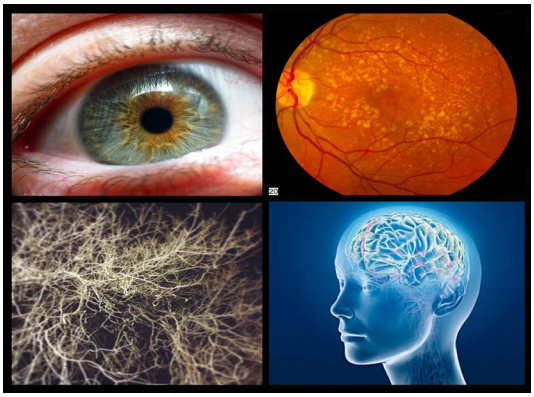
AAV Vector that Promotes Antioxidant Production for Treatment of Age-Related Macular Degeneration

Gene Therapy Requires Just One Intraocular Injection to Treat Eye Ailment Caused by Oxidative Stress



This AAV gene therapy approach provides a one-time treatment to oxidative stress. Sustained oxidative stress can lead to a variety of pathophysiological diseases including age-related macular degeneration, diabetic retinopathy, and amyotrophic lateral sclerosis. In the United States, age-related macular degeneration affects 1.75 million people and diabetic retinopathy affects 10 million. When the human body overproduces reactive oxygen species and reactive nitrogen species, it can lead to the oxidation and degradation of proteins, lipids, and DNA in the body. This degradation of DNA and lipids can cause mutations in the DNA sequences, and damaged cellular components can induce an inflammatory reaction. Researchers at the University of Florida have developed an AAV vector that introduces a small protein into the patient's cells that promotes the production of detoxifying enzymes in the body. The AAV vector only requires one injection to deliver the secreted and cell-penetrating protein into the patient's tissue. Unlike current methods that require monthly intraocular injections, this treatment for age-related macular degeneration is a one-time treatment for oxidative stress.

Application

Effective treatment for pathophysiologic diseases attributed to sustained oxidative stress, including age-related macular degeneration, diabetic retinopathy, and neurodegenerative diseases such as amyotrophic lateral sclerosis, Parkinson's Disease and Alzheimer's Disease

Advantages

- Provides treatment without affecting the patient's vision, overcoming the obstacles of current treatments that can lead to vision loss
- Treatments consists of one intraocular injection, minimizing patient discomfort in in therapy for diabetic retinopathy and wet form of age-related macular degeneration
- Requires one-time treatment rather than monthly doses, providing an efficient and cost-effective therapy for patients

Technology

This AAV vector delivers a secreted and cell-penetrating peptide to inhibit reaction to oxidative stress. Nrf2-Keap1 is a signaling pathway that regulates the expression of detoxifying enzymes, or antioxidants. Keap1, by reducing the levels of the Nrf2, maintains a constant level of this antioxidant production. Researchers at the University of Florida have developed an AAV vector that acts as a delivery system to introduce a peptide that allows Nrf2 to increase detoxifying enzyme production. The peptide binds with the Keap1. As a result, free Nrf2 transcription factor is able to translocate to the nucleus of the cell and stimulate expression of

Technology (cont.)

detoxifying enzymes. AAV are small DNA viruses that do not integrate into the genome of the cells they infect. They are used in gene therapy treatments because of their ability to infect a wide spectrum of cells with minimal inflammatory response. This virus does not cause disease.

The Inventors

Alfred S. Lewin, Ph.D., is the Shaler Richardson Professor of Ophthalmic Sciences and a Professor in the Department of Molecular Genetics and Microbiology. He is considered a leader in the development of gene therapy for dominant retinal degenerations and in the use of RNA-based therapeutics in the eye. Dr. Lewin received his B.A. and Ph.D. from the University of Chicago and was postdoctoral fellow at the University of Basel in Switzerland. He was an Assistant Professor of Chemistry at Indiana University in Bloomington before coming to the University of Florida in 1987.

Christhian Ildefonso, Ph.D., is the Senior Postdoctoral Associate in Dr. Lewin's Laboratory at the University of Florida College of Medicine. He earned his B.Sc. in Biology and Chemistry from the University of Puerto Rico, and his Ph.D. in Translational Biology and Molecular Medicine from Baylor College of Medicine in 2011. Dr. Ildefonso's primary research interests are translational medicine, the development of AAV vectors for immunomodulation and neuroinflammation, and gene therapy.

Qiuhong Li, Ph.D., is an Associate Professor in the Department of Ophthalmology. Her research interest is focused on studying the mechanisms causing retinal diseases, inherited retinal degenerative diseases and age-related macular degeneration, retinal and choroidal neovascular diseases, with particular focus on diabetic retinopathy using both gene-based and pharmacological approaches. Dr. Li received a Ph.D. from University of Alberta, Canada in Molecular Genetics and Biology. She was a postdoctoral fellow in the Department of Ophthalmology at UF before becoming a faculty member.

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