Peering at Genes To Detec

The eyes are said to be the windows into the soul of humans, but in the case of cattle, they may hold clues to overall animal health. A closer look at pinkeye is offering insight into other costly bacterial diseases as well.

Researchers at the Agricultural Research Service's Roman L. Hruska U.S. Meat Animal Research Center (USMARC) in Clay Center, Nebraska, have found that genes are linked to the incidence of several diseases. Eduardo Casas, a geneticist in the Genetics and Breeding Research Unit at the time of the study, and former ARS scientist Gary Snowder discovered a quantitative trait locus (QTL), or location, on bovine chromosome 20 that is associated with pinkeye, foot rot, and bovine respiratory disease.

Looking Beyond the Pathogens

Scientists have known for some time what causes pinkeye, also known as "infectious bovine keratoconjunctivitis," and other diseases. The bacteria *Moraxella bovis* is the most common pathogen associated with pinkeye. Pathogens associated with bovine respiratory disease include viruses, such as bovine viral diarrhea virus, bacteria, like *Mannheimia hemolitica,* and mycoplasma. *Fusobacterium necrophorum* and *Porphyromonas* spp. are the main bacterial pathogens for foot rot, or infectious pododermatitis.

"Scientists have spent a lot of effort and money studying the pathogens that make animals sick," says Casas, who is now research leader for ARS's Ruminant Diseases and Immunology Research Unit in Ames, Iowa. "We've made a lot of progress, but the microbes are still around. Therefore, the main focus of this research was to look at diseases from the animal's point of view."

Casas' approach was to examine the genetic makeup of cattle for evidence of genes associated with conferring resistance or tolerance to diseases. His initial study focused only on pinkeye because it's easy to see and measure in cattle, he says.

Different breeds vary in their pinkeye tolerance. For example, Herefords are very susceptible, but Brahmans are highly resistant. With this in mind, a Brahman-Hereford crossbreed sire was mated to other breeds to yield more than 540 offspring.

"This particular bull was heterozygous for all genes that would confer tolerance to pinkeye," Casas says. "Half of the offspring inherited the resistant gene, and the other half inherited the susceptible gene."

When scientists looked at 36 offspring affected by pinkeye, they found that regions on chromosomes 1 and 20 harbored genes that influence the presence of bacteria, but no strong linkage to a QTL was identified. So the team took a different approach.

A Tale of Three

Following up on a theory that the immune system is influenced by various genes, Casas and Snowder conducted a second study. They combined the incidences of three highly prevalent bacterial diseases affecting feedlot cattle—pinkeye, foot rot, and bovine respiratory disease.

"When you put all three diseases together, you're looking at the overall health of the animal, or resistance to multiple diseases, rather than a disease-specific response," Snowder says. "In other words, the particular loci affecting an individual disease may not be easy to pick up, but it might be easier to pick up markers that are related to the general health of the animal."

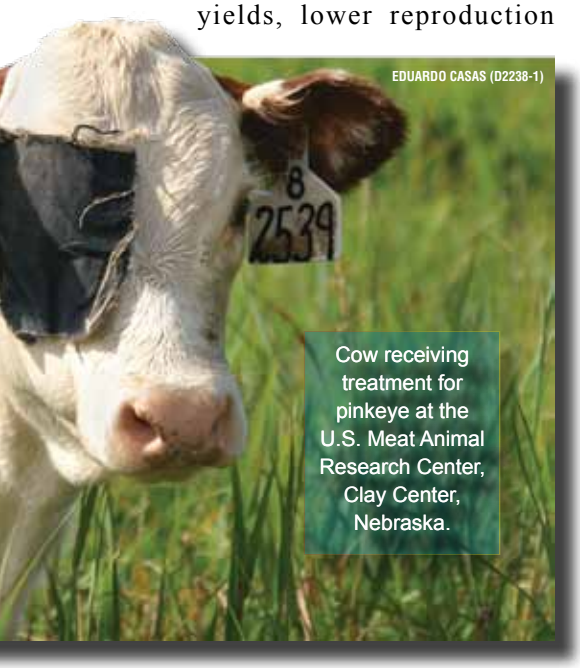
Selection for disease resistance is one of several possible interventions to prevent or reduce economic loss associated with animal disease and to improve animal welfare, according to Casas and Snowder.

A common condition affecting breeding-age beef heifers, pinkeye has a marked economic impact on the cattle industry—costing an estimated $150 million a year due to lower weight gains, decreased milk production, and treatment. Although not fatal, this highly contagious disease can affect up to 80 percent of a herd. Calves being weaned are even more susceptible and can lose as much as 10 percent of their body fat if they contract the disease.

