Proc. Assoc. Advmt. Anim. Breed. Genet. 19:131-134

THE EFFECTIVE MANAGEMENT OF DELETERIOUS GENETIC CONDITIONS IN CATTLE

C.F. Teseling and P.F. Parnell

The Angus Society of Australia, 86 Glen Innes Road, Armidale, NSW, 2350

SUMMARY

Genetic conditions exist in all populations and new mutations continue to occur making the eradication of all deleterious genetic conditions impossible. Several tools are available to assist in the management of genetic conditions. However, without supportive systems in place these tools can not be used optimally. Effective systems for the reporting of abnormal calves, for coordination of sample collection, for the conduct of DNA tests, and for the storage and reporting of results are necessary for the optimal management of genetic conditions.

The application of GeneProb to combine test results with pedigree information is a critical component of the strategy for the management of genetic conditions in the Angus breed in Australia. GeneProb is used to calculate the genetic status of all recorded animals in the breed for those genetic conditions for which DNA diagnostic tests are available. This is especially advantageous when only a relatively small number of animals have actually had the DNA test applied. This paper describes the systems used to facilitate and support the management of genetic conditions in the Angus breed.

INTRODUCTION

Deleterious genetic conditions can occur when genes are missing, in excess, mutated or in the wrong location. Usually when genes directly cause an abnormality these genes are recessive, meaning two copies of the mutated allele must be present at the specific locus to cause the associated abnormality. While affected animals of some conditions are born dead, carriers of these conditions in most instances don't show any clinical signs of the condition and can reproduce normally. When these carrier animals are used for breeding purposes they can pass the “defective” gene to their offspring thus increasing the prevalence of the mutation in the population.

The management of genetic conditions is an ongoing concern for most breed associations, especially where widespread use is made of individual sires. The increased utilization of artificial insemination and embryo transfer has allowed breeders to dramatically increase the number of progeny generated by an individual sire or dam. The use of accurate breeding value estimation and advanced reproductive technology results in rapid genetic progress but also leads to the accumulation of inbreeding in most livestock species (Weigel 2001). While most breeders avoid close inbreeding, it is not unusual for prominent sires to appear some generations back in pedigrees of both the sire and dam of individuals. In these instances there is an increased risk of progeny affected by recessive genetic conditions as two copies of the unfavourable alleles can occur at the same locus and cause the undesired characteristic to be expressed. An animal that has one undesirable recessive gene (carrier of a genetic condition) may have many desirable genes for particular production traits. The animal's desirable genes should be weighed against its undesirable genes. If the same desirable genes can be found in other animals without the undesirable gene, carriers of the undesirable genes should be replaced. Traditionally, when a superior bull or cow was found to be a carrier of a genetic condition, the only option available to produce a superior son that did not carry the undesirable gene was progeny testing. The first step would be to mate the superior animal with a small group of other outstanding individuals. A small number of the most superior sons produced were then selected and used in test matings to known carrier cows. The best son that didn’t produce any affected progeny would then be kept. The time and costs involved

in running such a program, and the availability of known carrier cows makes this process impractical in most circumstances (Schalles and Leipold 2008).

The rapid developments of the past two decades in molecular genetics and genomics resulted in the completion of the bovine genome sequence and the development of thousands of molecular markers. These advances have assisted in identifying causative mutations underlying many genetic conditions, even when relatively few samples are available for analysis (Meyers *et al.* 2010). This paper reviews some of the important considerations required to effectively manage genetic conditions in a cattle population.

CONSIDERATIONS FOR THE MANAGEMENT OF GENETIC CONDITIONS

Surveillance and reporting. General warnings and information about genetic conditions are important to inform industry about the potential risk and to emphasise the importance of reporting abnormalities. Early detection of potential genetic conditions requires breeders and veterinary practitioners to be vigilant and informed about abnormalities and prepared to report them to the breed association. Without the assistance of veterinarians and astute producers, many of the currently recognised genetic conditions of cattle would have gone undiscovered (Whitlock *et al.* 2008). For any surveillance program to be successful the recognition of a potential genetic condition is the first but very important step. At the time when an abnormal calf is reported as much information as possible should be collected. Beever (pers. comm. 2011) regards detailed pathology of affected calves, diligent sample collection, proper sample care, a set of informative pictures and accurate pedigree information as indispensable for the development of a DNA test.

Determining the genetic basis of the condition. It is important to develop an accurate clinical description of any potential genetic condition as soon as possible. This usually requires post mortems to be done on up to five suspected cases by a veterinary pathologist. Once a clinical description has been developed it is important to determine the method of inheritance. This could be done either through pedigree analysis or through test matings. The ideal situation is where a homozygous (expressing the condition) female is flushed to a homozygous male to produce at least 15 embryo calves. If only heterozygotes (carriers) are available for test matings, larger numbers of progeny will be needed to determine the method of inheritance. When test matings are used to determine the method of inheritance it is essential to monitor the pregnancies to ensure premature embryonic deaths don't alter the frequency of affected versus non-affected progeny.

