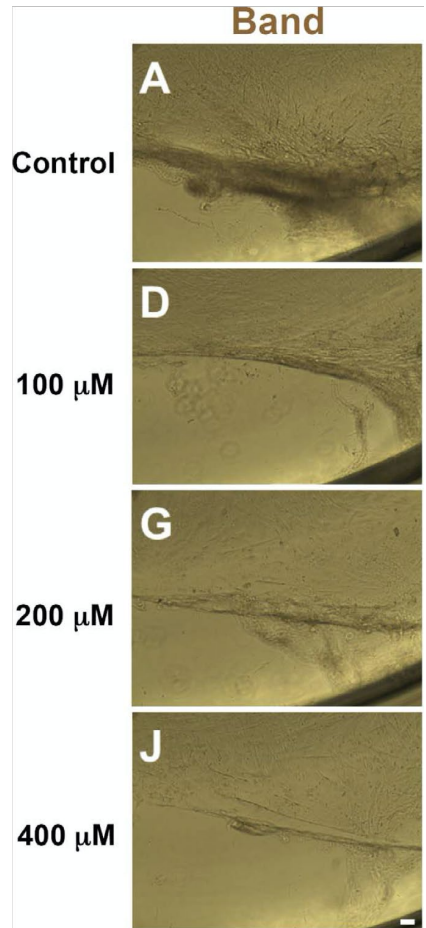
ECM-RECEPTOR INTERACTION



Fold change idiopathic ERM vs. PVR

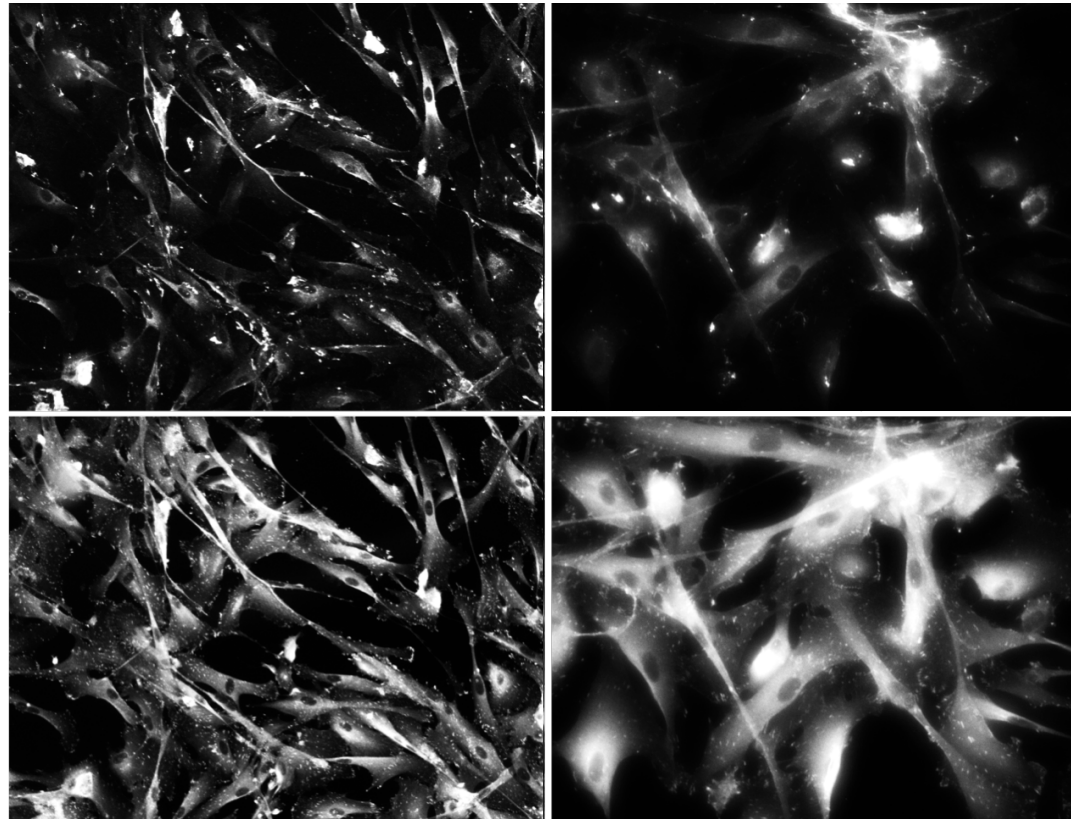


An *in vitro* model of PVR



Amarnani et al., 2017

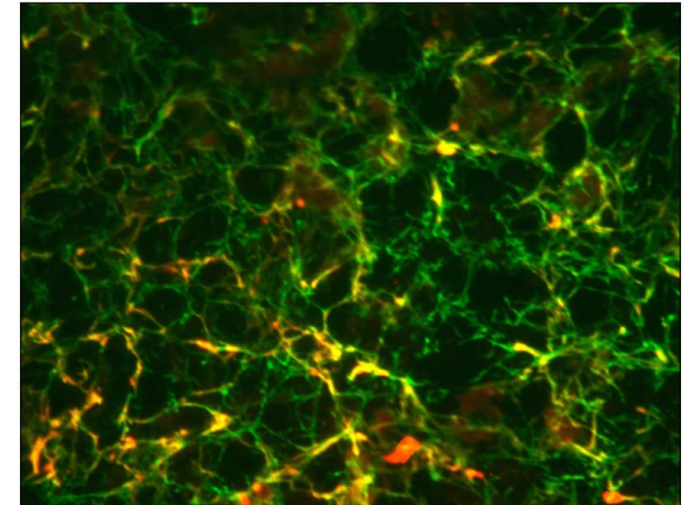
← Fibronectin →



Phalloidin

Vinculin

Fibronectin + Collagen



Acknowledgements

RUTGERS
Robert Wood Johnson
Medical School



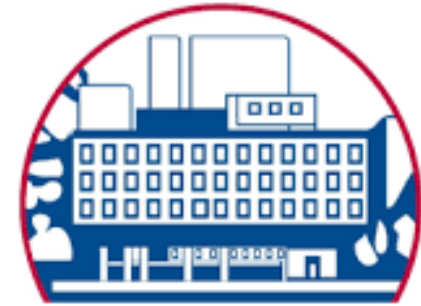
Jonathan Prenner, MD



PRINCETON
UNIVERSITY



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Scheie Eye Institute



Penn Medicine



Alexander Brucker, MD