

Angus GS

A new genomic era for American Angus

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The Angus GS™ genomic test was officially launched at the 2017 Angus Convention in Fort Worth. This test, designed by Angus Genetics Inc. (AGI) scientists in conjunction with experience and expertise from Neogen GeneSeek Operations, marks a new era in genomics for the Angus breed. To appreciate the full significance of this test, breeders need to understand how different genomic tests influence their expected progeny differences (EPDs) and how a test designed specifically for Angus can have an impact. The Angus GS test is not just a test for today; it is also an investment in Angus's future. It is a strategic test, designed to position Angus to fully capture future genomic opportunities on the horizon.

Progress

There are likely few Angus breeders who would not acknowledge genomics as a game-changer for selection and progress in the breed. Since genomics was launched in 2010, the Angus breed has seen some marked improvement in genetic progress. Fig. 1 shows genetic progress standardized to a unit of the trait. This allows us to compare a trait like growth (yearling weight), which is reported in pounds, directly with a trait like heifer pregnancy, which is reported as a percent.

Angus GS content includes a number of SNPs the research community has identified as having a potential impact on Angus for traits such as tenderness, feed efficiency, pulmonary arterial pressure (PAP) and fescue tolerance.

This progress was determined by a linear regression from the breed genetic trend table, considering 2001-2010 and 2010-2016 as different time periods. In general, what is realized is a greater rate of genetic progress after 2010 than before. Comparing traits like yearling weight (YW) and ribeye area (RE), we see a greater increase after 2010 in RE. This greater increase in progress for hard-to-measure traits such as carcass coincides with the known benefit of genomics, enabling selection with greater accuracy at younger ages for traits not measured on the animal.

Milk is a trait that is still increasing, but not as quickly, likely reflecting more moderate selection pressure. Heifer pregnancy and docility see marked increases in progress, as would be expected with newly recorded traits.

The pattern of implementation of genomics in the Angus breed has kept pace with the general implementation of genomics across livestock in general. The genomic revolution in cattle was really kicked off with the release of the Illumina Bovine SNP50 assay in 2007, which was quickly deemed the "50K." Early research with this new tool showed that "genomic selection" was possible and accurate utilizing this new 50K SNP (single-nucleotide polymorphism) chip, first in dairy cattle, with beef cattle to follow.

This original 50K assay has formed the backbone of genomic evaluation in cattle, although many custom chips have been created using the Illumina technology since then.

After the implementation of genomic selection based on this original 50K assay, the technology of imputation, where the full 50K profile of SNP markers can be determined based on only a subset of SNPs with relatively high accuracy, allowed AGI to provide genomic predictions based on low-density tests. Producers would soon recognize these tests as the GGP-LD and i50K, which reduced costs compared to the full 50K tests.

The implementation of genomic selection at Angus has included a genomic prediction based off a common set of markers from the 50K. Using imputation, despite the panel genotyped, the same set of markers was used on every animal. Although there were potentially 54,069 SNP genotypes that could have been used for genomic prediction in Angus, a number of these SNPs are not informative in the breed.

With the current single-step analysis, about 40,000 SNPs are used in the evaluation after culling SNPs that are not informative in Angus for reasons such as all animals having the same genotype (no variation). These culled SNPs reside on the SNP chips because they are informative in other breeds like Holstein. As the same chips are used across many different breeds, they have not been specific to Angus.

Angus-specific

The advent of Angus GS has come about as a result of four independent events: new genomic technology (Illumina XT), new genetic evaluation technology (single step) and the size of the Angus database (volume) coupled with the science team (Fig. 2). The original 50K chip from Illumina in 2007 ran with eight animals per slide in the lab. The new XT technology puts 96 animals on a slide and enables AGI to deliver a full 50K profile at a much lower price (\$37).

