

Developing Gene Therapy

Researchers at the University of Pennsylvania School of Veterinary Medicine are testing methods for transferring normal genes into the cells of animals affected by enzyme deficiencies that cause severe and often fatal disorders in both humans and animals.

The enzyme deficiency diseases, called mucopolysaccharidoses, or MPS diseases, are progressive degenerative disorders of children and young animals usually characterized by severe bone abnormalities, heart defects, impaired vision, mental retardation, and premature death. The diseases are caused by deficiencies in enzymes whose normal function is to break down specific molecules in the cell.

The current research at Penn has focused on developing and testing vectors, or carriers, that can successfully deliver healthy enzyme genes into MPS affected cells.

In a presentation in Washington, D.C. at the American Veterinary Medical Association conference on genetic engineering, Dr. John Wolfe of the Gene Therapy Research Group at Penn said the group had developed a vector that is an effective carrier for one of the healthy genes. When transferred, the gene corrected the abnormalities of the diseased cell.

"The preliminary tests indicate that retroviral vector gene transfer may be a feasible approach for treating MPS diseases," Wolfe said.

Retroviral vectors act as a delivery system for placing the normal gene into the diseased cell. Retroviruses have proven to be good carriers, Wolfe said, because they are capable of inserting the gene into the DNA of the host cell, and they are relatively simple viruses that have been extensively modified so they do not harm the cells in which they are placed.

The initial testing, which has taken place within the last six to eight months, has been performed in tissue culture using diseased cells from animals affected

with an MPS disorder, Wolfe said. The newly-developed vectors have been able to transfer the gene to MPS cells, where the transferred gene has corrected the defect in the diseased cells.

The work at Penn has been performed in collaboration with the Memorial Sloan-Kettering Cancer Center and the Mt. Sinai School of Medicine in New York.

The next step, Wolfe said, will be to begin testing to determine if the vectors can be transferred to and function in diseased animals to actually alter the course of the disease.

Although MPS disorders are quite rare in the general population, they often occur with high frequency within families that carry the defective gene. Besides the MPS disorders, there are several thousand other forms of genetic disease. Effective treatments are available now for only a few of those disorders. Many researchers believe the new field of gene therapy research offers an approach to the treatment of previously incurable genetic disorders of animals and humans.

In gene therapy, Wolfe explained, cells are removed from the patient and placed into tissue culture; the normal gene is inserted; and the corrected cells are returned to the patient.

"It is replacing something that is missing from the cell," Wolfe said. "In effect, it is similar to giving insulin for the treatment of diabetes. However, unlike insulin, the effect of the gene therapy treatment would be permanent."

Researchers face several challenges in achieving successful gene therapy. The gene involved in the disease must be identified — which has not yet been accomplished for many genetic diseases; the gene must be cloned, or duplicated; an effective vector, or delivery system, must be constructed to transfer the new gene into the diseased cells; the vector must be capable of transferring the gene to the correct target cell; the transferred gene must function correctly



Dog with MPS VII

once it reaches the diseased cell; and, finally, the transferred gene must be able to cure or substantially alter the course of the disease for gene therapy to be considered successful.

The MPS diseases are good subjects for gene therapy research because the defective genes have been identified and can be duplicated. And, Wolfe said, since the MPS diseases that occur in animals are very similar to those that occur in humans, what is learned from studying the MPS affected animals should be highly applicable to treating the diseases in humans.

"This is a good example of reciprocal benefit in human and animal medicine," Wolfe said. MPS was first discovered in humans, and that led to its discovery in animals.

"The information and benefits flow back and forth between animal and human medicine."

Phyllis Holtzman

Equine Symposium for Students

Students organized an all-day equine symposium, consisting of hands-on demonstrations and lectures on November 19. The topics offered in the presentations and laboratories were: familiarization with the YAG Laser; cytology; cardiology and useful equipment; semen handling and processing; embryo transfer; mare reproductive tract; oblique radiographs for common equine problems; neonatal intensive care; lameness diagnosis; principles of internal fixation; low power laser and acupuncture; diagnostic ultrasound of the equine limb; colic; and endoscopy. In the afternoon a lecture on the prepurchase exam and its legal implications was presented. The following clinicians and residents participated and volunteered their time for event: Dr. Eric Tulleners, Dr. Ellen Ziemer, Dr. Johanna Reimer, Dr. Charles Love, Dr. Patricia Sertich, Dr. Martin Burton, Dr. Curtis Schelling, Dr. Wendy Vaala, Dr. Dan Dreyfuss, Dr. James Orsini, Dr. Benson Martin, Dr. Virginia Reef, Dr. Janet Johnston, Dr. Alan Ruggles, Dr. Yves Rossier, Dr. Lin Klein, Dr. William Moyer, and Dr. James Wilson.



SCAVMA Activities

The second annual Student Teaching Awards Dinner will be held on Sunday, April 2, 1989, 6:00 pm at the Hotel DuPont in Wilmington, DE. Tickets will be \$17.00 each for students and \$30.00 each for faculty. Look for the invitations in the mail. Last year 200 students and 150 faculty, staff and alumni attended the dinner at Longwood Gardens. All enjoyed the feast and ceremonies and are looking forward to this year's event.

SCAVMA's annual December auction exceeded all expectations. Support was tremendous. \$9,000 were raised. The funds will be used by the Faculty/SCAVMA fund to provide money for the student emergency loan fund. Part of the proceeds will help defray the cost of student tickets to the Dinner Dance.

Bigger and better than ever—SCAVMA's latest fund raising effort is a 'Boutique' in the student lounge. It offers a great selection of sweatshirts, sweatpants, T-shirts, jogging shorts, mugs and can coolers—available in a variety of colors and graphic designs. Also beginning in January, merchandise will be available at New Bolton Center in the cafeteria on Fridays.

This year's SCAVMA student symposium will be held at North Carolina State University, in Raleigh-Durham. Approximately 80 students from Penn will participate in the event. Funds raised by SCAVMA throughout the year will be used to defray the costs of transportation and accommodations.