Transplanting Brain Cells Shows Promise for Treating Some Causes of Mental Retardation

Researchers from the University of Pennsylvania School of Veterinary Medicine and Harvard Medical School have successfully treated in mice brain lesions which may contribute to mental retardation. The results were published in the March 23 issue of the journal *Nature*.

The researchers transplanted healthy immature brain cells into the brains of young diseased mice. As the mice aged, the donor cells planted themselves throughout the brain, secreted a missing enzyme, and appeared as normal components of the central nervous system. This resulted in a widespread correction of the disease process. This strategy was successfully accomplished by John H. Wolfe, V.M.D., Ph.D., of the School of Veterinary Medicine at the University of Pennsylvania in Philadelphia, Evans Y. Snyder, M.D., Ph.D., of Harvard Medical School and Children's Hospital in Boston, and colleagues.

"The immature brain cells that we transplanted into the diseased brains matured into normal brain cells. Apparently, these young cells, whose mature form was still undetermined, migrated into regions of the brain and developed into the appropriate cells of each region," said Evan Snyder, of the departments of Neurology and Pediatrics at Harvard and Children's Hospital.

The researchers have been studying mice with a disease called mucopolysaccharidosis type VII. This is the animal model for the human disease called Sly disease which afflicts fewer than 1 in every 100,000 humans. Because of an inherited deficiency of an enzyme called bela glucuronidase, substances called glycosaminoglysanas accumulate in the brain and other tissues where they cause damage that leads to a progressive and ultimately fatal degenerative disease accompanied by mental retardation. Sly disease belongs to a broader group of inherited diseases characterized by defects in the breakdown of biomolecules, and which affect approximately 1 in every 1,500 humans.

To correct this deficiency in mice, the researchers transplanted a cell line of neural progenitor cells into the cerebral ventricles within the brains of the newborn mice. By the time the mice reached maturity, the donor cells which secreted the missing enzyme, had engrafted throughout the brain and appeared as normal constituents of the central nervous system, resulting in widespread correction of the disease process. This may be a model for treating other genetic diseases affecting the brain or delivering other types of therapeutic substances to the brain in other types of diseases. It is the first report of using these novel vehicles to treat a widespread genetic central nervous system disease.

Many metabolic diseases of the central nervous system do not respond to treatment because the blood-brain barrier blocks the entry of drugs and therapeutic molecules in the brain. One way of getting around this dilemma is to transplant healthy immature nerve cells, or "neural progenitor cells" directly into the brain.

Even mice with transplanted cells that lived to an old age showed a dramatic absence of pathology in the brain, indicating a permanent improvement. "Someday we would like to translate what we learn from these mice to humans, but we still are far away from that," said John H. Wolfe of the Laboratory of Pathology and the Section of Medical Genetics at Penn's Veterinary School. It will entail a better understanding not only of the diseases that cause mental retardation, but also the basic biology of the immature donor nerve cells, cautioned Wolfe and Snyder.

Elizabeth R. Moran Honored

The School honored Elizabeth Ranney Moran during a special dinner in May. Shown here are Dean Kelly, Mrs. Moran and Mrs. Kelly. Mrs. Moran was presented with the following citation:

In recognition of your generous spirit and great devotion to the equine athlete

Your insight into the needs of the horse industry, your commitment to so many of its worthy causes, and your joy in all aspects of the sport horse make you, Betty, an inspiration to all equine enthusiasts. Your gracious philanthropic efforts in support of New Bolton Center have left an indelible mark on NBC faculty and facilities through the Moran Heart Station; the Surgical Suite and Creme Fraiche Nursing Station; through the Allam Professorship; and through research, especially in sports medicine and comparative orthopedics. The Center and all of us personally are indebted to you for your outstanding and steadfast leadership and immeasurable kindness in support of programs for the care of horses.