Biomarkers reveal how patients with glaucoma may respond to treatment

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Mitochondrial respiration in PBMCs. Credit: Nature Medicine (2024). DOI: 10.1038/s41591-024-03068-6

Over 700,000 people in the UK have glaucoma and it is the leading cause of irreversible blindness worldwide. The condition occurs when the cells in the eye that help you see (called retinal ganglion cells) start to die.

The main risk factors for glaucoma are high eye pressure and older age.

Currently, all licensed treatments are designed to lower pressure in the
eye—also known as intraocular pressure. However, some patients still continue to lose their sight following treatment.

To help doctors better understand who will lose their vision faster, the new study, published in *Nature Medicine*, asked whether mitochondrial function, measured in white blood cells, is lower in people with glaucoma than those without glaucoma and if mitochondrial function is associated with the rate at which glaucoma patients lose vision.

Mitochondria are the "batteries" inside cells that produce energy for the cells to function. Cells in the eye use a lot of energy.

The researchers assessed 139 participants who were already receiving treatment to lower intraocular pressure and 50 healthy people acting as a control (comparison) group.

They measured how well cells in the blood use oxygen, how much vision was lost over time and nicotinamide adenine dinucleotide (NAD) levels.

NAD is a molecule in the body that helps cells produce energy and is made from vitamin B3 in the diet.

Firstly, the researchers discovered that certain cells in the blood, known as peripheral blood mononuclear cells, use oxygen differently in people with glaucoma.

The team measured how much oxygen these cells use and found that people whose blood cells used less oxygen tended to lose their vision faster, even if they were being treated to lower intraocular pressure. This measurement explained 13% of the differences in how fast patients lost vision.

Additionally, people with glaucoma were found to have lower levels of
NAD in their blood cells compared to people without glaucoma. These lower NAD levels were linked to the lower oxygen use in the blood cells.

Senior author, Professor David (Ted) Garway-Heath (UCL Institute of Ophthalmology and Moorfields Eye Hospital), said, "White blood cell mitochondrial function and NAD levels, if introduced as a clinical test, would enable clinicians to predict which patients are at higher risk of continued vision loss, allowing them to be prioritized for more intensive monitoring and treatment.

"If further research shows that low mitochondrial function or low NAD levels are a cause for glaucoma, then this opens the way for new treatments.

"UCL and Moorfields Eye Hospital are currently leading a major clinical trial funded by the Medical Research Council and the National Institute for Health and Care Research, to establish whether high-dose vitamin B3 can boost mitochondrial function and reduce vision loss in glaucoma.

"We hope that this will open a new avenue for treatment of glaucoma patients which does not depend on lowering the eye pressure."

**More information:** Bledi Petriti et al, Peripheral blood mononuclear cell respiratory function is associated with progressive glaucomatous vision loss, *Nature Medicine* (2024). [DOI: 10.1038/s41591-024-03068-6](https://doi.org/10.1038/s41591-024-03068-6)

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