Understanding Genetics

and

Complete Genetic Disease and Trait Definition

(Expanded Edition)

INDEX

Understanding Genetics:

DNA is essential to building all parts of all living things. Most people are familiar with the double helix structure discovered in 1953, but don't fully understand what it is or why we care about it. In the most basic terms, DNA is the building blocks of life. It is composed of 4 nucleotides, also called **bases**, adenine (A), cytosine (C), guanine (G), and thymine (T). These nucleotides are arranged on a sugar and phosphate backbone and when they are matched up, make up the double helix we have all become familiar with (Figure 1 A-C).

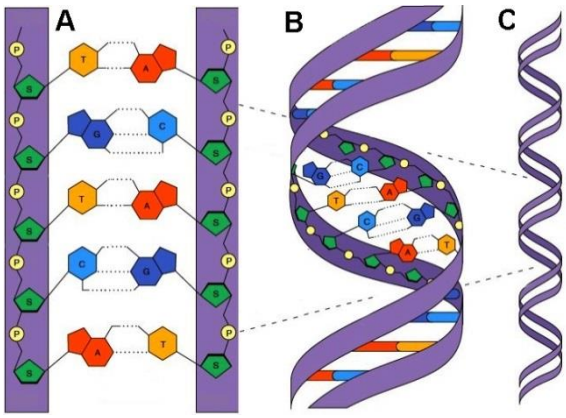


Figure 1:
A- If you were to zoom in, untwist the double helix, and flatten it out, it would look like this. Notice that the nucleotides in the centre are paired up, and the sugar and phosphate backbone, highlighted in purple, are on either side. This is what makes up every part of all living things.
B- Reassembling it into its double-helix structure and showing one twist of the helix.
C- Zooming out further to see multiple twists of the DNA helix.

The cattle genome has approximate 3 billion DNA bases, the same number as found in the human genome. To help store all this information DNA are packaged in **chromosomes**. These chromosomes can be broken down into 3 categories: autosomes, sex determining chromosomes- X and Y, and mitochondria. While most animals will share the same DNA code throughout the genome there are differences in the code which cause each animal to look and perform differently. Some of these differences in the DNA code (called **alleles** or mutations) can cause genetic diseases or a difference in **phenotype** (physical traits of the animal). Figure 2 is a pictorial depiction of alleles.

Over 100 of these differences that are known to cause a disease or trait are on the IDB chip. When the alleles are described below you'll see A>T (or T>G, G>C, …) what this means is that most animals have the first base and the allele we test for is the second base given. So for the G>T mutation in the SLC35A3 gene that causes Complex Vertebral Malformation (CVM) disease the 'G' is the allele most animals have, and 'T' is the allele that causes the disease. Animals that have CVM will be homozygous (have 2 copies) for the 'T' allele.

