

Genome-Wide Association Studies for Important Economic Traits in Domestic Animals Using High Density SNP Genotyping

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Summary and implications

New methods for genotyping large numbers of genetic markers have been developed, which are cheaper and faster than previous techniques. Iowa State University researchers helped to develop a tool known as the porcine 60K SNP chip that can genotype 64,232 genetic markers simultaneously in a single pig. Similar SNP chips are available for many other species, including sheep, chicken, cattle and dog. These new chips allow for trait association studies to be conducted using many more genetic markers spread across the genome (known as genome-wide association studies or GWASs). In our lab GWASs were performed for a variety of traits in pigs, sheep, and dogs. In pigs, a number of candidate genetic markers and chromosomal regions were associated with feed intake, average daily gain, body composition (such as 10th rib backfat and loin muscle area), feet and leg structure (such as overall leg action, front and rear leg pasterns), and reproductive traits. Other work in pigs involved looking for duplicated regions of the genome to identify genes that were duplicated, which could impact many traits in the pig. In sheep, chondrodysplasia (a condition in which the legs are malformed and other problems arise) was found to be associated with a group of consecutive markers on one chromosome. SNP chip research in dogs is ongoing to look for genes associated with cryptorchidism (retained testicles). These findings offer a promising list of genetic markers that can hopefully be used in the near future to improve animal production via lowered input costs and reduced incidence of disease.

Introduction

Many livestock traits are known to have a genetic basis but are difficult or expensive to measure. Without accurate measurements of these traits, traditional selection methods fail and genetic markers are needed to make selection successful. Sow productive lifetime is one such trait that can only be calculated after the sow has left the herd. By selecting for genetic markers that are associated with

reasons sows are frequently culled, such as reproduction problems and lameness, producers can predict which sows will stay in the herd the longest before they are selected for breeding.

Another trait for which genetic markers will be useful is feed intake. This trait is expensive to measure and difficult to select for without negatively impacting growth rate. Residual feed intake is a trait that is designed to measure the difference between what an animal is consuming and what an average animal would need to consume to maintain the same levels of growth and maintenance. By selecting for genetic markers associated with residual feed intake, producers should be able to reduce feed costs without the expense and difficulty of measuring feed intake and without reducing growth levels.

Finally, diseases such as chondrodysplasia (where the limbs are shortened and other defects arise) in sheep and cryptorchidism (retained testicles) in dogs could be reduced or eliminated if genetic markers were used to predict the offsprings' genotype prior to mating.

Markers from across the genome can be tested for association with each of these traits faster and cheaper than ever before through use of the newly developed genotyping method known as the SNP chip. SNP is an abbreviation for single nucleotide polymorphism or a type of genetic marker. Iowa State University helped to develop the pig 60K SNP chip, which can simultaneously genotype 64,232 genetic markers in a single pig for a cost of about 0.3 cents per genotype or \$150 per pig. Similar technology is available for sheep, dogs, cattle and chickens. These new SNP chips will revolutionize the way livestock are genotyped, moving industry from genotyping animals for tens of markers to genotyping for thousands of markers with minimal impact on costs.

Materials and methods

A total of 820 commercial female pigs (408 Large White, 412 Large White × Landrace) from Newsham Choice Genetics (West Des Moines, IA, USA) were genotyped with the porcine 60K SNP chip. Data on each animal included 10th rib backfat (BF), loin muscle area (LMA), body conformation (three body size and three body shape traits), overall leg action and five leg scoring traits per leg pair. A total of 442 of these sows also had reproduction data from 3 parities. The BF and LMA were measured by ultrasound when animals weighed ~260 lbs. The scoring traits were independently evaluated by two experienced scorers using a 9-point scale. Statistical analyses were conducted to look for genetic markers and gene regions associated with each of the traits listed.

To look for genes associated with residual feed intake (RFI), a measure of the difference between how much a pig actually consumes and how much it should need to consume based on its growth and maintenance needs, 730 animals were genotyped. These animals came from 2 Large White lines: a line selected for better RFI and a line selected for worse RFI. Average daily gain, average daily feed intake, BF, LMA, and intramuscular fat were also measured on these animals.

Duplications in the pig genome were examined based on the genome of a single Duroc female. The functions of genes that were found to occur multiple times in the genome were examined to determine which functions were over-represented.

A total of 15 sheep diagnosed with chondrodysplasia and an additional 8 animals known to carry a single copy of the mutant gene, all from New Zealand, were genotyped for the chondrodysplasia study.

Finally, we are planning to use 75 Siberian Huskies with cryptorchidism and 75 normal dogs in the cryptorchidism study following genotyping with the canine SNP chip.

All SNP chips were purchased from Illumina (Illumina, San Diego, CA, USA), and all genotyping was performed by GeneSeek (Lincoln, NE, USA). A computer program written by Drs. Dorian Garrick and Rohan Fernando at Iowa State University was used to determine which markers were associated with each trait.

Results and Discussion

Multiple genetic markers were found to be associated with each pig trait examined. To reduce the number of sows culled each year due to lameness, the markers found to be associated with overall leg action, front and rear leg pastern conformation, toes turned in or out, uneven toe size, foot size, buck knees, or weak rear legs could be included in a selection program. Additional body conformation traits that could be selected for include top line, hip structure, rib shape, body length, depth, and width. Considerable variation in each of these traits was explained by genetic markers.

Lameness is not the only reason for culling sows from a herd. Reproduction problems account for a large percentage of the sows culled, as well. We found genetic markers for total number of piglets born in each of three parities, as well as number born alive, number of stillborns and mummies, and gestation length. Together these markers may be successful in improving the reproductive performance of commercial sows over the next few years, while reducing the number of replacement gilts that must be purchased due to sows being culled for lameness issues.

Feed costs account for a large percentage of input costs in any swine production program. By reducing the amount that each pig eats without reducing growth rates, producers could save significantly on input costs. We found several genetic markers that explained a large percentage of the

difference between animals. These markers could be used to improve average daily gain, reduce average daily feed intake, and reduce residual feed intake, while decreasing backfat and intramuscular fat and increasing loin muscle area. Taken together, selection for these various markers could save producers several dollars per pig in the near future.

A search for genome duplications in the pig was also initiated and found several genes associated with fatness, reproduction, and immune response. Further work needs to be done to discover the effect of each duplication, but they could play a large role in the trait phenotype associated with each of these traits.

For sheep, a region of the ovine genome was found to be highly associated with the incidence of chondrodysplasia. Genotyping potential parents for this mutation could prevent lambs from being born with chondrodysplasia due to this genetic defect.

Work with dogs to find causative mutations involved in cryptorchidism is ongoing.

Though further validation is needed with each of these genetic markers, the current results look very promising for making a positive impact on producers' profits. Work will be completed as quickly as possible to make these markers available for commercial use.

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