



Genetic Improvement of Production and Adaptive Traits in Livestock

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State of Genomics Research in Livestock

In the previous century, technological advances like artificial insemination (Foote, 2002) and best linear unbiased prediction (Henderson, 1975) drove dramatic improvements in livestock species. For example, milk production has more than doubled (Abdallah and McDaniell, 2000). These genetic advancements have helped world farmers to generate more food more efficiently to feed the global population. However, to continue this trend additional improvements must be made.

Since the turn of the century, we have witnessed some dramatic changes in genetic improvement of livestock species. The advent of having access to a sequenced/assembled genome for species of interest has fueled these advancements (Elsik *et al.*, 2009; Groenen *et al.*, 2012; ICGS, 2004). The second major advancement was the development of genomic selection technologies (Meuwissen *et al.*, 2001). Finally, genome editing has great potential to alter what is possible (Kim, 2016).

For many species, their genome has been assembled and annotated – Chicken (ICGS, 2004), Cattle (Elsik *et al.*, 2009) and Swine (Groenen *et al.*, 2012). Technologies have been developed to genotype 10's of thousand of variants in thousands of individuals – SNPchips. Because of reference genomes and advances in sequencing technology, variant discovery, primarily single nucleotide variants and small insertions/deletions, is relatively easy. For example, the 1000 bulls project has identified and analyzed more than 25 million variants in cattle for association with traits and a similar project in sheep identified more than 46 million variants. These projects have just begun to identify the genetic variation that exists in livestock species.

For many years, marker assisted selection was practiced, but it wasn't until Meuwissen, Hayes and Goddard (Meuwissen *et al.*, 2001) proposed genomic selection that real progress in genetic selection using

molecular markers was even possible. Today, genomic selection is being practiced in all livestock species (Meuwissen *et al.*, 2013). The dairy industry has aggressively implemented genomic selection, with more than 1 million head of Holstein being genotyped in the United States. The dairy industry has gone as far as performing ovum pickup in pre-pubertal heifers, and genotyping *in vitro* fertilized embryos, to decide what embryos to implant in recipients. Genomic selection has dramatically decreased the generation interval in dairy cattle. Another leap forward was with the implementation of single-step GBLUP (Misztal *et al.*, 2009), in which genetic evaluation could utilise both genotyped and un-genotyped individuals in a single analysis. It was then possible to harness the power of both genomic selection and traditional quantitative genetic evaluation. Today, phenotypic not genotypic information is the rate limiting step to genetic progress. The genomic tools are in place. Now advancements in phenotype collection need to occur to fully utilise the genetic potential of livestock.

On-going Research Projects

The genome sequencing projects brought livestock research communities together on a scale never seen before. They ushered in the era of large collaborative multi-disciplinary research projects designed to tackle a problem larger than what one research lab could undertake. These projects have become to some extent the new norm. While there are more projects than can be summarized here, a couple projects will be discussed to high-light some unique aspects that they bring to the community.

The 1000 Bulls project (citation: <http://www.1000bullgenomes.com/>) (Daetwyler *et al.*, 2014) is the largest collaborative genome re-sequencing project in livestock. Researchers from around the world have re-sequenced more than 1,100 bulls. Variants were discovered in each of these individuals using

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a common variant detection pipeline. Run4 data has been imputed into more than 58,000 head and has been used in the analysis of stature (hip height) (unpublished results). Pooling of resources from across the world has allowed a project of this scope to be conducted. Project members have access to genotype information on all of the re-sequenced individuals to date. This provided an incredibly powerful resource for future research.

The Functional Annotation of Animal Genomes project (FAANG; <http://faang.org/>; (Tuggle *et al.*, 2016; Andersson *et al.*, 2015) aims to identify all functional elements in animal genomes. This project seeks to expand upon the human ENCODE (Consortium, 2012) and modENCODE (Celniker *et al.*, 2009) projects by identifying functional elements throughout. More than 300 researchers world-wide are working to set standards for sample collection, metadata, assays, bioinformatic pipelines, and data integration. It is expected that this project will have positive benefits on annotation of genomes, understanding gene function and predictive biology, which will continue to grow over time. This is an example of pre-competitive research that will have a powerful impact on biology.

