

# CAFÉ SCIENTIFIQUE

proposé par le Réseau de recherche en sciences de la vision (RRSV)



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MD, FRCPC, FAAP, PhD

Mercredi, **3 décembre 2025**  
10h à 11h30

Évènement **HYBRIDE**,  
ouvert à **tous!**



**Sylvie Castonguay**  
Directrice de l'AQDM



**Savsav**, 780 Brewster Ave RC-015, Montréal, QC (à proximité du Métro Lionel-Groulx)

OU



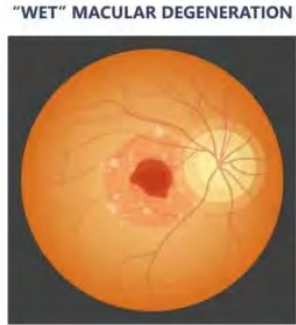
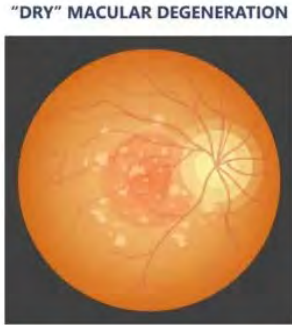
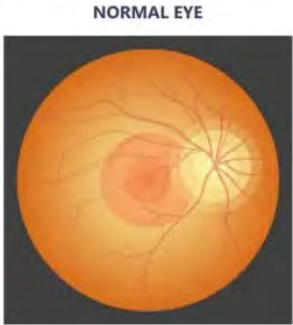
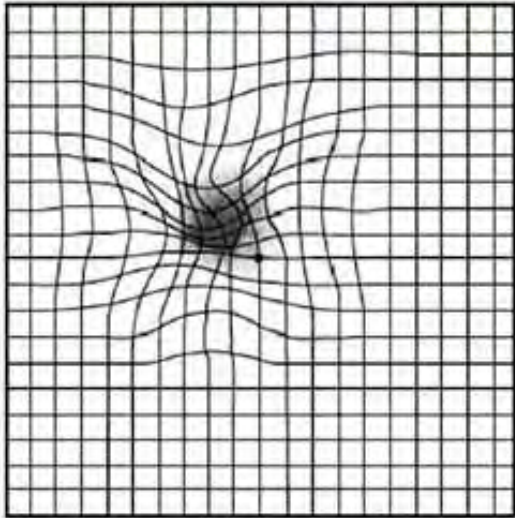
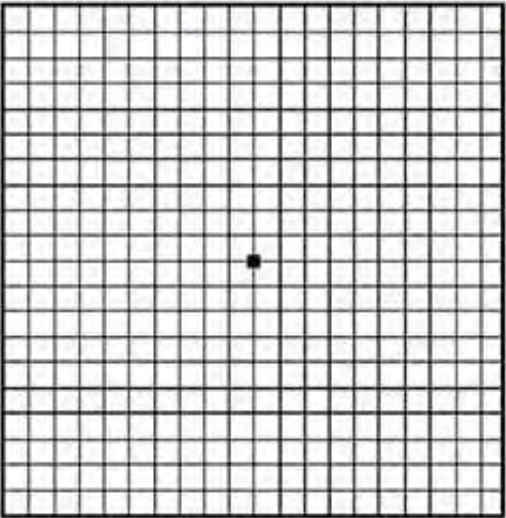
Lien *Microsoft Teams* à venir

## Thérapies médicamenteuses en émergence pour la DMLA type sèche

# AMD demographics

- ~190 million people affected worldwide; ~300 million expected by 2040 with aging population
- ~15% of >80 years old
- Highest prevalence in N America and Europe; fastest rise in Asia
- Women and Caucasian predilection

# Consequences of AMD on vision



CLEAR VISION OF NORMAL EYES

UNUSUALLY FUZZY OR DISTORTED VISION

BLIND SPOT IN CENTER OF FIELD OF VISION

# What is AMD?



## **Definition and Impact**

AMD damages the macula, reducing sharp central vision but preserving peripheral sight.

## **Symptoms and Progression**

AMD often starts without symptoms and progresses gradually, affecting reading and face recognition.

## **Importance of Early Detection**

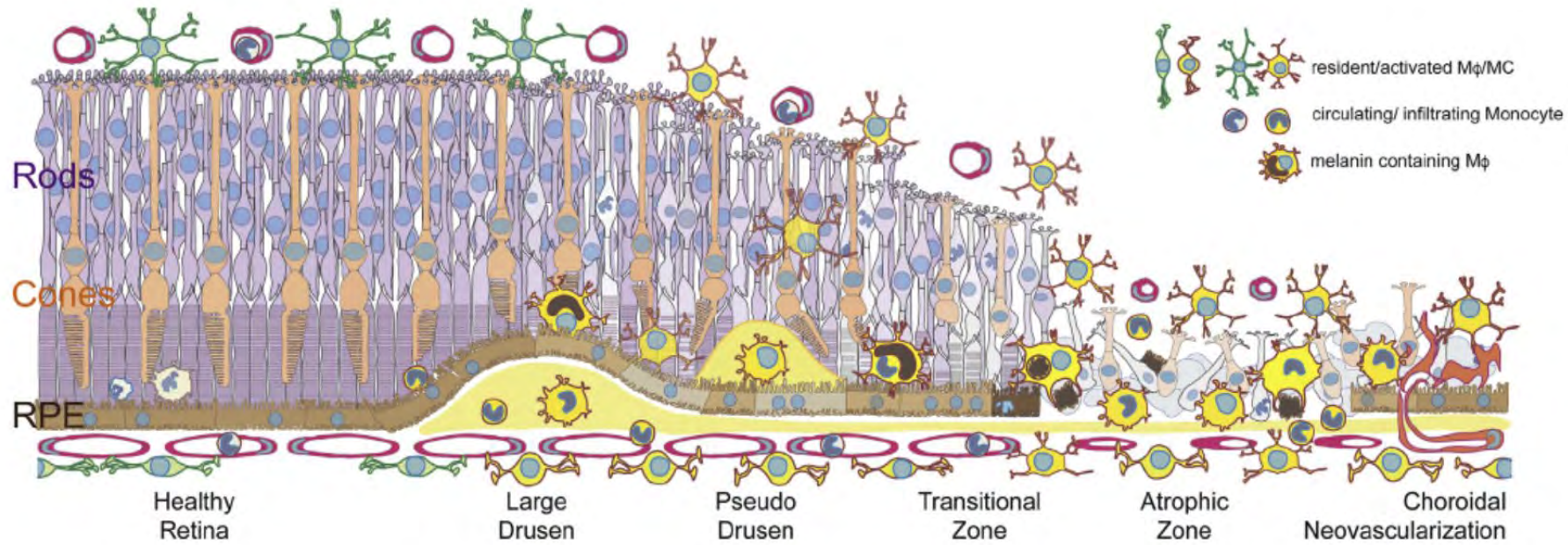
Regular eye exams help detect AMD early since initial stages may have no symptoms.

