

Identifying Variation in the U.S. Bovine Prion Gene

Bovine spongiform encephalopathy—BSE, or mad cow disease—is a serious threat to the U.S. beef industry.

While the first confirmed case of BSE on U.S. soil in December 2003 had little effect on domestic consumption, it carved into our international beef sales. According to USDA's Economic Research Service, the United States exported only \$552 million worth of beef in 2004—down from \$2.6 billion in 2002 and \$3.1 billion in 2003—a reduction due, in part, to the BSE case.

Are some cattle more susceptible to BSE? Is there a genetic component involved?

To address these and other questions, ARS scientists at the U.S. Meat Animal Research Center (USMARC) at Clay Center, Nebraska, have sequenced the bovine prion gene, *PRNP*, in 192 cattle representing 16 beef and 5 dairy breeds common in the United States. This work was partially funded by a grant from USDA's Cooperative State Research, Education, and Extension Service.

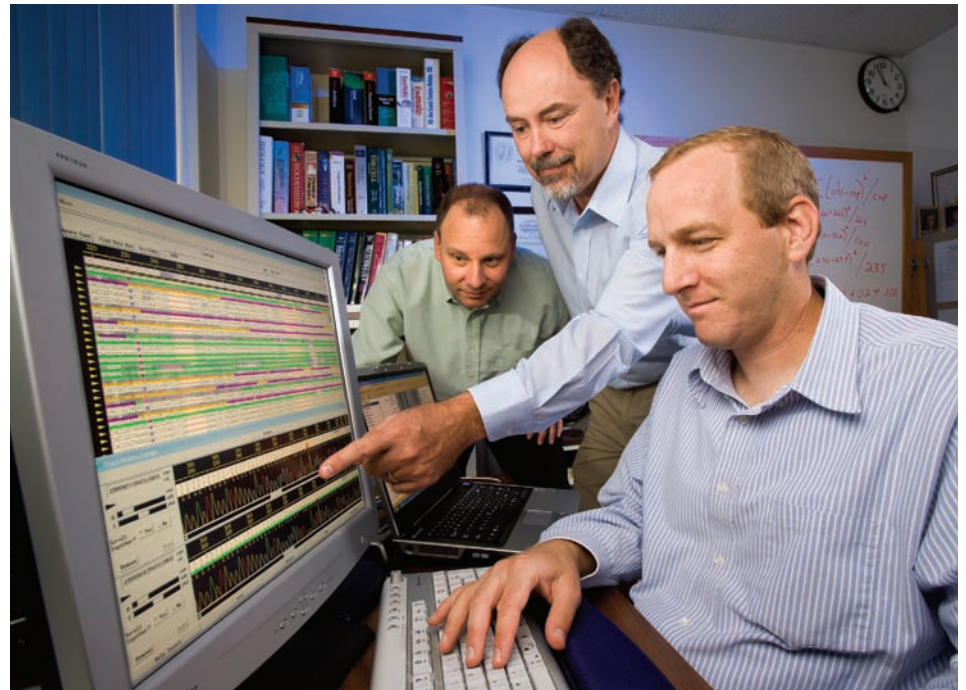
Prions are proteins that occur naturally in mammals. BSE is a fatal neurological disorder characterized by irregularly folded prions. Much is unknown about the disease, but scientists recognize a correlation between variations in the *PRNP* gene in some mammals and susceptibility to transmissible spongiform encephalopathies, such as scrapie in sheep.

"Evidence indicates that this could also be true in cattle," says molecular biologist Mike Clawson. He is among the USMARC scientists examining *PRNP* variation to learn if and how different forms, or alleles, of the prion gene correlate with BSE susceptibility.

A thorough characterization of *PRNP* variation in a U.S. cattle population will provide a reference framework for researchers to use in analyzing *PRNP* sequences from cattle afflicted with BSE.

From the 192 *PRNP* genes sequenced, Clawson and his colleagues have identified

STEPHEN AUSMUS (D663-1)



Microbiologist Michael Heaton (left), research leader William Laegreid (center), and molecular biologist Michael Clawson view DNA sequence variation within the cattle prion gene.

388 variations, or polymorphisms, of which 287 were previously unknown. Some of these polymorphisms may influence BSE susceptibility in cattle, he says. Ongoing studies with European collaborators are testing the newly identified variants for association with BSE. If these studies show some cattle to be genetically less susceptible to the disease, this information could shed light on BSE's transmission and development.

The United States has had only three confirmed cases of BSE. Laboratory tests showed that the second and third of these appear to differ significantly from the first case, says Clawson.

"By comparing the *PRNP* sequence from BSE-infected cattle to healthy cattle, we may be able to identify genetic markers in the prion gene that predict BSE susceptibility," he says.

In addition to *PRNP*, the team is currently sequencing several genes closely related to it. These too will be tested for their association with BSE.

"The prevalence of BSE in the

United States is extremely low and is declining worldwide," Clawson says. "Well-characterized genetic markers that correlate to resistance could improve our understanding of the disease and prepare the cattle industry to respond if another prion disease arises in the future."—By **Laura McGinnis, ARS.**

This research is part of Animal Health, an ARS National Program (#103) described on the World Wide Web at www.nps.ars.usda.gov.

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