Fig. 1: Recent pre- and post-2010 standard genetic trends

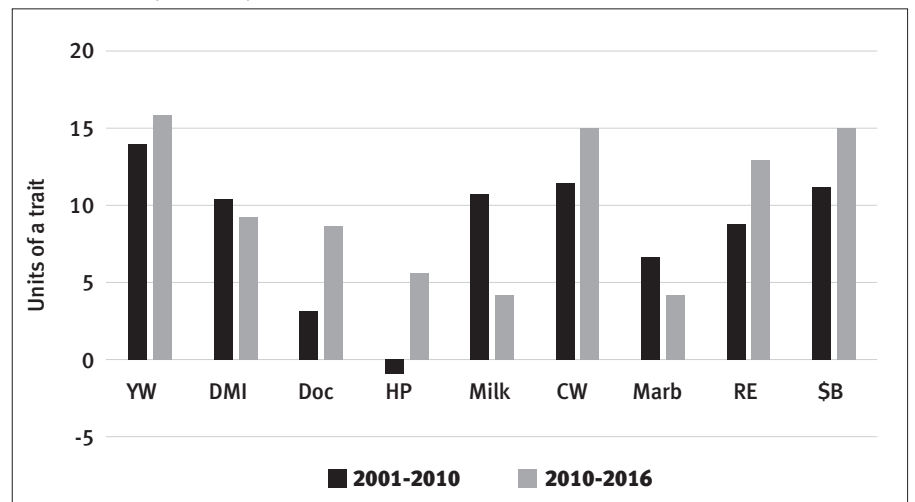


Fig. 2: Multiple factors contributed to the creation of Angus GS

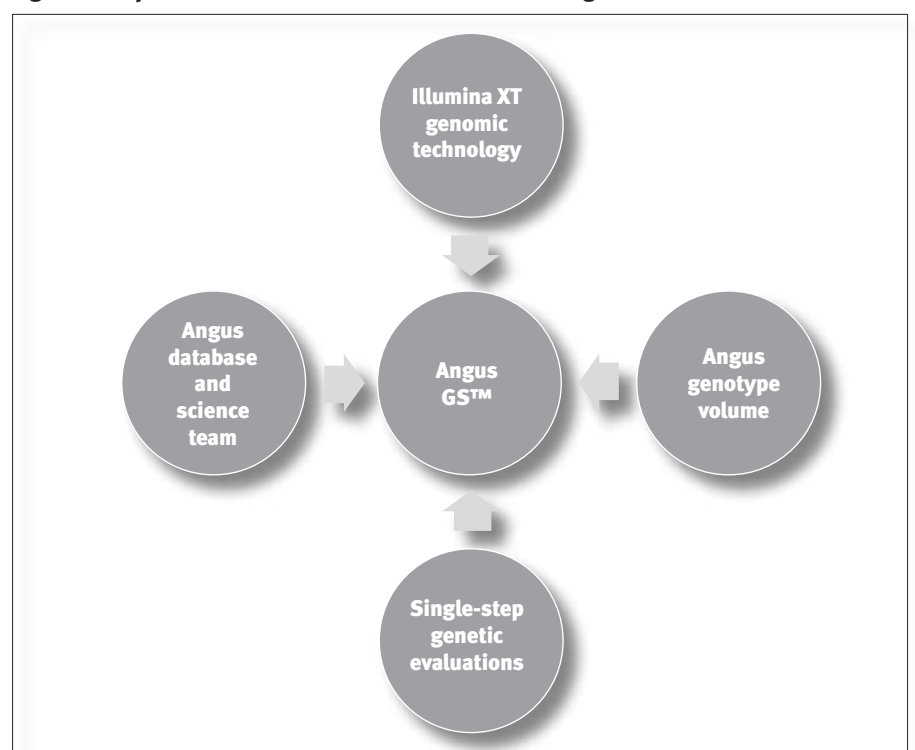
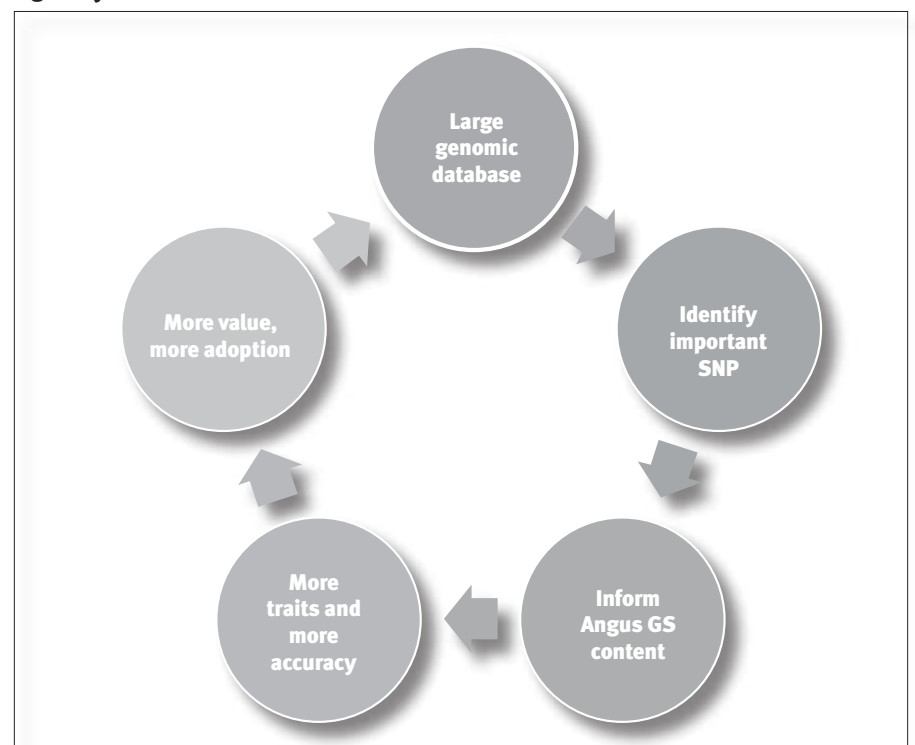


