# Update IVOM 2024 –

# Therapie der Geographischen Atrophie bei AMD

Amelie Pielen

DOC Kongress Nürnberg 20.06.2024

## Prof. Dr. med. Amelie Pielen – conflict of interest (COI)

Ärztliche Klinikleitung, Maximilians-Augenklinik Nürnberg

Gastwissenschaftlerin, Medizinische Hochschule Hannover

**Mitgliedschaft in Fachgesellschaften**:

DOG, BVA, BDOC, Retinologische Gesellschaft, Retina.net e.V.

**Klinische Studien und Forschungsprojekte:**

Novartis, Bayer, Allergan, Roche, Chengdu Kanghong, Böhringer Ingelheim, Sanofi Aventis, Recordati Rare Diseases, ICON, TFS, iveriqbio

**Referentin und Beraterin**:

abf Campus, Apellis, Bayer, Allergan/ Abbvie, Novartis, Roche, med update, Heidelberg Engineering, Stada Pharm

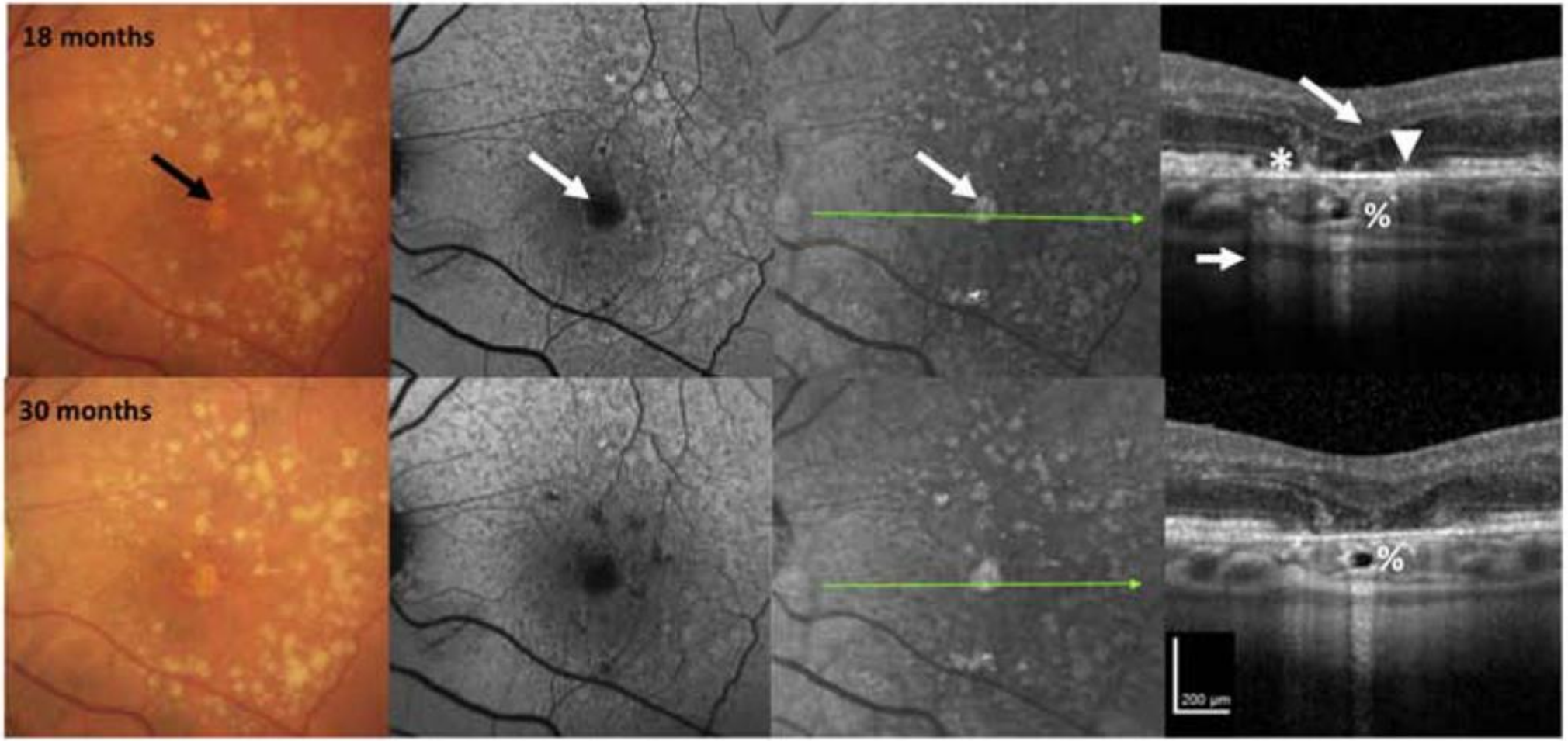
# AMD – Spätform trockene AMD – geographische Atrophie

**Spätform – trockene AMD**

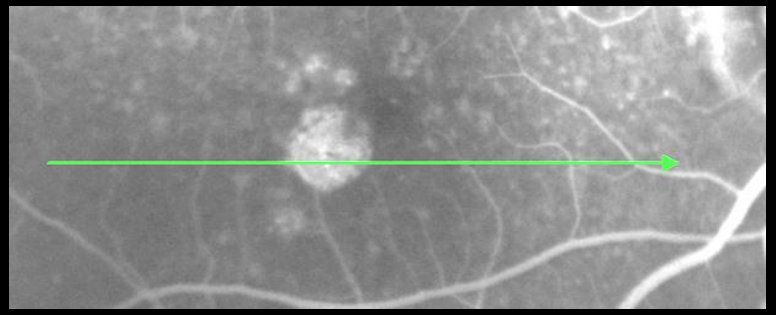
**(noch)**
**KEINE Therapie**

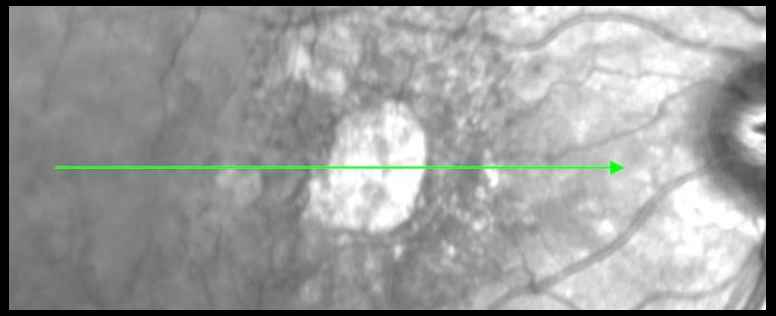
Quelle: C. Framme, MHH

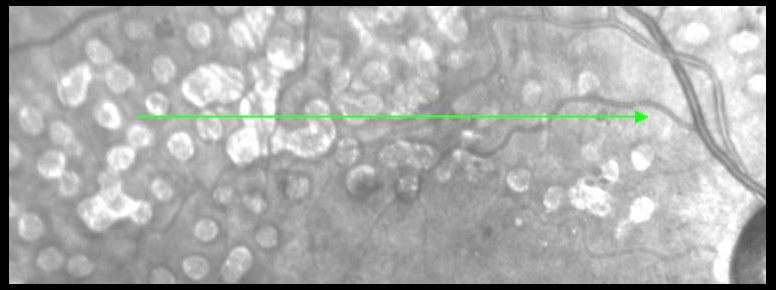
# Multimodal Imaging of AMD – progression from incomplete to complete RPE and outer retinal atrophy (iRORA and cRORA)

