

## Scientist working to break vicious cycle causing vision loss in diabetes

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it's a vicious cycle that robs people with diabetes of their vision.

The hallmark [high glucose](#) of the disease causes inflammation that produces [free radicals](#) that cause inflammation that produces more free radicals, explains Dr. Manuela Bartoli, vision scientist at the Medical College of Georgia at Georgia Regents University.

If that's not bad enough, the body's endogenous system for dealing with free radicals also is dramatically impacted by diabetes, said Bartoli, who recently received a \$1.8 million grant from the National Eye Institute to try to bolster that system and interrupt the destructive cycle.

Nearly 10 percent of the U.S. population has diabetes, according to the National Diabetes Foundation, and nearly half those individuals will develop [diabetic retinopathy](#), according to the National Eye Institute.

Culprit free radicals are actually normal byproducts of the body's constant use of oxygen and, despite their derivative status, also are important signaling molecules in the body. Problems result when there are too many, like in diabetes, and their natural tendency to bond starts [wreaking havoc](#) on cells and DNA. In fact, excessive levels are thought to be a major contributor to a wide variety of diseases as well as aging.

The thioredoxin system typically works to maintain a healthy level of free radicals by neutralizing excess but, like many body systems, the thioredoxin system slows with age and diabetes hastens the process.

"This increase in free radicals results in an inability to put them to good use," Bartoli said. "Instead, we accumulate the damage they induce." In the case of the eyes and diabetes, over time the overwhelmed system destroys blood vessels that deliver blood and nutrition. In another biological irony, the starving eyes grow new blood vessels but they are fragile, leaky and often misplaced so ultimately they destroy vision.

Bartoli believes a selenium supplement could give the thioredoxin system the shot in the arm needed to stay efficient and effective. Selenium is a byproduct itself, resulting from copper-refining and used to make glass, alloys and more. It is also found in fish, nuts and grains.

Thioredoxin reductase, a protein essential to the recycling of the system, is dependent on selenium and Bartoli has found that protein's activity is reduced in an animal model of diabetic retinopathy and in retinas of human diabetic donors. Bartoli believes the cascade of cellular change resulting from high glucose levels impairs thioredoxin reductase. So she wants to better understand how the system works, exactly what happens to thioredoxin reductase and whether supplements of selenium can help the natural antioxidant system work better in diabetes.

In a related study, funded by the International Retinal Research Foundation, she is looking for an early sign of eye damage and possibly another window of intervention.

Currently, swelling of the macula – the central part of the retina responsible for central vision – is the first sign of treatable trouble. Anti-inflammatories injected into the eyes can help.

However increased blood levels of uric acid, a part of the inflammatory process that leads to swelling, may be an earlier indicator, Bartoli said. Uric acid is a byproduct of purine metabolism and is typically eliminated in the urine. High uric [acid levels](#) are associated with cardiovascular

disease and gout as well as diabetes but it hasn't been well studied in the eye.

"We want to validate hyperuricemia as a risk factor for progression of diabetic retinopathy," she said. So she and her colleagues are measuring levels in the blood and eye fluid to see if they correlate with each other and with progressive eye damage. They also are reducing uric acid levels by giving two drugs already on the market, one that blocks formation and another that enhances excretion. Thinking that uric acid levels also may be a biomarker, she eventually wants to see how uric acid levels correlate with disease progression in humans.

"As the ancients said: 'The eyes are the mirror of the soul.' We also know that whatever happens in the eye is an expression of what is happening in the rest of the body," Bartoli said. "We want to better understand the causes of inflammation in the eye in [diabetes](#) and find better ways to manage it as well as [byproducts](#) such as [uric acid](#). Ultimately, of course, we hope to protect sight."

A National Eye Institute fellowship to GRU Graduate Student Folami Lamoke also is supporting the thioresoxin studies. Bartoli is a faculty member in the MCG Department of Ophthalmology and the GRU James and Jean Culver Vision Discovery Institute.

Provided by Medical College of Georgia

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