## **Coping and Management**

Assistive devices and prevention strategies help maintain independence despite AMD vision loss.

# AMD characteristics

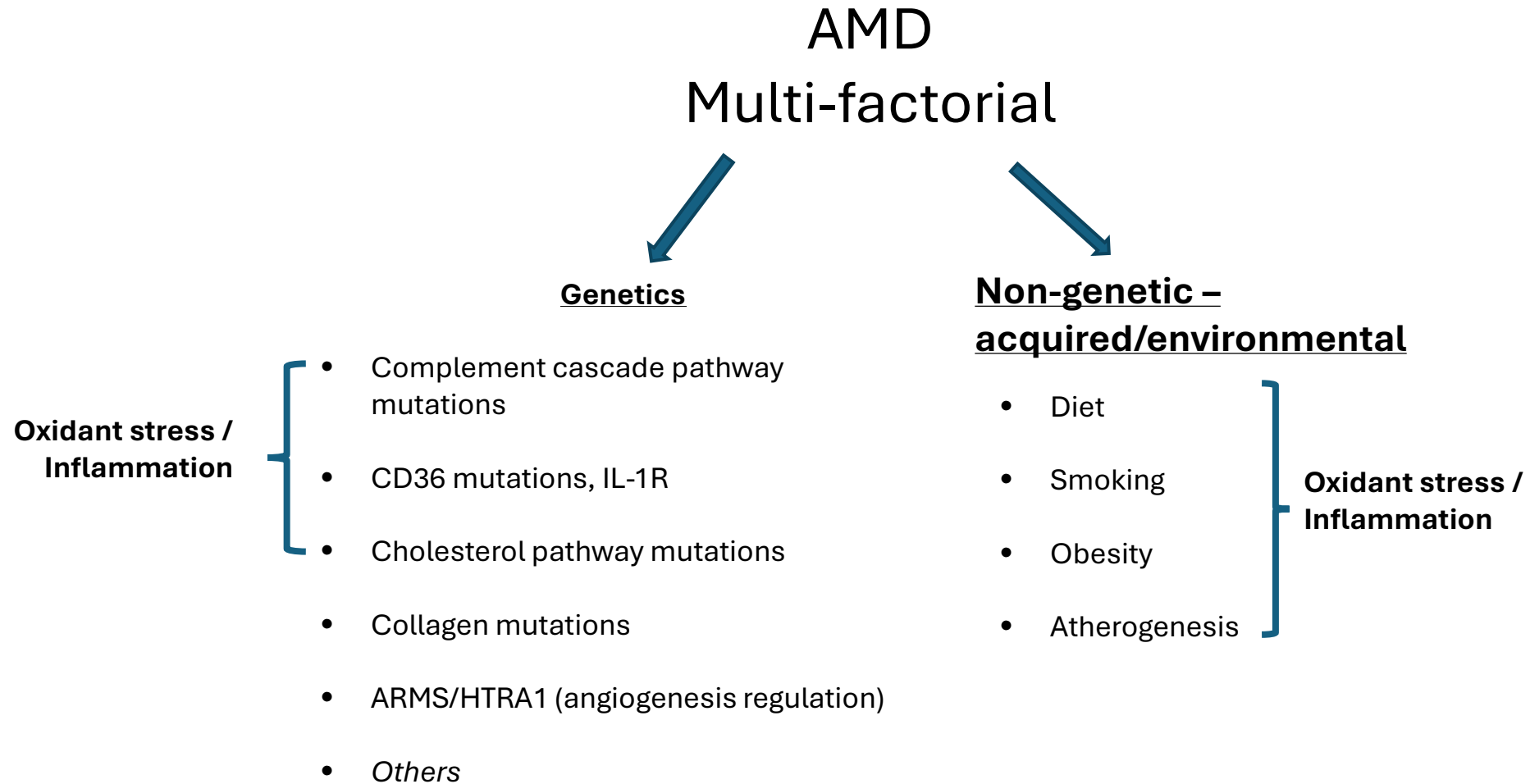
Progressive, degenerative, multifactorial, polygenic disease



Sennlaub et al, 2017

Faculté de médecine

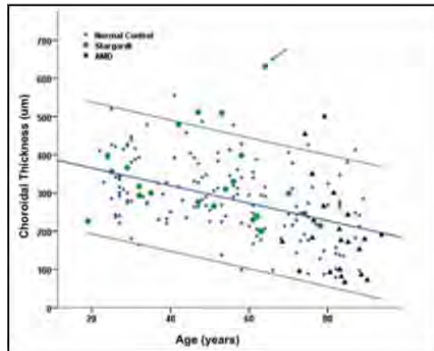
# Causes/Factors of AMD



# The choroid – main supply of oxygen and nutrients to RPE and photoreceptors

## Inflammation is associated with photoreceptor degeneration and choriocapillary involution

Choroid thickness as function of age in AMD



Nunes, 2015

### Choroidal thinning is regularly observed in AMD and ischemic retinopathies

**Age-related macular degeneration:** Capuano V, Br J Ophthalmol, 2016  
Esmaeelpour M, PLoS One, 2014  
Cincinelli MV, Br J Ophthalmol, 2017  
Seddon JM, JAMA Ophthalmol, 2016  
Nittala MG, Ophthalmol Retina, 2019