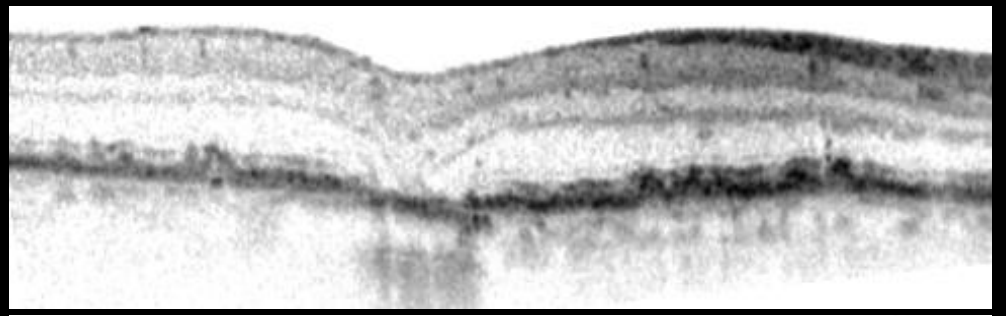


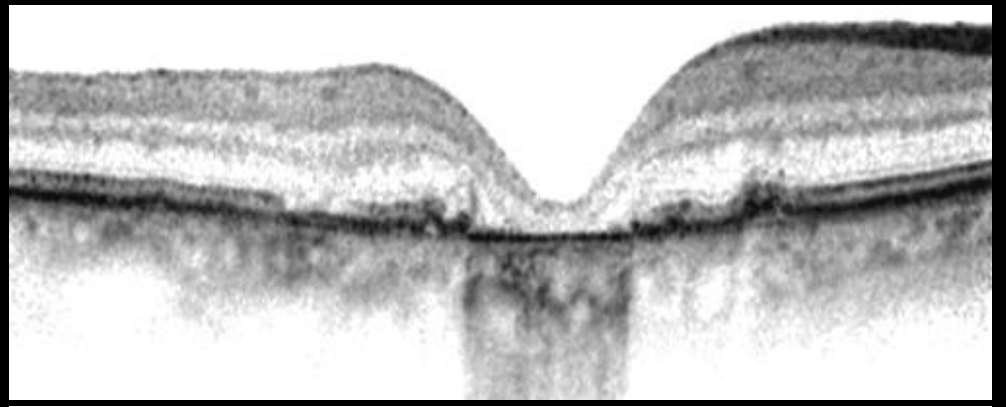

Guymer et al. 2020 Ophthalmology; 127(3):394-409 **CAM** Report 4

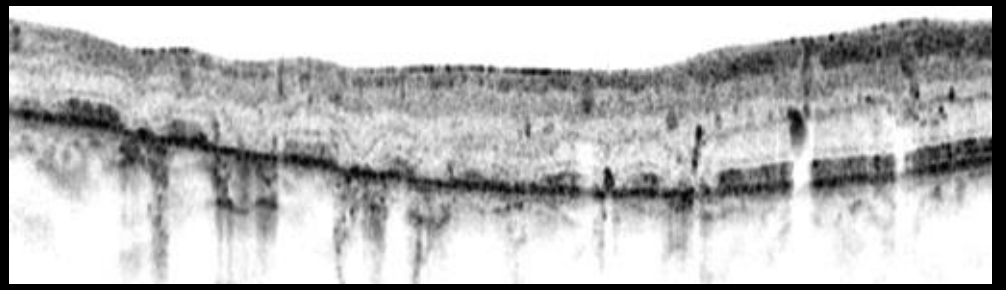


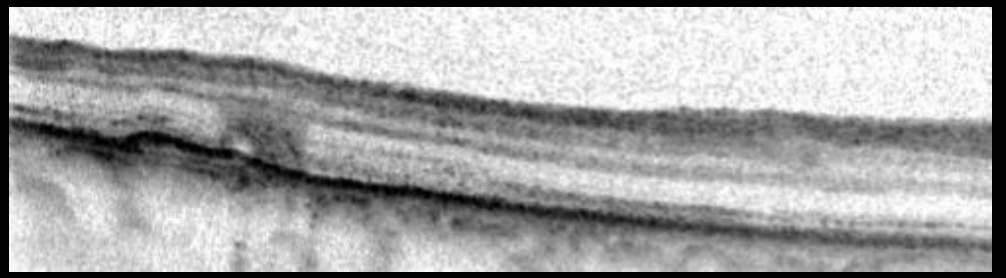


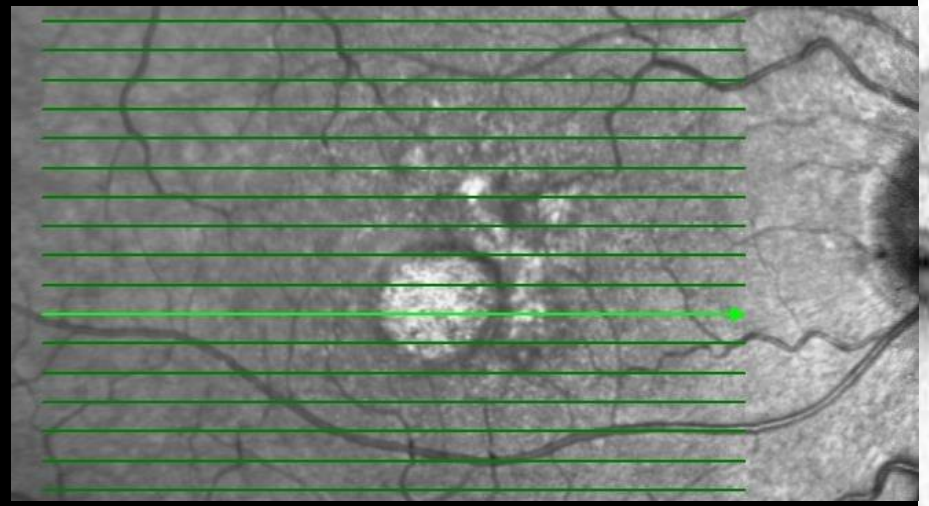


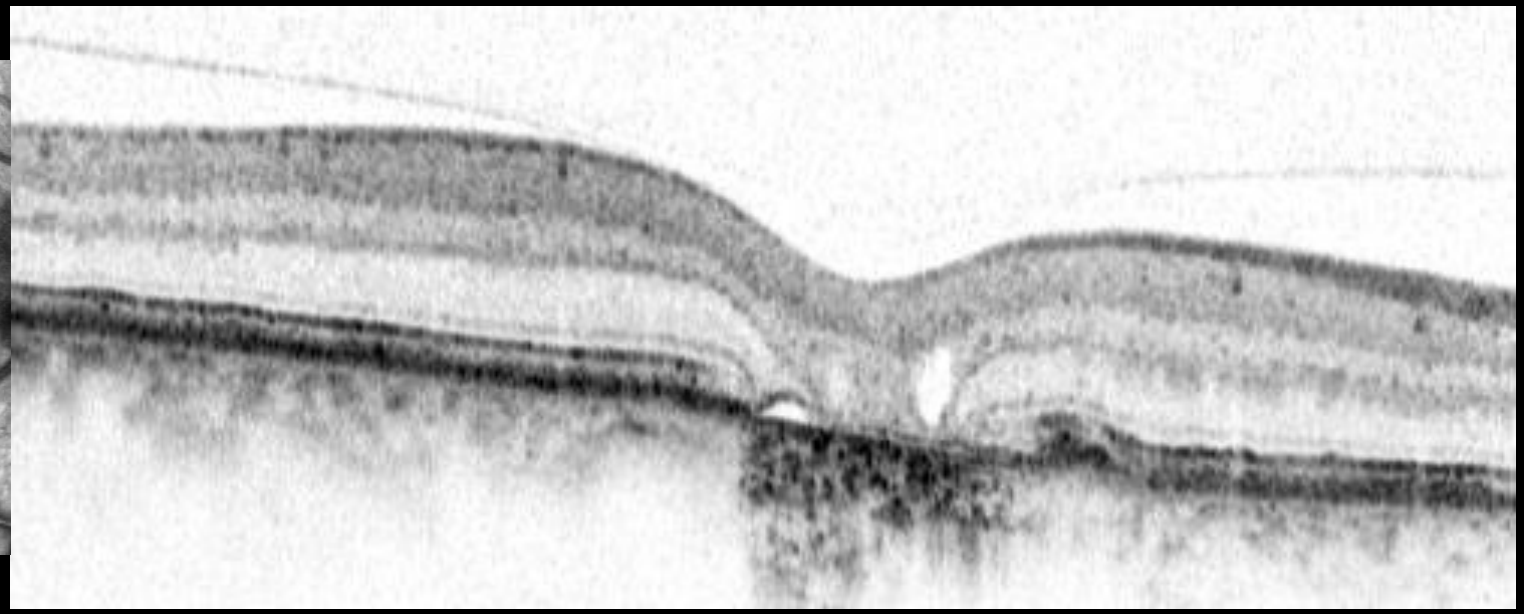






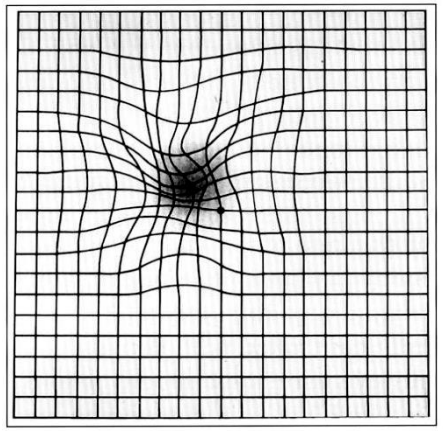


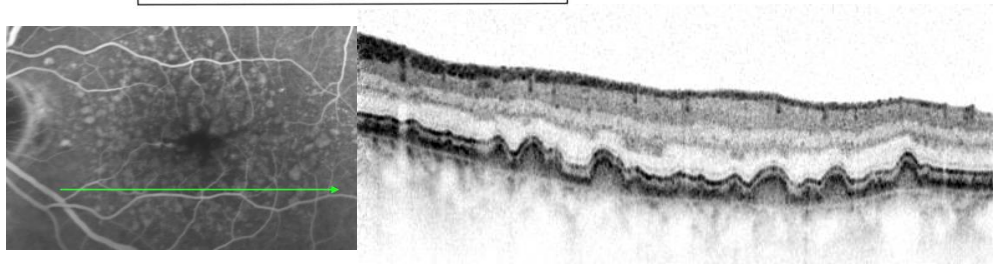




CAVE: Hohlräume über Atrophie – keine IVOM !

