Genetic Basis for Establishment of EAV Carrier State

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New research from the University of Kentucky (UK) suggests that genetic factors play a role in determining stallion susceptibility to equine arteritis virus (EAV) infection.

Results from the laboratory of Udeni Balasuriya, BVSc, PhD, professor of virology at the UK Gluck Center, demonstrated a correlation between horse genetic factors and establishment of EAV carrier state in stallions. Genome-wide analysis shows that the equine chromosome 11 (ECA11) carries genes that are likely involved in cellular susceptibility to the virus.

Equine viral arteritis (EVA) outbreaks result in significant economic losses to the equine industry due to high rates of abortions, death in young foals, and establishment of the carrier state in stallions. Persistently infected carrier stallions function as the natural reservoir of EAV, and they disseminate the virus to susceptible mares at breeding.

Results of previous studies by Yun Young Go, DVM, MSc, PhD, a former graduate student in Balasuriya's laboratory, identified that horses can be divided into two groups based on in vitro (in the lab) susceptibility of their lymphocytes (white blood cells) to EAV infection. One group of horses had lymphocytes susceptible to in vitro EAV infection and the other group had lymphocytes resistant to in vitro EAV infection. Based on this finding, the investigators hypothesized that there must be a genetic basis for this phenomenon.

In their study, the researchers randomly selected 310 horses representing four different breeds (Thoroughbreds, American Standardbreds, Standardbreds, and Quarter Horses) from Kentucky farms. They collected blood samples and divided the samples into two groups according to the susceptible and resistant types of lymphocytes to in vitro infection with EAV. Then, using genome-wide analysis tools, they analyzed DNA from each group's cells to determine which genes might contain markers involved in viral infection of the cell.

Of the 310 horses, 167 had the susceptible lymphocytes and 143 had the resistant type. By breed, 95% of the Standardbred horses had the susceptible cell type, and approximately 90% of the American Standardbred horses had the susceptible type. Thoroughbreds and Quarter Horses had the lowest prevalence of the susceptible type (23%). Quarter Horses had evenly distributed resistant and susceptible cell types.

The genome-wide analysis of EAV susceptibility showed that Standardbreds were most fixed for susceptibility markers, meaning that almost all Standardbreds have the genetic markers associated with cell susceptibility to EAV. Of the four breeds, Thoroughbreds had the lowest number of markers associated with the susceptible type.

Thoroughbreds have less diversity for genetic markers than other breeds. By analyzing this breed first, the researchers were able to uncover a specific marker for lymphocyte susceptibility indicating

that EAV infection is highly associated with the ECA11 chromosome. The genes on this chromosome encode proteins that are involved in virus attachment and entry into the cells, the inflammatory response, and cellular immunity.

EAV might interact with some of these cellular proteins to evade the equine immune response and establish persistent infection in some, but not all, stallions infected with the virus, as only some stallions become persistently infected carriers, according to the authors. Recently, the same researchers demonstrated that stallions with lymphocytes susceptible to EAV infection might have a higher risk of becoming carriers.

"These studies can help us develop working hypotheses about why horses become infected, and how persistent infection is established in the stallion," said Balasuriya. "The next step is to test semen samples using the same techniques. To continue these studies, we have recently been awarded a \$2.9 million five-year grant by the United States Department of Agriculture-Agriculture and Food Research Initiative to specifically identify the genetic factors responsible for establishment of the EAV carrier state in stallions."

These papers are available at http://jvi.asm.org/content/85/24/13174 and http://jvi.asm.org/content/86/22/12407.