The ADAPTmap project (<http://www.goatadaptmap.org/>) is an international effort to coordinate independent genomics based projects on goats. It is interesting in that it involves coordination of projects ranging from genomic selection for improved milk production on commercial populations to surveying of genetic diversity throughout the world. A goal of the project is to disentangle the genetics of adaption of goats throughout the world.

These projects and others like them will have a positive impact on both scientific knowledge and in meeting the challenge of feeding the world in the future.

Traits of Interest

Traditionally, genetic improvement has focused on easy to measure traits that have an economic impact on livestock, e.g. yearling weight in beef, number of eggs laid in chicken, milk yield in dairy cattle, growth rate in swine to name a few. The impact of genetics on these production traits cannot be under estimated, for what has occurred in nothing short of incredible. Furthermore, these production traits will continue to be selected on well into the future.

Unfortunately, elite genetics do not fair well in many parts of the world. Selection for traits of economic importance has adapted these animals to their environment. In order to thrive in other environments other adaptive traits need to be selected upon. Disease resistance is a trait that could have a dramatic impact upon livestock production world-wide. However, disease resistance/susceptibility traits are not easy to measure. What constitutes a sick animal? How do you objectively measure incidence and severity? New technologies are needed to drive genetic progress in these traits. Unfortunately, the heritability of many disease resistance trait is low, which means that selection for improvement will be slow as well. Furthermore, the number of livestock diseases that we know about continues to increase. Taken together, disease resistance is a topic in need to increased emphasis.

Climatic stress is one of the main limiting factors of production efficiency in many areas of the world and is expected to become even more of a limitation due to climate changes associated with global warming. Substantial differences in thermal tolerance exist among breeds and among animals within breeds indicative of opportunities to improve it by selection. However, many of the physiological pathways underlying thermotolerance are interconnected with metabolic changes and nutrient partitioning resulting in suboptimal productivity. Unfortunately, this is a trait that we do not fully understand the metabolic/physiological mechanisms at play, which makes it hard to know whether the right phenotypic data is being collected. We have room for a lot of improvement in this trait.

There are a myriad of other traits, e.g. feed efficiency, green house gas production, reproduction to name only a few, that the livestock industry needs to select for improvement. Many of these traits are hard to measure and as a result are costly to measure. Thus, there is a real need to invest in development of new measurement technologies to take what is hard and expensive to measure today to become cost-effective in the future.

Limitations to Genetic Progress and Conservation of Genetic Diversity

In many parts of the world, the basic infrastructure needed for genetic progress just does not exist. In many places, it is not possible to measure a trait of interest (e.g. no scale to collect an animal weight or no way to cost effectively measure something like methane

production), record it (i.e. there is no organized data recording site), and then use it in a genetic evaluation (i.e. there is no organized genetic analysis provider; e.g. a breed association). This all starts at the level of the producer. There needs to be a basic understanding of the economic benefit of genetic selection. Someone can invest all they want into the newest latest genomic technology, but unless a strong foundation for genetic improvement is in place, real genetic progress throughout the country will not take place. This is a fundamental difference between livestock and plant species. Genetic improvement of plant species can be accomplished in limited locations and then improved seeds can be distributed and rapidly deployed. In livestock, hundreds of thousands of producers own the genetic resources. A large percentage of them need to be actively involved for genetic progress to occur. Generally in livestock, genetic improvement has been implemented in larger operations first. Then as the technology costs drop due to volume application, smaller and smaller operations can benefit. Smaller producer will be able to benefit from the ability to have access to genetically superior animals that they can breed their animals too.

The tools exist today in some species like cattle, pigs, sheep, goat and chicken to utilise genomic technologies, i.e. SNPchips, for conservation of genetic diversity. Most of these resources have been used to large surveys of the genetic diversity differences between breeds. Once a breed has been characterised, these same SNPchips can be used to minimise the inbreeding within a limited population (Saura *et al.*, 2013). Along with an estimate of the effective population size of the breed, selective breeding can be employed to minimise inbreeding and maximise the potential to conserve the breed. Unfortunately, this process is expensive requiring a long-term investment in the conservation of that breed. Thus, a well thought out breeding goal and plan need to be in place to maximise the return on investment.

