



DEAD COWS DON'T LIE!! MOO NEWS TELLS YOU WHY!

Special tear-out
insert for future
reference

The gene gurus have been busy this decade: recessive defect, mutations and DNA-based tests

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DNA testing has changed the beef business – not only in terms of traits important to production or the consumer, but also in our ability to identify and manage deleterious recessive genetic defects. In the US, molecular geneticist Dr. Jon Beever (U. of Illinois) and veterinary pathologist Dr. Dave Steffen (U. of Nebraska, Lincoln) have been leaders in identifying genetic disorders, characterizing the pathology, determining the genetic mutation and then developing a test. This work requires cooperation of both breeders and associations. In the past 5 years, there have been several defects identified that have had significant impact on specific cattle populations. In the near future, it is likely that the mutations in fawn calf syndrome, marble bone in Black Angus, spastic paresis, and the “itty bitty” calf will be identified. The purpose of this article is to review those genetic defects recently described for which the mutation has been identified and a test is available.

All the defects described in this edition of “Dead Cows Don’t Lie” are recessive, meaning that in order to have an affected calf BOTH sire and dam must be carriers. The status of animals (carrier of the defect vs. free of the defect) can be determined with DNA tests. These defects affect not only registered cattle but also commercial cattle, and they can affect purebred as well as crossbred cattle. Additional information about these defects can be found on the breed association web pages. Different laboratories require different samples for testing – consult your breed association for approved laboratories and the laboratory web site for required sample type.



3-year-old long-nosed dwarf and dam

Defect: Long-nosed dwarf

Breed of origin: Angus

Breeds affected: Angus

What is it? An autosomal recessive genetic defect

How did we find it? In the beginning of the 21st century astute Angus breeders in the northwest US noticed a group of calves that appeared normal at birth but failed to grow. Breeders thought these calves could be dwarfs and submitted calves for necropsy. Gross and histopathological examination diagnosed these calves as the “long-nosed” dwarf

Where did it come from? This form of dwarfism traces to the bull High Valley 7D7 of 4G9 (AAA # 12,838,783; born 1997). Neither his sire nor dam have been tested for dwarfism.

What does it look like? Calves are normal looking at birth, but as they age, when compared to similar age-mates, they are shorter in stature because the long bones in the legs fail to grow. Consequently, their legs are shorter and the body appears thicker. The head is of normal size. Dwarfs appear to have normal fertility. The long-nose dwarf

is not the same as the “snorter” dwarf or the “bulldog” dwarf – both of which have abnormal heads/faces.

Mutation: A long-nose dwarf and her (carrier) dam were donated to Dr. Jim Reecy at Iowa State. Both were bred to a known carrier. Information from these matings was used to identify the mutation that causes the long nosed dwarf. It involves a single base pair substitution in the PRKG2 gene – a gene important in, among other things, the development of cartilage.

DNA test: MMI



Osteopetrosis (OS or Marble bone) Marble bone in an aborted Red Angus calf. Note the shortened lower jaw.

Defect: Osteopetrosis (OS; Marble bone disease)

Breed of origin: Red Angus (NOTE: Most likely independent mutations in several different breeds.)

Breeds affected: Red Angus (marble bone has been identified in other breeds, however the mutations are most likely different from the Red Angus mutation)

What is it? A lethal autosomal recessive genetic defect

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How did we find it? Marble bone has been described in many different breeds, including Angus, Red Angus, and Hereford. Most recently an increased frequency of calves has been reported in the Red Angus breed. Within the past two years several prominent AI sires have been classified as carriers of OS based on parental verification of two or more affected calves. Analysis of pedigrees plus historical information suggests that the mutation may have originated in the 1950's. The oldest known carrier bull, as determined by DNA testing, is BKT STRM 751626 (RAAA #8605, born 1964). Pedigree analysis of other known carriers suggests that the mutation may have occurred at least two generations prior to "751626".

Where did it come from? The Red Angus mutation is NOT the same as the mutation that causes marble bone in Black Angus cattle. This could mean that the mutation in Black Angus evolved or that they are 2 distinctly different mutations. To date the black Angus mutation has not been identified.

What does it look like? Calves are aborted 10 to 30 days early. In many cases the fetus is not found and the cow (checked pregnant in the fall) is open in the spring. Aborted calves have a short lower jaw and impacted molars. The long bones contain no marrow cavity, but are very fragile and can be easily broken.

Mutation: Samples from the "751626", as well as samples from the identified carriers, were used by Dr. Beever to identify the mutation. The disease is caused by a deletion (missing piece) of the SLC4A2 gene on chromosome 4 – this gene is necessary for bone remodeling during development.

DNA test: AgriGenomics, Pfizer, MMI Genomics, Igenity (NOTE – the OS test is for the mutation in Red Angus ONLY).



Idiopathic epilepsy

Hereford calves with IE appear normal unless having a seizure.

