Genomics—What It Means to You and Your Cattle

Lee A. Bulla, Jr.

A particularly noteworthy accomplishment for the cattle industry was the completion of the sequence of the cow genome, published in the journal *Science* in April, 2009. The subject of the sequencing project was a brown and white Hereford cow named L1 Dominette 01449. This achievement almost certainly will have a major impact on livestock breeding in years to come. The most likely consequence will be improving efficiency of cattle production, which should help provide more sustainable food stores for an ever-increasing world population. From a science perspective, sequencing of the bovine genome adds new information to cattle biology, contributes to the study of animal evolution and provides a platform for further genomics investigations of cattle in general.

From time to time, I am asked by various people associated with the cattle industry, "What is genomics and why will studying the genome be beneficial?" These questions are important, especially at this time in the cattle industry and, certainly, there is no uncomplicated answer. So, I would like to begin by defining a genome and describing some of its features.

Life as we know it is specified by the genomes of all of the organisms with which we share the planet. Every organism possesses a genome that contains the biological information needed to construct and maintain a living example of that organism. Most genomes, including the bovine genome and those of all other cellular life forms, are made of DNA (deoxyribonucleic acid), although a few viruses (viruses are not considered living organisms because they require a host cell to survive) have RNA (ribonucleic acid) genomes. DNA and RNA are polymeric molecules made up of chains of monomeric subunits called nucleotides (building blocks).

The bovine genome, which is typical of the genomes of all multicellular animals, consists of two distinct parts:

- The nuclear genome comprises approximately three billion nucleotides of DNA, which are distributed on 30 linear molecules, each contained in a different chromosome. These 30 chromosomes consist of 29 autosomes (non-sex chromosomes) and either of two sex chromosomes, X or Y. Altogether, some 22,000 genes are present in the bovine nuclear genome.
- The mitochondrial genome is a circular DNA molecule of about 16,000 nucleotides, multiple copies of which are located in the energy-generating compartments (mitochondria) within cells. The bovine mitochondrial genome contains just 37 genes.

Each of the approximately 100 trillion cells in a cow has its own copy or copies of the genome, the only exceptions being those few cell types, such as red blood cells, that lack a nucleus in their fully differentiated state. The vast majority of cells are diploid and, therefore, have two copies of each autosome, plus two sex chromosomes, XX for females or XY for males—60 chromosomes in all. Diploid cells are called somatic cells, in contrast to sex cells, or gametes, which are haploid and have just 30 chromosomes, comprising one of each autosome and one sex chromosome. Both types of cell have about 9,000 copies of the mitochondrial genome, 10-12 or so in each mitochondrion.

Obviously, the definition of genome is not a straightforward one although we could simplify it by saying that the genome of a cow refers to all of its genes represented in one complete haploid set of chromosomes. And, a genome, any genome, is a reservoir of biological information but, on its own, is unable to release that information to the cell. Utilization of the biological information contained in the genome requires coordinated activity of enzymes and other proteins, which participate in a complex series of biochemical reactions referred to as genome expression.

Back to the original question—what is genomics? Simply stated, it is the study of the functions and interactions of many genes or other DNA sequences, or of comparing genomes. The central consideration of such a study is determining the genome sequence of an organism and comparing it to those of other organisms, i.e., cow vs. human vs. mouse vs. horse, and so on.

Because the sequence *per se* is not self-explanatory, scientists now are beginning to interpret it. The sequence itself is a string of only four letters A, G, C and T (shorthand for those molecules that are a part of the building blocks of DNA) without any spaces or punctuation. Most importantly, they are not indexed. Annotation or interpretation can provide explanatory notes that will accompany the overall sequence.

Indeed, genome annotation specifies functionality of the various regions of a genome, i.e., genes that code for proteins, various elements that regulate these genes and an array of other components associated with the dynamics of the entire genome. Because much of the DNA in a cow's genome does not code for proteins (ca. 2%), parsing out those genes from the remaining 98% of the genome is a daunting challenge. Although the genomes of all cattle breeds have not been sequenced, several comparative studies indicate that all breeds share almost exactly Dominette's genome sequence.

With a somewhat basic understanding of a genome and genomics, the second question pertaining to the benefits of genomics still remains. Let me address this issue by first saying that scientists have identified a number of locations in the genome of individual cows where single-base DNA differences occur. We already know that certain single nucleotide polymorphisms (SNPs) in genes correlate directly with various hereditary diseases of cattle. Identification of genes and SNPs should provide focused targets for the development of effective new diagnostic techniques and therapies for some of the more common diseases of cattle.

Disease-susceptibility prediction based on gene sequence variation soon should be possible as well as identification of those genes involved in complex traits and multi-gene diseases. Chromosomal structure and organization now can be determined along with better understanding of which genes and gene networks contribute to the development of a cow from embryo to a mature animal.

One of the greatest impacts of having the cow sequence along with a great many others, including human, may well be in enabling an entirely new approach to biological research. The classical approach involves studying one or a few genes at a time. With whole-genome sequences and new high-throughput technologies, biological questions can be approached more systematically and on a grand scale. All genes in a genome can be studied, for example, in a particular tissue or organ, and it can be ascertained how tens of thousands of genes and proteins in these body parts work together in interconnected networks to orchestrate their overall functionality.

Even with the full cow genome sequence in hand, there is a myriad of unanswered questions. However, the eventual upshot of studying the bovine genome will be accumulation of meaningful knowledge that will define biological research not only of the cow but other animal species as well.

Biosketch for Lee Bulla

Dr. Bulla is Professor of Molecular Biology at The University of Texas at Dallas where he teaches courses in Human Genetics and Genomics. His research involves the construction of transgenic lines of some of the major plant commodities of the world, including rice, corn and cotton. He also is involved in genomics studies of horses and cattle.

Dr. Bulla will be the featured speaker at the September 2011 meeting of the Red River Angus Association.