Researchers develop new tool for gene delivery

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Researchers at Tufts University School of Medicine and the Sackler School of Graduate Biomedical Sciences at Tufts have developed a new tool for gene therapy that significantly increases gene delivery to cells in the retina compared to other carriers and DNA alone, according to a study published in the January issue of *The Journal of Gene Medicine*. The tool, a peptide called PEG-POD, provides a vehicle for therapeutic genes and may help researchers develop therapies for degenerative eye disorders such as retinitis pigmentosa and age-related macular degeneration.

"For the first time, we have demonstrated an efficient way to transfer DNA into cells without using a virus, currently the most common means of DNA delivery. Many non-viral vectors for gene therapy have been developed but few, if any, work in post-mitotic tissues such as the retina and brain. Identifying effective carriers like PEG-POD brings us closer to gene therapy to protect the retinal cells from degeneration," said senior author Rajendra Kumar-Singh, PhD, associate professor of ophthalmology and adjunct associate professor of neuroscience at Tufts University School of Medicine (TUSM) and member of the genetics; neuroscience; and cell, molecular, and developmental biology program faculties at the Sackler School of Graduate Biomedical Sciences at Tufts.

Safe and effective delivery of therapeutic genes has been a major obstacle in gene therapy research. Deactivated viruses have frequently been used, but concerns about the safety of this method have left

scientists seeking new ways to get therapeutic genes into cells.

"We think the level of gene expression seen with PEG-POD may be enough to protect the retina from degeneration, slowing the progression of eye disorders and we have preliminary evidence that this is indeed the case," said co-author Siobhan Cashman, PhD, research assistant professor in the department of ophthalmology at TUSM and member of Kumar-Singh's lab.

"What makes PEG-POD especially promising is that it will likely have applications beyond the retina. Because PEG-POD protects DNA from damage in the bloodstream, it may pave the way for gene therapy treatments that can be administered through an IV and directed to many other parts of the body," said Kumar-Singh.

Kumar-Singh and colleagues used an in vivo model to compare the effectiveness of PEG-POD with two other carriers (PEG-TAT and PEG-CK30) and a control (injections of DNA alone).

"Gene expression in specimens injected with PEG-POD was 215 times greater than the control. While all three carriers delivered DNA to the retinal cells, PEG-POD was by far the most effective," said first author Sarah Parker Read, an MD/PhD candidate at TUSM and Sackler and member of Kumar-Singh's lab.

Age-related macular degeneration, which results in a loss of sharp, central vision, is the number one cause of vision loss in Americans age 60 and older. Retinitis pigmentosa, an inherited condition resulting in retinal damage, affects approximately 1 in 4,000 individuals in the United States.

More information: Read SP, Cashman SM, Kumar-Singh R. The Journal of Gene Medicine. 2010 (January). 12(1): 86-96. "A

poly(ethylene) glycolylated peptide for ocular delivery compacts DNA into nanoparticles for gene delivery to post-mitotic tissues in vivo." doi:10.1002/jgm.1415

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