Studies Shed Light On Role Of Melanin In Preventing Macular Degeneration

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FULL STORY

Two studies from an unusual research partnership at the University of Chicago appear to have resolved a long-standing dispute about the role of melanin in the eye. The studies, one published in the Proceedings of the National Academy of Sciences (PNAS) and one early online in the Journal of the American Chemical Society (JACS), also suggest a new way to prevent a common cause of blindness.

Chemist James Norris, Ph.D., and retina surgeon Kourous Rezai, M.D., combined resources to show that melanin, a pigment found throughout the human body, acts like a neutralizing sponge inside cells in the retina to soak up and destroy reactive oxygen species. Reactive oxygen species, or free radicals, energized by light, are thought to play a major role in macular degeneration, the leading cause of blindness in people over the age of 60.

"We now have the first persuasive evidence that melanin plays an important protective role within the eye," said Norris, professor in the Department of Chemistry and the Institute for Biophysical Dynamics at the University of Chicago and one of the senior authors of both papers. "Although melanin contains its own intrinsic free radical, we found that it absorbs a far more damaging form of free radical, converting its destructive energy into harmless heat before it can hurt the retina."

An estimated 1.75 million Americans have decreased vision from age-related macular degeneration (AMD), with about 200,000 new cases each year. The incidence of AMD is expected to double within the next 25 years as the number of older persons continues to increase. The disorder is far more prevalent among whites than among black persons.

It causes gradual loss of central vision by damaging the retinal pigment epithelial (RPE) cells that lie underneath the macula, the small region of the retina responsible for fine detail at the center of the field of vision. Without RPE cells, the photoreceptors, which are the light detectors, also die. Patients lose the ability to see detail and soon they can't read.

"This is a devastating disease," said Rezai, director of the vitreoretinal service at the University of Chicago. "We do not have a cure for this disease. We can only treat the secondary complications, such as growth of abnormal blood vessels."

"Since we don't know how to replace or repair the dead or damaged retinal cells," he said, " we need to find ways to protect them."

Because people stop producing new RPE cells after birth, these cells have to last a lifetime. They live, however, in a toxic environment. Oxygen concentrations at the back of the eye are very high. At the same time the eye is constantly bombarded with light energy, which interacts with oxygen and can lead to the production of harmful free radicals – which can damage cell membranes and DNA. "It's amazing," noted Norris, "that the eye lasts as long as it does."

"To prevent the damage," Rezai said, "we need to understand exactly how it happens." He grows human RPE cells in culture in his lab, but "until now, we have had no direct way to measure the production of most dangerous free radicals. They are too small and too fast."

Norris studies photosynthesis, in which energy from sunlight is converted into electrochemical energy, a process with many parallels to vision. To study the early steps, he uses a tool called electron paramagnetic resonance (EPR). EPR is similar to magnetic resonance imaging except that it measures the spin of electrons rather than of protons.

Because photochemical reactions happen extremely fast, the Norris laboratory has one of the world's few high-speed EPR spectroscopy devices, able to record actions that occur in nanoseconds, about 1,000 times faster than standard EPR.

"Free radicals are dangerous chemicals and dangerous chemistry takes place rapidly," said Norris. "This lets us see some of it."

Norris and Rezai have another valuable asset, an ambitious student, interested in chemistry and medicine, experienced with EPR and looking for a project. This was a unique opportunity for Brandon-Luke Seagle, a third-year student in the College at the time. His knowledge of chemistry and medicine enabled him to be the link between Rezai's cells and Norris's techniques. He is the first author on both papers.

Using Rezai's cells, Norris's technology and Seagle's leg work, the team was able to capture convincing and dramatic evidence that melanin protects the retinal cells. In the PNAS paper (21 June 2005), they show that increased melanin aggregation and radical migration within melanin aggregates can protect RPE cells from free-radical damage and help prevent cell death. In the JACS paper (17 August 2005, but available online) they demonstrate how melanin actually scavenges the harmful free radicals produced by high-energy blue or ultraviolet light as it flows into the eye, soaking them up and neutralizing their effects.

"We now have molecular-based evidence to support the epidemiologic data that points to the protective effects for melanin," said Rezai, who is testing ways to boost melanin levels, first in cells grown in culture and, if that appears promising, in animal models.

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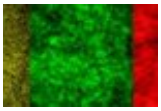

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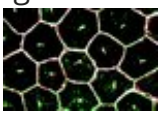

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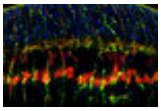

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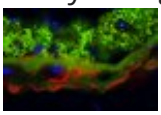

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