

Retinal Penetration and Distribution of Avastin (Bevacizumab) Following Intravitreal Injection

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Informatics**

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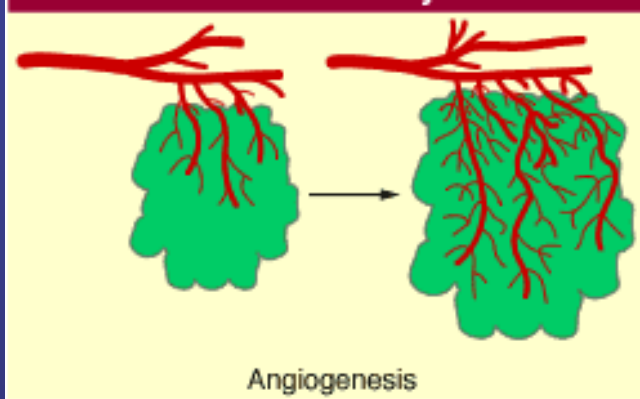


Avastin - Background

- Avastin is a relatively new drug used to treat specific cancers due to its anti-angiogenic properties.
- Recently, Avastin has been shown to be effective in treating the new vessel growth that is the cause of the devastating effects of age-related macular degeneration.



Angiogenesis and Cancer



- VEGF is the protein produced by tumors that stimulates vessel growth.

How **Avastin** Starves a Tumor

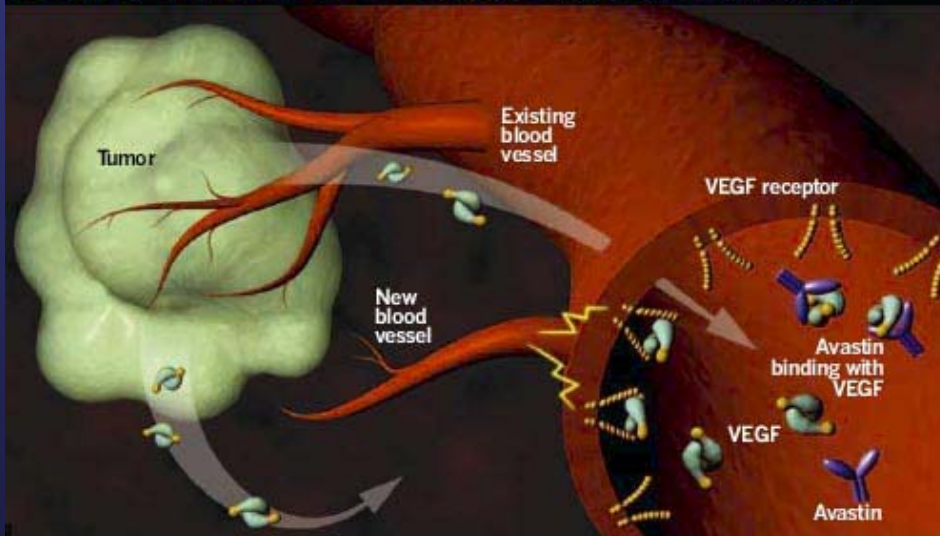
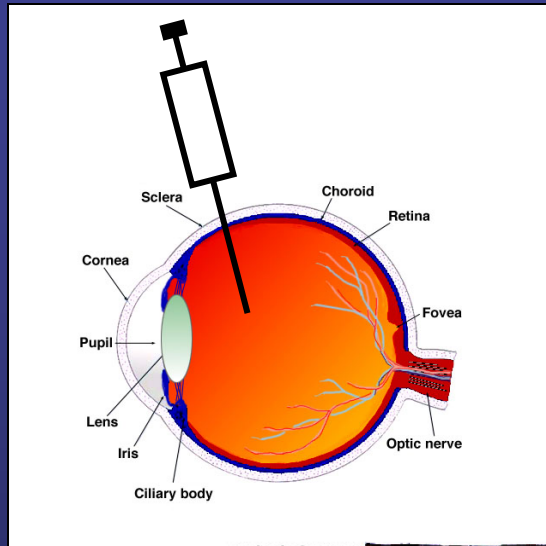