# AMD – eine Erkrankung?





**Früh: Trockene AMD**

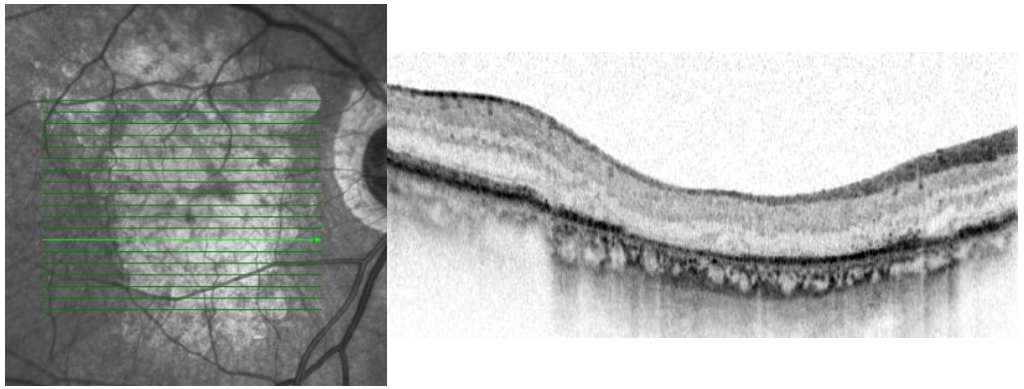
50%

**Spät: Feuchte AMD**

**IVOM**
- **aVEGF**
- **aPDGF**
- **aAng2**

**Spät: Trockene AMD**

50%

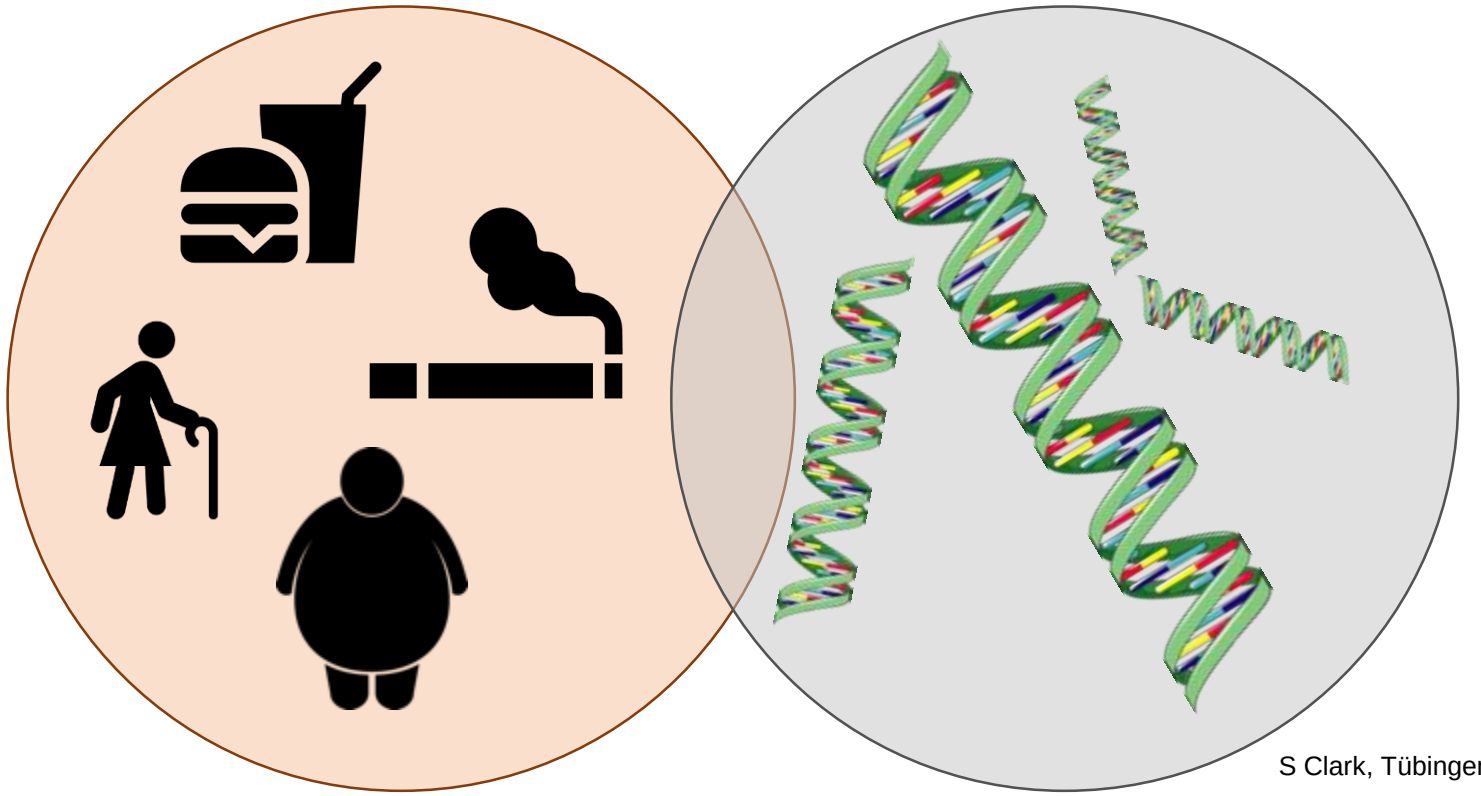


**IVOM?**
- **aC3**
- **aC5**

Quelle: B Junker, A Pielen

# Risikofaktoren AMD – multifaktorielle Erkrankung

Umwelt

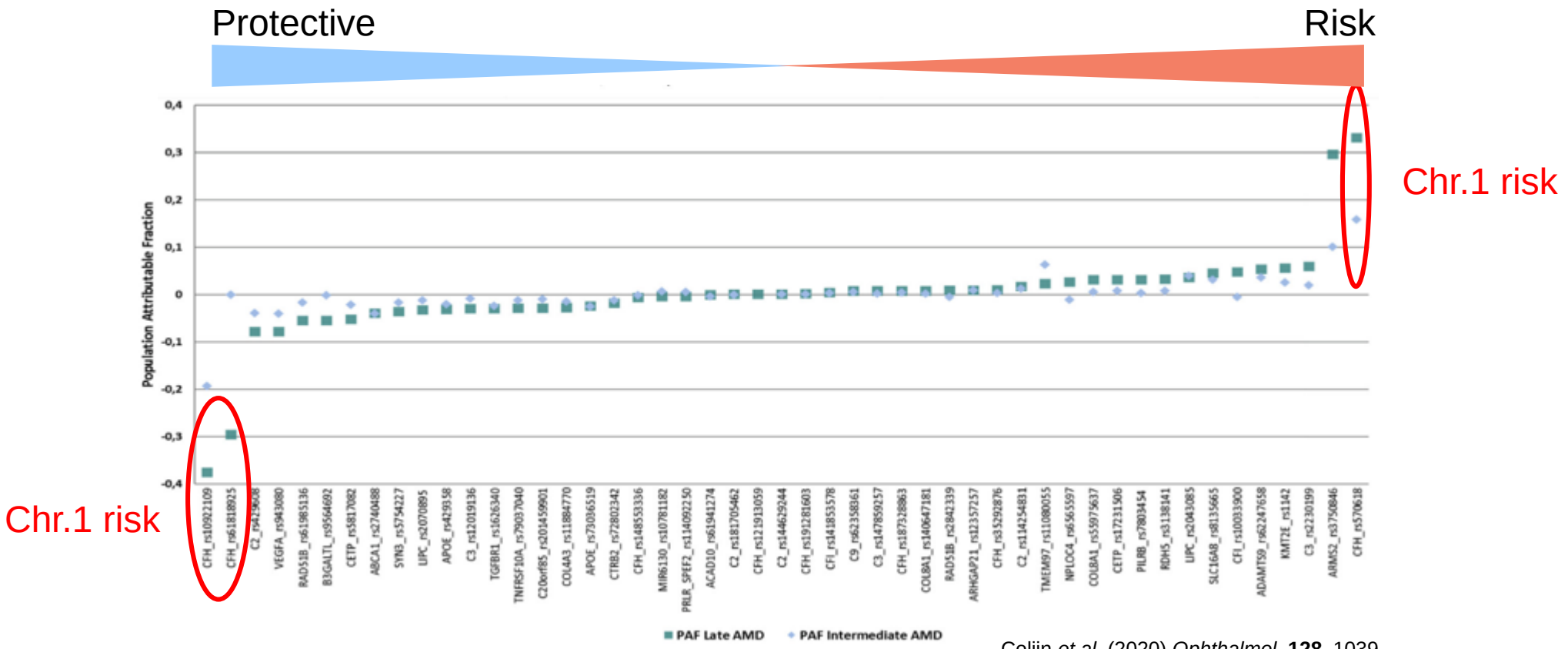


Genetik

S Clark, Tübingen

Unterschiedliche Faktoren verursachen individuelles Krankheitsbild
Therapeutika adressieren bislang je nur 1 von sehr vielen Aspekten