### Diabetic retinopathy:

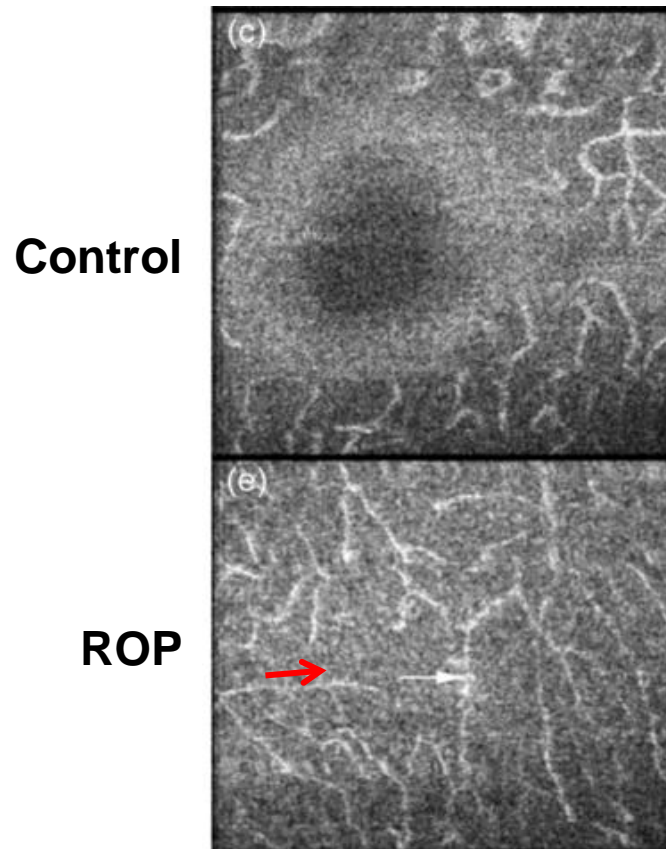
Yolcu U, Postgrad Med, 2016  
Adhi M, JAMA Ophthalmol, 2013  
Esmaeelpour M, IOVS, 2012  
Orduna-Hospital E, Diagnostics, 2020

### Retinopathy of prematurity:

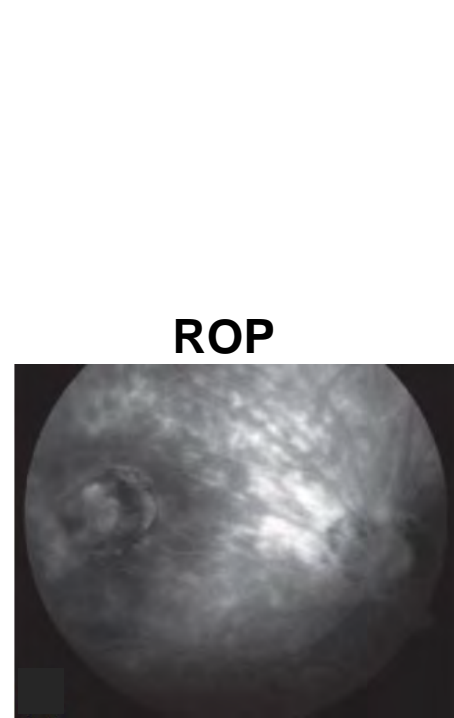
Erol MK, Retina, 2016\*  
Park KA, IOVS, 2012  
Wu WC, JAMA Ophthalmol, 2013  
Anderson MF, Eye, 2014  
Hansen R, Prog Ret Eye Res, 2017\*  
Lavric A, Acta Ophthalmol, 2020

Faculté de médecine

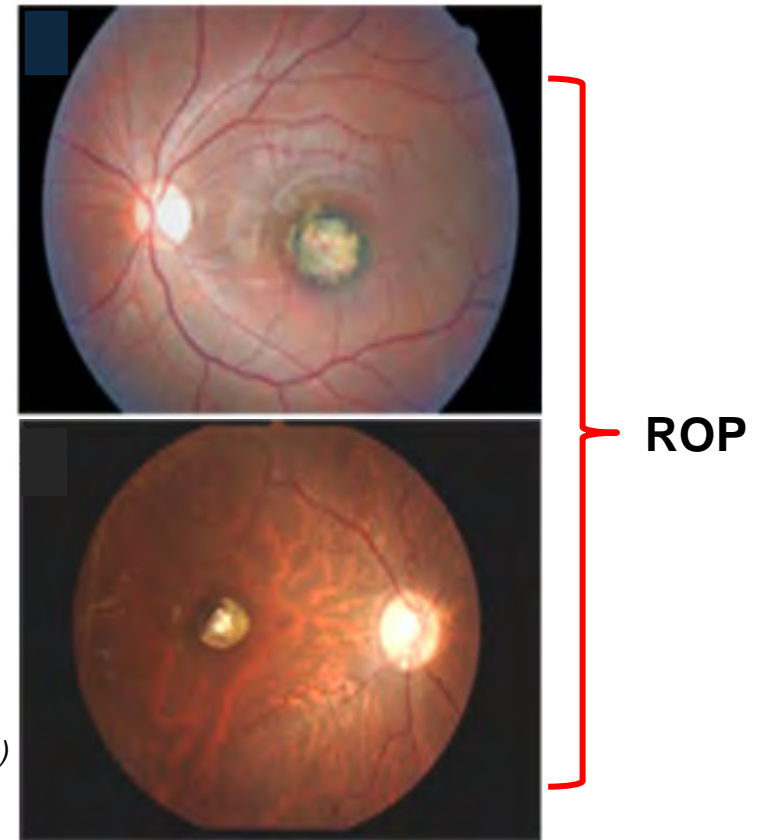
# Progressive vascularized fovea, macular angiogenesis and depigmentation in former ROP patients (age: 8-45 years)



(Hammer DX, IOVS, 2008)

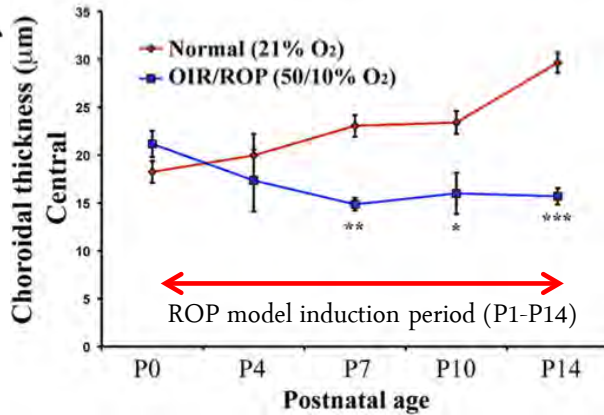


(Fiedelius HC, Acta Ophthalmol, 2011)

