Genomic tools: genetic testing for genetic defects in various breeds

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Over the last several years the beef seedstock sector has had to deal with a number of recessive genetic defects. The utilization of assisted reproductive technologies including embryo transfer and artificial insemination has allowed breeders to concentrate selection to a relatively small number of animals. While many breeders avoid matings of half-sibs or sires to daughters to reduce the accumulation of inbreeding, it is not unusual for very prominent sires to appear several generations back in pedigrees of both the sire and dam of a particular individual. It is in this case when there is an increased chance for the appearance of a progeny affected by a recessive genetic defect.

Autosomal recessive genetic defects are inherited congenital abnormalities. These genetic mutations occur on one of the 29 pairs of autosomal (non-sex coding) chromosomes. Animals that inherit a single defective or mutated gene and one normal copy of the gene are called heterozygotes and are not affected by the disease but are carriers of the defect passing it on to half of their progeny on average. Animals that have two copies of the normal or unmutated gene are called homozygous normal. Animals that inherit two copies of the defective gene are homozygous for the recessive forms of the gene and are phenotypically affected by the abnormality. The carriers (heterozygotes) and homozygous normal animals do not exhibit the deleterious condition and are phenotypically indistinguishable. The fact that the normal animals and heterozygotes are indistinguishable makes phenotypic selection to eliminate defect carriers ineffective.

To illustrate this difficulty in phenotypic selection to eliminate recessive carriers consider a more common trait like coat color. Both homozygous black animals and heterozygous black (red carriers) are phenotypically black and indistinguishable. Only when two black animals produce a red calf can we infer the genetic makeup of the color parents as both being heterozygotes (red carriers).

All breeds carry some genetic defects. Presumably some of the autosomal recessive lethal genetic conditions affect embryos during gestation and cause early embryonic loss. These defects are difficult to detect and may simply be diagnosed as 'reproductive failure'. A number of defects have been documented in beef breeds, several quite recently. A brief description of several genetic defects are listed below. Due to space limitations this is not a complete listing of defects.

Condition	Description	Breeds Affected
Tibial Hemimelia (TH)	Affected calves are born with twisted rear legs with fused joints, malformed or missing tibia, large abdominal hernias and/or a skull deformity. DNA test available to identify carriers.	Shorthorn Maine-Anjou Chianina
Pulmonary Hypoplasia with Anasarca (PHA)	Underdeveloped heart and lungs, marked increase in calf size caused by fluid retention (anasarca) of fetus. DNA test available to identify carriers.	Shorthorn Maine Anjou Chianina
Ideopathic Epilepsey (IE)	A neurological disorder in which affected calves have seizures. DNA test available to identify carriers.	Hereford

Arthrogryposis -Multiplex (AM)*	Many environmentally caused forms appear but one form is inherited as a simple recessive trait. The joints of all four legs are fixed symmetrically and a cleft palate is present. AM in Angus includes twisted malformation of spine and fixed leg joints. DNA test available to identify AM carriers.	Charolais Angus*
Contractual Arachnodactyly (CA)	Inherited as simple recessive, CA is caused by a deletion of genomic DNA. Calves are abnormal at birth and exhibit arched spine, hyperextension of fetlocks, muscle contracture resulting in inability to straighten the upper limb joints. Post-natal improvement of clinical signs.	Angus
Dwarfism	At least three types of dwarfism documented in cattle and thought to be caused different simply inherited recessive genes.	Angus Hereford Brahman Dexter
Hypotrichosis (Hairlessness)	Partial to complete lack of hair. Hair grows in and falls out so affected animals may have varying appearance over time. DNA test available to identify carriers.	Hereford
Protoporphyria	Light sensitivity causing open sores and scabs. Liver function is also affected and animals may suffer from seizures. Inherited as simple recessive. DNA test available to identify carriers.	Limousin
Osteopetrosis (Marble Bone)	Long bones are solid and without developed marrow. Bones are brittle and break easily . Calves are usually born dead 2 to 4 weeks pre-term. DNA test available to identify carriers in Red Angus.	Angus Red Angus Holstein
Hydrocephalus -Internal * -Neuropathic Hydrocephalus(NH)**	Excessive fluid in brain ventricles (internal) or in cranium (external). DNA test available to identify NH carriers.	Hereford* Many other breeds Angus**

Management of genetic defects in seedstock or commercial beef herds can be quite challenging. In the case of seedstock herds, suspect animals or those known to be the progeny of carriers should be tested when DNA diagnostic tools are available and economically practical. Carrier animals may be retained in the breeding herd, but breeders should test all progeny to determine carrier status prior to marketing as breeding stock. Carrier calves should only be sold to feeders and designated for slaughter only. The table below details the expected results if a homozygous normal sire is mated to a carrier (heterozygote) cow the resulting progeny will include on average one-half defect free and one-half carrier calves with no affected calves. Also included in the table is the expected proportion of progeny of various genotypes when a carrier sire is mated to a carrier dam. On average one-quarter of the calves will be free of the defect, one-half will be carriers and one-quarter will be affected. If the animals are affected by a lethal defect, the surviving animals will include one-third defect free calves and two-thirds will be carriers of the defect. If you have a calf born with a suspected congenital defect, photograph the affected calf and contact your breed association immediately to arrange for tissue collection and reporting instructions.

In a commercial herd that has had affected calves or is striving to prevent introduction of a known defect, bulls should be DNA tested as the primary means of control. Pedigree inspection and reduction of matings of closely related animals may provide reductions in the production of affected calves but not as effective as DNA marker testing. Mating of carrier cows to non-carrier or clean bulls will result in the production of no affected calves. It is frequently not economically practical to cull commercial cows on the basis of their carrier status. If a DNA test is available, all new sire purchases or semen used for artificial insemination should be from sires that are not carriers. Non-carriers may also be determined by pedigree if both sire and dam have tested free of the defect. If a DNA test for a defect is not available, the strategic use of a planned crossbreeding system may eliminate the appearance of affected calves. Care should be taken to select a breed that has not had any calves produced in recent generations that are affected by the same defect one is trying to eliminate. At the commercial level, autosomal recessive defects can be effectively managed through careful sire and/or breed selection without extensive culling of the beef cow herd.

Table . A.) Expected calf genotypic frequencies from mating of non-carrier sire to carrier dam for deleterious recessive genetic defect. B.) Expected calf genotypic frequencies from mating of carrier sire to carrier dam.

A.

	Non-carrier Sire Genotype (AA)	
Carrier Dam Genotype (Aa)	**A**	**A**
A	AA	AA
a	Aa	Aa

Genotypes	**Frequency**
AA (homo. Normal)	50%
Aa (hetero. Carrier)	50%
aa (Homo. Recessive Affected)	0%

B.

	Carrier Sire Genotype (Aa)	
Carrier Dam Genotype (Aa)	**A**	**a**
A	AA	Aa
a	Aa	aa

Genotypes	**Frequency**
AA (homo. Normal)	25%
Aa (hetero. Carrier)	50%
aa (Homo. Recessive Affected)	25%

Phenotypes	**Frequency**	**Frequency in Surviving Calves**
AA (Normal)	25%	33%
Aa(Normal)	50%	67%
aa (affected-dead)	25%	NA

A = Normal genotype

a = Defective/mutated genotype