Conclusions

Many livestock species have a wealth of genomic and quantitative genetic tools that can be used for genetic improvement or conservation of genetic diversity. Therefore, it is possible to accomplish most breeding goals/plans if sufficient resources or economic incentives are in place to drive them forward.

References

- Foote RH (2002) The history of artificial insemination: Selected notes and notables. *J. Anim. Sci.* **80**(E-Suppl_2): 1-10.
- Henderson CR (1975) Best linear unbiased estimation and prediction under a selection model. *Biometrics* **31**(2): 423-447.
- Abdallah JM and McDaniel BT (2000) Genetic parameters and trends of milk, fat, days open, and body weight after calving in North Carolina experimental herds. *J. Dairy Sci.* **83**(6): 1364-1370.
- Elsik CG, RL Tellam, KC Worley, RA Gibbs, DM Muzny, GM Weinstock, DL Adelson, EE Eichler, L Elnitski and R Guigo (2009) The genome sequence of taurine cattle: a window to ruminant biology and evolution. *Science* **324**: 522-528.
- Groenen MA, AL Archibald, H Uenishi, CK Tuggle, Y Takeuchi, MF Rothschild, C Rogel-Gaillard, C Park, D Milan and HJ Megens (2012) Analyses of pig genomes provide insight into porcine demography and evolution. *Nature* **491**(7424): 393-398.
- International Chicken Genome Sequencing C (2004) Sequence and comparative analysis of the chicken genome provide unique perspectives on vertebrate evolution. *Nature* **432**(7018): 695-716.
- TH Meuwissen, BJ Hayes and ME Goddard (2001) Prediction of total genetic value using genome-wide dense marker maps. *Genetics* **157**(4): 1819-1829.
- Kim JS (2016) Genome editing comes of age. *Nat. Protoc.* **11**(9): 1573-1578.
- Meuwissen T, B Hayes and M Goddard (2013) Accelerating improvement of livestock with genomic selection. *Annu. Rev. Anim. Biosci.* **1**: 221-237.
- Misztal I, A Legarra and I Aguilar (2009) Computing procedures for genetic evaluation including phenotypic, full pedigree, and genomic information. *J. Dairy Sci.* **92**(9): 4648-4655.
- Daetwyler HD, A Capitan, H Pausch, P Stothard, R van Binsbergen, RF Brondum, X Liao, A Djari, SC Rodriguez and C Grohs (2014) Whole-genome sequencing of 234 bulls facilitates mapping of monogenic and complex traits in cattle. *Nat. Genet.* **46**(8): 858-865.
- Tuggle CK, E Giuffra, SN White, L Clarke, H Zhou, PJ Ross, H Acloque, JM Reecy, A Archibald and Bellone RR (2016) GO-FAANG meeting: a Gathering On Functional Annotation of Animal Genomes. *Anim. Genet.*
- Andersson L, AL Archibald, CD Bottema, R Brauning, SC Burgess, DW Burt, E Casas, HH Cheng, L Clarke and C Couldrey (2015) Coordinated international action to accelerate genome-to-phenome with FAANG, the Functional Annotation of Animal Genomes project. *Genome Biol.* **16**: 57.
- Consortium EP (2012) An integrated encyclopedia of DNA elements in the human genome. *Nature* **489**(7414): 57-74.
- Celniker SE, LA Dillon, MB Gerstein, KC Gunsalus, S Henikoff, GH Karpen, M Kellis, EC Lai, JD Lieb and DM MacAlpine (2009) Unlocking the secrets of the genome. *Nature* **459**(7249): 927-930.
- Saura M, A Fernandez, MC Rodriguez, MA Toro, C Barragan, AI Fernandez, B Villanueva (2013) Genome-wide estimates of coancestry and inbreeding in a closed herd of ancient Iberian pigs. *PLoS One* **8**(10): e78314.