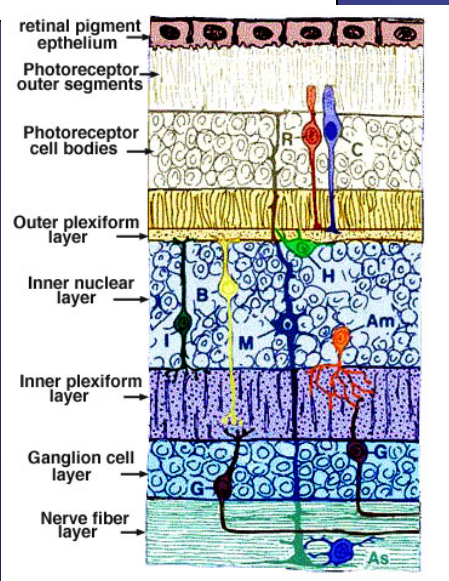
Image courtesy of Genentech

- By binding to VEGF, Avastin prevents the protein from binding to cells, thereby inhibiting new vessel growth in macular degeneration.

Experimental Method in Evaluating Avastin

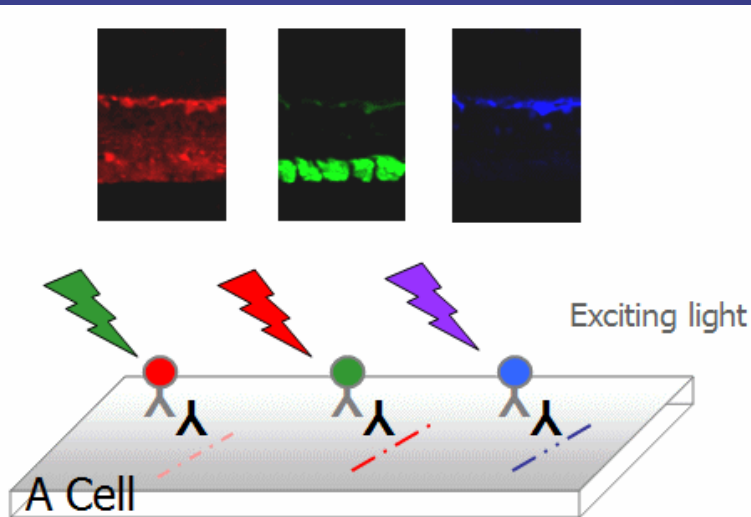


- Ten rabbits were injected intravitreally with 0.1 mL of Avastin in the right eye and with 0.1 mL of phosphate buffered saline (PBS) in the left eye (control).



- The eyes were fixed and processed for immunocytochemistry at 24 hours, 7 days, and 28 days post-injections.