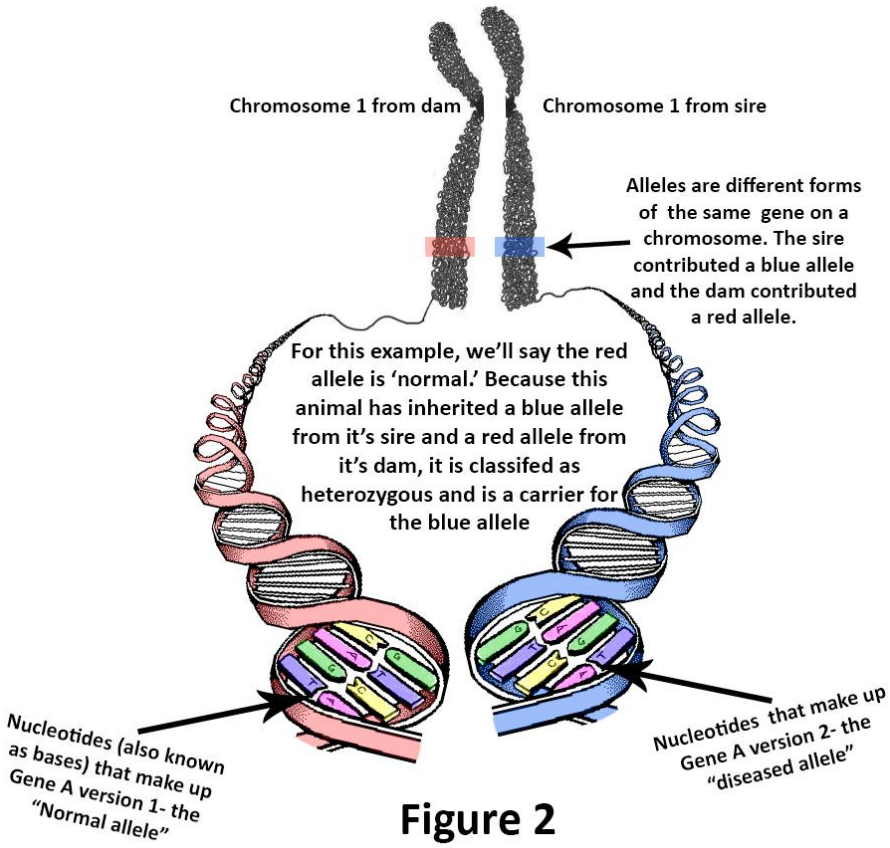


Figure 2

Figure 2: This image shows what happens in an animal produced from a sire and dam with different allele types for one gene. The dam has contributed a normal (red) allele while the male contributed a diseased (blue) allele to the offspring. This results in the offspring being a carrier of the diseased gene.

An animal's genetic disease status is described as Normal, Carrier, or Homozygous for X, where X is the disease name. These are defined below:

Normal= animal has 0 copies of the trait allele

Carrier = animal has 1 copy of the trait allele

Homozygous = animal has 2 copies of the trait allele

A trait can be recessive, dominant, additive, or have interactions with other genes.

A **Recessive** trait means that an animal has to have 2 copies of the trait allele for the animal to be affected with the disease. Those with 1 or 0 copies have the normal phenotype. An example of this is the Complex Vertebral Malformation (CVM) disease allele. Animals with 2 copies of the CVM allele are aborted or born dead while those with 1 or 0 copies are normal.

A **Dominant** trait means that an animal with 1 or 2 copies of the allele will show the trait, while those with 0 copies have the normal phenotype. An example of this is the Polled allele. Animals with 1 or 2 copies of the Polled allele are polled while those with 0 copies of the allele have horns.

An **Additive** trait means each copy of the trait allele increased the trait effect, and animal with 1 allele will have a phenotype that is between what is seen in an animal with 2 or 0 copies of the allele. An example of this is the Silver Dilutor 1 allele. Animals with 0 copies will be the breed's base colour such as Black, animals with 1 copy will be light grey, and animals with 2 copies will be white.

Sometimes an allele has **Incomplete Penetrance.** When this occurs, even if an animal is homozygous for a disease it may not express the phenotype. This is usually because there are multiple genes that influence the trait and one of those other genes masks the effect of the mutation.

Examples of the mating risk of having a genetic disease affected calf born when the dam and sire are normal, carrier, or homozygous for recessive or dominant disease alleles are shown below.

Recessive Disease Mating Risk

Animals with 2 copies of the trait allele have the trait phenotype (affected), those with 1 or 0 copies have the normal phenotype. A common way to write these different allele types is by using a capital letter (i.e. **A**) to designate the normal gene and a lower case letter to designate the affected gene (i.e. **a**). For these examples, we'll call an animal that is homozygous for the desirable trait, **normal**. This animal would have a gene designation as 'AA.' Animals that are **carriers** would get the designation 'Aa,' and we'll call the animals that have 2 copies of the diseased allele **homozygous** because they are homozygous for the diseased allele. These animals would have the designation 'aa.'

1. Mating a **normal** to **normal** results in a 0% chance of having an affected calf born

2. Mating a **normal** to a **carrier** results in a 0% chance of having an affected calf born

3. Mating a **normal** to **homozygous** results in a 0% chance of having an affected calf born

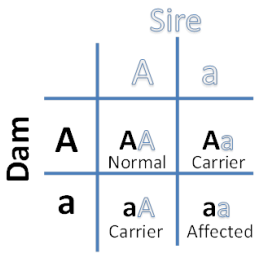
4. Mating a **carrier** to **carrier** results in a 25% chance of having an affected calf, a 50% chance of having a carrier calf, and a 25% chance of having a normal calf born

5. Mating a **carrier** to **homozygous** results in a 50% chance of having a carrier calf and a 50% chance of having an affected calf born

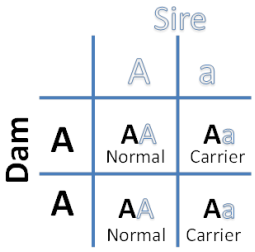
6. Mating a **homozygous** to **homozygous** results in a 100% chance of having an affected calf born

