MedicalXpress

Clearer day for gene therapy: New vector carries big genes linked to inherited blindness

April 16 2008

For some inherited diseases, one barrier to successful gene therapy is that a commonly used vector (package into which the curative gene is placed) cannot accommodate the large size of the curative gene. However, a newly developed vector derived from the AAV5 form of adeno-associated virus has been used to successfully carry large genes into cells and to improve eye function in a mouse model of an inherited disease causing progressive loss of sight.

Some clinicians and researchers hope that individuals with inherited diseases (such as cystic fibrosis and recessive Stargardt disease, which causes progressive loss of sight) might one day be cured by providing them with a corrected version of their disease-causing faulty gene, i.e., by gene therapy.

In gene therapy, the curative gene is packaged in an agent known as a vector, which carries the gene into cells where it is required. One of the most common vectors is derived from a virus, adeno-associated virus (AAV). However, for some diseases, such as recessive Stargardt disease, one barrier to successful gene therapy is that AAV is not able to accommodate the large size of the curative gene.

New data, generated by Alberto Auricchio and colleagues, at the Telethon Institute of Genetics and Medicine, Italy, has revealed that vectors derived from a specific form of AAV known as AAV5 can accommodate large genes, including that missing in a mouse model of recessive Stargardt disease.

In the study, it was found that much larger genes could be packaged into vectors derived from AAV5 than from vectors derived from other forms of AAV. Further, it was shown that AAV5 could be used to induce cells to successfully convert the information in the large genes into protein.

When AAV5 containing the mouse gene Abca4, which is the mouse correlate of the gene mutated in individuals with recessive Stargardt disease, was injected into the eye of mice lacking Abca4, improvement in the function of the eye was observed. The authors therefore concluded that vectors derived from AAV5 could be useful for treating individuals with recessive Stargardt disease.

Source: Journal of Clinical Investigation