Immunocytochemistry

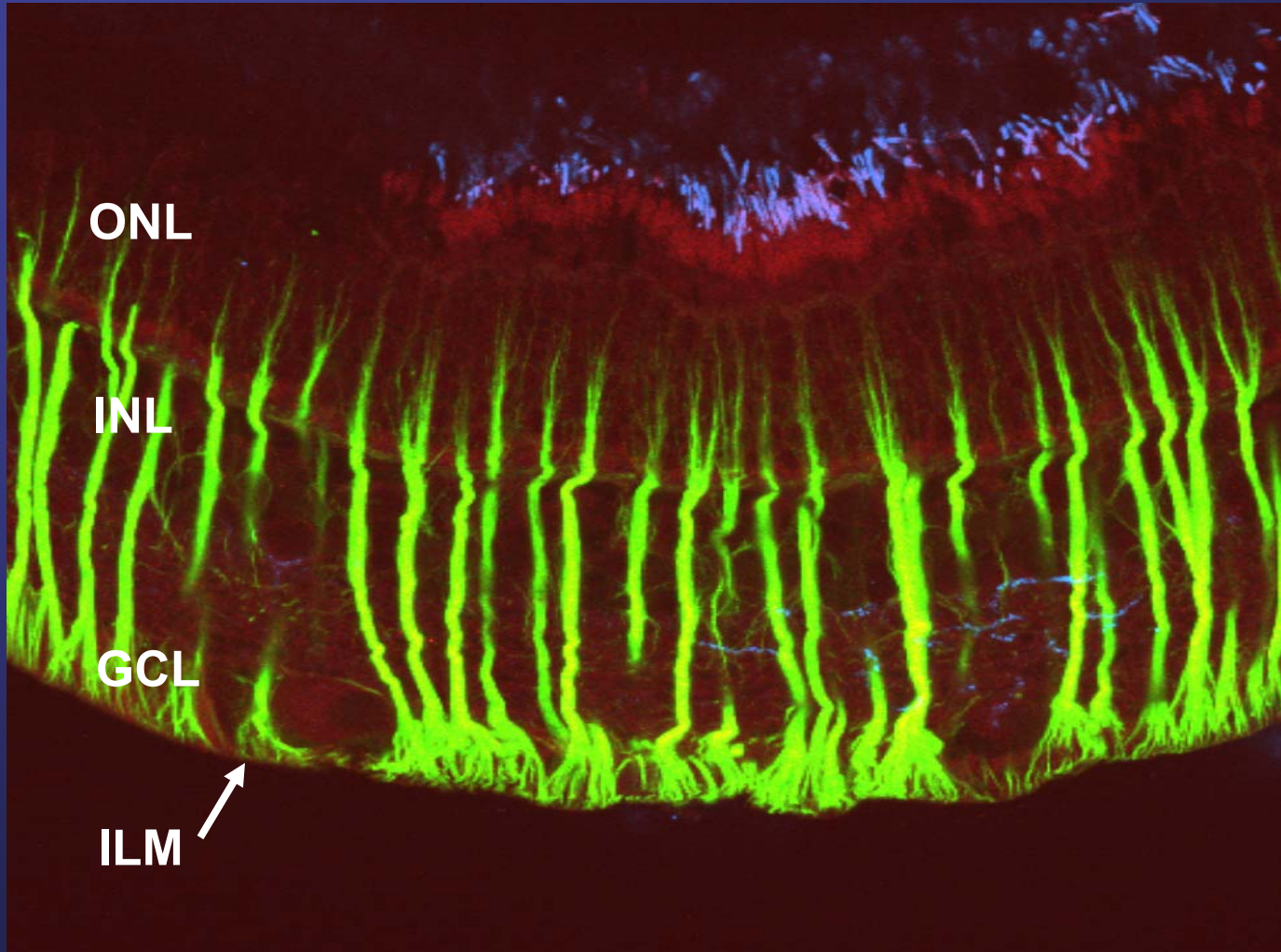


- Retinal sections of 100 μm thickness were triple labeled with antibodies to the humanized Avastin IgG (red), vimentin (Müller cells, green), and isolectin B4 (microglia cells, blue).