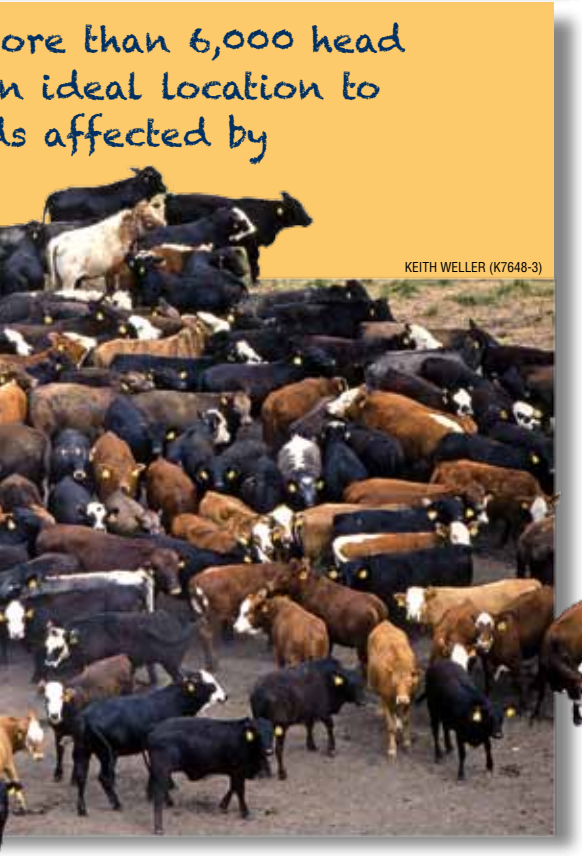
Bovine respiratory disease—pneumonia—is the most common and costly feedlot disease in the United States. It accounts for 75 percent of feedlot morbidity and up to 70 percent of all deaths. Economic losses to cattle producers exceed $1 billion annually from animal deaths, reduced weight gain, lower feed efficiency, treatment costs, and poor-quality meat and hide products.

t Origin of Cattle Diseases

While foot rot is not as expensive as other diseases, it is estimated to cost dairy producers about $120 to $350 per animal. Foot rot causes lameness and leads to reduced milk yields, lower reproduction performance, increased involuntary cull rates, and discarded milk.



Cow receiving treatment for pinkeye at the U.S. Meat Animal Research Center, Clay Center, Nebraska.



Producers have been managing these diseases with various treatments and management practices. USMARC, which has more than 6,000 head of cattle, provided an ideal location to study different breeds affected by pathogenic diseases.

Breeds Apart

In addition to the Brahman-Hereford family studied in the pinkeye experiment, three other half-sibling families were produced to detect QTLs associated with combined incidences of the three diseases.

The second half-sibling family was developed from a Brahman-Angus sire and produced 176 offspring. A Piedmontese-Angus sire fathered 209 calves, and a Belgian Blue-MARC III (part Red Poll, Pinzgauer, Hereford, and Angus) sire produced 246 offspring.

Researchers used microsatellite markers—short, repetitive DNA sequences used as genetic markers to track inheritance—to screen the genome of each family. Informative markers were chosen within a family based on their location in each chromosome.

All animals were observed daily throughout their lifespan for pinkeye, pneumonia, and foot rot and treated when symptoms occurred. The 240 calves infected by one or more of the diseases were classified as affected by a microbial pathogenic disease and coded. Analysis of DNA blood samples taken from these animals revealed QTLs for disease activity.

Though scientists have discovered genetic locations that may influence resistance or susceptibility to bacterial diseases, there's more to do.

"We don't know what the gene or genes are yet, and that's what we are working on," Casas says. More study needs to be done to confirm the association between the genes and disease.

"What's interesting about the markers on chromosome 20 is that they are in very close proximity to other markers related to other diseases. That particular region may have a significant effect on the general health of animals," Casas says.

Additional studies are under way to detect genes associated with reduced susceptibility to bacterial diseases, including Johne's disease and bovine viral diarrhea.

"The costs for treating animals that have these diseases are enormous," Casas says. "Identifying genes responsible would provide an opportunity for effective crossbreeding to produce animals with increased disease tolerance, which would greatly reduce the economic impact to the cattle industry."—By **Sandra Avant,** ARS.

This research is part of Food Animal Production (#101), an ARS national program described at www.nps.ars.usda.gov.

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Geneticist Eduardo Casas (right) and technician Sandra Nejezchleb prepare bovine DNA samples for mass-spectrometry. Results are used to assess whether changes in DNA sequence are associated with pinkeye, also known as "infectious bovine keratoconjunctivitis."

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