

Using Nanoparticles, In Vivo Gene Therapy Activates Brain Stem Cells

July 26 2005

Using customized nanoparticles that they developed, University at Buffalo scientists have for the first time delivered genes into the brains of living mice with an efficiency that is similar to, or better than, viral vectors and with no observable toxic effect, according to a paper published this week in Proceedings of the National Academy of Sciences.

The paper describes how the UB scientists used gene-nanoparticle complexes to activate adult brain stem/progenitor cells in vivo, demonstrating that it may be possible to "turn on" these otherwise idle cells as effective replacements for those destroyed by neurodegenerative diseases, such as Parkinson's.

In addition to delivering therapeutic genes to repair malfunctioning brain cells, the nanoparticles also provide promising models for studying the genetic mechanisms of brain disease.

"Until now, no non-viral technique has proven to be as effective as the viral vectors in vivo," said co-author Paras N. Prasad, Ph.D., executive director of the UB Institute for Lasers, Photonics and Biophotonics, SUNY Distinguished Professor in UB's Department of Chemistry and principal investigator of the institute's nanomedicine program. "This transition, from in vitro to in vivo, represents a dramatic leap forward in developing experimental, non-viral techniques to study brain biology and new therapies to address some of the most debilitating human diseases."

Viral vectors for gene therapy always carry with them the potential to revert back to wild-type, and some human trials have even resulted in fatalities.

As a result, new research focuses increasingly on non-viral vectors, which don't carry this risk.

Viral vectors can be produced only by specialists under rigidly controlled laboratory conditions. By contrast, the nanoparticles developed by the UB team can be synthesized easily in a matter of days by an experienced chemist.

The UB researchers make their nanoparticles from hybrid, organically modified silica (ORMOSIL), the structure and composition of which allow for the development of an extensive library of tailored nanoparticles to target gene therapies for different tissues and cell types.

A key advantage of the UB team's nanoparticle is its surface functionality, which allows it to be targeted to specific cells, explained Dhruva J. Bharali, Ph.D., a co-author on the paper and post-doctoral associate in the UB Department of Chemistry and UB's Institute for Lasers, Photonics and Biophotonics.

While they are easier and faster to produce, non-viral vectors typically suffer from very low expression and efficacy rates, especially in vivo.

"This is the first time that a non-viral vector has demonstrated efficacy in vivo at levels comparable to a viral vector," Bharali said.

In the UB experiments, targeted dopamine neurons -- which degenerate in Parkinson's disease, for example -- took up and expressed a fluorescent marker gene, demonstrating the ability of nanoparticle technology to deliver effectively genes to specific types of cells in the

brain.

Using a new optical fiber in vivo imaging technique (CellviZio developed by Mauna Kea Technologies of Paris), the UB researchers were able to observe the brain cells expressing genes without having to sacrifice the animal.

Then the UB researchers decided to go one step further, to see if they could not only observe, but also manipulate the behavior of brain cells.

Their finding that the nanoparticles successfully altered the development path of neural stem cells is especially intriguing because of scientific concerns that embryonic stem cells may not be able to function correctly since they have bypassed some of the developmental stages cells normally go through.

"What we did here instead was to reactivate adult stem cells located on the floor of brain ventricles, germinal cells that normally produce progeny that then die if they are not used," said Michal K. Stachowiak, Ph.D., co-author on the paper and associate professor of pathology and anatomical sciences in the UB School of Medicine and Biomedical Sciences. Stachowiak is in charge of in vivo studies at the UB Institute for Lasers, Photonics and Biophotonics.

"It's likely that these stem/progenitor cells will grow into healthy neurons," he said.

"In the future, this technology may make it possible to repair neurological damage caused by disease, trauma or stroke," said Earl J. Bergey, Ph.D., co-author and deputy director of biophotonics at the institute.

The group's next step is to conduct similar studies in larger animals.

The UB research was supported by the John R. Oishei Foundation, the National Science Foundation, the American Parkinson Disease Association and UB's New York State Center of Excellence in Bioinformatics and Life Sciences.

Research at UB's Institute for Lasers, Photonics and Biophotonics has been supported by special New York State funding sponsored by State Sen. Mary Lou Rath.

Source: University at Buffalo

Citation: Using Nanoparticles, In Vivo Gene Therapy Activates Brain Stem Cells (2005, July 26)
retrieved 26 April 2024 from

<https://phys.org/news/2005-07-nanoparticles-vivo-gene-therapy-brain.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.