Genomics

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What is it?

Genomics is a dynamic field of biology that focuses on the genome of organisms. A genome is an organism's complete set of Deoxyribonucleic acid (DNA), including all of its genes that, as a whole, influence growth and development. There are four molecules ("bases") found in a DNA molecule, adenine, cytosine, guanine, and thymine, known more commonly as A, C, G and T. This four-letter alphabet is found in every living organism, they pair up in a swirling shape known as the double helix of chromosomes. The number of base pairs in every cell of a farm animal (mammal) is approximately 3 billion. If typed out on a ribbon in 11-point font, the cattle genome in a single cell would roughly cover the distance from Halifax, Nova Scotia to Victoria, British Columbia. Within this long sequence of base pairs, groupings have different functions, and these are known as genes.

Using a combination of DNA sequencing methods and bioinformatics, genomics studies the structure, function, evolution, and mapping of genomes. Understanding the genes in organisms allows for faster selection for traits of importance (e.g., healthier and more efficient animals). The cost of genomic analysis has decreased exponentially in recent years making it more affordable as a component of animal breeding programs.

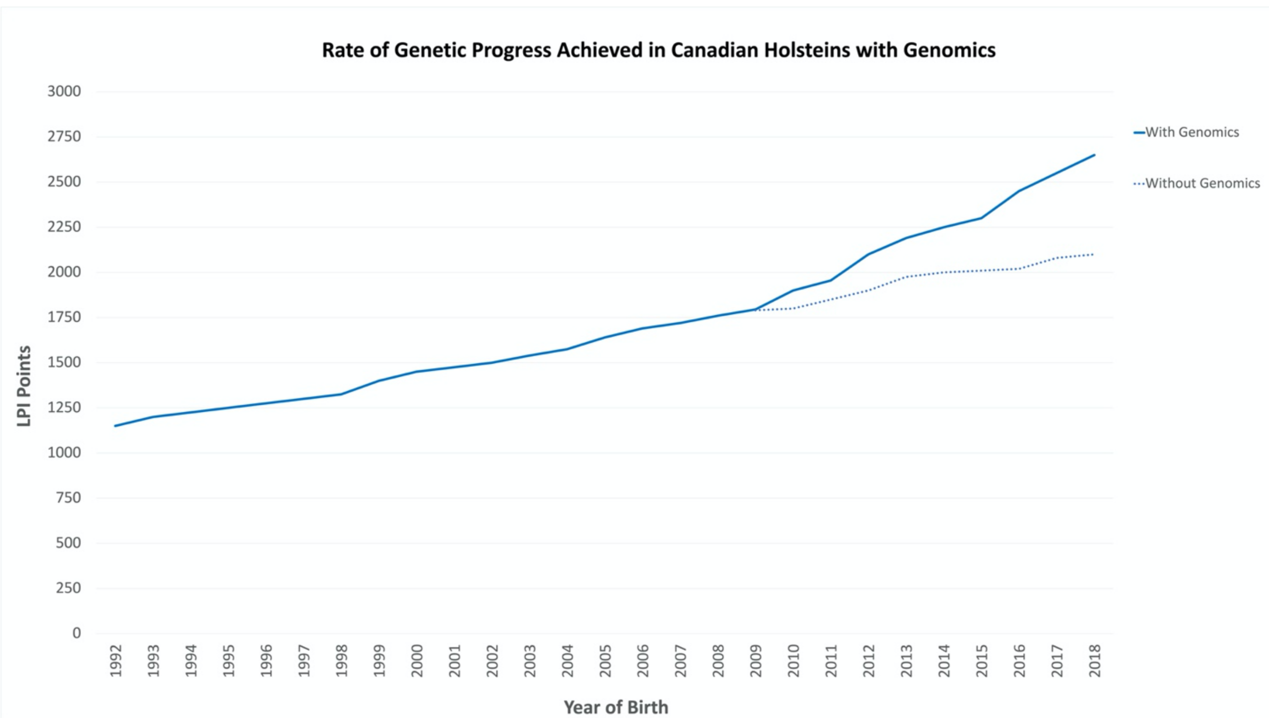
Why it matters to the Ontario livestock industry:

Ontario livestock has a role to play in global protein production, fostering innovation amongst producers in the global quest to produce more, with increasingly scarce resources. Livestock production across the world is also under scrutiny with concerns including the impact of livestock on climate change, water use, influence on human health (zoonoses) and antimicrobial resistance. Genetics, including genomics can play a significant role in creating a robust future for Ontario livestock producers as they meet these challenges and satisfy consumers globally.