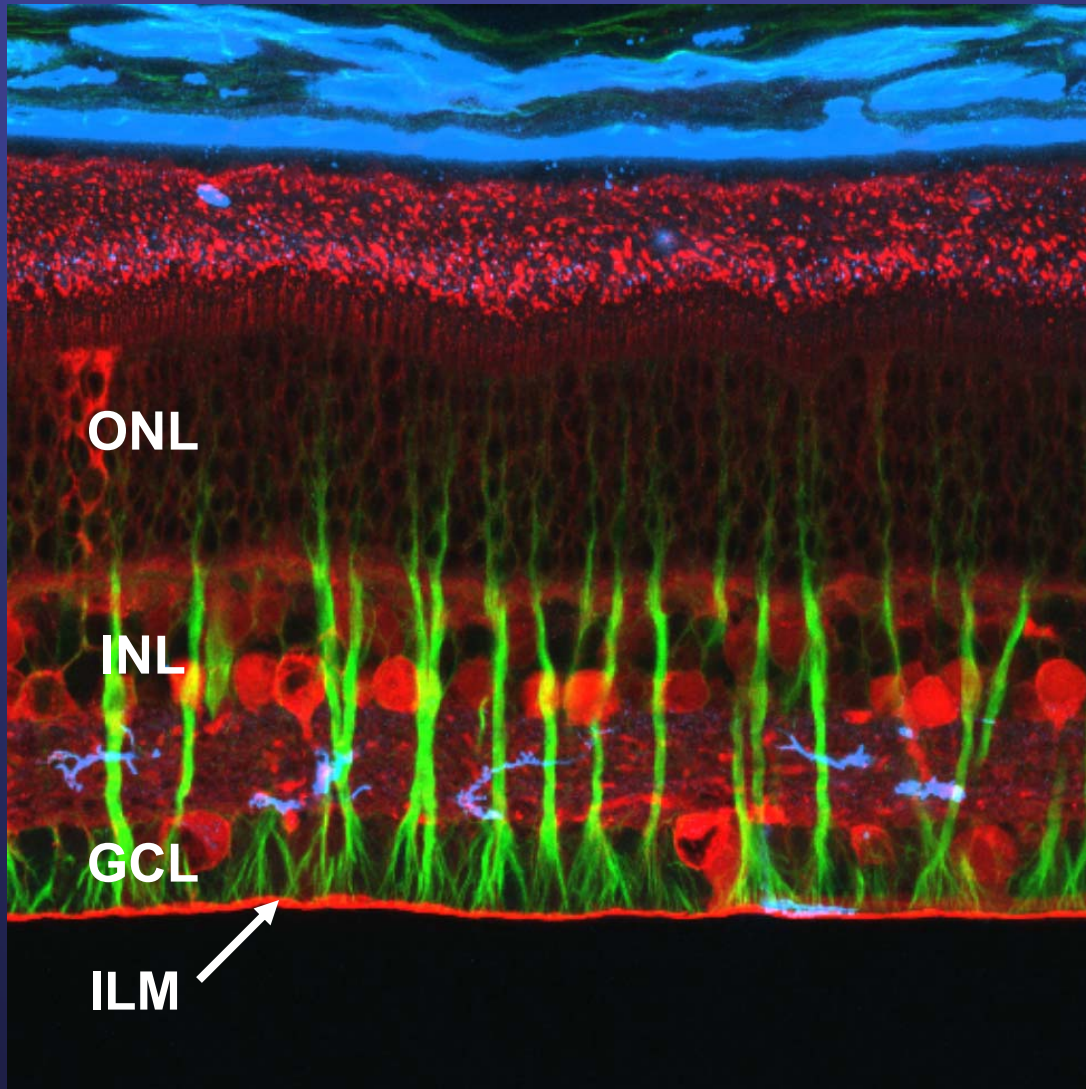


- Application of light excites the fluorochrome, causing the tissue to emit fluorescence.
- The sections were then viewed using a laser scanning confocal microscope.

