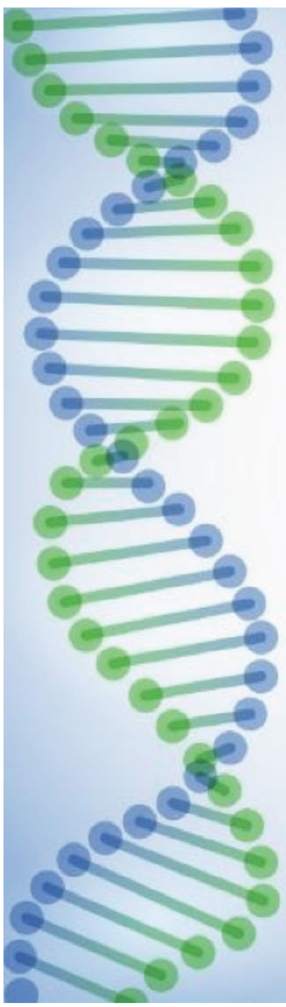
Improving Livestock with Genomics

Livestock genetics are big business - and have helped drive substantial improvements in global agricultural productivity over the last half century. Canada has been a key player, exporting nearly $100 million worth of bull semen in 2013 alone[1]. In 1960, the average Canadian Holstein cow produced about 4500 L of milk per year; today that figure has more than doubled to about 9700 L per year[2]. Over that same period of time, the average percentage of lean (as opposed to fat) content of pork has increased by about a third, from 40 to 55 percent[3]. An additional 98 kg of beef per cow was achieved in 2012 relative to 1970[4]. Genes aren't everything - an animal's traits are determined by the interaction between its genes and its environment. Still, the economic value of good genetics is clear: and the steady increase in the quality and quantity of food available to consumers is the result.



What's a genome?

An organism's genome is the 'blueprint of life,' the complete set of instructions for making the molecules, cells and tissues that control how an animal can perform throughout its life. Every cell in the body contains the complete genome, encoded in the form of DNA. DNA is a long chain molecule made by combining four possible types of building blocks: organic molecules named adenine (A), cytosine (C), guanine (G) and thymine (T). Thus, the genome can be thought of as a book written in a code that contains four possible letters: A, C, G and T. The study of genomics has enabled scientists to learn some of the words in this code, for example, sequences that describe how to make a particular protein molecule are called genes. These genes influence observed traits, everything from eye and coat colour to milk production and bone quality. Mammals have two copies of every gene; one from each parent. These genes could be the same or different, and some versions could confer improved traits.

Today, genomics allow us to quickly and easily sequence DNA from an animal in order to help understand its impact on observed traits. While genomic technology can be applied to change the genome of an organism - including inserting genes from one species into another - this approach is used primarily in plants, not livestock. Instead, genomics provides breeders with more timely and accurate information to improve the quality of their herds.

Starbuck the Superstar

It was a chance meeting at a restaurant outside Port Perry Ontario in May of 1979 that helped make Canadian cattle history. Robert Chicoine and Harley Nicholson worked at the Centre d'insémination artificielle du Québec (CIAQ). Part of their job was to look for young bulls with the potential to become sires for dairy cows. At dinner they ran into Peter Heffernan, owner of Hanover Hill Holsteins, who offered to show them his herd. They selected Hanoverhill Starbuck - a two-week-old bull with exceptional stature, a balanced frame and excellent bone quality - for their breeding program.

It turned out to be one of the best decisions they ever made. Starbuck's daughters had his excellent frame, as well as high quality udders that produced lots of milk. Starbuck himself won many prizes and was voted Premier Sire 27 times. His sperm was exported to 42 countries, and many of his sons became prominent sires in their own right, exerting a major influence on the global dairy herd. By the time he died in 1998, Starbuck produced over 685,000 doses of semen, generating more than $25 million in semen sales and siring over 200,000 daughters around the world[5].

Born in 1979 near Port Perry, Ontario, Starbuck became a world-famous sire to over 200,000 cows around the world, significantly impacting the global Holstein herd and generating millions in semen sales. (Photo credit: Jim Rose/Centre d'insémination artificielle du Québec (CIAQ))