A Punnett Square is a great way to graphically to express these matings. When making up a Punnett's square you make a 3X3 grid. The allele for the sire goes into the top middle and top right of the square, and the dam's allele type goes into the left bottom and left middle square (see below). Once set up, you carry the sire's alleles down and the dam's allele's across giving you the possible allele combinations if you mated those two animals. Punnett's square examples of mating 2 animals that are Normal (AA), Carrier (Aa), or Homozygous(aa) for a **RECESSIVE** trait are below:

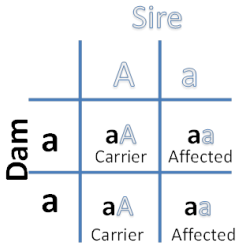
Carrier sire X Carrier dam. How do we know they are both carriers? When looking at the gene designations at the top of the squares, they have one copy of the normal allele (**A**) and one copy of the affected allele (**a**).



Carrier sire (Aa) X Normal dam (AA)



Carrier sire (Aa) X Homozygous dam (aa)



Dominant Disease Mating Risk

Animals with 1 or 2 copies of the trait allele have the phenotype (affected), those with 0 copies have the normal phenotype. This is just like above, but this time if a calf gets ANY copies of the affected allele (a), it will be affected.

1. Mating a **normal** to **normal** results in a 0% chance of having an affected calf born

2. Mating a **normal** to **carrier** results in 50% chance of having a normal calf and a 50% chance of having a affected calf born

3. Mating a **normal** to **homozygous** results in a 100% chance of having a carrier calf born that is affected with the trait

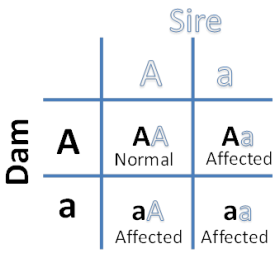
4. Mating a **carrier** to **carrier** results in a 75% chance that the calf born will be affected and a 25% chance that it will be normal

5. Mating a **carrier** to **homozygous** results in a 100% chance of having an affected calf born

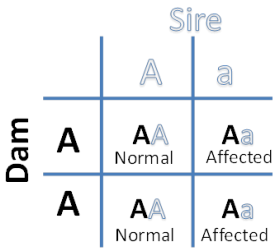
6. Mating a **homozygous** to **homozygous** results in a 100% chance of having an affected homozygous calf born

Punnett Square examples of mating 2 animals that are Normal, Carrier, or Homozygous for a **DOMINANT** trait are below:

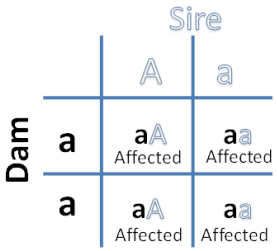
Carrier sire (Aa) X Carrier dam (Aa)



Carrier sire (Aa) X Normal dam (AA)



Carrier sire (Aa) X Homozygous dam (aa)



The pages below list information about the validated trait probes on the IDB chip in the following format.

Trait definition layout:

Full Trait Name

Abbreviations: Abbreviations and alternative names for the trait

Royalty Fee: If this trait is free in Ireland or if a Royalty fee is required

For traits that require a Royalty fee please contact Weatherbys Ireland for cost and reporting

Genetic Mode: If the trait is recessive, dominant, or additive

Trait Type: If the trait is Lethal, Unwanted, Beneficial, Milk, Muscle, or Coat Colour related

Breeds found in: Breed lineages this trait is known to occur in

General: A general description of the trait

Common Ancestor: If carriers of the trait can be traced back to a common ancestor(s)

Clinical: A more clinical description of the trait, geared for veterinary and research

Image: If available an image of an animal with the trait will be provided

OMIA: This is the disease/trait ID on the Online Mendelian Inheritance in Animals website

Gene: The gene symbol and name where the mutation lies

Genetic: Genetic description of the mutation and it affect. If an allele is breed specific it will be noted here

The gene symbol and full name will be provided. The mutation's location and effect is shown as:

Genome: X:g.Y R>A where 'X' is the chromosome, 'g' denotes genome, 'Y 'is the position, 'R' is the reference DNA allele, 'A' is the alternative DNA allele. Position is based on the *Bos taurus* genome assemble (UMD3.1 build)

Gene: c. Z R>A where 'c' denotes gene, 'Z' is the gene position, 'R' is the reference DNA allele, 'A' is the alternative DNA allele

Protein: p.Qaa x Saa where 'p' denotes protein, 'Qaa' is the reference amino acid, 'x' is the codon position, 'Saa' is the alternative amino acid