Defect: Idiopathic epilepsy (IE)

Breed of origin: Hereford

Breeds affected: Hereford

What is it? An autosomal recessive genetic defect that is incompatible with life

How did we find it? There had been rumors circulating about a seizure disorder in Herefords for some time, Dr. Beever, a Hereford breeder and molecular geneticist, began receiving reports of seizing calves and samples from them in 2003. He was able to obtain 3 carrier cows and flushed them to bulls known to produce IE offspring. This material was used to identify the mutation.

Where did it come from? Over 15,000 Hereford samples have been tested for IE. To date all carriers of IE trace to a single bull born in 1982, however DNA is not available to test this bull. IE is predominately seen in horned Herefords, but can be seen in polled Herefords with horned animals in their pedigrees

What does it look like? IE is a seizure disorder. Affected calves can have their first seizure anywhere from birth to several months of age. The seizures are grand mal and can last from minutes to more than an hour. Environmental stressors (heat, cold, weaning, processing) can trigger the seizures. There is no treatment. Calves with IE look perfectly normal when not seizing.

Mutation: The mutation is more complicated than a single substitution or a deletion, base pairs are duplicated, and deleted, with the result being an addition of 5 base pairs.

DNA test: AgriGenomics, American Hereford Association, Igenity



Tibial hemimelia (TH)

TH in a Shorthorn calf. Note the twisted hind limbs and large abdominal hernia.

Defect: Tibial hemimelia (TH)

Breed of origin: Shorthorn

Breeds affected: Shorthorn and Shorthorn composites

What is it? A lethal autosomal recessive genetic defect

How did we find it? In 2000, Dr. Dave Steffen described TH in Shorthorn calves in an article published in Veterinary Pathology. They described 6 calves with similar pedigrees and thought the condition was genetic. Somewhat later, veterinarian Dr. Chuck Hannon and Shorthorn breeders in the mid-west cooperated to provide tissue samples and pedigree information to Dr. Beever and Brandy Marron, ultimately resulting in identification of the defective gene.

Where did it come from? The TH mutation was traced to the Irish bull Deerpark Improver (ASA # 3,684,142; born 1972), one of a few direct imports to North America. Improver was used extensively in the U.S. in the 1970s, as there are 635 direct progeny registered with the American Shorthorn Association.

What does it look like? Calves are born dead or die (or are euthanized) shortly after birth. TH consists of a constellation of abnormalities, including abnormally twisted legs, fused joints, abdominal hernia, meningocele (part of the brain covering coming out of a hole in the skull), and cryptorchidism.

Mutation: The gene involved (ALX4) is a major regulator of hind limb formation. The mutation is a deletion of an important part of the gene. The Improver deletion removes approximately one-third of the ALX4 gene. After identification of the Improver deletion, it was noted that although the parentage of some TH calves was DNA-verified, some parents did not test positive for the Improver deletion. Additional studies revealed a second (rare) TH mutation called the Outcast mutation. The Shorthorn bull TKA Outcast (ASA # 4,046,304; born 2001) possessed a larger deletion of 450,000 base pairs that overlapped the Improver deletion, and removed four genes, including ALX4.

DNA test: AgriGenomics, Igenity, Pfizer (NOTE: Does test for both the Improver and Outcast deletions.)



Pulmonary hypoplasia with anasarca (PHA)

Calf with PHA delivered by C-section. Note the water logged appearance.

Defect: Pulmonary hypoplasia with anasarca (PHA)

Breed of origin: Maine-Anjou

Breeds affected: Maine-Anjou, Shorthorn, and composites

What is it? A lethal autosomal recessive genetic defect

How did we find it? At the time that Dr. Hannon was examining calves with TH, he also identified another group of calves with a very different lethal defect. These calves were Maine-Anjou, cross-bred, or Shorthorn with Maine-Anjou in their pedigree. Seeing similarities in both the physical presentation of the PHA calves and the pedigrees Dr. Hannon provided samples to Dr. Beever and Brandy Marron for identification of the causative mutation.

Where did it come from? Originally PHA calves were identified as Maine-Anjou, Shorthorn or their crosses. The apparent link was three popular bulls: two registered Maine-Anjou bulls (Draft Pick, born 1989; AMAA # 165,744 and Stinger, born 1985; AMAA # 111,205) and a bull registered with the American Chianina Association (Payback, born 1992; ACA # 232,907). Subsequent genetic testing suggested a common ancestor of the three bulls. Draft Pick's maternal great grand sire, Paramount (AMAA # 77; born 1973), a full-blood Maine-Anjou bull exported from England to Canada, was a PHA carrier. Due to incomplete or inaccurate pedigrees or inability to obtain samples from older full-blood Maine-Anjou cattle, the origin of the mutation in Stinger and Payback has not been positively identified. Molecular markers surrounding the gene suggest the French import Dalton (AMAA # 15; born 1970) as a common source for Stinger and Payback. In the USA, the Maine-Anjou breed is considered the origin of PHA. In registered Maine-Anjou cattle, Draft Pick is primarily responsible for the widespread dispersion of the mutation, whereas in registered Shorthorn cattle, Stinger is considered primarily responsible. A second mutation in the same gene has been identified in the Dexter breed of cattle.

