

Untapped Potential of Physiological Genomics

While recent accomplishments have revolutionized the field of animal-health research, scientists at ARS's National Animal Disease Center (NADC) in Ames, Iowa, know that we are all still in the early stages of a whole new era.

NADC is the nation's largest federal animal-health research center. Recently, its scientists have made highly significant contributions to the list of organisms whose genomes have been sequenced and genetically mapped. Remarkably, they and their collaborators have completely sequenced the genomes of several species of pathogenic bacteria that infect livestock, including ones that cause brucellosis, Johne's disease, and bovine leptospirosis.

Genome sequencing is the process of determining the arrangement of nucleotides that make up an individual's entire genetic code. Sequence data makes it possible to identify genes that ultimately determine traits associated with health and disease. These genes can also help us pinpoint traits that we do or don't want in plants, animals, bacteria, or viruses.

An extension of genome sequencing in which I see explosive potential is physiological genomics, an emerging discipline in which scientists study the specific physiological functions that genes produce when they're expressed. Now that we have key genetic sequences in hand for many organisms, it's vital that we use them to advance our knowledge about the specific functions of these gene products when they are expressed—especially during various states of animal health and disease.

Recent advancements have left animal-health research rife with untapped opportunities to use physiologic genomics. At NADC, we're already using it in discovering, understanding, and managing host-response and disease-pathogenesis mechanisms in livestock.

Veterinary medical officer Juergen Richt recently evaluated cattle that had been genetically modified to be incapable of producing prion proteins. He determined that the animals' lack of prions had no observable adverse effects on their health! This is big news, because abnormal prions are believed to cause devastating illnesses called "transmissible spongiform encephalopathies," the best known of which is bovine spongiform encephalopathy—or mad cow disease.

The story on page 4 of this issue explains how comparing the genomes of different species of *Leptospira* bacteria led to a key discovery: that certain strains express genes that enable them to persist in the environment, but other strains do not.

Another NADC study is applying comparative genomics to identify genes in the swine influenza virus genome that convey varying levels of cross-reactivity and protection when different viral strains are used as a swine vaccine.

A particularly intriguing possibility resulting from this new world of science is an increase in collaborative research between veterinary and human medical researchers to combat potential emerging zoonotic diseases—those that can pass from livestock or wildlife to humans.

NADC has had an early upper hand in this work. Veterinary medical officers Ray Waters and Mitchell Palmer have found that whitetail deer are exquisitely sensitive to *Mycobacterium bovis*, the bacterium that causes tuberculosis in cattle and humans. With collaborators, they are using the cow as a scientific model through which to evaluate vaccines for tuberculosis.

Comparing immunological responses to *M. bovis* in whitetail deer and in cattle could yield important insights for identifying genes within this microbe that are keys to determining its host pathogenicity. This knowledge could ultimately help scientists develop better vaccines against *M. bovis* in cattle, whitetail deer, and perhaps even humans.

Physiological genomics can also be used in determining how microbial ecology affects animal health, persistence of antimicrobial resistance, and potential colonization by foodborne pathogens.

Using genomics-based methods to describe the microbial communities growing within the turkey intestinal tract, microbiologist Alexandra Scupham found a dramatic change in intestinal communities two-thirds of the way through the production cycle. This change may be correlated to increased colonization of the gut by the foodborne pathogen *Campylobacter* and other animal pathogens.

Reasons for this apparent change are unknown. But further examination of microbial communities that hinder intestinal colonization by *Campylobacter* will help scientists develop interventions.

Despite all the recent gains, there are still important challenges to meet. One is to find new ways to study gene function and its role in health and disease.

Now that physiological genomics enables us to evaluate thousands of genes simultaneously, we must become more adept at studying how genes of the host and of the pathogen interact over time to cause disease.

To accomplish such a large task, ARS must take a leading role in establishing teams of veterinarians, animal scientists, molecular biologists, and information technologists that are capable of working freely across several locations and management units.

Breaking existing barriers between scientific disciplines will help science in general break other barriers—ones that prevent us from curing diseases of animals and humans alike.

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