Normal Retinal Morphology

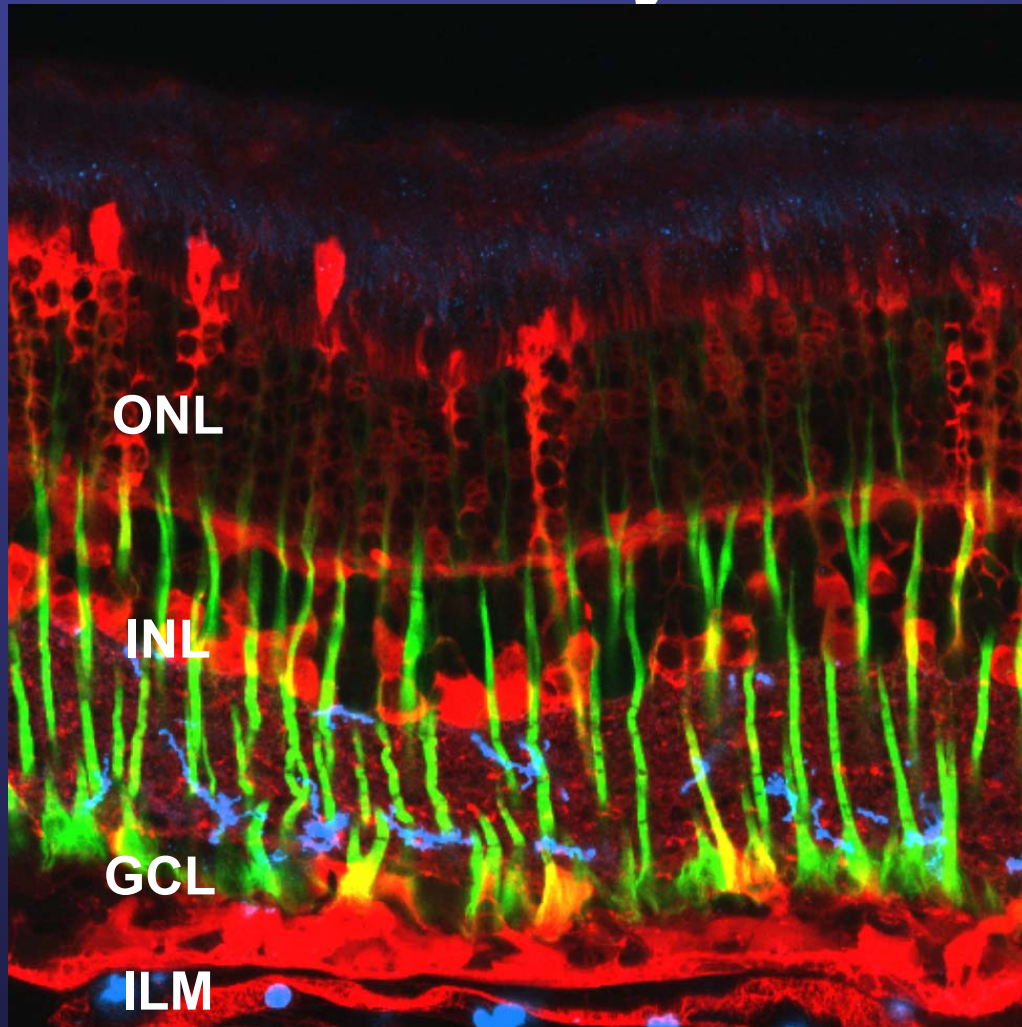


24 Hours Post-Injection



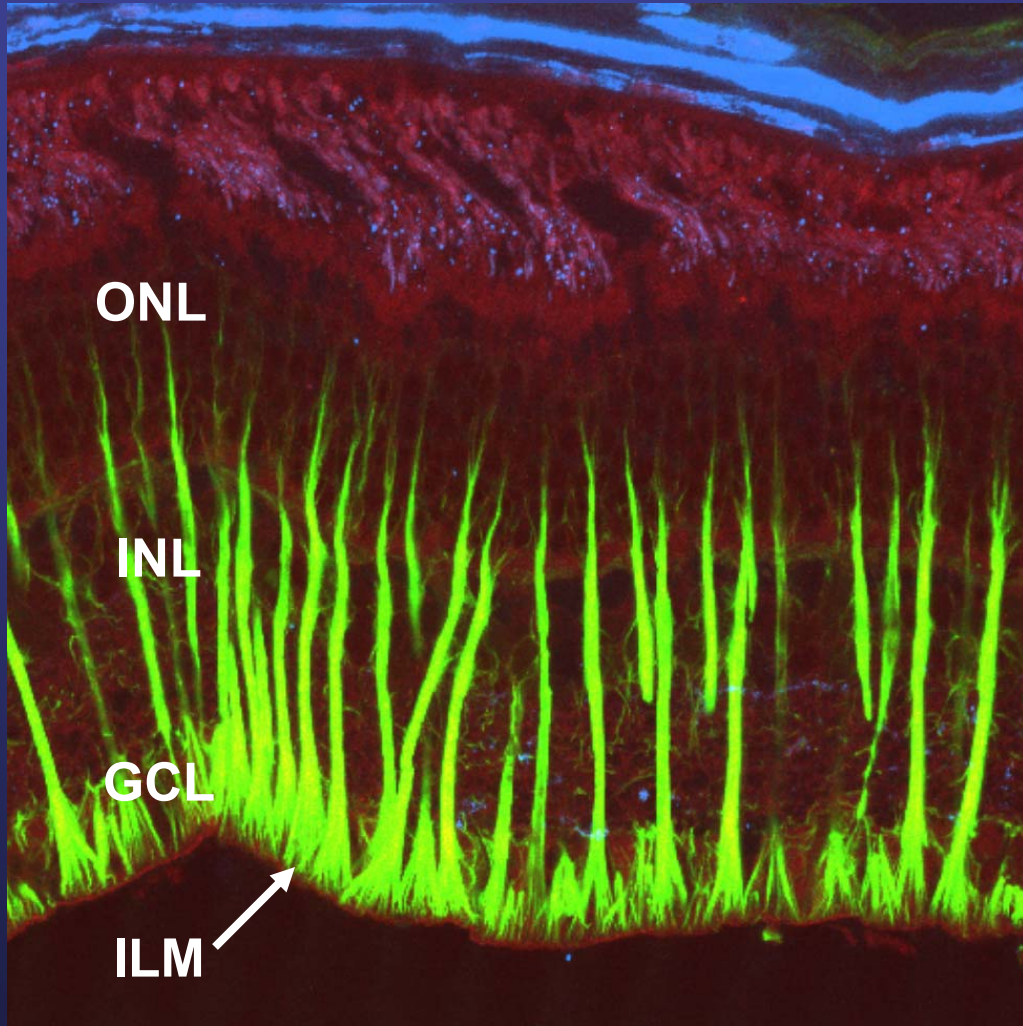
- Avastin (red) penetrated the entire width of the retina