Note: ones like this "p.Glu275ArgfsX14" read that at the 275th amino acid Glutamic acid (Glu) is replaced by Arginine (Arg). The "fs" notes a frame shift. The "X14" notes that a termination codon is introduced 14 codons after the mutation

dbSNP ID: rs# or ss#, Scientific reference to the mutation

Flanking Seq: Flanking DNA sequence around the alleles in brackets and bold. The reference allele is listed first then the alternative allele

References: Scientific publications that the information about the trait and mutation came from

NOTE: For mutations/traits covered by Royalty fees, Patents, or Intellectual Property rights the **Genetic**, **Flanking Sequence**, and **Reference** information might not be provided or be minimal

Traits are grouped by the following:

1) Lethal: Alleles that result in mortality before the animal can provide an economic return

2) Unwanted: Alleles that have a negative economic effect, but are non-lethal

3) Beneficial: Alleles that are economically beneficial

4) Meat: Alleles that affect meat or muscle quality or quantity

5) Milk: Alleles that affect the quantity of milk produced or the milk components

6) Colour: Alleles that affect an animal's coat colour

DNA Allele and Amino Acid abbreviations

DNA	One letter code
Alanine	A
Cytosine	C
Guanine	G
Thymine	T
Insertion	" -/" or ins
Deletion	"/-" or del
Duplication	dup

Amino acid	Three letter code
Alanine	Ala
Arginine	Arg
Asparagine	Asn
Aspartic acid	Asp
Asparagine	Asx
Cysteine	Cys
Glutamic acid	Glu
Glutamine	Gln
Glutamine	Glx
Glycine	Gly
Histidine	His
Isoleucine	Ile
Leucine	Leu
Lysine	Lys
Methionine	Met
Phenylalanine	Phe
Proline	Pro
Serine	Ser
Threonine	Thr
Tryptophan	Trp
Tyrosine	Tyr
Valine	Val
STOP	X

List of IDB reported diseases and traits

LETHAL

1. Alpha Mannosidosis
2. Arachnomelia Syndrome
3. Beta Mannosidosis
4. Brachyspina
5. Bulldog Dwarfism
6. Cardiomyopathy and Woolly Haircoat Syndrome
7. Citrullinaemia
8. Congenital Muscular Dystonia 1
9. Congenital Muscular Dystonia 2
10. Complex Vertebral Malformation
11. Deficiency of Uridine Monophosphate Synthase
12. Holstein Haplotype 1
13. Holstein Haplotype 3
14. Holstein Haplotype 4
15. Idiopathic Epilepsy
16. Jersey Haplotype 1
17. Maple Syrup Urine
18. Montbeliarde Haplotype 2
19. Neuropathic Hydrocephalus
20. Osteopetrosis
21. Paunch Calf Syndrome
22. Pulmonary Hypoplasia with Anasarca 1
23. Spinal Muscular Atrophy
24. Tibial Hemimelia

UNWANTED

1. Axonopathy
2. Bovine Leukocyte Adhesion Deficiency
3. Bovine Progressive Degenerative Myeloencephalopathy (Weaver)
4. Chediak Higashi Syndrome
5. Congenital Myoclonus
6. Crooked Tail Syndrome
7. Developmental Duplication
8. Dystrophic Epidermolysis Bullosa
9. Factor XI Deficiency
10. Hypotrichosis
11. Mulefoot
12. Neuronal Ceroid Lipofuscinosis
13. Protoporphyria
14. Pseudomyotonia
15. RNF11 Growth Retardation
16. STAT1
17. STAT3
18. STAT5A
19. Thrombopathia

BENEFICIAL

1. Infectious Bovine Keratoconjunctivitis (Pinkeye)
2. Poll

MEAT

1. Calpain1
2. Calpastatin
3. Myostatin

MILK

1. ABCG2
2. AcylCoA:Diacylglycerol Acyltransferase
3. Growth Hormone
4. Growth Hormone Receptor
5. Casein Beta
6. Casein Kappa
7. Lactoglobulin Beta

COLOUR

1. Dun
2. MC1R
3. PMEL17

LETHAL

Alpha Mannosidosis

Abbreviations: AM_662, AM _961

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Lethal

Breeds found in: Angus, Galloway, Murray Grey

General: Affected calves are either aborted, born dead, die soon after birth, or die within the first year. Those born alive can show signs of ataxia, head tremor, aggression, and paralysis before death.

Common Ancestor: None identified

Clinical: This lysosomal storage disease is caused by a build-up of mannose-rich compounds caused by deficiency of the alpha-mannosidase enzyme.

