

## **Bovine genome provides clue to evolution, better beef and milk**

Sequencing of the bovine genome provides new information about mammalian evolution as well as cattle-specific biology and points the way to research that could result in more sustainable food production in a world challenged by global population growth. “The future challenge will be to explore the bovine genome sequence in greater depth to fully understand the genetic basis of the evolutionary success of ruminants as this will provide opportunities to address some of the crucial issues of the present time – efficient and sustainable food production for a rapidly increasing human population,” The cattle sequence took six years to complete, annotate and analyze and has involved over 300 scientists from 25 countries. Most of more than 25 companion reports describing detailed analyses of the two projects by the Bovine Sequencing Project and the Bovine Hapmap Consortia appear online at [www.biomedcentral.com](http://www.biomedcentral.com) in a special electronic issue of the BioMed Central journal group.

The Bovine (cow) Genome Sequencing Project sequenced the genome of a female Hereford cow.

“The mammals we have looked at previously have been laboratory animals and humans,” said Dr. Kim C. Worley, associate professor in the sequencing center and a corresponding author. “This is the first mammalian livestock animal we have studied.”

The authors concluded that the bovine genome, consisting of at least 22,000 genes, is more similar to that of humans than that of mice or rats. They note that most cattle chromosomes correspond to part or all of human chromosomes, although the DNA is rearranged in some areas.

“During evolution, domesticated cattle and other ruminants diverged from a common ancestor that gave rise to humans about 95 million years ago, yet cattle and humans still share a high degree of conservation in the organization of their chromosome architectures, far more so than humans and mice” do, said Dr. Harris Lewin, one of the lead analysts from the University of Illinois at Urbana-Champaign. “We were surprised to find that, like humans, duplicated segments appear to have played a major role in the rearrangements of chromosomes in the cattle lineage.”

Some of these rearrangements appear important to cattle biology because they affect genes involved in immunity, lactation, metabolism and digestion. These changes could help explain the amazing ability of cattle to convert low-quality forage efficiently into energy-dense meat and milk, a fact that benefits humans.

One particular genetic rearrangement involves the histatherin gene in mammary tissue, which undergoes special regulation during lactation to produce a novel protein in milk that has

anti-microbial activity. Other gene changes aid in the transfer of immunoglobulin G to milk and the subsequent transference of innate immunity to suckling calves from their dams.

The researchers said, "Observation suggests that species-specific changes in genome organization and gene regulation may help tailor the functional components of milk to the specific needs of newborn mammals. They also add to the mounting evidence that milk contains 'innate immune' proteins that may be important for gut protection and gut development in the suckling young as well as the health of the mammary gland."

"More generally, it appears that the cow has significant rearrangements in many of its immune genes and enhanced innate immune defense capacity. This may be in response to increased risk of opportunistic infections at mucosal surfaces caused by the large number of microorganisms carried in the rumen (the largest of the four compartments that make up the bovine stomach)," said Dr. Ross Tellam of the Commonwealth Scientific and Industrial Research Organization of Australia.

The knowledge gleaned from this sequencing could lead to more efficient beef and milk production, the researchers noted.

In a companion report, the bovine HapMap (a literal map of genetic diversity among different populations) described genetic variation among different branches of the bovine tree, starting with the major division between the humpless taurine cattle most commonly found in Europe, Africa and East and West Asia and the indicine found in India, South and West Asia and East Africa.

The researchers used the complete sequence from a single Hereford cow and comparative genome sequences from six more breeds to look for changes called single nucleotide polymorphisms or SNP in 497 cattle from 17 geographically and biologically diverse breeds and two related species (Anoa and Water Buffalo).

Their studies indicate the cattle have a diverse ancestral population that has undergone a recent rapid decrease in effective population size, probably because of domestication, selection and the development of breeds. The evolution of humans and cattle intertwined between 8,000 and 10,000 years ago, and today there are more than 800 cattle breeds selected for different economic, social and religious reasons.

"Domestication and artificial selection appears to have left detectable signatures of selection within the cattle genome yet the current level of diversity within breeds is at least as great as exists within humans," the authors noted.