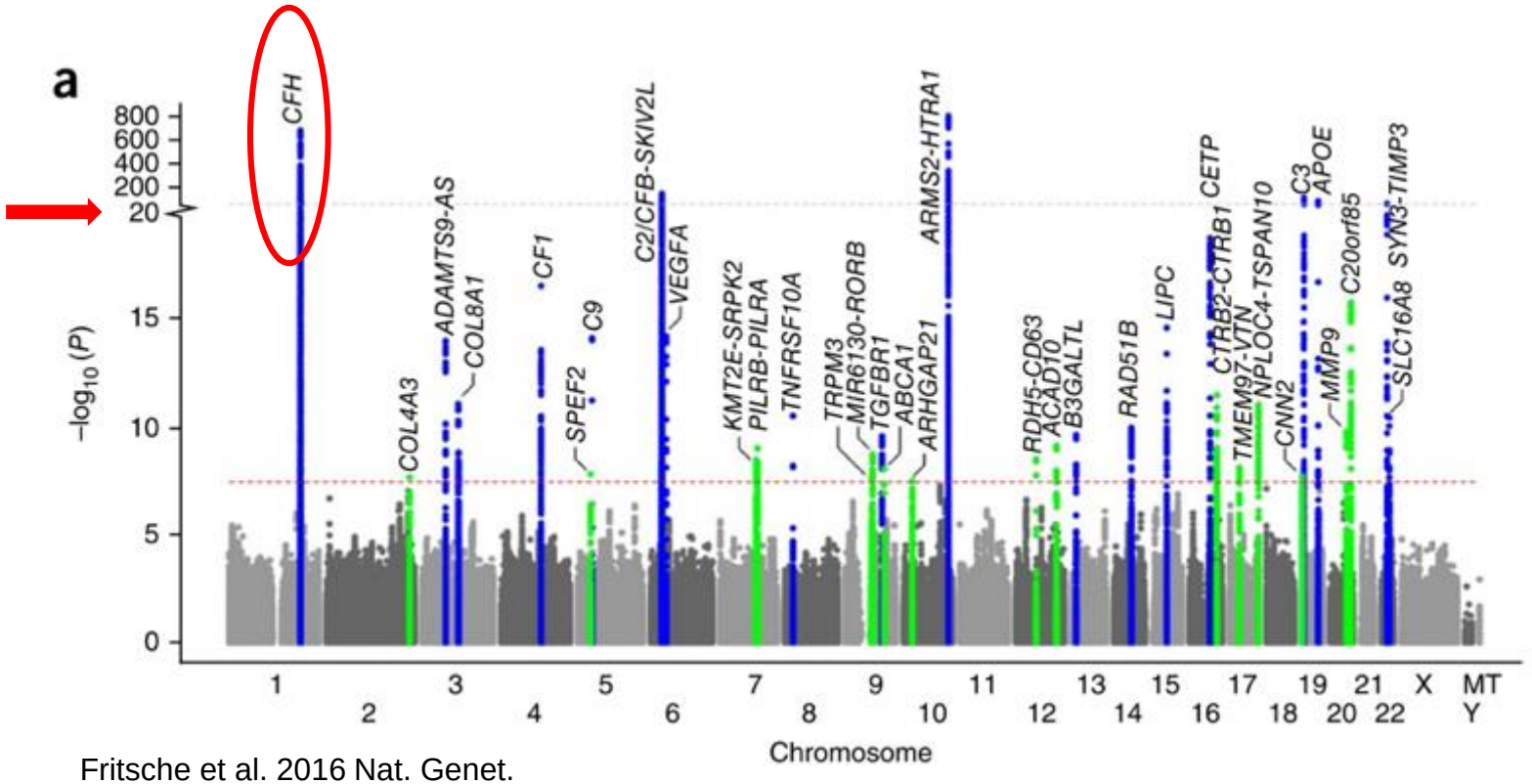
# Risikofaktoren AMD - Genetik




Colijn *et al*. (2020) *Ophthalmol*. **128**, 1039

Beispiel: Diskussion um Chr. 1 und Chr. 10 – 2 unabhängige Loci mit genetischem Risiko für AMD – offene Frage: unterschiedliche Erkrankungen?

# Risikofaktoren AMD – Genetik




Fritsche et al. 2016 Nat. Genet.

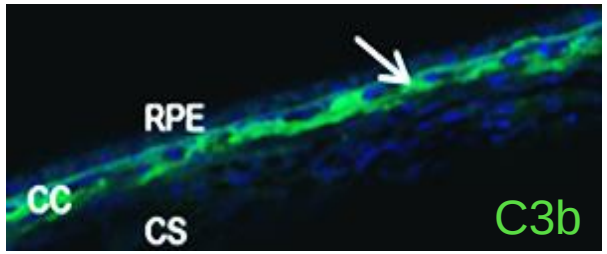
***CFH***

- Assoziiert mit exzessivem Turnover von Komplement im Auge

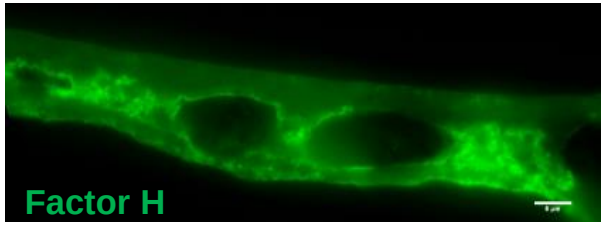
# Komplement in AMD

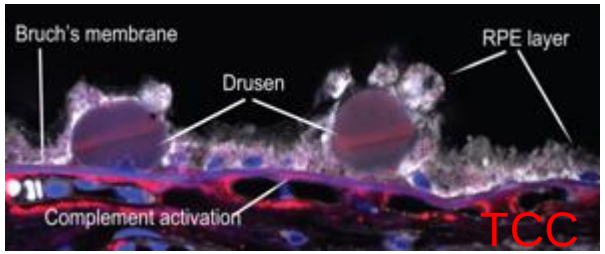
Complement Aktivierung:

Extracelluläre Matrix der Choriocapillaris

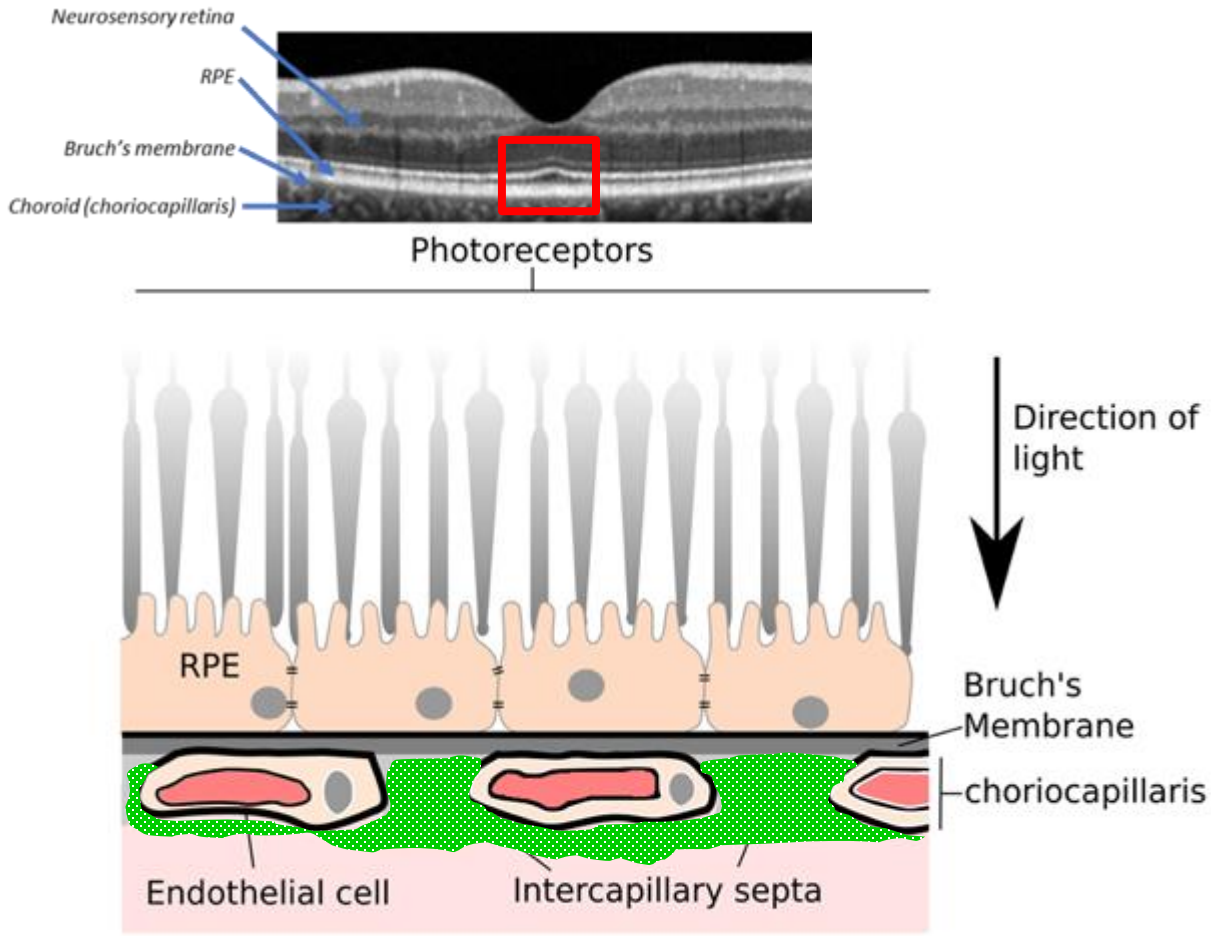



Keenan *et al*. (2015) *IOVS.* **56**, 4870



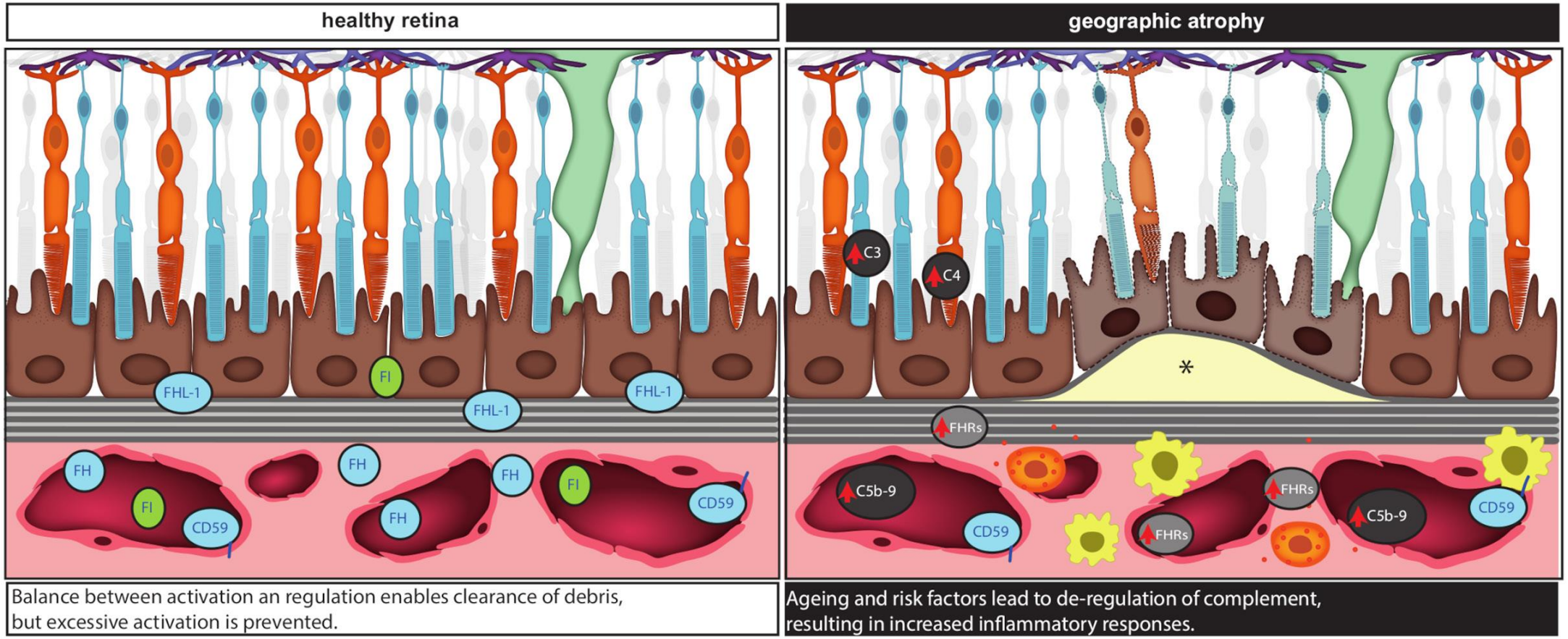




Forest *et al*. (2015) *Dis. Model Mech.* **8**, 421




*Complement activation*

# Komplement in AMD – gut und schlecht



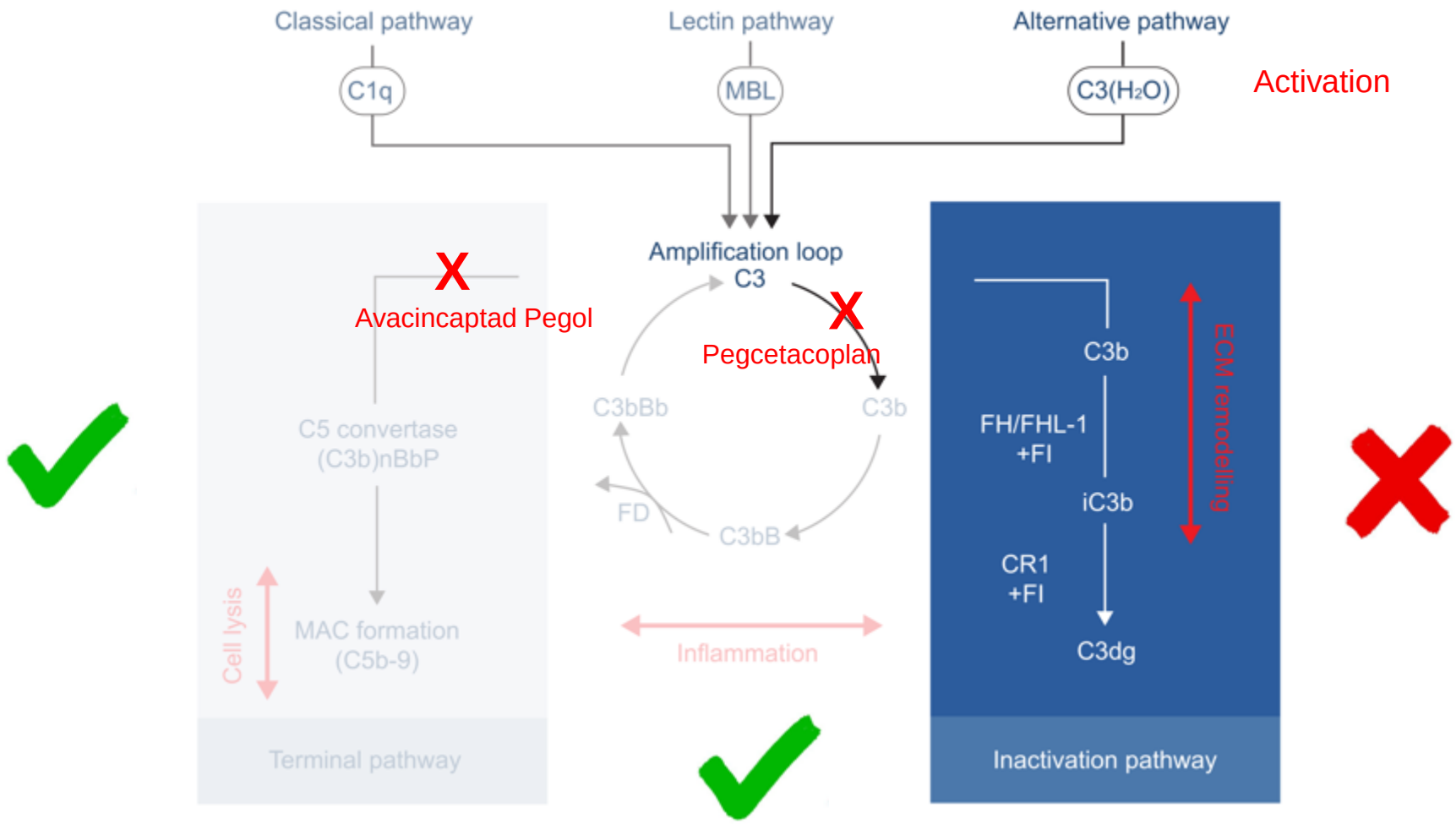

Gesund: Balance, Aufräumen

Krank: Altern, Ungleichgewicht, Entzündung

de Jong S, Tang J, Clark SJ. 2023 *Immunol. Rev.* **313**, 1

Maximilians-Augenklinik

# Komplementsystem und AMD



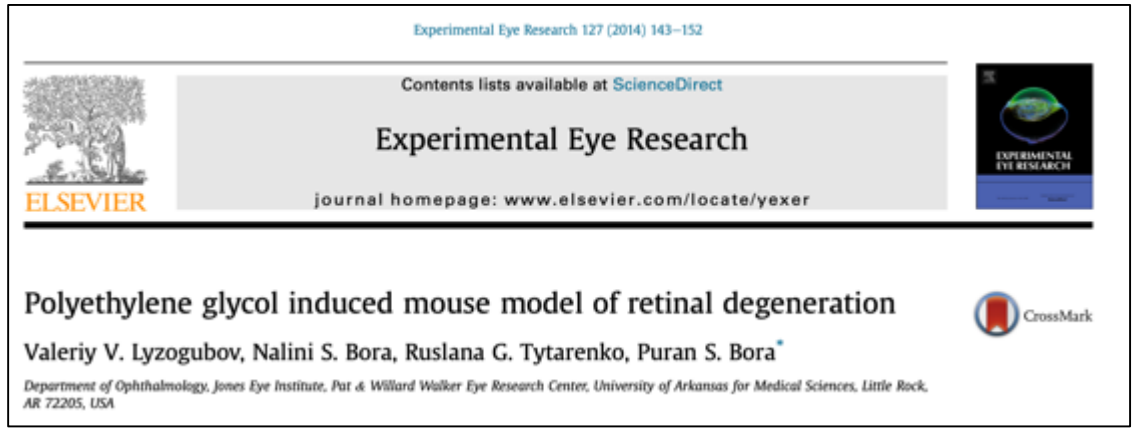

de Jong S, Tang J, Clark SJ. 2023 *Immunol. Rev.* **313**, 1

Maximilians-Augenklinik

# Komplementinhibition in der Klinik – Erkenntnisse

- Pegceptacoplan und Avacincaptad Pegol sind von der FDA zugelassen. Die klinischen Studien zeigen, dass Komplement als Target positive Effekte bei GA/ AMD haben kann

- Limited efficacy:
  - Nur ~20% Verlangsamung der GA Progression
  - Keine Wiederherstellung des Sehens
  - Negatives Votum der EMA


Experimental Eye Research 127 (2014) 143–152

Contents lists available at ScienceDirect

Experimental Eye Research

journal homepage: www.elsevier.com/locate/yexer

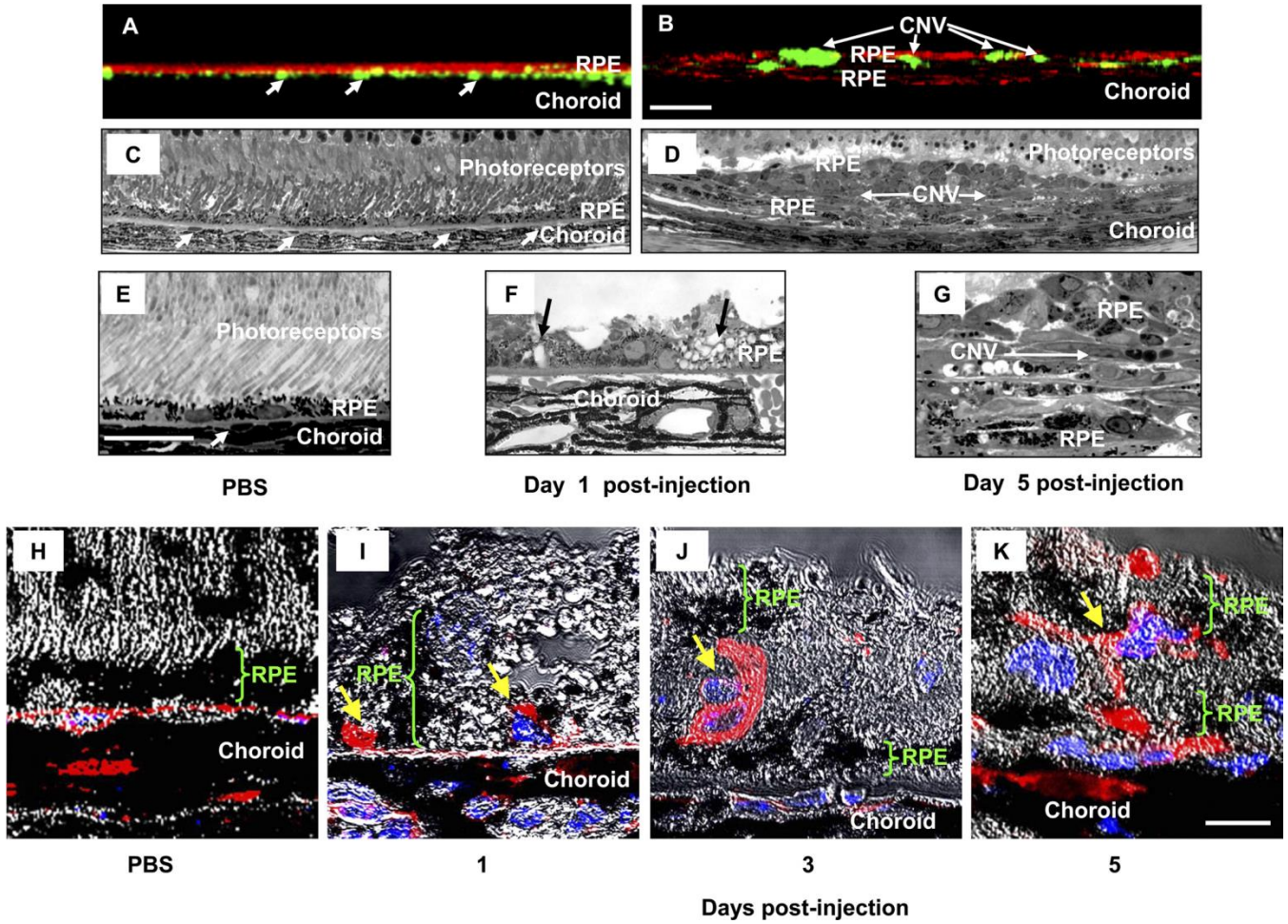
Polyethylene glycol induced mouse model of retinal degeneration

Valeriy V. Lyzogubov, Nalini S. Bora, Ruslana G. Tytarenko, Puran S. Bora*

*Department of Ophthalmology, Jones Eye Institute, Pat & Willard Walker Eye Research Center, University of Arkansas for Medical Sciences, Little Rock, AR 72205, USA*

- Unerwünschte Effekte:
  - ~ 10% Konversionsrate zu MNV/ nAMD
  - Möglicher Zusammenhang: Pegylierung der Medikamente – Methode für CNV im Tiermodell

# PEG-induced Mouse Model of CNV




Lyzogubov et al. 2011 *J biological Chemistry.* **286(18),** 16229-37

Maximilians-Augenklinik

# Release Details

## Apellis Announces Pegcetacoplan MAA Review Has Been Reset to Day 180 of Initial Assessment by European Medicines Agency (EMA)

April 26, 2024

- *Decision by EMA follows recent judgment by the Court of Justice of the European Union regarding the organization of EMA's expert groups*
- *Apellis anticipates a CHMP opinion no later than July 2024*

WALTHAM, Mass., April 26, 2024 (GLOBE NEWSWIRE) -- Apellis Pharmaceuticals, Inc. (Nasdaq: APLS) today announced that the European Medicines Agency (EMA) has reset the review of the marketing authorization application (MAA) for intravitreal pegcetacoplan for geographic atrophy to the last phase of the initial assessment (day 180). The procedure is expected to be led by the original rapporteurs, and EMA has stated their intent to convene a new expert group meeting. Apellis anticipates an opinion from the Committee for Medicinal Products for Human Use (CHMP) no later than July 2024.