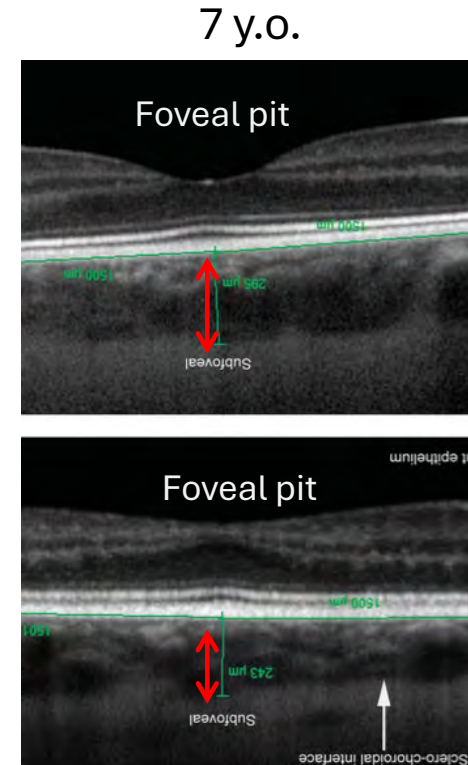


(Lee KM, Graefes Arch Clin Exp Ophthalmol, 2010)

# Persistent choroidal thinning (involution) in animal models and in patients – prematurity may accelerate AMD development

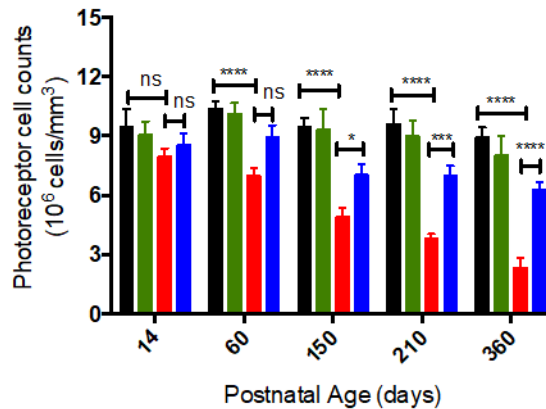
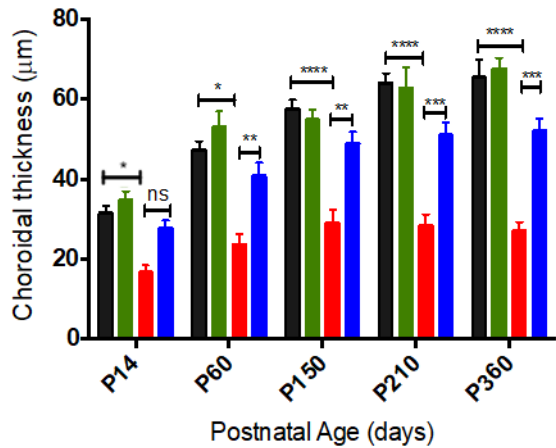


Shao, IOVS, 2011; Zhou, Am J Pathol, 2016



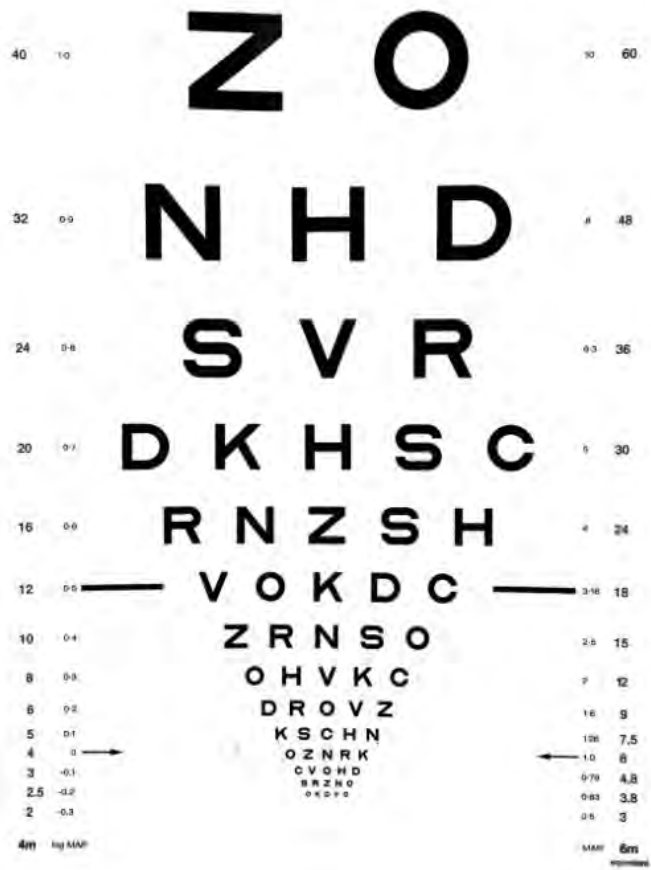
7 y.o.  
Control patient  
Retina  
Choroid  
Subfoveal  
ROP (regressed)  
Retina  
Choroid  
Subfoveal  
Sclero-choroidal interface

Anderson, et. al., Eye, 2014.



Legend:  
 ■ NOR  
 ■ NOR+IL-1ra  
 ■ OIR  
 ■ OIR+IL-1ra

# Detection / Diagnostic of AMD



## Comprehensive Eye Exam

Dilating eye drops widen the pupil to allow detailed retinal and macula examination for AMD signs.

## Amsler Grid Test

The Amsler grid detects visual distortions or blind spots in central vision indicating AMD progression.

## Advanced Imaging Techniques

Optical coherence tomography and fluorescein angiography identify fluid leakage and abnormal blood vessels in wet AMD. **Enhanced by Deep learning OCT analysis.**

## Inflammatory serum metabolites

CRP, cytokines, OH-cholesterol.

