DEUTSCHES KREBSFORSCHUNGSZENTRUM IN DER HELMHOLTZ-GEMEINSCHAFT

No. 18 März 09, 2006 (Bm)

Tamed AIDS Viruses as Safe Gene Ferries for Treating Hereditary Eye Diseases

An international research team used an altered AIDS virus for gene transfer into the retina of mice. Thus it was possible, for the first time ever, to treat an inherited eye disease by gene therapy. The researchers have now published their results in the latest issue of the journal *Nature Medicine**.

The search was on for a viral vector which is able to transfer genes for therapeutic purposes into the retina of a mouse without causing mutations. The therapeutic gene should act as a substitute – for as long as possible – for the cell's own defective copy and be multiplied by the cell. The solution in the form of an altered AIDS virus was found by London scientists **Dr. Rafael Yáñes-Muños** and **Professor Adrian Thrasher**. **Professor Christof von Kalle** of the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) and the National Center for Tumor Diseases Heidelberg and his group collaborated by investigating the efficiency and safety of these vectors.

Gene therapy is the treatment of hereditary diseases by intoducing genes into the cells of affected tissues. Thus, the function of the introduced gene can compensate the defective regulation or loss of function of mutated genes. In the method studied, a severely altered version of the AIDS virus was used to deliver the genetic material to the cells. To this end, scientists removed the sequences of viral genetic material that make the virus dangerous and added the required gene instead. Possible risks of this method include uncontrolled insertion of the genes into the genome of the host cell – an event that can change important information (insertion mutagenesis). Depending on the location of such an insertion, it can cause cancer to develop.

Yáñes-Muños and colleagues avoided this problem by altering the viral genetic information in such a way as to prevent integration into the host cell genome. In order to check whether the cells nevertheless were reading the new information and translating it into proteins, they made the virus inject a jellyfish gene into the retinal cells. It contained the blueprint for a protein that fluoresces green when illuminated by light of a different wavelength. Since the new information was constantly translated, the eyes of the mice glowed green, even nine months later. Correspondingly, the method proved to be effective with the therapeutic gene. Yáñes-Muños and Thrasher are convinced that the curing of this rare retinal disease in the mouse model points the way to the treatment of other inherited eye diseases. Clinical trials to study the approach in humans should be possible in one or two years time.

Gene therapy has been successfully used in earlier studies for treating hereditary blood diseases, but caused a leukemia-like disease in three cases. Von Kalle found out that this happened because a cancer-causing gene was activated unintentionally. The therapeutic gene had become inserted into the DNA close to such a gene and, thus, caused abnormal cell growth. As in the work presented, von Kalle attempts to discover and understand the molecular processes of the vector function in order to make gene therapy free of such side effects.

* *Rafael J Yáñez-Muñoz, Kamaljit S Balaggan, Angus MacNeil, Steven J Howe, Manfred Schmidt, Alexander J Smith, Prateek Buch, Robert E MacLaren, Patrick N Anderson, Susie E Barker, Yanai Duran, Cynthia Bartholomae, Christof von Kalle, John R Heckenlively, Christine Kinnon, Robin R Ali & Adrian J Thrasher: Effective gene therapy with nonintegrating lentiviral vectors, Nature Medicine, March 2006, Volume 12 (3), pp 348 – 353*

This press release is available at www.dkfz.de/pressemitteilungen

Dr. Julia Rautenstrauch
Division of Press and Public Relations
Deutsches Krebsforschungszentrum
Im Neuenheimer Feld 280
D-69120 Heidelberg

T: +49 6221 42 2854

F: +49 6221 42 2968