The scientists found that genetic diversity among the taurine breeds was similar to that found in humans but less than that in the indicine breeds, giving support to the theory that cattle were separately domesticated on the Indian subcontinent from more diverse wild populations.

Although the decline in diversity among cattle is rapid enough to prompt concern among cattle breeders, the new tools will enable better conservation of genetic diversity in the species, the scientists reported.

The implications of the genome project for the beef and dairy industries loom large.

Dr. Gordon Doak, president of National Association of Animal Breeders, an industry trade group of organizations that market semen for breeding dairy and beef cattle, said, "The availability of very large numbers of SNP (single letter changes in the genetic blueprint) has allowed the development of gene chips that measure genetic variation in cattle populations and will allow the rapid selective breeding of animals with higher value commercial traits," he said. "This technology is quickly transforming the dairy genetics industry and has the potential to dramatically alter beef cattle industries as well."

These new tools provide a means of selection of more energy-efficient animals with a smaller environmental footprint, particularly animals with less greenhouse gas emissions.

The effort was a true collaboration. For example, researchers from the University of Houston also took part.

"As usual we analyzed compositional heterogeneity and used it to locate genes. We also analyzed potential errors due to quality of sequences by comparing the old draft genome with the finished version," said Dr. Dan Graur, UH professor of biology and biochemistry

The sequencing project was led by Drs. Gibbs and George Weinstock, co-directors of the BCM-HGSC, Dr. Steven Kappes of the United States Department of Agriculture, Dr. Christine Elsik of Georgetown University and Dr. Ross Tellam of CSIRO Australia. The HapMap project was led by Gibbs, Dr. Curt Van Tassell of the United States Department of Agriculture and Dr. Jeremy Taylor of the University of Missouri. A full listing of participants can be found in the article at [www.sciencemag.org](http://www.sciencemag.org).

Funding was provided by an international group that included the International Atomic Agency (IAEA) and the Food and Agriculture Organization of the United Nations (FAO), through its Animal Production and Health (APH) programme of the Joint FAO/IAEA Division for Nuclear Applications to Food and Agriculture. Specifically, the Joint FAO/IAEA Division sponsored the inclusion in the study of the Sheko breed, which is native to Ethiopia. The Sheko breed is resistant to trypanosomosis and has the ability to achieve good productivity under difficult environmental conditions in Africa.

It is hoped that the information obtained from the study can be a first step in the greater utilization of the Sheko and other related indigenous breeds to improve livestock productivity in Africa and, as a result, the livelihoods of farmers. Technical Officers of the APH also contributed to data analysis.

Other organizations that supported the study are the National Human Genome Research Institute, which funded more than half of the project; the U.S. Department of Agriculture's Agricultural Research Service and Cooperative State Research, Education, and Extension Service National Research Initiative; the state of Texas; Genome Canada through Genome British Columbia; The Alberta Science and Research Authority; The Commonwealth Scientific and Industrial Research Organization of Australia (CSIRO); Agritech Investments Ltd., Dairy Insight, Inc. and AgResearch Ltd., all of New Zealand; the Research Council of Norway; the Kleberg Foundation; and the National, Texas and South Dakota Beef Check-off Funds. Funding for the genetic diversity work was provided by: American Angus Association, American Hereford Association, American Jersey Cattle Association, AgResearch (New Zealand), Beef CRC and Meat and Livestock Australia for the Australian Brahman Breeders Association, Beefmaster Breeders United, The Brazilian Agricultural Research Corporation (Embrapa), Brown Swiss Association, GENO Breeding and Artificial Insemination Association - Norway, Herd Book/France Limousin Selection, Holstein Association USA, International Atomic Energy Agency - FAO/IAEA Vienna, International Livestock Research Institute – Kenya, Italian Piedmontese Breeders - Parco Tecnologico Padano, Italian Romagnola Society - Università Cattolica del Sacro Cuore, Livestock Improvement Corporation, Meat & Wool New Zealand. North American Limousin Foundation, Red Angus Association of America, The Roslin Institute for UK Guernsey, and Sygen (now Genus).

The full report is available at [www.sciencemag.org](http://www.sciencemag.org).

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