Genetics are the raw materials in an animal's development, but environment also plays a key role, particularly for some traits. The relationship between an animal's performance, also known as "phenotype" and their genetics is not perfect. Environmental factors such as feeding, housing and health can all have significant impacts on animal performance. That said, genetics determines potential. The environment is a limiting factor in an animal's ability to reach its genetic potential and it's the producer's role to ensure that the animal's management best matches its genetic potential for optimum performance. In fact, matching an animal's genetic potential to its environment is a key component of extensive livestock systems. It is incredibly important to understand that the results of genetic change, unlike changes due to nutrition, health and other management interventions, are permanent, and they accumulate over generations. The Canadian dairy sector for example has seen phenomenal improvements via genetic selection when compared to change from management strategies.

SNPs ("snips") or single nucleotide polymorphisms each indicate a difference in a base pair at a particular location (e.g. G rather than C). The SNPs that are related to differences in traits of interest (disease resistance, better weight gain, higher milk yield, lower GHG emissions) can be used in genetic selection. The Angus cattle breed, for example, has about 20 million known SNPs across the 3 billion bases on their genome.

In the Canadian dairy sector, genetic merit is expressed as a Lifetime Profit Index (LPI) and takes into account many traits. The graph below shows positive genetic change towards 2009 using traditional breeding values (estimated breeding values or EBV) which were calculated using animal performance measures along with pedigree relationships amongst animals. A big boost in the rate of progress is obvious once the LPI index was based on genomic breeding values (GEBV) that takes into account analysis of the genomics of each animal using the SNPs that they carry, in addition to the performance and pedigree information. The dashed line in the graph indicates the genetic progress that would have been expected without the introduction of genomics, whereas the solid line indicates the gain actually achieved by taking genomics into account (Van Doormaal, 2019).



Data retrieved from Lactanet 2019

A similar increased rate of genetic progress has been achieved in Angus cattle following the implementation of genomically enhanced genetic evaluations in 2010. Genomics is now being used in dairy, beef, swine and turkeys in Ontario as well as other species. The full extent to what genomics can do for the Ontario livestock industry is not yet known but the possibilities seem endless. It must be realized, however, that the predictive ability of these genomic tests cannot be determined without on-farm data. In fact, the genomic predictions are only possible with the collection of phenotypes for the traits of interest such as weight in Angus cattle or milk yield in Holsteins. The implementation of genomics, instead of replacing the need for animal measurements to inform selection decisions, has actually made these measures more important. Traditionally, animals were evaluated based on their performance for a trait, or through the performance of their progeny, for example, milk yield records on daughters of a sire. This approach, although highly effective, had the limitation that only the animals with measurements, or those with progeny measured had any significant accuracy. Those measures had little predictive ability for new animals and this is where genomics has really changed the game. A genomic prediction can be developed based on a reference set of animals and this prediction developed from the reference dataset can be applied to new animals, without measurements. The result is such that a DNA sample can be pulled on a beef calf at birth and the genetic potential of that calf for weaning weight can be predicted with better accuracy than would be possible from previous methods based on the weaning weight of that calf. This ability to predict with accuracy what an animal's genetic merit is without waiting to obtain a measure on the animal or its progeny is the primary driver in increased genetic progress with genomics. Breeding companies now have no need to wait until a bull has daughters in milk before deciding if he is worthy of use or not. With genomics the merit of this bull for future use can be determined at birth and in some cases even prior to birth as genotyping embryos is now possible.

