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Expanding the understanding of equine and human diseases

By Dan Gurvich



A Cornell veterinary immunologist and a mare from his research herd are at the center of what may turn out to be the most important breakthrough for horses since the advent of the horseshoe some 2,000 years ago. The completed map of the horse genome has already enabled advances in equine medicine, from the study of simple genetic traits to complex multi-gene conditions and the genetic regulation of development and healing. In addition, the horse genome holds the potential to shed light on human genetics and disease.

A paper published in this week's edition of the journal *Science*—written by the international Horse Genome Project team that includes Dr. Doug Antczak, Dorothy Havemeyer McConville Professor of Equine Medicine at the Baker Institute for Animal Health—provides a high quality draft of the approximately 2.7-billion DNA base pair sequence, as well as comparative analysis and population genetics of the horse. Among the paper's findings is that the arrangements of genes on individual chromosomes between horses and humans are actually quite similar. This high degree of conserved synteny between horses and humans will assist comparative and translational researchers in using insights from one species to illuminate the other. The study's authors also note that horse population history has led to important genetic similarities across horse breeds, increasing the feasibility of across-breed mapping.

"The horse genome sequence is changing equine research and clinical medicine fundamentally and completely," said Antczak, who noted that it also promises insights for human medicine. "Researchers in many areas are rapidly adopting this technology, and those who are not using it may soon find themselves behind the times."

Antczak has been a leading member of the Horse Genome Project from its inception in 1995. An immunologist, Antczak became involved in genetics while investigating the mechanism that allow a placenta and fetus to avoid destruction by the maternal immune system in pregnant mares. Twilight, a young Thoroughbred mare from Antczak's research herd at McConville Barn had the distinction of being chosen as the DNA donor for the entire horse genome, which was sequenced in 2006 at MIT and Harvard's Broad Institute.

The Horse Genome Project was originally supported by the Dorothy Russell Havemeyer Foundation, and later by other funding agencies, including the U.S. Department of Agriculture. However, in 2005 it received funding through the National Human Genome Research Institute at the National Institute of Health, which recognized the value of genomics work in the horse for its power to illuminate the human genome and generate knowledge valuable to human health.

In the area of translational medical application, genome mapping has already enabled the development of genetic tests for approximately 10 simple inherited genetic diseases, including Severe Combined Immunodeficiency Disease of Arabian horses, Lethal White of Paint horses, HERDA and HYPP of Quarter Horses. Genetic testing for these single-gene disorders, some of them fatal, is becoming standard practice for certain horse breeds and may soon eradicate these conditions.

Another highly promising application of the horse genome is the development of expression arrays. These miniature devices contain probes for all of the 20,000+ genes of the horse on chips that can be used to profile gene activity across the genome, illuminating unknown functions and mechanisms of normal physiology and disease. Expression profiling may one day produce breakthroughs in areas as diverse as lameness, lung disease, reproduction, and immunology. For example, at the College of Veterinary Medicine, Dr. Alan Nixon, Professor of Large Animal Surgery and Director of the Comparative Orthopedics Laboratory, is using equine expression arrays to investigate osteochondritis dissecans, a common and debilitating cartilage disease in growing animals and children. Dr. Dorothy Alnsworth, Professor of Large Animal Medicine, is utilizing the technology to study equine chronic lung disease. And Dr. Tracy Stokol, Assistant Professor of Clinical Pathology plans to apply the expression array developed in Antczak's laboratory to study aspects of equine herpes virus disease.

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