What does it look like? PHA calves are born dead or die shortly after birth. The calves are water logged (anasarca) and on necropsy have very small lungs and virtually no lymphatic system. Calves begin to accumulate excess fluid in the 5th or 6th month of gestation and can

reach enormous size (>200lbs). Delivery often requires C-section and the cow may die or require euthanasia.

Mutation: PHA is the result of a single mis-sense mutation common to Draft Pick, Stinger, and Payback, and identified in modern Shorthorn, Maine Anjou, and composite cattle.

DNA test: AgriGenomics, Igenity (NOTE: Does test for the Dexter mutation)

Defect: Arthrogryposis multiplex (AM; "curly calf syndrome")

Breed of origin: Angus

Breeds affected: Angus, Red Angus, Angus crosses

What is it? A lethal autosomal recessive genetic defect



Arthrogryposis multiplex (AM)

Calf born dead with AM. Not the severely twisted legs and spine.

How did we find it? On September 5, 2008, the American Angus Association posted a notice on its website requesting assistance in obtaining reports of any abnormal calves believed to fit the description of what was then called "Curly Calf Syndrome". On November 3, Dr. Jon Beever posted a description of the mutation and identified the status of over 700 AI bulls. It is quite remarkable that in a mere 2 months, researchers obtained samples and pedigrees from affected calves and their parents, the mutation was identified, and the DNA test was developed and validated.

Where did it come from? The genetic cause of AM was suspected when pedigree analysis of the original cases found that all affected calves trace on one or both sides of their pedigree to GAR Precision 1680 (#11520398) – a bull born in 1990 used heavily for his carcass traits. Later investigation revealed that those AM calves that did not trace to 1680 on both sides of the pedigree did trace to his dam 9J9 GAR 856 (#10895323) whose sire Rito 9J9 of B156 7T26 (#9682589) has subsequently been determined to be a carrier of AM.

What does it look like? Calves with AM are born dead or die shortly after birth. They are small for gestational age and have markedly diminished muscle mass. It appears that in AM an essential protein that allows communication between nerves and muscle tissue is absent, thus the calf (which fails to move in utero) is born with the joints of all 4 limbs fixed and the legs twisted. There are several characteristics of AM including arthrogryposis (fixed, twisted joints), kyphoscoliosis (twisted spine), and decreased muscling.

Mutation: Dr. Jon Beever and Brandy Marron of the University of Illinois have identified the mutation involved in AM. The mutation is a deletion that involves 3 genes – one of these genes is involved in the development of nerve and muscle. Affected calves are missing ~23,000 base pairs. These missing base pairs results in complete loss-of-function of all three genes in homozygous calves.

DNA test: AgriGenomics, Igenity, Pfizer, GeneSeek, MMI



Neuroathic hydrocephalus (NH)

Calf born dead with NH. Note the huge head.

Defect: Neuroathic hydrocephalus (NH)

Breed of origin: Angus

Breeds affected: Angus, Red Angus, Angus crosses

What is it? A lethal autosomal recessive genetic defect

How did we find it? At the same time that AM calves were being submitted, 15 calves with a severe form of hydrocephalus (“water on the brain”) were also submitted. These calves were similar in description and pedigree to calves described by Dr. Laurie Denholm in Australia. Interestingly, calves submitted for both AM and NH generally had GAR Precision 1680 on both sides of the pedigree.

Where did it come from? It is believed that the NH mutation originated with the bull GAR Precision 1680 (AAA #11520398) as both his sire (Tehama Bando 155, #9891499) and dam (9J9 GAR 856, #10895323) test negative for NH.

What does it look like? Calves are born near term and have 25-35 pound birth weights. The head (cranium) is markedly enlarged (volleyball to basketball sized). The bones of the skull are malformed and appear as loosely organized bony plates that fall apart when the cavity is opened. The cranial cavity is filled with fluid and no recognizable brain tissue is evident. The spinal canal is also dilated and no observable spinal tissue is found.

Mutation: The mutation identified by Dr. Beever and Brandy Marron is a change of a single DNA base pair in a gene that is involved in development and maintenance of central nervous system tissue. This single base pair change results in abnormal function of an important protein and the NH syndrome.

DNA test: AgriGenomics, Igenity, Pfizer, MMI

Laboratories

AgriGenomics
2399 N. 1000 E. Rd.
Mansfield, IL 61854
217-762-9808

<http://www.agrigenomicsinc.com/cattle.html>

MMI Genomics
1756 Picasso Avenue
Davis, CA 95618
(800) 311-8808 ext 3016
<http://www.mmigenomics.com>

Pfizer Animal Genetics
250 Plauche St.
Harahan, LA 70123
1-877-BEEF DNA
1-877-233-3362
<http://www.pfizeranimalgenetics.com>

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4701 Innovation Drive, CB 101
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