AAV Vector-Based Anti-Inflammatory Therapeutic for Macular Degeneration and Other Tissue-Specific Inflammatory Diseases

Gene Therapy Vectors Deliver Secretable, Cell-Penetrating Viral Therapeutics to Targeted Host Cells

This AAV vector-based therapeutic treats inflammatory responses in mammals by delivering tissue-specific anti-inflammatory therapeutic proteins to targeted host cells. These transvected host cells then inhibit a variety of pro-inflammatory syndromes, which cause or exacerbate diseases and disorders caused by chronic inflammation. AAV vector-based gene therapy is useful in treating a number of diseases, including congestive heart failure, Parkinson’s disease, and hemophilia, by delivering therapeutics to targeted cells. Unfortunately, no available treatments combat tissue-specific inflammation, such as dry age-related macular degeneration. Age-related macular degeneration affects as many as 11 million people with global cost of visual impairment at $343 billion in the United States alone. University of Florida researchers have developed AAV vector constructs that are optimized for delivering anti-inflammatory peptides to selected mammalian cells and tissues. This tissue-specific treatment addresses symptoms of oxidative stress and inflammation by delivering secretable, cell-penetrating anti-inflammatory proteins to treat specific inflammatory diseases, such as dry age-related macular degeneration.

Application

AAV vectors deliver modified viral protein as tissue-specific therapy for chronic inflammation

Advantages

- Delivers viral proteins to host cells, providing gene therapy treatment for inflammation
- Delivers gene product directly to affected cells, increasing chance it can be used for many other tissue-specific inflammatory diseases
- Targets two key pro-inflammatory signaling pathways within cells, giving it the capacity to treat diseases over prolonged period of time

Technology

AAV vector-based therapy has been utilized in treating a number of genetic diseases; however, gene therapy has not traditionally been used to treat inflammatory diseases. This tissue-specific method of treating inflammation targets inflammatory responses by administering AAV vectors coupled with secretable, cell-penetrating anti-inflammatory proteins derived from viruses. These modified viral proteins penetrate target host cells; these suitably-transvected host cells then inhibit the key cellular inflammatory pathways that cause or exacerbate a variety of chronic progressive diseases, disorders, and conditions. Researchers have used this AAV vector-based therapy to treat dry age-related macular degeneration as an example of the therapy’s use in inhibiting pro-inflammatory responses in a number of mammalian diseases.
The Inventors

Dr. Grant McFadden, Ph.D., is a professor in the Department of Molecular Genetics & Microbiology at the University of Florida. He earned his doctorate in Biochemistry from McGill University in 1975 and was a postdoctoral fellow at the University of Western Ontario in Canada. He earned the Hellmuth Prize in 2002, and was named the Canada Research Chair in Molecular Virology in 2001. He was inducted as a Fellow of the Royal Society of Canada in 2004 and as a Fellow of the American Academy of Microbiology in 2007. His research interests include the use of viral proteins for therapeutic purposes against inflammatory diseases.

Dr. Alfred S. Lewin, Ph.D., is the Shaler Richardson Professor of Ophthalmic Sciences and a Professor and Program Director in the Department of Molecular Genetics and Microbiology at the University of Florida. 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. He 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.

Dr. Alexandra R. Lucas, M.D., is a Professor of Medicine and the Ethel Smith Chair in Vasculitis Research at the University of Florida. She earned her doctor of medicine from the University of Alberta in 1982 and completed fellowships at the University of Alberta and Tufts University School of Medicine. She is a member of the Canadian Society for Atherosclerosis and serves on an American Heart Association grant panel. Her research interests include vascular innate immune responses and interventional cardiology.

Dr. Cristhian J. Ildefonso, Ph.D., is a postdoctoral associate in the Department of Molecular Genetics & Microbiology at the University of Florida. He earned his doctorate at Baylor College of Medicine in 2011 and was a postdoctoral student at Baylor College of Medicine. His research interests include AAV vectors to treat dry AMD and retinitis pigmentosa.

Dr. Mohammed Masmudur Rahman, Ph.D., is a research assistant professor in the Department of Molecular Genetics & Microbiology at the University of Florida. He earned his doctorate at the Indian Institute of Science in Bangalore, India, in 2004. He conducted postdoctoral research at the Roberts Research Institute in Ontario, Canada. His research interests include innate immune responses modulated by DNA viruses and virus-host protein-protein interactions.

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