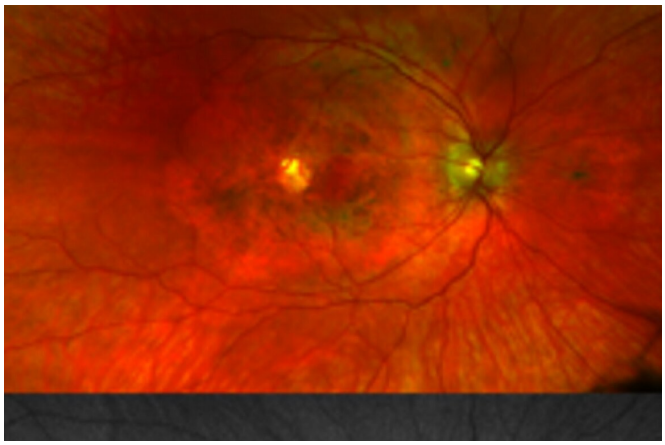
Researchers discover new genetic eye disease

9 June 2022



Retinal images of a patient with a TIMP3 mutation causing atypical symptoms. While there is visible damage in the retina (dark circles), there is no CNV present. Credit: NEI

Researchers from the National Eye Institute (NEI) have identified a new disease that affects the macula, a small part of the light-sensing retina needed for sharp, central vision. Scientists report their findings on the novel macular dystrophy, which is yet to be named, in *JAMA Ophthalmology*.

Macular dystrophies are disorders that usually cause central visual loss because of mutations in several genes, including ABCA4, BEST1, PRPH2, and TIMP3.

For example, patients with Sorsby Fundus Dystrophy, a genetic eye disease specifically linked to TIMP3 variants, usually develop symptoms in adulthood. They often have sudden changes in visual acuity due to choroidal neovascularization– new, abnormal blood vessels that grow under the retina, leaking fluid and affecting vision.

TIMP3 is a protein that helps regulate retinal blood flow and is secreted from the retinal pigment epithelium (RPE), a layer of tissue that nourishes and supports the retina's light-sensing photoreceptors. All TIMP3 gene mutations reported are in the mature protein after it has been "cut" from RPE cells in a process called cleavage.

"We found it surprising that two patients had TIMP3 variants not in the mature protein, but in the short signal sequence the gene uses to 'cut' the protein from the cells. We showed these variants prevent cleavage, causing the protein to be stuck in the cell, likely leading to retinal pigment epithelium toxicity," said Bin Guan, Ph.D., lead author.

The research team followed these findings with clinical evaluations and genetic testing of family members to verify that the two new TIMP3 variants are connected to this atypical maculopathy.

"Affected individuals had scotomas, or blind spots, and changes in their maculas indicative of disease, but, for now, they have preserved central vision and no choroidal neovascularization, unlike typical Sorsby Fundus Dystrophy", said Cathy Cukras, M.D., Ph.D., a Lasker tenure-track investigator and medical retina specialist who clinically evaluated the patients.

NEI's Ophthalmic Genomics Laboratory gathers and manages specimens and diagnostic data from patients who have been recruited into multiple studies within the NEI clinical program to facilitate research of rare eye diseases, including Sorsby Fundus Dystrophy.

"Discovering novel disease mechanisms, even in known genes like TIMP3, may help patients that have been looking for the correct diagnosis, and will hopefully lead to new therapies for them," said Rob Hufnagel, M.D., Ph.D., senior author and director of the Ophthalmic Genomics Laboratory at NEI.

More information: Bin Guan et al, Early-onset TIMP3-related retinopathy associated with impaired signal peptide. *JAMA Ophthalmology* (2022). DOI: 10.1001/jamaophthalmol.2022.1822

Provided by National Institutes of Health

APA citation: Researchers discover new genetic eye disease (2022, June 9) retrieved 12 June 2022 from https://medicalxpress.com/news/2022-06-genetic-eye-disease.html