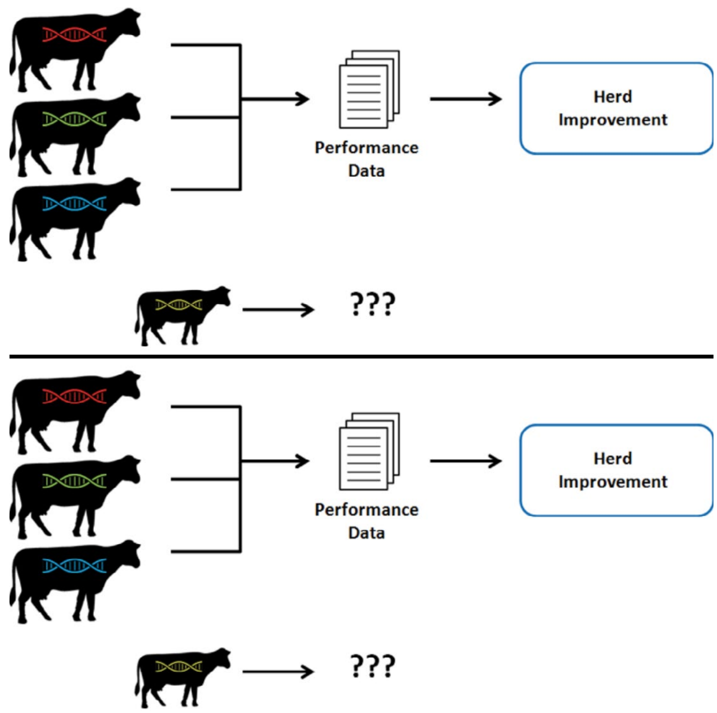
How it works - SNPs and chips

Farmers have always used breeding to improve their herds, but starting in the 19th century they formed associations to keep written records on traits that are of economic value: for example, milk production in the dairy industry, or rate of weight gain in the beef industry. This process became even more streamlined with the widespread adoption of artificial insemination, beginning in the 1950s. As computing power increased, researchers developed complex algorithms that combined data on a number of traits; the Canadian Dairy Network's Lifetime Profit Index is a good example, combining data on 70 separate traits into a single, easy-to-understand number that reflects the animal's value.

Such systems have been very successful, but they provide only an indirect measure of animal's genetic makeup. A given animal's DNA is more than 99 percent identical to every other member of the same species; it's the tiny differences that all together can help determine why one animal performs better than another. One type of difference is called a single nucleotide polymorphism, or SNP (pronounced 'snip'). A SNP is a location in the genome where some members of the population have one letter (e.g. an A) and other members have a different letter (e.g. a G). By looking at a number of different SNPs and determining which version of each an animal has, it's possible to map out a 'SNP profile' for that particular animal; the process is called genotyping. These SNP profiles can then be matched with information on animal performance collected by breed associations and milk recording agencies. Computer programs mine this data to identify which genetic differences have the strongest influence on the desired traits.

While a complete genome may contain billions of SNPs, in practice it's only necessary to track a few of these to identify beneficial differences. The technology that makes this possible is the SNP chip which provides a simple, fast and inexpensive way to test a DNA sample from the animal - a few hair follicles would be enough - against many possible SNPs in order to create a SNP profile/genotype that can be correlated to real-life traits. Such chips began to become available in the early 2000s, first for dozens of SNPs, then for hundreds. In 2007, a consortium that included the American biotech company Illumina, the US Department of Agriculture, the University of Missouri, and the University of Alberta developed the Illumina BovineSNP50 BeadChip, which tracked 54,609 different SNPs and led to explosive growth in the use of genomics in improvement of agricultural livestock.

Today, there are high-density chips available for cows that track up to 770,000 SNPS and one for pigs that tracks over 60,000 SNPs. It's also possible (but more costly) to sequence the complete genome of an animal. However, given that most SNPs will not be associated with beneficial traits, this level of detail isn't usually required, and is typically only done for key animals, such as bulls that have sired many offspring.



Top: Breeders have always kept data on animal performance to improve the herd. However, young animals have no data; their performance must be estimated based on their parentage, or through time-consuming processes such as proving. Bottom: Genomics allows breeders to link real genetic data with past performance, providing faster data and speeding up herd improvement.

Benefits

A glimpse at greatness

Back in 1979 the genetic value of a bull like Starbuck was determined through a process known as proving which involves tracking performance information from his first 100 daughters. It's a lengthy process: a bull takes nearly a year to reach sexual maturity, and his first daughters will not be born until at least 9 months later. By the time those daughters have each had a calf and begun producing milk, up to five years may have elapsed.

If another Starbuck were born today, we'd be able to compare his SNP profile with that of previous high-performing bulls using a SNP chip; in other words, we might be able to predict his superstar status earlier. Such glimpses into the future are still blurry; current estimates are that genomics alone can only predict a bull's genetic value with about 75 per cent reliability, whereas going through the multi-year proving process predicts this with about 85 per cent reliability[4]. Still, having an early estimate of a bull's genetic worth is a big advantage; it means that fewer bulls will have to be 'proven' and those who are chosen as the best sires for the next generation can start to be used sooner, accelerating the rate at which genetic improvement can be made. Genomics and proving can also be used together, which can bump the reliability of estimates even higher, up to 90 per cent[6]. As databases get bigger and software becomes more sophisticated, the accuracy of these estimates will continue to increase.

