

A novel ferrochelatase inhibitor as a therapy for ocular neovascularization

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Background and Hypothesis:

Ocular neovascularization, characterized by the abnormal growth of new blood vessels, underlies blindness-inducing diseases such as wet age-related macular degeneration (AMD) and proliferative diabetic retinopathy (PDR). This neovascularization can be either choroidal (in the case of wet AMD) or retinal (in the case of PDR).

Inhibition of vascular endothelial growth factor is the target of current FDA approved therapies, however the need for intravitreal injections poses a drawback to such treatments. Furthermore, many patients are non-responders or refractory. Given this, the discovery of novel therapeutic targets is warranted.

Ferrochelatase (FECH) is an enzyme involved in heme synthesis. The Corson lab has previously shown FECH to be necessary for angiogenesis both in vitro and in vivo. The Corson lab has been successful in developing novel compounds that inhibit FECH in vitro, based on high-throughput screening hits. The objective of this project was to test one such novel FECH inhibitor in a choroidal neovascularization mouse model.

Experimental Design:

FECH inhibition was investigated in the laser-induced choroidal neovascularization model. This model involved creating a laser-induced lesion into the retinal pigment epithelium/choroid of mice aged 6-8 weeks; this promotes neovascularization. The FECH inhibitor compound was delivered once intravitreally at the time of the laser. Neovascularization was analyzed in vivo using optical coherence tomography and fluorescein angiography one and two weeks after laser, then quantified ex vivo by isolectin staining.

Results:

There was a trend toward decreased ocular neovascularization with the administration of a FECH inhibitor, as measured by optical coherence tomography seven days after laser treatment. However, further analyses are ongoing to validate this finding.

Conclusion and Potential Impact:

The administration of a FECH inhibitor compound intravitreally may result in a decrease in CNV. This may be useful as it could lead to FECH serving as a target for future therapies.