## B-Amyloid detection by hyperspectral laser

Optina Diagnostics.

## Early Detection Importance

Routine eye exams enable early AMD detection, allowing timely treatment to preserve vision.

# Most common 'treatments' of ARMD

## Neurodegenerative ARMD ('dry form')

### **AREDS2 SUPPLEMENT**

These vitamins, which you can find at pharmacies, are helpful in stopping the progression of the disease and are most used as an intervention for dry AMD.



Negligible efficacy;  
essentially no therapy

## Neovascular ARMD ('wet form')

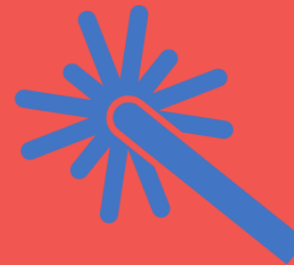
### **ANTI-VEGF INJECTIONS**

These eye injections are used to treat wet AMD, and they help stop the development of abnormal blood vessels. They're usually given every month to every six months.



### **PHOTODYNAMIC THERAPY**

Another treatment for wet AMD specifically, photodynamic therapy uses a combination of medication and a laser to seal off leaky blood vessels in the retina.



**Inhibits neovascularization (eventual refractoriness)**

# Dry AMD pipeline

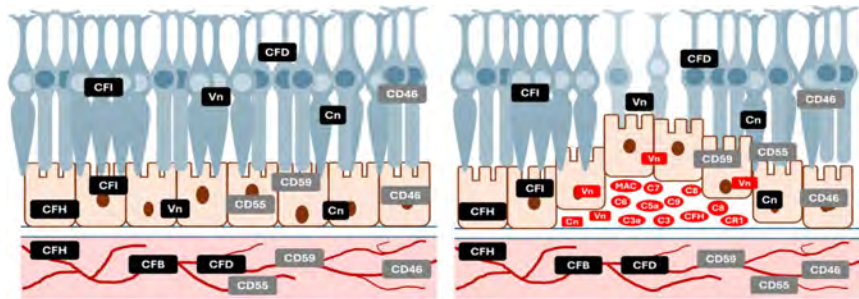
Compound	Type/Mechanism	Companies	Stage	MoA
Pegcetacoplan*	Complement C3, C3b inhibitor	Apellis	Phase IV	IVT
Zimura (Avacincaptadpegol)**	Complement C5 convertase inhibitor pegylated RNA aptamer	Iveric Bio	Phase IV	IVT
ANX-007	Complement C1 inhibitor	Annexon	Phase II	IVT
CB2782	Complement C3 inhibitor	Catalyst	Preclinical	IVT
ALXN1720	Complement C5 inhibitor	Alexion	Phase I	
MC-1101	Anti-oxydant	MacuClears	Phase III	topical
Ethamsylate	FGF inhibitor	Dobecure	Phase III	IVT
Alk-001	Vitamine A aggregation inhibitor	Alkus Pharma	Phase III	oral
HMR59	Potentiator of formation of sCD59	Hemera	Phase I	IVT
Kamuvudine	Inflammasome inhibitor	Inflammasome Therap.	Preclinical	IVT
Xiflam	Connexin-43 / inflammasome inhibition	InflammX Therap.	Phase II	oral

\*FDA-approved (Syfovre: 02-2023)

\*\* FDA approval (08-2023)

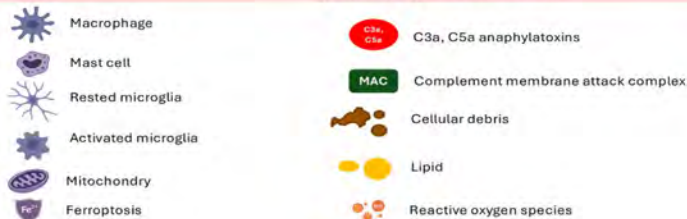
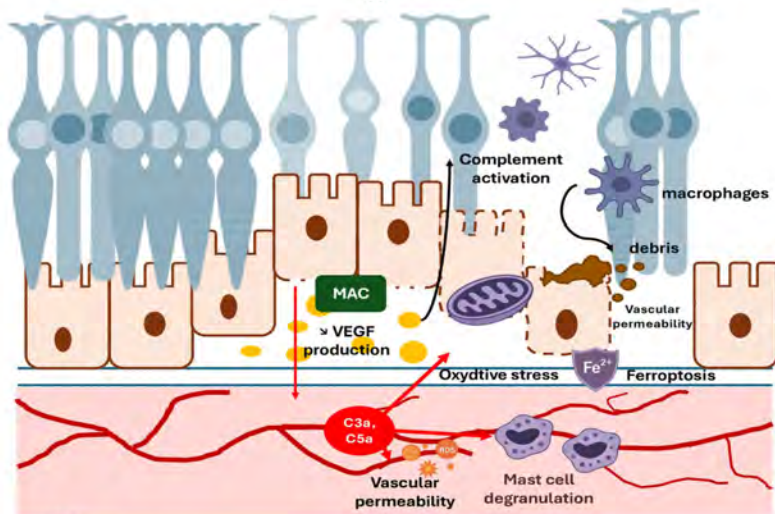
MoA: mode of administration; IVT: intravitreal

# Anti-Complement role and trials for AMD



A

B



C

## Failures of anti-Complement trials

Table 2

### Summary of failed complement-targeted therapies in GA.

Drug	Target	Sponsor	Trial phase/ID	Outcome
Lampalizumab	Factor D (alternative pathway)	Genentech/Roche	Phase III — Chroma and Spectri	No significant reduction in GA lesion growth; trials failed to meet primary end points.
Eculizumab	C5 (terminal pathway)	Alexion	Phase II — COMPLETE (NCT00935883)	Well tolerated but did not significantly slow GA progression.
Tesidolumab (LFG316)	C5 (terminal pathway)	Novartis	Phase II — NCT01527500	No anatomical or visual benefit observed compared to sham.
CLG561	Properdin (alternative pathway)	Novartis	Phase II — NCT02515942	No significant effect on GA progression, both as monotherapy and in combination.
POT-4 (AL-78898A)	C3 (central component)	Alcon	Phase II — NCT01603043	Trial terminated early due to intraocular deposits and formulation issues.
GEM103	CFH (alternative pathway)	Gemini Therapeutics	Phase IIa — ReGAtta (NCT04643886)	Well tolerated with biomarker evidence of complement regulation (CFH elevation, C3a and Ba reduction); development discontinued after early trials; no efficacy data on GA progression.
NGM621	Complement C3 (central component)	NGM Biopharmaceuticals	Phase II — CATALINA (NCT04465955)	Did not meet primary end point of statistically significant reduction in GA lesion growth; favorable safety profile with no increase in CNV; development discontinued after Merck declined licensing option.
IONIS-FB-LRx	Complement factor B (alternative pathway)	Ionis Pharmaceuticals/Roche	Phase II — GOLDEN (NCT03815825)	Phase II trial initiated to assess safety and efficacy in GA; development discontinued following disappointing data; no further development plans announced.