Fig. 3: Cycle of innovation



One of the primary reasons AGI can deliver a custom Illumina assay is because of the genotyping volume Angus breeders are doing, with volumes now exceeding 100,000 per year. There is significant overhead to bring a genotyping chip to market, which requires a significant genotype volume to do this affordably. Simply put, a custom chip just for Angus is a luxury Angus breeders can afford due to the sample volume they do.

Each week a new genetic evaluation is completed, which incorporates all the genotype, pedigree and performance information. The genomic information is

Genotypes on Angus GS will provide important information in the science team's endeavor to characterize these important fertility regions. There are more than 8,000 SNPs on Angus GS that reside in these regions of interest. Increased density in these regions will allow scientists to more accurately track the genetic variants influencing this trait and enable a faster route to discovering the

causative mutations. Once discovered, we can incorporate them directly into future versions of Angus GS.

The 40,000 SNPs currently used in genomic prediction of Angus are spread over 29 chromosomes. There are actually 30 pairs of chromosomes in cattle, and the chromosomes that determine sex (X and Y) have not been included in genomic predictions. Angus GS

has much better coverage of each of these sex chromosomes to enable research to determine how genetic inheritance of these chromosome segments could influence predictions of important traits such as fertility in the future.

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Implementation of the new single-step methodology for genetic evaluation on July 7 marked another important development for Angus breeders, but also an important change in the process of calculating EPDs. With single step, the entire EPD process is in-house at AGI.

“retrained on the fly” each week.

The data submitted by Angus members determines the influence genomics has on the EPD, and the SNP markers used in the calculations can be optimized. The new Illumina XT technology has capacity for 50K SNPs, and we maximized the use of this chip real estate for benefit to the Angus genetic evaluation, where every one of the 50,000 SNPs that were put in the design have been proven to be informative in the breed.