OMIA: 000625-9913

Gene: MAN2B1 (Mannosidase Alpha Class 2b Member 1)

Genetic: There are 2 mutations in MAN2B1 that cause this disease:

AM_662 (Found in Galloway lineages)

Genetic: 7:g.13956640G>A, c.662G>A, p.Arg221His

Flanking Sequence:

CCGGTCCCTTATGCATCCTGCCCTCTCTTGTTCTCCCATCCCACTCGTCATCCCTCCCCATCTCCAGATGGGTTTTGA
CGGCTTCTTCTTTGGAC**[G/A]**CCTGGATTATCAAGACAAGAAGGTGCGGAAAAAGACGCTGCAGATGGAGCAGG
TGTGGCGGGCCAGCACCAGCCTGAAACCTCCCACTGCCGACC

AM_961 (Found in Angus and Murray Grey lineages)

Genetic: 7:g.13957949, c.961T>C, p.Phe321Leu

Flanking Sequence:

ACAGGGGTGGGCCAGGACACCCTAGCCTTAGGATACCCCCATCTTGCCTGCAGGGTAAGCTCTACCGCACCAAAC
ACACTGTGATGACCATGGGCTCAGAC**[T/C]**TCCAGTACGAGAATGCCAACACGTGGTTCAAAAATCTTGACAAGCT
CATCCAGTTGGTCAATGCCCAGGTGAGTGTGCCTGCCCCGTGGGCACTT

TOLLERSRUD, O. K., BERG, T., HEALY, P., EVJEN, G., RAMACHANDRAN, U. & NILSSEN, O. 1997. Purification of bovine lysosomal alpha-mannosidase, characterization of its gene and determination of two mutations that cause alpha-mannosidosis. *Eur J Biochem,* 246**,** 410-9.

Arachnomelia Syndrome

Abbreviations: SAA_SUOX **Genetic Mode: Recessive**

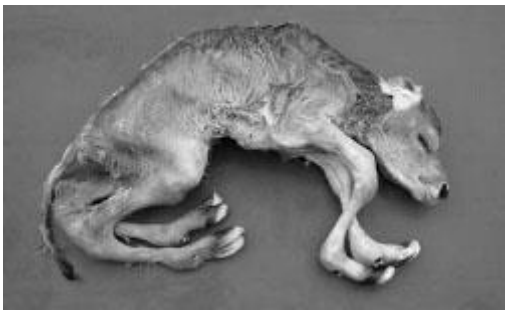
Royalty Fee: No **Trait Type: Lethal**

Breeds found in: Brown Swiss

General: Affected calves are usually stillborn with a spidery appearance and an abnormally shaped skull. Leg bones can be thin, fragile, and easily broken.

Common Ancestor: Liason, Beautician, Leon, Amaranto, Prealba Pete Rose

Clinical: Primary pathological changes are skeletal malformations of the skull, legs and spinal column. Facial deformation leads to brachygnathia inferior and concave rounding of the maxilla forming a dent ('pointer-head'). The legs show abnormally thin diaphyses of the long bones and stiffened, hyperextended fetlocks ('spider-legs', dolichostenomelia), leading to frequent fractures of the metacarpus and metatarsus in the course of forced birth assistance. Vertebral formation failure results in kyphosis and scoliosis. In some cases, there is a cardiac element to the deformities. The mutation is believed to have appeared de novo in the bull Liason who was born in 1957.



Arachnomelia calf from Gentile & Testoni 2006, Slov Vet Res 43:17-29

OMIA: 000059-9913

Gene: SUOX (Sulfite oxidase)

Genetic: 5:g.57641332-57641333insC, c.363–364insG, p.Ala124GlyfsX42

OMIA: 000059-9913

Flanking Sequence:

TACTGAGCTAGTATCTCTCGCACGTGGGGCTGGTTGTGAACAGCATAGAGGGCCCAGAAGGGCTCTAAAGGACC
CCCGGCTGCTAGCATCAGCTTTGATG**[-C]**CCCCCCCTGGGTGTATGTCCACAAATTCTGTGATATCAAAAACCTCAC
AGCCCAAAGTTACCCAGACCCCAGTCTCAGGGCTGCTGTGGGATTTCACTTC

DROGEMULLER, C., TETENS, J., SIGURDSSON, S., GENTILE, A., TESTONI, S., LINDBLAD-TOH, K., LEEB, T., Identification of the bovine Arachnomelia mutation by massively parallel sequencing implicates sulfite oxidase (SUOX) in bone development. *PLoS Genet* 2010, 6(8).