A unique benefit of genomics in this regard is related to traits that are very important, but difficult to measure. Without genomics, such traits are not viable to pursue as the measures are typically expensive and in some cases not possible on breeding candidates. A sire could be proven based on progeny performance at great cost, but this only provided information on the limited sires whose progeny were measured and provided little information on the general breeding population. With genomics, measures in dedicated reference populations can be used to develop a prediction, which can be applied more generally. Thanks to genomics, these difficult traits can now be addressed with breeding. Health traits are a good example of this, collecting good health data in a commercial environment is difficult, but with genomics, such a dedicated effort to obtain such a reference population can generate a genomic prediction that has accuracy and can be applied to the larger population. Genomics has given research facilities a new purpose as the more specialized and detailed measures they are capable of generating, can be used to develop these genomic reference populations. The new Dairy Research facility in Elora is a good example, where measurements of feed intake of cows are now contributing to a feed efficiency evaluation across North America. Animals which use their feed more efficiently are good examples of breeding animals that produce more with less. The North American Angus evaluation includes a reference of 30,000 animals with intake measured, this core is used to provide genomic predictions on the close to 1 Million animals now genotyped in that evaluation. Genomics has greatly expanded the industry's ability to deal with more difficult problems such as identifying animals that are more efficient, healthier (less need for antimicrobials) and produce less methane.

History of Genomics:

- In the 1970's and 1980's Fred Sanger, recipient of two Nobel Prizes in Chemistry, and his team at the Medical Research Council were responsible for establishing techniques to sequence, genome map, store data and conduct bioinformatic analyses. This work prefaced the human genome project in the 1990's (Bentley et al., 2008).
- The global collaboration on the human genome yielded the sequence (the complete set of the alphabet in order) that was publicized in 2003.
- Following the human genome came sequencing of livestock species.
- The cost to sequence a human genome, $100 million in 2001, is now well under $1,000 (Wetterstrand, 2020).
- CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) technology has been a ground-breaking advancement in genetic editing as it is more accessible economically, more efficient and more accurate than other editing technologies. First found in 1987 in E Coli, and with many developments thereafter, CRISPR-Cas9 was harnessed for genome editing.
- Following the Bovine Genome Project, an array to genotype cattle efficiently for 50,000 SNP was developed in 2006, which started a genomic revolution in cattle breeding with other species to soon follow.
- In August 2009 the first genomic evaluations were published in Canada starting with the Holstein breed (Van Doormaal, 2019).
- Since 2009, over 3.2 million genotypes have been accumulated in the Canadian dairy genetic evaluation database at Lactanet. In 2019 approximately 53,000 Canadian-born Holstein females were genotyped compared to the 1,887 in 2009 (Van Doormaal, 2019).
- In 2021, genomic evaluation of Angus cattle including US, Canada and Australia surpassed 1 million genotypes, the first for a beef breed.
- In 2016 and 2018 scientists published their success using CRISPR-Cas9 to genetically edit pigs to become resistant to one of the industry's most economically important infectious disease, Porcine reproductive and respiratory syndrome virus (PRRSV) (Whitworth et al., 2016; Burkard et al., 2018). This enormous feat opened a world of opportunities for the future of improving animal welfare and productivity.
- In 2008 researchers introduced, through gene editing, the 'slick hair' gene into a Red Angus beef animal in Brazil in an effort to improve heat tolerance (Agricultural Resource Magazine). Using gene editing and the TALEN (Transcription activator-like effector nuclease) technology, a single base pair was cut from the Angus chromosome sequence to make the hair 'slick' and provide more heat resistance, key for success in warmer climates (Wallstreet Journal Digital Network). The land use and greenhouse gas footprint of Angus cattle are much lower than what Brazil currently has with the Nelore Cattle breed (Brazeau, 2019).
- Advancements in gene editing such as the pigs resistant to PRRSV and Angus cattle more resilient to heat stress are examples of how gene editing is improving the livestock industry to become more sustainable, improve animal welfare and meet consumer demand.

