Gene therapy slows progression of Batten Disease

June 2 2008

Gene therapy that helps defective brain cells get rid of "garbage" appears both safe and effective at slowing down Batten disease, according to promising findings from NewYork-Presbyterian Hospital/Weill Cornell Medical Center.

Batten disease (late infantile neuronal ceroid lipofuscinosis) is a rare genetic, degenerative neurological disorder that usually becomes fatal in children by age 12.

The clinical trial found that the procedure, which involves injecting a harmless gene-bearing virus into the brain, is safe; and that, on average, it significantly slowed the disease's progression during the 18-month follow-up period.

"The virus is used as a Trojan horse that houses and then delivers a healthy, functional gene into the cells of the brain," said lead author Ronald Crystal, M.D., chairman of the Department of Genetic Medicine and chief of the Division of Pulmonary and Critical Care Medicine at NewYork-Presbyterian/Weill Cornell. "The genes are incorporated within the genetic material of the cells, which are then able to produce a protein that is deficient in Batten disease."

The results are published in the May 13 online issue of Human Gene Therapy.

The gene in question -- CLN2 -- is mutated in children with the disease,

causing a deficiency in the enzyme TTP-1, which is responsible for ridding waste from central nervous system cells. Small organelles within the cell, called lysosomes, become clogged with toxic material within the neurons of the brain.

"It's like the garbage man of the cell is not able to do its job," said Crystal. "The trash keeps getting backed up inside the cell until the cells can no longer function properly and then eventually die throughout the entire brain."

Children with the disease start showing such neurological symptoms as impaired muscle coordination (ataxia), involuntary twitching (myoclonus) and speech and developmental disorders, starting around age 4. A gradual decline in vision follows. Affected children usually become wheelchair-bound by age 6 and ultimately become bedridden.

Because the disease is fatal early in life, there are only about 200 cases of the disease in the world at a given time. Subjects were selected from around the world to take part in the trial.

Six tiny holes were made in the skull of each subject, and then a liquid containing the healthy CLN2 gene, within the harmless adeno-associated virus (AAV), was injected into the brain. Neurological surgeons from NewYork-Presbyterian/Weill Cornell, led by Mark Souweidane and Michael Kaplitt, performed the gene therapy procedure.

"Before now, we had no hope of a therapy for Batten disease, but today we can say that there is some hope," said Crystal. "These results are not just promising for sufferers of the disease, but suggest that gene therapy can work and should be studied for other neurological disorders. Each gene in our body has the potential to become a target to study for human disease."

Co-researchers include Stefan Worgall, Dolan Sondhi, Neil R. Hackett, Barry Kosofsky, Minal V. Kekatpure, Nurunisa Neyzi, Jonathan P. Dyke, Douglas Ballon, Linda Heier, Bruce M. Greenwald, Paul Christos, Madhu Mazumdar, Mark M. Souweidane and Michael G. Kaplitt -- all from NewYork-Presbyterian/Weill Cornell.

Source: Cornell University