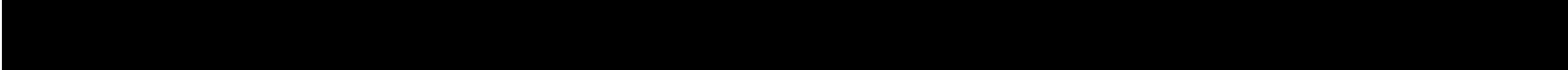
# Dry AMD pipeline

Compound	Type/Mechanism	Companies	Stage	MoA
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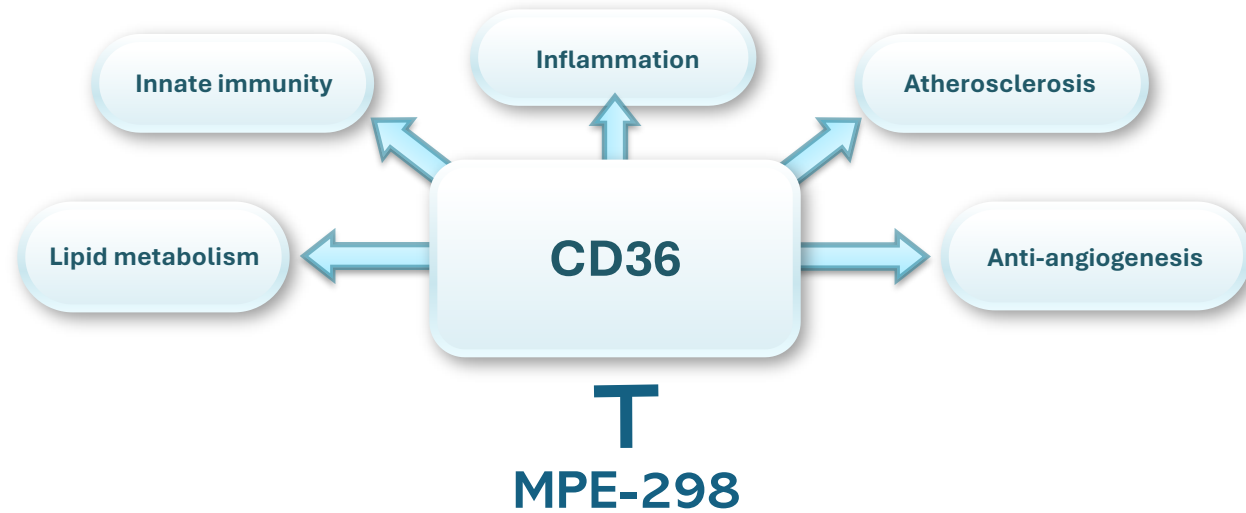
Molecule	Indication	Mechanism	Stage
<b>Vonaprunent (ANX007)</b>	Dry AMD (GA)	C1q complement inhibitor (Fab)	Phase 3 (enrolled)
<b>Elamipretide</b>	Dry AMD	Mitochondrial protective peptide	Phase 3
<b>GAL-101</b>	Dry AMD	Amyloid- $\beta$ aggregation modulator	Phase 1 (oral/eye)
<b>SREDS (PDE inhibitors)</b>	Dry & other retinal degeneration	Stress resilience enhancers	Preclinical



# AMD emerging therapies in pre-clinical trials

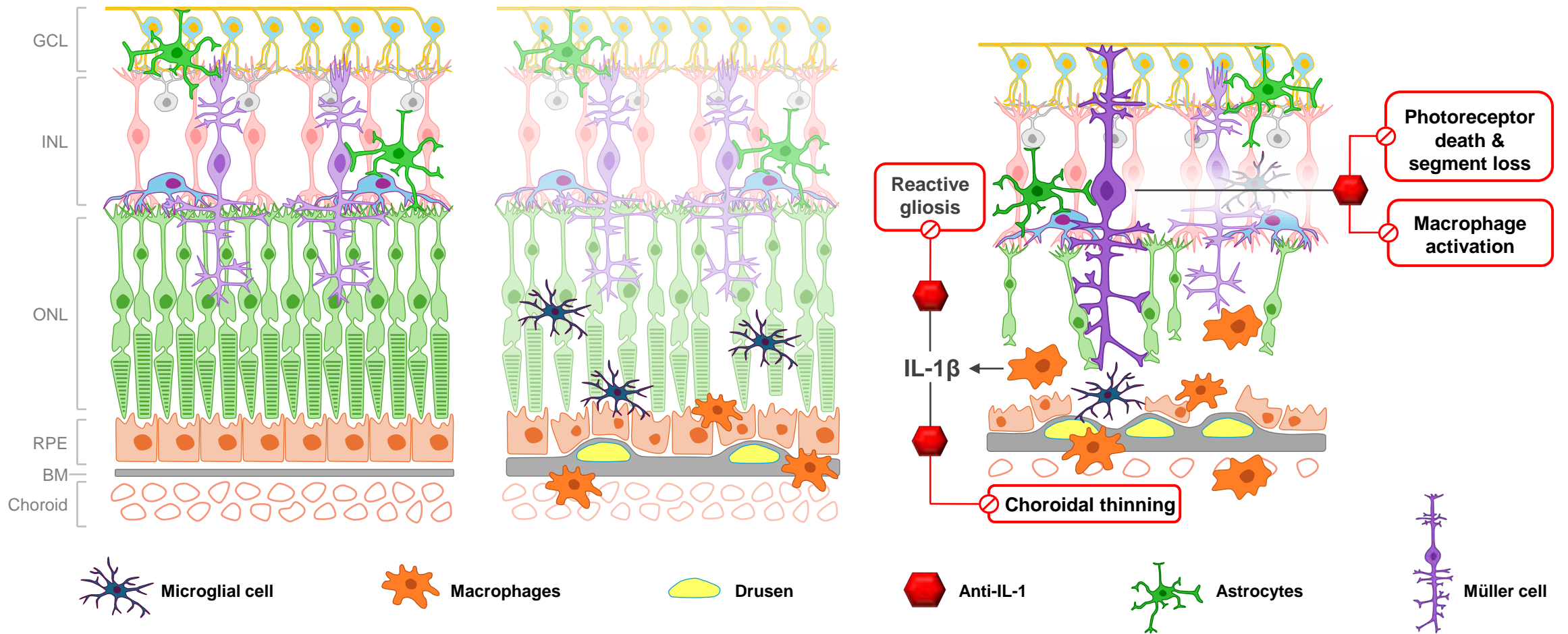
Mechanism	Candidate	Model evidence
Lipid regulation	sHDL-T0 (LXR agonist)	Decreases inflammation
Lipid regulation	MPE-298	Decreases cholesterol & inflammation
Autophagy enhancer	Flubendazole	Drusen clearance
Mitochondrial rescue	Bevemipretide	Protects retinal thickness
Neuroprotective	ONL1204; CT1812	PR protection
Inflammasome suppression	NLRP3 inhibitor	Anti-inflammatory
IL-1R antagonist	Rytvela	Anti-inflammatory in NaIO <sub>3</sub> model