Single step and Angus GS can be considered a matched set. The GS in Angus GS stands for genomic selection. Genomic-enhanced EPDs calculated by AGI are a result of this genomic selection methodology. The Angus GS assay is designed and optimized for accuracy into AGI's single-step analysis.

The size of the Angus database and the commitment of the membership to testing has enabled the possibility of a customized assay. It simply is not economically feasible for low genotyping volumes. The Angus database coupled with the AGI science team has enabled further customization of the content to reflect results from analyses from existing Angus genotypes.

Early in 2017, an extensive analysis of Angus's genotype database revealed a number of regions of the genome that appear to be impacting fertility and early survival outcomes in Angus. This advanced analysis was only possible due to the large number of genotypes in the Angus database. Further validation of these regions is required before the genotypes can influence EPD predictions and mating programs.

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remaining 29 chromosomes, certain segments of the genome have low SNP or no SNP coverage within the current SNP set used in prediction. The development of Angus GS employed sophisticated algorithms that optimize placement of SNPs to minimize these gaps.

By making the coverage as complete as possible across the genome, Angus GS has

been built to better track inheritance across the genome, but also to increase accuracy of imputation to higher-density levels. We know there are millions of SNPs that could be influencing traits in Angus cattle.

As genomic sequencing projects and other research projects identify these causative variants, we will want to impute these variants for animals genotyped on Angus GS. In

this way, Angus GS is designed not only for genomic prediction today, but it is also prepared for future applications such as high-density or sequence imputation that we will be facing in the future, as we continue to apply the latest in technological advancements to make the EPDs ever more accurate.

Angus GS is built with input from AGI scientists, and the Angus database was used

to inform just what SNPs were most informative to include. This SNP list will evolve over time as the AGI science team learns of new genetic variants that are important to include or as analyses of the Angus data reveal important variants. Not only will internal analyses reveal variants to include, but information from universities and government research agencies in the United States and abroad will also be gleaned for important SNPs.

Angus GS content includes a number of SNPs the research community has identified as having a potential impact on Angus for traits such as tenderness, feed efficiency, pulmonary arterial pressure (PAP) and fescue tolerance. Once Angus GS is in use and 100,000 new genotypes have come in, we will be able to better identify important variants to include. At this time we will top up, or add to, the content with another 1,000 SNPs. This process will be repeated after another 100,000 samples, this time with a potential redesign of the entire content, which will also take advantage of new technology that may be available.

Genotyping platforms will continually evolve. It is important that the AGI team continually harnesses the best tools for Angus breeders and keep Angus GS the best it can be for genomic selection in the Angus breed.

Continuous innovation







As the above features and process illustrate, Angus GS is simply not a new DNA test, but the start of a new process of innovation for Angus breeders. Fig. 3 describes this cycle of innovation. Starting at the top of this cycle is the large Angus genotype database. This large database and sample volume is what makes a custom Angus SNP chip possible.

Moving on to the second bubble, through analyses of this database we can identify important variants to include on the chip. With these variants on the chip, we can increase accuracy for existing traits, but also begin to predict new traits. With this increased sample volume and improved accuracy, the value of genotyping increases.

Angus breeders have already experienced immediate benefits with the launch of Angus GS with the lowest price ever for a 50K assay for U.S. beef cattle. With this greater value, more cattle will be genotyped and, as a result, the genotype database will grow. We are back at the top of the innovation wheel now with a larger database, which will enable us to identify more informative variants; add these to future Angus GS content; and increase value, which drives genotyping.

Over time this innovation wheel will continually pick up speed, with Angus GS becoming more informative, presenting greater value to members. Angus GS marks a new era of innovation, which would not be possible without the embracement and adoption of genomics by Angus breeders. This level of adoption is the envy of the beef breeding world, and Angus GS is poised to accelerate this adoption and resulting impact in the breed by accelerating the rate of genetic progress.

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