Market Pull

The use of genomics has become mainstream in many sectors. Many breed associations now require a DNA sample for analysis as part of registration of animals. Genomics are used in a variety of genetic evaluation systems and will be a key tool for the livestock sector as they respond to demands for healthier animals that have a reduced impact on the environment. The ability to use a reference population of animals with key measurements to inform breeding candidates increases the value of phenotypes. This will result in increased investment in phenotyping by industry, to enable breeders to address these challenging traits.

Research gaps

We have come a long way, but a full understanding of genomics is on a distant horizon. In fact, we really know very little about the genome. We can sequence it, so we know the order, but understanding the function of each gene and how they interact will take more research. Many of the tools used in livestock genomics were driven in their development by demands in human research. Next generation sequencing and high-density genotyping technologies have been applied in livestock, but the developments were originally for human genetics applications. The recent COVID-19 pandemic has seen a surge in sequencing applications to better understand and rapidly identify the different variants. The livestock industry will benefit from developments in this area in the future.

Innovation gaps

The innovation gap in livestock genomics involves physical measurement. Lower cost and more powerful genotyping continue to be developed but to take advantage of this, we need animal measurements for the traits that farmers want changed. If it can be measured, it seems genomics provides a path for sustainable genetic improvement for most traits.

Cultural Change

Genomic selection, which has contributed to great increases in genetic progress, and which will enable the industry to address the very difficult to measure traits of the future, is a “natural” process in the eyes of the consumer. The analysis of DNA is simply used to select the best animals as parents of the next generation. The process of selective breeding has been a part of animal production for centuries, genomics only improves the accuracy of selection. The adoption of genomics by farmers has required a change in culture. Livestock genetic improvement over the centuries was based first on the “eye” of the breeder along with lineage (pedigree) followed by measurement of traits and these were all compiled with statistical software in modern times to provide objective predictions of genetic merit for traits. Prior to genomics, there has always been a close connection between the objective measures on an animal or its progeny and the genetic merit prediction for that animal. Now with genomics, farmers must take a “leap of faith” to use the technology, when there is no direct measure on an animal or it’s progeny, just a DNA sample.

Similarly, given the role the environment plays in animal performance, choosing an animal with a poor phenotype and a superior genomic prediction over an animal with a superior phenotype but a poor genomic prediction has taken some adjustment for breeders as it goes against generations of experience.

The implementation of genetic modification is something that will need to be accepted by the public before commercial use. Consumer understanding of genetic modification and gene editing varies. Kilders and Caputo conducted a survey to understand consumer preferences and willingness-to-pay (WTP) for milk produced from conventionally and genetically dehorned cows, in their results they found that responses are heavily impacted on the information provided to respondents (2021). Shew et al., conducted a study assessing the willingness-to-consume (WTC) and the WTP for CRISPR-produced food compared to genetically modified (GM) foods in a multi-country assessment (2018). The WTC of the respondents were equivalent for both CRISPR and GM food, valuing them comparably as well, however the value placed on CRISPR and GM food was significantly less than conventional food. Similar to Kilders and Caputo's study, familiarity with the biotechnology and respondents' perceptions of safety were the primary drivers in their WTC.

In Canada, new GMOs are assessed by Health Canada and the Canadian Food Inspection Agency (CFIA) to determine whether they are novel foods (different to what is currently available). If they are considered to be 'novel' they are required to undergo regulatory oversight. Not all genetically edited food products are considered 'novel' and thus for 'non-novel' traits they are not subject to regulatory oversight. Reducing the amount of regulation for GM foods and crops could reduce the price of these foods in the grocery store. In 2016 the first genetically modified animal, AquAdvantage salmon was sent to market in Canada (Health Canada, 2021).

For more information

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Additional resources

- *The Gene: An Intimate History* by Siddhartha Mukherjee
- The Canadian Dairy Network https://www.cdn.ca/home.php
- The National Human Genome Network https://www.genome.gov/
- Angus Genetics Inc. https://www.angus.org/agi

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