# CD36: A Lipid Sensor with Multiple Functions



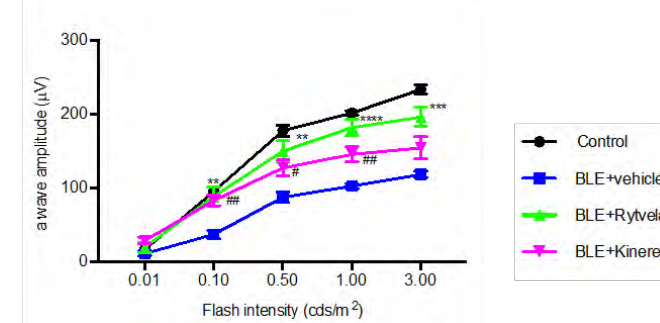
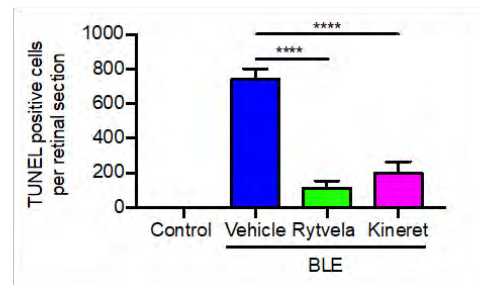
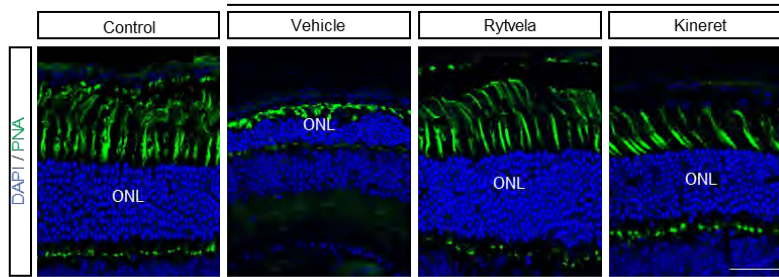
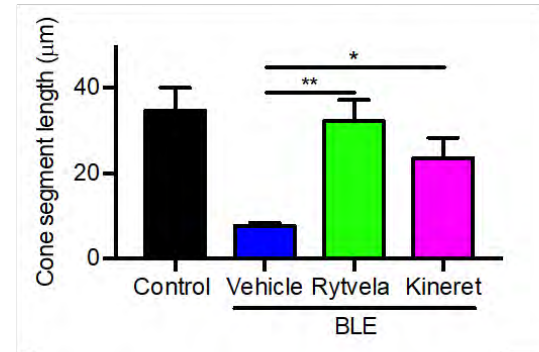
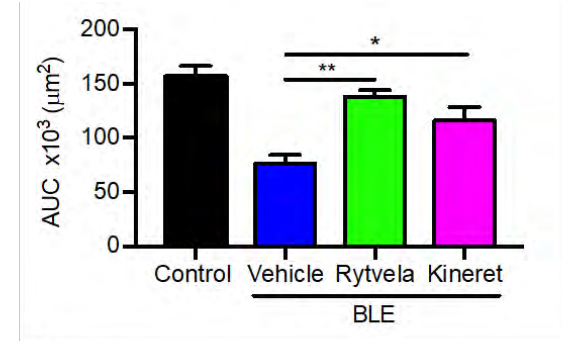
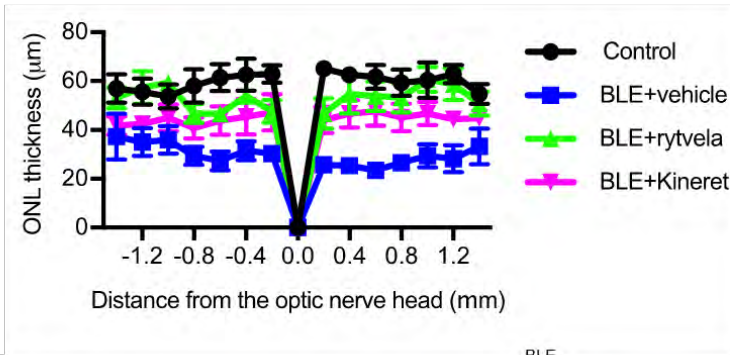
- CD36 is a multi-ligand scavenger receptor: binds oxLDL, AGE and Thrombospondin
- CD36 is involved in different activities: lipid metabolism, inflammation, angiogenesis
- CD36 is expressed in macrophage/microglia, microvascular endothelium, RPE
- CD36 is a co-receptor for TLR2, and enhances TLR2-mediated inflammation
- Positive association of common genetic variants in CD36 with neovascular AMD