DNA based test development. Before a sample is considered for use to develop a DNA test all associated information should be scrutinised carefully to ensure the sample represents the expected genotype (i.e. affected, carrier or free). Any misclassified samples will have a negative impact on the mapping process. Normally the parents used and progeny generated by test matings form the basis of samples used for the development of a DNA test. Depending on the complexity of the mutation, between 10 and 40 calves (representing affected and carriers) and their parents would be enough to map a recessive condition to a small enough region of the genome to make it practical to select against the defect (Tallman *et al*, 2009). New genomic technologies insure rapid DNA sequence analysis to develop a DNA-based test. In the case of Neuropathic Hydrocephalus 6 affected and 10 "control" samples were analysed on the Illumina BovineSNP50 Genotyping BeadChip. Two weeks after sample collection the mutation location was reduced to less than 6.6 Mb (Beever 2009). Beever (pers. comm. 2011) used 10, 6 and 3 affected samples, and 11, 11 and 17 control samples in the development of a DNA based tests for Arthrogryposis Multiplex (AM), Neuropathic Hydrocephalus (NH) and Contractural Arachnodactyly (CA) respectively.

DNA sample and results management. The importance of accurately recording the identification of the animal from which a sample is collected can not be over-emphasised. The potential for human transcription errors should be minimised through the extensive use of electronic file transfer between the different parties involved in the testing process. The testing process is defined as all actions necessary from when the sample is collected from the animal to the point when the result is reported to the breeder.

Genotype probability prediction. Manual segregation analysis to determine the expected genotype of an animal is only feasible where the genotypes of only a few animals need to be resolved. In a population where the expected genotypes of many animals need to be determined an efficient procedure is required that considers the genotypes of all parents, the animals themselves, matings and the resultant progeny. GeneProb is a software program developed by Kinghorn (2000) for the analysis of large datasets to indicate the probability of each animal being of the AA, Aa or aa genotype.

Angus Australia uses GeneProb to manage five genetic conditions, with a weekly analysis involving almost 1.3 million animals. Electronic reports for each condition are made available through a secure file download area to members each time an analysis is conducted. The use of GeneProb has significantly reduced the number of animals needed to be tested for AM, NH and CA. It is estimated that its use has reduced the number of required tests from as many as 150,000 to 30,000 per genetic condition. Saving the industry in excess of $12 million (120,000 x 3 conditions x $35 per test).

Publishing DNA test results and probabilities. As soon as preliminary testing of individuals is completed and the gene frequency in the population and economic impact determined, results should be released to bull owners and breeders concerned with the genetic condition. It is important to promptly complete research about the accuracy of a DNA test and the financial impact of the condition before this information is made available to the broader industry. Withholding information from industry may put the organization and its members at risk for allowing defective animals to be marketed without disclosure of the condition (World Holstein-Friesian Federation, 2011).

CONCLUSIONS

Historically, in an effort to eradicate genetic conditions, many breed associations would revoke the registration status of carrier animals, making some breeders antagonistic about reporting abnormal calves in their herds. Consequently, there is a high risk that the condition will be forced "underground" as many breeders could stop reporting abnormal calves. The ability to analyse DNA test results in conjunction with pedigree information enables breed associations to effectively change from a policy of eradication to that of management of genetic conditions.

Modern genomic technology can greatly speed up the process of developing DNA based diagnostic tests for recessive genetic conditions. With the combined use of GeneProb and genetic testing there is essentially no reason for known genetic conditions to ever become a significant problem. An important benefit resulting from the development of GeneProb is that breeders can now manage genetic conditions much more efficiently by identifying the most informative animals for initial testing and assisting with the decision of which other animals to subsequently test.

ACKNOWLEDGEMENTS

The input the Agricultural Business Research Institute (ABRI) in the application of GeneProb, and the financial support of Meat and Livestock Australia is acknowledged.

REFERENCES

Beever J.E. (2009) http://www.rangebeefcow.com/2009/documents/Beever2009RBCS.pdf

Kinghorn B.P. (2000) In 'Animal Breeding – Use of New Technologies', pp. 112-117, editors B.P. Kinghorn, J.H.J. Van der Werf and M. Ryan, The Post Graduate Foundation in Veterinarian Science of the University of Sydney, Sydney.

Meyers S.N., McDaneld T.G., Swist S.L., Marron B.M., Steffen D.J., O'Toole D., O'Connell J.R., Beever J.E., Sonstegard T.S. and Smith T.P.L. (2010) *BMC Genomics* **11:** 337.

Schalles R.R and Leipold H.W. (2008) http://www.csubeef.com/dmdocuments/1026.pdf

Weigel K.A. (2001) *J. Dairy Sci*. **84** (Supplement E), E177.

Whitlock B.K., Kaiser L. and Maxwell H.S. (2008) *Theriogenology* **70:** 535

World Holstein-Friesian Federation (2011) http://www.whff.info/info/geneticrecessives/Genetic Recessives_Harmonisation.pdf