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# Herpes Virus as a Vector to Deliver Healthy Genes to Brain

## New, faster *Salmonella enteritidis* Test

The current tests used to identify *Salmonella enteritidis* take almost two weeks. Dr. Linda Keller, research associate professor at Penn's Veterinary School, has developed an ELISA (enzyme-linked immunosorbent assay) that can determine in just under 30 hours whether *Salmonella enteritidis* is present in a sample. "This test is based on a very specific monoclonal antibody to *Salmonella enteritidis*,"

said Dr. Keller. "We incubate the eggs for 24 hours at 37 C°. Then we take a sample of the material and "sandwich" it between the monoclonal antibodies. We can get a reading of the sample in about three hours."

Because of the large number of eggs being cultured at the Cooperative Poultry Diagnostic Laboratory at New Bolton Center, Dr. Keller has been able to compare

the results of the ELISA test to those from the conventional test and verify the accuracy of the new test. "It's been very exciting and may be a commercial kit can be developed."

When a reading is negative in a suspect house, eggs can be diverted back faster to the grade market. This helps the farmer. And on the other side, if the results are positive, control measures can be instituted much quicker."

## Herpes Virus as a Vector to Deliver Healthy Genes to Brain

Herpes virus, after an acute short infection, becomes latent in the nerve cells. This latency factor plays a key role in research by Dr. John Wolfe, assistant professor of pathology and medical genetics at the School, and Dr. Nigel Fraser of the Wistar Institute. Dr. Wolfe, a specialist in gene therapy, and Dr. Fraser, an expert on herpes virus, have collaborated to construct a herpes virus vector to deliver a healthy gene to central nervous system cells of mice afflicted with mucopolysaccharidosis (MPS) VII (Sly disease).

"The herpes virus is uniquely able to transfer genetic material to a brain cell without killing it because it is a latent virus," notes Dr. Fraser. "The advantage of the herpes virus is that it can transfer the gene directly to the target organ, without removing cells from the body and then reimplanting them," says Dr. Wolfe. "The healthy gene remains active in the brain cells, which is important for achieving permanent correction of the deficiency."

The researchers modified a herpes simplex virus (HSV-1) and inserted a normal gene for enzyme production near the location of the virus' latency gene to take advantage of that gene's ability to activate the normal gene. The reconstructed virus was injected into a group of mice with MPS VII and it was found that a small number of central nervous system cells then produced the proper enzyme over a prolonged period of time.

This is the first time that a genetic deficiency in diseased cells of the brain has been corrected by gene therapy. Drs. Wolfe and Fraser caution that further development is needed to correct enough cells to improve the disease in patients. It has been shown, in previous studies, that vector-transferred enzyme activity in MPS VII can result in correction of the metabolic defect. Thus the expression of vector-transferred gene in the central nervous system should correct the metabolic deficiency.

Sly disease, an inherited lysosomal storage disease, causes mental retardation and affects the liver, skeletal system, heart, eye and brain. It is a rare, but devastating fatal disease of humans, and has been identified in dogs and mice. It is estimated that 1 in 25,000 human births will result in some form of MPS. The disease is caused by a genetic deficiency where cells are unable to produce an enzyme needed to break down complex sugar molecules.

The molecules accumulate in the cells, interfering with normal function.

Dr. Wolfe points out, that at this time, the number of cells showing activity of the corrected gene is small. However, as knowledge increases, the herpes virus vector could become an important vehicle to deliver corrective genes to the brain and other parts of the central nervous system.

The medical genetics group at the School has a long history of investigating the genetics, biochemistry, pathology, and treatments of animals with genetic diseases. Studies of these naturally-occurring counterparts of human genetic diseases have contributed to understanding both human and animal health. The Wistar Institute is an independent basic science research center located on the Penn campus with programs in virology, molecular genetics, cell and developmental biology, cancer therapies, structural biology and immunology.

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A mouse afflicted with MPS VII.