**Modulation of CD36 provides an desirable encompassing treatment for AMD.**



**Vision:** Small molecule anti-IL-1 MU-010 and parent rytvela underscore a breakthrough technology effective in safely suppressing inflammation, while displaying retinal neuroprotective properties in models of AMD. We thus aim to decrease health, social and personal costs by introducing a safe effective new therapy for treating dry AMD prior to late severe deleterious consequences on vision


# Rytvela preserves photoreceptor density and function in neurodegenerative retinopathy, and is superior to Kineret



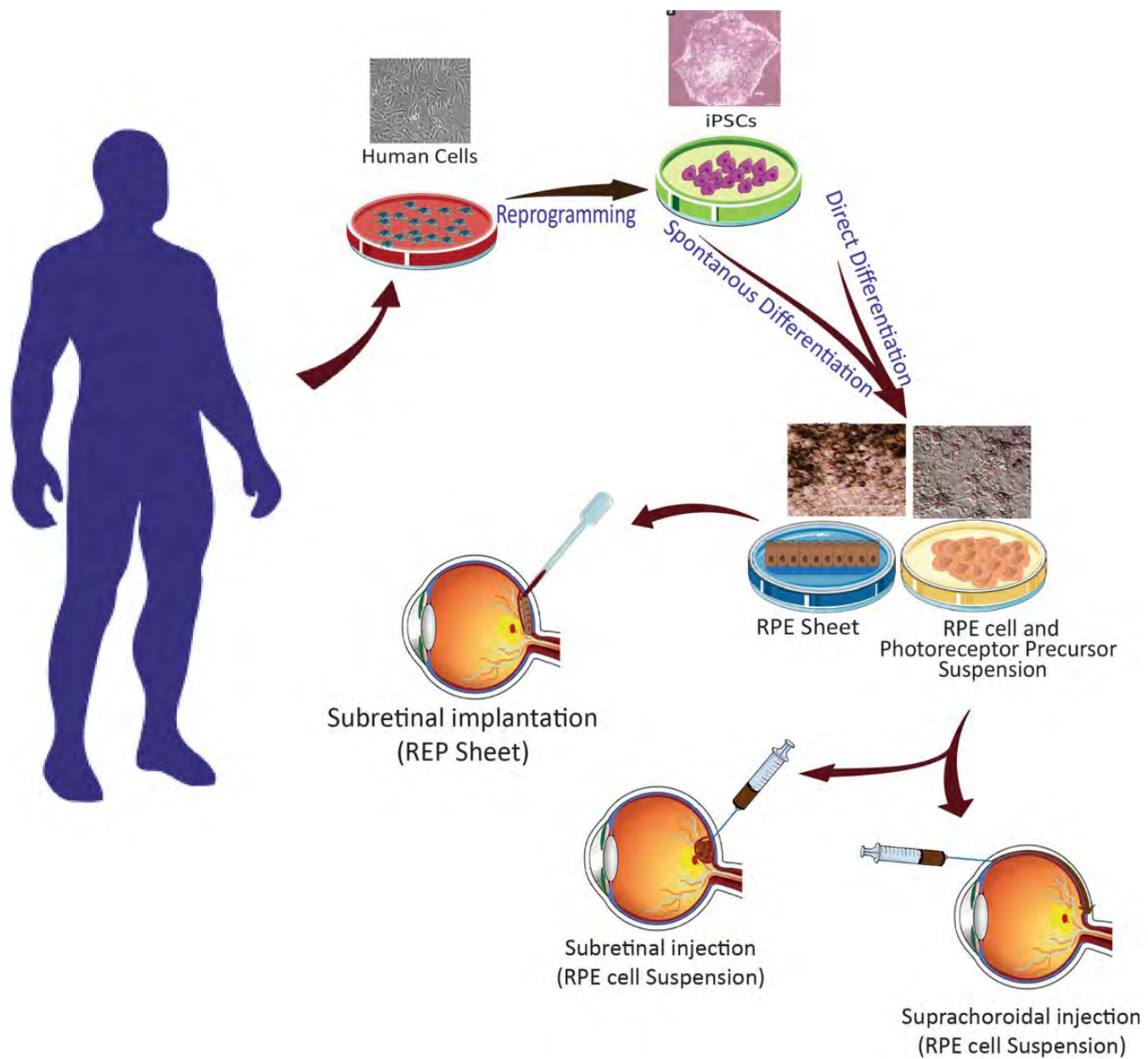
# Comparative outcomes between rytvela and complement inhibitors

Comparative outcomes	Drug candidates	
	Rytvela	Complement inhibitors
Targets a central point of inflammation regardless of trigger	+++	---
Avoid mitigated results	+++	---
Decreased risk of neovascularization upon treatment	+++	---
Targeted pathway facilitates timing of intervention	+++	---
Pathway selectivity conveys immunovigilance	+++	---

## Partners:

- Altus Drug Corporation  - assist in commercial advances and development; in-kind support)
- Studio Biosciences (formulation development – fully implicated)

# Stem cell therapy for AMD



# Stem cell therapy for AMD

## Objectives:

- **Replacing damaged cells:** The primary goal is to replace lost RPE cells, which are critical for supporting the eye's light-sensing photoreceptor cells.
- **Cell transplantation:** Stem cells are differentiated into specialized retinal cells, such as RPE cells, and then surgically implanted into the eye's retina.
- **Supportive function:** The transplanted cells may also release factors that help keep the remaining host cells alive and functioning, and recent research suggests they can transfer material to host cells to provide support.
- **Clinical trials:** Research is ongoing in clinical trials to assess the safety and efficacy of these therapies, with some preliminary results showing promise in stabilizing or improving visual function.

# Perspectives for dry AMD treatments

## Other than anti-VEGF and complement inhibitors)

- Anti-inflammatory drugs
- Mitochondrial preservation
- Neuroprotectants
- Cell therapy / Gene therapy (?)
- Enhanced early diagnostics: AI, imaging, molecular detection
- **Combination therapy, personalized therapy, non-invasive modalities (enhanced formulations)**

**Hopeful future in tackling AMD**



*Merci*