

Zinc Found to Be a Link in AMD

REVIEWED BY ERIK VAN KUIJK, MD, PhD

An international research team including scientists at the University of Texas Medical Branch at Galveston (UTMB) and the Galveston-based spinoff Neurobiotex, Inc., has found high levels of zinc in the drusen that are an indication of age-related macular degeneration (AMD)—the leading cause of blindness in the elderly in the developed world. The finding, published in *Experimental Eye Research*,¹ contributes to a better understanding of AMD and could facilitate the development of effective treatments, said UTMB ophthalmologist Erik van Kuijk, MD, PhD, senior author of the study.

“We have discovered that the drusen in the eyes of those with AMD have very high levels of zinc,” said Dr. van Kuijk, Associate Professor in the UTMB Department of Ophthalmology and Visual Sciences, in a university news release.

Zinc previously had been shown to contribute to the formation of brain plaques in patients with Alzheimer’s disease. Dr. van Kuijk and his colleagues used a reagent called ZP-1 to test the idea that zinc might also contribute to the formation of the plaque-like drusen in the eye. ZP-1 was developed by Neurobiotex scientist Christopher Frederickson, PhD.

AMD: ALZHEIMER’S OF THE EYE

From the findings, Dr. Frederickson suggested that AMD be considered “the Alzheimer’s disease of the eye,” in that both disorders involve the aggregation of misfolded amyloid proteins and metals like zinc and copper into microscopic plaque clumps.

“What is particularly important is that within the zinc we found a small pool—about 5% to 10%—of what is known as ‘free or loosely bound’ zinc,” Dr. van Kuijk explained. “Generally, zinc is essential to keeping a molecule’s shape, but mobilized zinc can cause lots of problems. Since it is a small proportion of the overall zinc pool, however, it is straightforward to target it. That is what researchers are beginning to do with Alzheimer’s disease by developing methodologies and drugs that can capture this mobilized zinc and see if doing that slows down the degenerative

Drusen in the eyes of people with AMD contain very high levels of zinc. Zinc has been shown to contribute to brain plaque in Alzheimer’s patients.

process. This study shows that we could now potentially take a similar route for AMD treatment.”

COMPARED DEPOSITS

The researchers examined eyes procured by the Montana Eye Bank from deceased patients with AMD that contained several large subretinal pigment epithelium deposits and compared them with postmortem eyes from a similar age group that had no known eye disease and no deposits in the macula. They analyzed these using zinc-sensing molecules like ZP-1, which glow when they bind with zinc. The glowing molecules bind only to the free or loosely bound zinc, which is particularly crucial in causing disease.

Currently there is no treatment for the non-neovascular form of AMD, but there has been considerable progress in treating the neovascular form, including use of new drugs like ranibizumab (Lucentis; Genentech, San Francisco) that stop new vessel growth.

“The pioneering work by Dr. van Kuijk and his colleagues is an important development in our understanding of AMD” said Michael Boulton, MD, Director of the new Macular Degeneration Center at UTMB. “The possibility of targeting zinc or stopping or reversing drusen growth is important because doing so has the potential to arrest the progression of AMD early, before irreversible damage to the retinal cells occurs.” ■

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1. Lengyel I, Flinn JM, Peto T, et al. High concentration of zinc in sub-retinal pigment epithelial deposits. *Exp Eye Res.* 2007;84:772-780.