# Therapieansätze zur Modulation von Komplement

TABLE 1 List of complement-targeting therapeutics directed against AMD

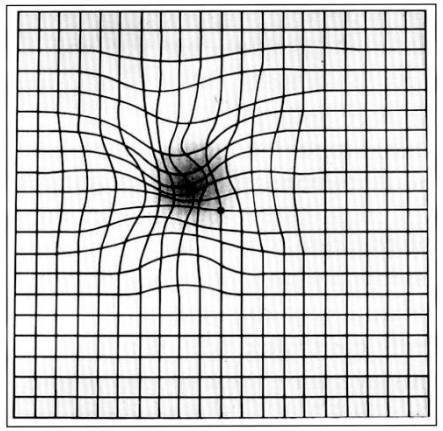
| Therapeutic candidate | Drug Type | Delivery methodology | Complement focus | Company | Sub-type of AMD | Clinical trial |
|---|---|---|---|---|---|---|
| *IONIS-FB-LRx* | siRNA | Subcutaneous injection | FB | Ionis Pharmaceuticals | Dry | NCT03815825<br>Phase II |
| *Iptacopan (LNP023)* | Small molecule | Oral | | Novartis | Early-Intermediate | NCT05230537<br>Phase II |
| *GT005* | AAV gene therapy | Single sub-retinal injection | FI | Gyroscope Therapeutics | Dry | NCT04437368<br>Phase II |
| *Danicopan* | Small molecule | Oral | FD | Alexion Pharmaceuticals | Dry | NCT05019521<br>Phase II |
| *AAVCAGsCD CD59* | AAV gene therapy | Single Intravitreal injection | CD59 | Janssen Research & Development | Wet | NCT03585556<br>Phase I |
| *VOY-101* | Biologic[a] | Single Intravitreal injection | *Undisclosed* | Perceive Biotherapeutics | Dry | NCT05380492<br>Phase I |
| Previously completed/terminated/withdrawn trials | | | | | | |
| *Zimura* (ARC1905) | Aptamer-based inhibitor | Monthly Intravitreal injection | C5 | IVERIC bio. | Wet | NCT03362190[b]<br>Phase II |
| *CLG561 (in combination with LFG316)* | Monoclonal antibody | Monthly Intravitreal injection | Properdin | Alcon/Novartis | Dry | NCT02515942[b]<br>Phase II |
| *Lampalizumab (FCD4514S)* | Antibody Fab fragment | Monthly Intravitreal injection | Factor D | Genentech/Roche | Dry | NCT02247479[c]<br>NCT02745119[c]<br>NCT02247531[c]<br>Phase III |
| *AAVCAGsCD CD59* | AAV gene therapy | Single Intravitreal injection | CD59 | Hemera Biosciences | Dry | NCT04358471[d]<br>Phase II |
| *GEM103* | Biologic—pure protien | Monthly Intravitreal injection | FH | Gemini Therapeutics | Dry | NCT04643886[e]<br>Phase II |

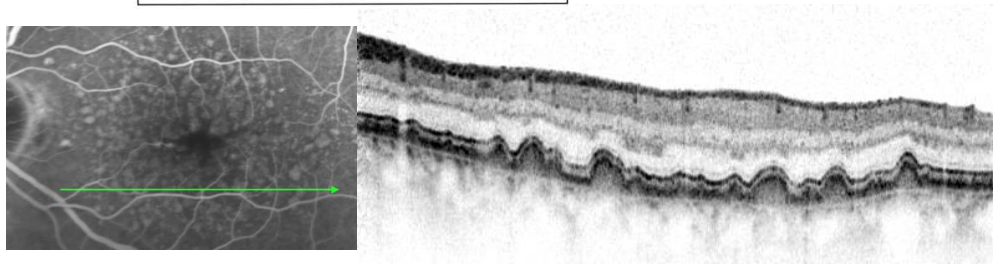
[a]Undisclosed nature of "Biologic".
[b]Completed, with results.
[c]Terminated, with results.
[d]Withdrawn, no results (withdrawn after transfer to Janssen Research and Development).
[e]Terminated, no results.

de Jong *et al* (2023) *Immun. Reviews* **313**, 1

- Breites Spektrum:
  - Subkutan (siRNA)
  - IVOM
  - Gentherapie
  - Nicht-pegylierte Moleküle
  - ….

# Fazit – AMD – Atrophie





**Früh: Trockene AMD**

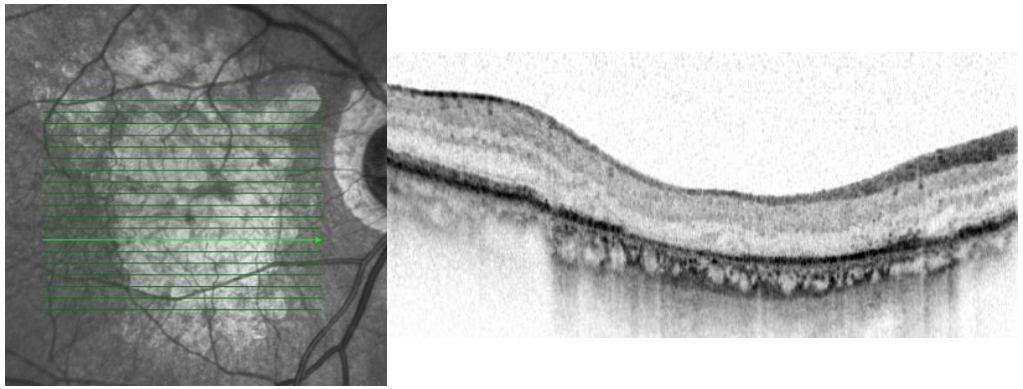
50%

**Spät: Feuchte AMD**

**IVOM**
- **aVEGF**
- **aPDGF**
- **aAng2**

50%

**Spät: Trockene AMD**



**IVOM?**
- **aC3**
- **aC5**
- **…**

Quelle: B Junker, A Pielen

Maximilians-
Augenklinik

Menschlich.
Miteinander.
Modern.


*Vielen Dank!*

Prof. Dr. med. Amelie Pielen
Erlenstegenstraße 30
90491 Nürnberg
Tel.: 0911 - 91 994 - 0
**E-Mail: pielen@maxiklinik.de**
**www.maximilians-augenklinik.de**

Maximilians-
Augenklinik