Tracking more traits, more comprehensively

Tracking some traits - for example, how efficiently animals transform feed into muscle - over an animal's entire lifetime can be costly and tedious; doing so for all animals in a herd would be almost impossible. Genomics offers a way forward by allowing results from a smaller sample group sizes to be applied to the entire herd. For example, imagine if a group of 1000 animals were genotyped and then tracked throughout their lives for some difficult-to-measure trait. This 'training set' could be used to create computer programs that determine which SNPs influence feed efficiency. Once that is done, any animal could be genotyped to get a quick estimate of feed efficiency. Researchers from the Centre for Genetic Improvement of Livestock at the University of Guelph and Livestock Gentec, a research centre at the University of Alberta, and other institutions are already using this approach to identify SNPs that influence feed efficiency in beef cattle[7,8].

Maintaining diversity

If a herd is too genetically similar, certain animals may start to suffer from inbreeding, or accumulate the recessive mutations which lead to more genetic disease. Computer programs can compare SNP profile across a herd, allowing breeders to accurately track how diverse it is and manage inbreeding to appropriate levels.

Limitations and risks

Genes aren't everything

An animal's genetics are not the only factor in determining its performance. Genes describe the potential of an animal, but the environment - feed, nutrition, stess, herd management, etc. - has a strong influence on whether that potential is actually reached, in most cases a stronger influence than genetics alone. Genomics is not a panacea.

Emergence of unknown traits

Over the years, herd managers have learned that selecting for particular traits can come at the expense of others. For example, in the past, the dairy industry emphasized milk production, but eventually discovered that fertility, which is harder to measure, was dropping. Today fertility traits are tracked and the trend has been reversed, but it took years.

While genomics can help track more traits, it also increases the speed at which these traits can be changed. Because we don't always know what negative traits to look for, it's possible that new ones could emerge, for example, genetic vulnerability to a particular disease. If so, they would do so more quickly than in the past.

Success in Canada's Dairy Industry

Dairy farmers almost exclusively raise a single breed of cow - the Holstein - and have been keeping detailed records on the genetic value of their livestock for decades, so it's not surprising that dairy farmers have had a 'head start' when it comes to implementing the new methods. Groups like the Canadian Dairy Network, began to gather genomic information on Holsteins in the late 2000s. By 2010 over 50,000 Holstein cows in North America had been genotyped; today that number is closer to 250,000.

In Canada, genomic technology has already had a major impact on livestock health and productivity since it gained widespread use around the year 2009-2010. According to the Canadian Dairy Network, overall, the genetic value of the cow as measured by the Lifetime Profit Index (LPI) has increased twice as quickly after the introduction of genomics. It's estimated that this increased rate of improvement brings in an additional $125 million in year-on-year profits[9].

Most dairy cows are Holsteins for which lots of performance data is available, making this industry ideally suited to adopt genomic technology. (Credit, Jess Johnson, via Flickr)

Availability/cost of data

Genotyping an animal using a SNP chip takes approximately a week and the cost ranges from about $40 to $100 depending on how many SNPs you want to track. However, what's required is not a single animal, but a database of hundreds of animals so that computer models can match genotype information to data on animal performance. Because such database are costly to build and maintain, they are typically funded by large breed associations or government agencies; it's no surprise that common breeds like Holsteins tend to have larger databases, while local, heritage or specialty breeds (e.g. Canadienne) may not have as much information available.

Even when the data is plentiful, it takes time to develop the computer models that predict which SNPs will impact which traits; in many cases, researchers are still at the beginning of such a process.

The Canadian Cattle Genome Project

2014 is the final year of the three-year Canadian Cattle Genome Project (CCGP) which aims to build on the successful model of the dairy industry and expand it to other industries, such as beef. Its goal is to create a database of complete genome sequences for dozens of bulls within each breed, as well as 50K and 770K SNP profiles for hundreds more. By tying the genetic information to records on each animal's performance, the CCGP hopes to provide a 'training set' of data that can be used to develop new computer models to guide genetic improvement for purebred and crossbred animals. In particular, they hope to focus on traits that are difficult to measure in larger data sets, such as feeding efficiency.

As of April 1, 2014, the project has completely sequenced 382 animals and genotyped over 10,000 more. Some of these are historically famous bulls going back as far as 1900 (their DNA samples were obtained from archives and from samples held by breeders) which have had a major influence on today's herds.

Seven Forty Seven, a world renowned Grand Champion bull at the Iowa state fair in 1980, is a key founder of the Canadian Limousin herd and one of the bulls to be genotyped by the Canadian Cattle Genome Project. (Photo credit: Fred Stevens/Canadian Cattle Genome Project)

The future

In principle, genomic technology could be taken further through the process of 'genome editing' which would allow scientists to tailor the genetic makeup of cows by adding or deleting certain SNPs. That approach could raise a variety of technological, ethical and legal issues, and commercial application is still far from being a reality. In the meantime, genomics will see its biggest success in accelerating the rate of genetic improvement by making the underlying cause - variation in genome sequences between animals - visible. This means increased profits for farmers through more efficient production, but it also means improvements in product quality and animal health that matter to consumers.

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