

The Washington Post

March 24, 2008

Therapeutic Cloning Works in Mice With Parkinson's

BY ALAN MOZES

MONDAY, March 24 (HealthDay News) -- Therapeutic cloning successfully treated Parkinson's disease in mice, researchers report.

Using the process to develop dopamine-producing neurons with an identical genetic profile to each mouse being treated allowed scientists to significantly improve the neurological performance of the diseased animals, without provoking any evidence of immune system rejection.

"This is the first time that anyone has done this kind of cloning experiment to show the therapeutic aspect of the process in this customized way," said study author Dr. Viviane Tabar, an associate professor of neurosurgery in the department of neurosurgery at the Memorial Sloan-Kettering Cancer Center in New York City.

The finding -- which has not yet been replicated in human trials -- was published in the March 23 online issue of *Nature Medicine*.

Parkinson's is a neurodegenerative disorder that severely impairs motor skills and speech. According to the National Parkinson Foundation, 1.5 million Americans suffer from the disease, and men and women over 65 are at the greatest risk of developing the debilitating condition.

The illness is sparked by the breakdown of nerve cells in the brain and a resulting drop in the production of the dopamine -- a chemical key to the proper function of muscles and movement. In recent years, the effort to slow or halt dopamine loss has focused on the promise of therapeutic cloning.

Controversy over the ethical ramifications of cloning has led many researchers to draw a clear distinction between therapeutic cloning and reproductive cloning.

Both processes begin with the removal of the nucleus from a single cell taken from any part of the body of a living adult organism. In the laboratory, this isolated nucleus is then inserted into an egg cell that has been stripped of its own nucleus. This egg cell is then stimulated to grow and divide into an increasing number of cells that are all an identical genetic match to those of the original host.

At that point, the two procedures part company. On the one hand, reproductive cloning continues the cell division process to the birth of a whole new organism possessing the exact same DNA as the host. In the absence of any human reproductive cloning to date, the 1996 birth of Dolly the sheep -- the first animal ever to be cloned -- is perhaps the most famous example of this process.

Therapeutic cloning is limited to the generation of a very early-stage embryo comprised of a small collection of undifferentiated stem cells. These malleable cells are then stimulated to develop into specified cells that could be reintroduced into the body of the original host to treat any number of diseases. Such an approach circumvents a patient's natural immune response.

Tabar and her Sloan-Kettering colleague Lorenz Studer joined researchers at the RIKEN Center for Developmental Biology in Kobe, Japan, to test the viability of therapeutic cloning in mice that had been induced to develop Parkinson's.

The research team extracted cells from the tail tips of each of 24 young mice and therapeutically cloned 187 distinct stem cell lines --including at least one DNA-specific line per mouse.

After inducing the stem cells to develop into dopamine neurons, each Parkinson's mouse was "treated" with the insertion of only those neurons derived from its own cells.

Subsequent behavioral tests revealed that this one-to-one therapeutic cloning technique significantly improved the neurological function of the mice without any adverse immune response. The observed improvement was found to be much better than that achieved by a group of control mice that were given dopamine cells cloned from a single mouse line, as in prior studies.

Compared with the one-to-one treated mice, the non-matched mice had poorer immune responses, poorer motor control improvements, and a mild degree of inflammation.

"It had been thought that this process would be way too cumbersome to carry out," said Tabar. "But this validates that it is feasible and superior to using non-matched genetic material."

Michael Jakowec, an assistant professor of neurology with the George and MaryLou Boone Parkinson's Disease and Movement Disorders Research Center at the University of Southern California Keck School of Medicine in Los Angeles, cautioned that the leap to humans might be "gigantic."

"You see a lot of failures in studies that try to translate success from rodents to humans," Jakowec said. "So, it may be premature to take this to human trial just yet. Perhaps it should first be replicated in primates. But it certainly does open up a new avenue of therapeutic strategy, which may ultimately benefit patients down the road."