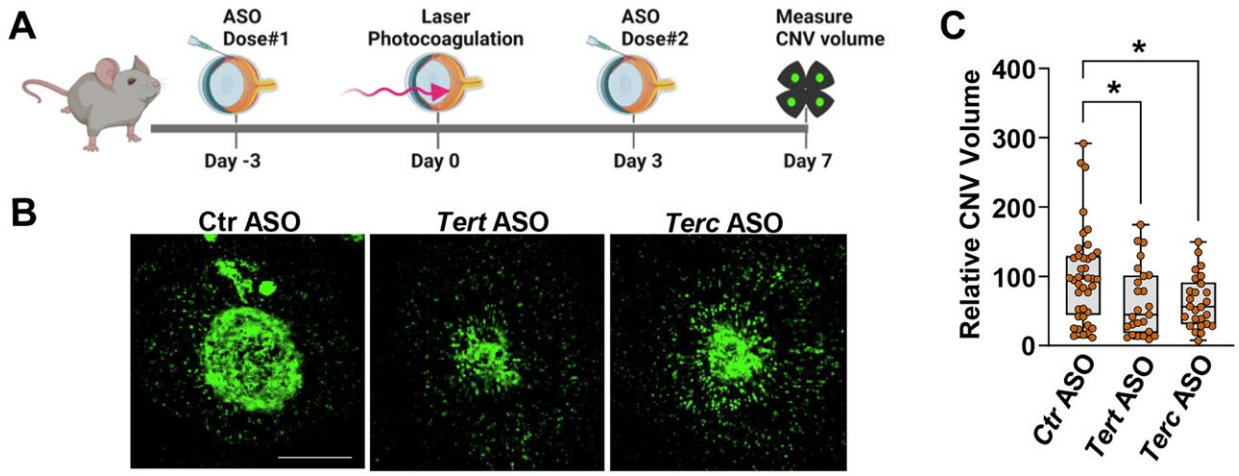
A new target for treatment of one type of macular degeneration

July 2 2024, by Emily Caldwell



Tert and Terc specific antisense oligonucleotides (ASOs) suppress CNV growth. A) Schematic representation of the ASO treatment in laser-induced CNV mouse model. B) Representative confocal images of FITC- isolectin B4 stained RPE/choroid/scleral flatmount showing CNV lesion C) Quantification of CNV volume. Credit: *Biochimica et Biophysica Acta (BBA)—Molecular Basis of Disease* (2024). DOI: 10.1016/j.bbadis.2024.167156

A new study in mice hints at the promise of an eventual alternative treatment option for the "wet" version of age-related macular degeneration (AMD).

Researchers determined in mice that an enzyme related to cell growth

and division is a culprit in the blood vessel invasion in the back of the eye that causes blurred central vision in wet AMD. Targeting the enzyme, called telomerase, with an experimental drug suppressed abnormal vascular growth in the animals' retina.

The only current treatment for wet AMD is injection into the eye of a medication that blocks the activity of a growth factor protein, called VEGF, which is also known to prompt formation of abnormal blood vessel growth in this condition.

"Anti-VEGF treatment has shortcomings—after two years, about half of people stop responding. And patients can develop scarring under the retina," said senior study author Nagaraj Kerur, associate professor of ophthalmology and visual sciences in The Ohio State University College of Medicine.

"There is a need for better understanding of the mechanisms behind this problem, which, to me, means newer targets need to be tested."

The study was published recently in the journal *Biochimica et Biophysica Acta (BBA)—Molecular Basis of Disease*.

Dry age-related macular degeneration constitutes about 80% of all AMD cases, and occurs when the macula, a part of the retina, gets thinner, leading to buildup of proteins and cell death, which blur a person's central vision.

Wet AMD, also known as neovascular AMD, is caused by the growth of new blood vessels that invade the retina, a space normally free of vascular activity.

"You don't want to have blood vessels there," said Kerur, who also has a faculty appointment in microbial infection and immunity at Ohio State.

"And the blood vessels that invade are often not healthy—they leak their contents and cause inflammation."

Previous cancer research has linked high activity of telomerase to rapid production and migration of cells lining blood vessels that enables tumor growth, and has also shown the enzyme can stimulate production of VEGF. Based on those findings, Kerur and colleagues sought in this study to see if telomerase could have a similar damaging effect in the eye.

A series of experiments first confirmed telomerase has a role in abnormal blood vessel formation in a mouse model of wet AMD. Researchers found that, compared to control mice, expression and activity of one of two genes carrying instructions for making telomerase were higher in the eyes of mice in which rapid growth of new blood vessels was induced with a laser.

In addition, the abnormal blood vessel response to laser injury was significantly lower in mice lacking both telomerase genes, "providing genetically clear evidence that telomerase plays a critical role in development of the disease," Kerur said.

The team then tested the effects of an experimental compound that inhibits telomerase activity. They confirmed that the drug lowered telomerase activity in healthy mice, and found that injecting it into the eyes of mice with symptoms mimicking wet AMD significantly reduced the abnormal blood vessel invasion.

Telomerase's job is to rebuild telomeres, which function as protective caps at the end of chromosomes. Telomeres are known to shorten in many types of cells as a consequence of aging, but Kerur said the study suggested localized blocking of telomerase in the eye had no bearing on the enzyme's telomere-building function.

The experimental treatment's effectiveness at curbing abnormal blood vessel growth in mice was similar to the current anti-VEGF treatment, Kerur said. But the researchers made an intriguing finding when testing both drugs at lower doses: Individually, a lower dose did not have much of a therapeutic effect, but a combination of both drugs at lower doses gave the best results of all.

"Possibly, one goal would be using a combination therapy rather than one alone," Kerur said. "But telomerase inhibition by itself can also be pursued independently, and that is the plan."

More information: Aman Kumar et al, Therapeutic targeting of telomerase ameliorates experimental choroidal neovascularization, *Biochimica et Biophysica Acta (BBA)—Molecular Basis of Disease* (2024). DOI: 10.1016/j.bbadis.2024.167156

Provided by The Ohio State University

Citation: A new target for treatment of one type of macular degeneration (2024, July 2) retrieved 2 July 2024 from https://medicalxpress.com/news/2024-07-treatment-macular-degeneration.html

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.