7 Days Post-Injection



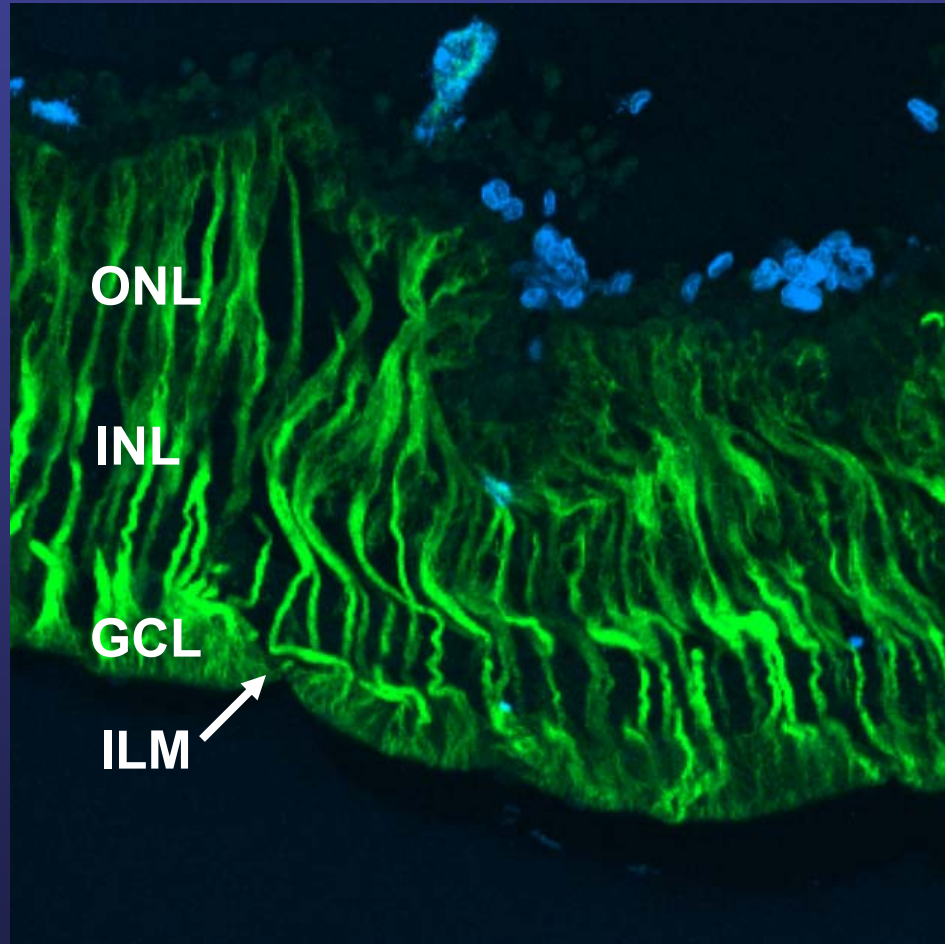
- Avastin labeling can still be seen at high levels throughout the retinal layers.
- Increased intensity of Avastin labeling is evident in the Müller cells.

