

Discovery of 'Canavan Rat' Thrills Researchers

Parents Looking to Stem-Cell Therapy After Suspension of Trials

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Researcher Morris Baslow's greatest hope for a cure for Canavan disease lies within a Japanese rat.

Until now, investigators have performed experiments and trials directly on children with Canavan, a genetic disorder that causes progressive brain damage, leading to death. The research has progressed slowly. Because Canavan is rare and those afflicted seldom live past age 10, researchers have a limited number of patients to study.

Now, however, investigators will be able to work more quickly by breeding the rat, which suffers from a rodent form of Canavan, to produce more rats with the disease.

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The rat was discovered by Japanese epilepsy researchers, who noticed that one of their rodents had tremors in its feet. They tested the rat and found that it was lacking N-acetyl aspartate, a key indication of Canavan disease.

"We can have 100 of these animals every week," Dr. Baslow, a biochemist at the Nathan S. Kline Institute for Psychiatric Research in Orangeburg, N.Y., said. "It's an infinitely faster route."

Canavan disease, which is found most often in Saudi Arabians and Ashkenazic Jews, is a neurological disease in which a defective gene causes brain damage by not allowing for the production of myelin, a fatty tissue that protects the body's nerves. Canavan patients suffer from muscle weakness, stunted



RATS: Disease bearers may provide cures.

mental development and the inability to speak. One in 41 Ashkenazic Jews is a carrier of the Canavan gene. One in four children born to parents who both carry the gene suffers from the disease. An estimated 500 to 1,000 American children suffer from Canavan disease.

The discovery of the Canavan rat, along with a Canavan mouse currently being studied at the University of Texas, could not have come at a better time for researchers and parents of Canavan children. In the wake of last year's death of a gene-therapy patient at the University of Pennsylvania, the Food and Drug Administration has put many gene-therapy experiments on hold — including Thomas Jefferson Medical University researcher Paola Leone's trials with Canavan patients. The FDA canceled Dr. Leone's gene-therapy trials in July, saying she needs to perform more experiments before she will be allowed to conduct clinical trials on children with Canavan.

Dr. Leone said the FDA's decision reflects a lack of sensitivity to the plight of Canavan patients. "It's understandable that the FDA is under pressure," Dr. Leone said. "It's not understandable to not realize the seriousness of Canavan disease."

Dr. Leone's proposed trials incor-

porated her findings from the experience of children treated during the past few years with the gene for an enzyme that breaks down N-acetyl aspartate. Children with Canavan accumulate excessive amounts of NAA, causing brain damage. However, the previous experiments succeeded in reducing NAA to a normal level, causing the children's health to improve. Some of the children developed myelin after being treated with gene therapy.

Now that the gene-therapy trials have been postponed, some parents of Canavan children are turning to stem cell therapy, a new treatment pioneered by a neurology professor at Harvard University, Dr. Evan Snyder. Stem cells are basic, "primordial" cells that are thought to give rise to all cells in the nervous system. Dr. Snyder hopes that injecting these cells into the brains of Canavan patients will result in the stem cells evolving into normal oligodendrocytes, the cell responsible for breaking down NAA.

Other researchers have tried injecting mature oligodendrocytes into patients' brains, but these cells do not spread throughout the brain like stem cells do. Dr. Snyder hopes that his therapy will "not only arrest ongoing degeneration [of Canavan patients], but allow some recovery of function and restoration of brain tissue." However, he said that any practical application of stem cell therapy is still "a good three to five years away. We may not see home runs immediately, but we'll settle for singles and doubles and even bunts."

Dr. Baslow, too, remains "tremendously optimistic" about the possibility of a forthcoming cure for Canavan. He said researchers already have "some pretty good ideas" about the mechanics of Canavan, and the discovery of rodents with the disease will help further.