

Vitamin B3 prevents glaucoma in laboratory mice

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Credit: Martha Sexton/public domain

In mice genetically predisposed to glaucoma, vitamin B3 added to drinking water is effective at preventing the disease, a research team led by Jackson Laboratory Professor and Howard Hughes Medical Investigator Simon W.M. John reports in the journal *Science*.

The vitamin administration was surprisingly effective, eliminating the vast majority of age-related molecular changes and providing a remarkably robust protection against [glaucoma](#). It offers promise for developing inexpensive and safe treatments for glaucoma patients.

Glaucoma is one of the most common neurodegenerative diseases, affecting an estimated 80 million people worldwide. In most glaucoma patients, harmfully high pressure inside the eye or intraocular pressure leads to the progressive dysfunction and loss of [retinal ganglion cells](#). Retinal ganglion cells are the neuronal cells that connect the eye to the brain via the optic nerve. Increasing age is a key risk factor for glaucoma, contributing to both harmful elevation of intraocular pressure and increased neuronal vulnerability to pressure-induced damage.

"We wanted to identify key age-related susceptibility factors that change with age in the eye," John says, "and that therefore increase vulnerability to disease and in particular neuronal disease." By understanding general age-related mechanism, there is the potential to develop new interventions to generally protect from common age-related disease processes in many people. Conducting a variety of genomic, metabolic, neurobiological and other tests in mice susceptible to inherited glaucoma, compared to control mice, the researchers discovered that NAD, a molecule vital to energy metabolism in neurons and other cells, declines with age.

"There's an analogy with an old motorbike," John says. "It runs just fine, but little things get less reliable with age. One day you stress it: you drive it up a steep hill or you go on really long journey and you get in trouble. It's less reliable than a new bike and it's going to fail with a higher frequency than that new bike."

The decrease in NAD levels reduces the reliability of neurons' [energy metabolism](#), especially under stress such as increased intraocular

pressure. "Like taking that big hill on your old bike, some things are going to fail more often," John says. "The amount of failure will increase over time, resulting in more damage and disease progression."

In essence, the treatments of vitamin B3 (nicotinamide, an amide form of vitamin B3, also called niacinamide) boosted the metabolic reliability of aging retinal ganglion cells, keeping them healthier for longer.

"Because these cells are still healthy, and still metabolically robust," says JAX Postdoctoral Associate Pete Williams, first author of the study, "even when high [intraocular pressure](#) turns on, they better resist damaging processes."

The researchers also found that a single gene-therapy application of *Nmnat1* (the gene for an enzyme that makes NAD from nicotinamide) prevented glaucoma from developing in this mouse model. "It can be a problem for patients, especially the elderly, to take their drugs every day and in the correct dose," Williams says. "So gene therapy could be a one-shot, protective treatment." He notes that gene therapies, through injections into the eye, have been approved for a handful of very rare, human genetic eye disorders, and their demonstration of an important age-dependent factor may enable gene therapy for more common eye disease.

John says that the team is pursuing clinical partnerships to begin the process of testing the effectiveness of vitamin B3 treatment in glaucoma patients. They are also exploring potential applications for the treatment in other diseases involving neurodegeneration.

More information: "Vitamin B3 modulates mitochondrial vulnerability and prevents glaucoma in aged mice," *Science*, [science.sciencemag.org/cgi/doi ... 1126/science.aal0092](https://science.sciencemag.org/cgi/doi/10.1126/science.aal0092)

Provided by Jackson Laboratory

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