28 Days Post-Injection

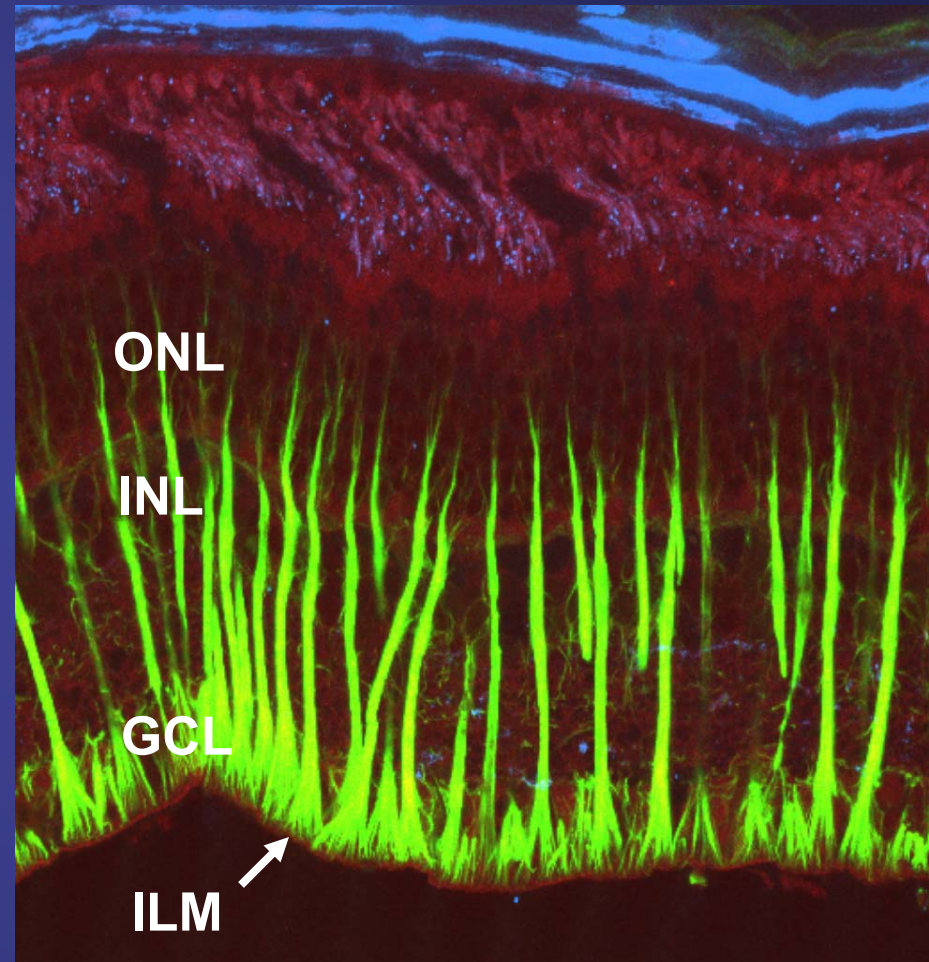


- Using increased gain settings, only slight ILM labeling of Avastin could be seen.

Comparison of Müller Cells and Microglia



Activated retina without Avastin
(3 day post retinal detachment)



Non-activated retina after Avastin
(28 days post-injection)

Summary and Conclusions

- Avastin is distributed across the retina within 24 hours.
- Avastin is taken up by specific cell types.
- It quickly reaches the region of new vessel growth in age-related macular degeneration.
- Neither Müller cells nor microglia became reactive as a result of the injected Avastin.
- Speculation: Avastin may be transported throughout the retina by the Müller cells.

Future Directions



- The dose of Avastin used in this study was twofold greater than that used in treating humans with eye disease.
- Further studies are being undertaken to evaluate the bioactivity of smaller doses, comparable to those used in a clinical setting.

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