

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



Studying the Prion Gene

by Laura McGinnis

Bovine spongiform encephalopathy (BSE) 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 the U.S. Department of Agriculture (USDA) Economic Research Service (ERS), 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 than others? Is there a genetic component involved?

To address these and other questions, ARS scientists at the Roman L. Hruska U.S. Meat Animal Research Center (MARC) at Clay Center, Neb., 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 (CSREES).

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 (TSEs), such as scrapie in sheep.

"Evidence indicates that this could also be true in cattle," says molecular biologist Mike Clawson. He is among the MARC 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 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, Clawson says.

"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."

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Editor's Note: Laura McGinnis is a public affairs specialist for the USDA's Agricultural Research Service (ARS). The research printed here is part of Animal Health, an ARS National Program (#103) available at www.nps.ars.usda.gov. For more information on this research, contact Michael Clawson at the USDA-ARS Roman L. Hruska U.S. Meat Animal Research Center, PO Box 166, Clay Center, NE 68933; phone (402) 762-4342, fax (402) 762-4375. "Identifying Variation in the U.S. Bovine Prion Gene" was published in the January 2007 issue of Agricultural Research magazine.