Réseau laitier canadien
Canadian Dairy Network

Genomic Testing Success

A desirable goal would be to guarantee that every animal that is genotyped, male or female, young or old, receive a published genomic evaluation. Quality assurance at every stage of the testing and analysis process currently negates this goal from being 100% attainable. Tissue samples must pass several quality control measures at the laboratory in order to extract sufficient DNA to enable successful genotyping. The resulting genotype must also undergo a verification of parentage to ensure herd book integrity and surpass quality assurance tests for the animal to receive a publishable genomic evaluation. In order to measure the probability that an animal will receive a publishable genomic evaluation when submitted to the GenoTest program, it is important to be cognisant of the quality control measures imposed at each phase of the testing process and how they impact the chances of success.

Samples submitted to the GenoTest program from September 2010 until January 2011 were investigated. Of the 6,429 samples in total, 93% were submitted for testing on the low density 3K panel, with the remainder having been tested on the 50K panel.

DNA Extraction and Genotyping

Holstein Canada conducts an initial visual inspection of the hair and nasal samples to increase the likelihood that there will be enough tissue for the laboratory to extract DNA. DNA Landmarks (laboratory) extracts the DNA from the tissue and performs an analysis to ensure the DNA meets sufficient quality standards for genotyping. The laboratory has not been able to obtain adequate DNA from 4.2% of the samples submitted to date. Next, each of the 3,000 or 50,000 SNPs on the genotype are inspected. If the technician is unable to read the result, the SNP is deemed “missing” or “unreadable”. If more than 10% of the SNPs are unreadable, the genotype is rejected. Only 1.6% of the genotypes that have been inspected at the lab did not meet these criteria and must be re-sampled and re-tested. Since September 2010, 94.2% of the samples that have been submitted to the laboratory have been successfully genotyped.

Parentage Verification

More than 78,000 Holsteins have now been genotyped in North America on either the 3K or 50K panels. This large-scale commercialization of genotyping has provided another conduit for verification of pedigree information. Less than 150 SNP are required to accurately determine if a genotyped animal’s parentage has been recorded correctly. For each animal that receives a quality genotype, its DNA profile is compared to that of its sire’s and/or dam’s DNA profiles (when available) to determine the likelihood that the genes were in fact received from the recorded parents. In cases where the animal’s DNA profile does not match those of a parent, the DNA profiles of other genotyped animals are investigated to find more probable matches. In cases where one or both parents are not genotyped, it is possible to identify parentage by tracing the transmission of genes further back into the pedigree. Under these investigations, several groups of animals (more than 175 sets) with identical genotypes have been discovered.

Approximately 3.5% of the animals tested in Canada had genotypes that were inconsistent with their recorded pedigree. Depending on the amount of inconsistency, a sire, or dam or both can be disqualified from being parent(s). In a similar way, using many more than 150 SNP, an animal’s breed constitution can be confirmed. Holstein Canada attempts to rectify all cases of parentage disputes as soon as they are identified. Until these inconsistencies are resolved, the animal's genotype is not included for genomic evaluation.

Imputation Procedures

All animals tested on the 50K panel that receive a quality genotype and have no parentage disputes are expected to receive a genomic evaluation. However, 3K genotypes must be accurately imputed to 50K genotypes before qualifying for inclusion in genomic evaluation. The accuracy with which an animal's 3K genotype can be imputed is directly related to the degree of pedigree completeness and the amount of genotyping conducted in ancestors. CDN and research colleagues are consistently researching to improve imputation procedures and methodology. To date, only 3.9% of the animals tested on the 3K panel have not received a publishable genomic evaluation.

A recent study conducted by CDN based on more than 11,000 animals showed the probability of successfully imputing a 3K to a 50K genotype given different scenarios for pedigree completeness and ancestral genotyping (Table 1). When both the sire and dam have 50K genotypes, imputing an animal's 3K genotype can be extremely accurate and is essentially 100% successful. If the dam was instead tested on the 3K panel or not genotyped at all, the probability of effectively imputing lessens (99.2% to 96.5%, respectively). For animals with an unknown dam, only 62% have had their 3K genotypes successfully imputed.

Table 1: Imputation success rates

Sire	Genotyped Dam?	% Success
Genotyped (50K is mandatory for official genomic evaluation)	Yes with 50K	99.9%
	Yes with 3K	99.2%
	No, but MGS is with 50K	98.5%
	No and MGS neither, but at least one other ancestor is genotyped	96.5%
	Dam is unknown	62%
Not Genotyped (but PGS is)	No, and MGS may or may not be genotyped	82%
Unknown	Any situation for dam	8%

Summary

Under today's criteria and methodologies, 88% of the animals that have been submitted for genotyping have passed all stages of quality control and received a publishable genomic evaluation. As more and more animals are tested and imputation procedures become increasingly effective and accurate, this success rate will only improve. In addition to boosting the accuracy of predicting an animal's genetic potential, genomic testing has supplied an alternative and cost effective means of verifying parentage and discovering genetically identical animals.

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