Understanding West Nile

A new "gene chip" developed at the University of Florida College of Veterinary Medicine sheds light on brain response in horses infected with West Nile virus and could lead to better ways to diagnose and treat both equines and humans, researchers said.

Using gene sequencing technology, the researchers developed a "brain and immunity chip" to characterize molecular changes in the equine brain during illness and recovery from West Nile virus. The findings were published in the journal *PloS One* in October.

"We hope this will help us understand why some animals and humans become sick and others succumb to the virus resulting in severe illness, lifelong neurological debilitation and even death," said senior author Maureen Long, an associate professor of infectious diseases and pathology. "Knowing this will allow us to come up with treatments that aid in recovery from illness."

University of Florida veterinarians hope new gene chip will help detect, treat West Nile Virus in horses and humans.

Lead author and Long's former graduate student Melissa Bourgeois, created a gene library enriched for neurological and immunological sequences to develop the novel chip, which will help target genes that are active during brain disease states.

A gene chip, or microarray, is a slide with hundreds of pieces of DNA strands arranged in a regular pattern. When those strands, called probes, are exposed to genetic material from equine cells, researchers can identify genes associated with equine brain disease. The UF group relied on Agilent Technologies, based in Santa Clara, Calif., which has patented the probes.

In the end, the equine brain chip consisted of 41,040 genes and included many targets that have counterparts in human psychiatric diseases, such as depression and schizophrenia; and

neurodegenerative diseases, such as Parkinson's and Lou Gehrig's disease.

West Nile virus

West Nile virus is a potentially serious illness often transmitted by mosquitoes. Since 1999, more than 24,000 cases of West Nile virus encephalitis have been reported in horses in the United States, with more than 1,000 cases reported in 2006, according to the American Association of Equine Practitioners. In 2006, there was a 14% increase in human cases and new expansion of the virus into 52 U.S. counties.

Long and Bourgeois investigated the basic idea that certain families of genes change expression in a consistent manner during West Nile virus infection, as well as during the disease and recovery from encephalitis caused by it.

"Although we knew there were microarrays that had previously been developed for horses, our goal was to create a brain and inflammation-based array to look specifically at how function was affected during brain infection," said Long, who is also a member of the UF Emerging Pathogens Institute. "This chip has applications to many brain and spinal abnormalities of the horse, including eastern equine encephalitis, equine protozoal myelitis, rabies, and even non-infectious diseases like Wobbler syndrome. This allowed us to detect changes that would not be common in normal horses."

The UF study took more than five years and relied heavily on sequencing and bioinformatics expertise provided by the university's Interdisciplinary Centers for Biotechnology Research.

"Analysis of the data found that many of the psychiatric, Parkinson genes and neuromuscular diseases were triggered," Long said. "Then a computer program that can analyze hundreds of genes simultaneously was used to build models of various disease processes that may be affected in the acute disease and may result in other diseases once the infection is long gone."

Data mining and testing of individual pathways of disease is the focus of current work in Long's laboratory.

"The wonderful resources and excellent collaborators at the University of Florida will allow us to use the power of comparative medicine to contribute to the biology of brain infection in humans in animals," Long said.

Bourgeois, who now works in the influenza division of the Centers for Disease Control in Atlanta, said, "Information discovered in this research could eventually be used to combat not only outbreaks of West Nile virus, but also as a model to understand and reduce the impact of viral encephalitis in general."

Other collaborators include UF's Nancy Denslow, a professor of physiological sciences; David Barber, formerly an assistant professor of physiological sciences at UF; and Kathy Seino, an assistant professor at Washington State University.

Editor's Note: *This article was provided by the University of Florida.*