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PRESS RELEASE
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Novel Approach May Spell Safer Gene Therapy

A novel strategy for circumventing safety problems that have plagued gene therapy has been offered by a complex multicenter group of researchers, including Professor Claudio Napoli, a Full Professor at the II University of Naples and Adjunct Professor at the Sbarro Research Institute for Cancer Research and Molecular Medicine and the Center of Biotechnology at the College of Science and Technology of Temple University. The study was published online in the prestigious scientific journal Cell (Cell 2008 Feb 8;132:397-409).

The study reports that adenovirus type 5, a common vector for delivering gene therapy, transfects liver cells by a different mechanism than previously thought. That mechanism offers a new target for modifying the viral vector to make it safe for clinical use.

A number of studies indicated that it would be possible to use adenovirus as a vector to deliver genes into specific locations, such as a solid tumor. But when it's injected intravenously, the virus accumulates in the liver instead of circulating in the body, raising the risk of toxicity and transfection of other cells. Basically, adenovirus consists of three major proteins - fiber, penton and hexon. Based on earlier work, most researchers held that the main mechanism of viral transduction was the fiber protein's interaction with a receptor on the target cell. But attempts to mutate the fiber protein did not block the virus's accumulation in the liver in vivo.

Professor Andrew Baker of the University of Glasgow, who led the current research, notes that all of these fiber-modified viruses still ended up transducing the liver. The Cell paper focused instead on the hexon protein. The researchers mutated the protein, disabling its ability to interact with a blood-clotting enzyme, Factor X. Those mutations, and pharmacological blockade of the interaction, did indeed block gene transfer, suggesting that the virus enters liver cells via the interaction of the hexon protein and Factor X.

The researchers noted that fiber-mediated transduction works when the virus is injected in muscle or cell culture, but when injected into the bloodstream, this mechanism takes over.

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"Now that we have learned the mechanism that an adenovirus uses we could modify that process by genetically engineering the virus, to improve uptake into several cell types, including stem cells," says Dr. Napoli.

The Sbarro Institute for Cancer Research and Molecular Medicine in Philadelphia was established in 1993.

"Our hope is that this new discovery will point to new avenues to develop important and safer delivery of genetic therapies," said Antonio Giordano, M.D., Ph.D., the President and Founder of SHRO.

About Sbarro Health Research Organization

Sbarro Health Research Organization is committed to excellence in basic genetic research to cure and diagnose cancer, cardiovascular diseases, diabetes and other chronic illnesses and to foster the training of young doctors in a spirit of professionalism and humanism.