Beta Mannosidosis

Abbreviations: BM

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Lethal

Breeds found in: Salers

General: Affected calves have symptoms of hypothyroidism (coarse, dry hair, cold intolerance, fatigue, weakness, etc.), are unable to rise with intention tremors, hidebound skin, slightly domed skull, slight underbite or overbite, and narrow eye slits. Calves born with this disorder do not get up after birth and soon die.

Common Ancestor: None identified

Clinical: Post-mortem calves usually have variable opening in a portion of the brain, observable paleness and smaller than normal white matter of the cerebrum and cerebellum, and mild to severe enlargement of the kidneys. The thyroid in affected calves show marked extensive vacuolation, with an associated reduction in the serum concentrations of thyroxine and tri-iodothyronine.

OMIA: 000626-9913

Gene: MANBA (Mannosidase Beta A)

Genetic: 6:g.2354228G>A, c.2574G>A, p.TRP858X

Flanking Sequence:

CCATCCCCATGGAAAAGAAATGCAAAAAAGCAAAATGGCTGTCTGAGGAGGACTTACAAATAGCTGTGAAAAGAAG
AGAAGTGAAAAGCAAAGGAGAAAA**[G/A]**GAAAGATATAAGCATCTGAATACAGAGTTCCAAAGAATAGCAAGGAG
AGATAAGAAAGCCTTCCTCAGCAATCGATGCAAAGAAATAAAGGAAAACAACA

LEIPPRANDT, J. R., CHEN, H., HORVATH, J. E., QIAO, X. T., JONES, M. Z. & FRIDERICI, K. H. 1999. Identification of a bovine beta-mannosidosis mutation and detection of two beta-mannosidase pseudogenes. *Mamm Genome,* 10**,** 1137-41.

LOVELL, K., JONES, M., PATTERSON, J., ABBITT, B. & CASTENSON, P. 1991. Thyroid structure and function in bovine β-mannosidosis. *Journal of inherited metabolic disease,* 14**,** 228-230.

Brachyspina

Abbreviations: BY

Genetic Mode: Recessive

Royalty Fee: Yes

Trait Type: Lethal

Breeds found in: Friesian, Holstein

General: Affected calves are either aborted in the first 40 days of gestation or stillborn. Stillborn calves are born after a prolonged gestation with reduced body weight, a short neck and body, a hump between the shoulder blades and a deformed lower jaw.

Common Ancestor: Sweet Haven Tradition, Bis-May Tradition Cleitus, Rothrock Tradition Leadman

Clinical: Stillborn calves are characterized by a severely reduced body weight, shortening of the spine, long and slender limbs, malformed internal organs including, liver, kidneys, reproductive organs, and heart. Intervertebral disks can have incomplete development or be fused. Limbs appear disproportionately long in relation to the body.

Brachyspina affected calf from Agerholm et al., 2006

OMIA: 000151-9913

Gene: FANCI (Fanconi anemia complementation group I)

Genetic: 21:g.21184870_21188198del, c.526-64495_526-67824del , p.Val876Leufs26X

Flanking Sequence:

TGTCACATACATAAATGTAAAATGGTGCAGCCACTTTGGAAAATAATTTGTCAGTTTCTTAAAAAGTTAAGCACACACC
TATCTTACGGTACACCCATTC**[CACTCTTAGGTATTTAC…3,329bp….AAATTTGCAGGAAATGGT/-]**CACCTTTCTAT
CCGTGTCCTCCATCTGTTCAGTTCTTCTCCCCCAGTAGCTAAATATCTTTTAGTGTCTTGTGTAAAGAATTCTTTTATTCC
TGTACAGC

AGERHOLM, J. S., MCEVOY, F. & ARNBJERG, J. 2006. Brachyspina syndrome in a Holstein calf. *J Vet Diagn Invest,* 18**,** 418-22.

CHARLIER, C., AGERHOLM, J. S., COPPIETERS, W., KARLSKOV-MORTENSEN, P., LI, W., DE JONG, G., FASQUELLE, C., KARIM, L., CIRERA, S. & CAMBISANO, N. 2012. A deletion in the bovine FANCI gene compromises fertility by causing fetal death and brachyspina. *PLoS one,* 7**,** e43085.

Bulldog Dwarfism

Abbreviations: BD1, BD2, Dexter Chondrodysplasia

Genetic Mode: Recessive

Trait Type: Lethal

Royalty Fee: No

Breeds found in: Dexter

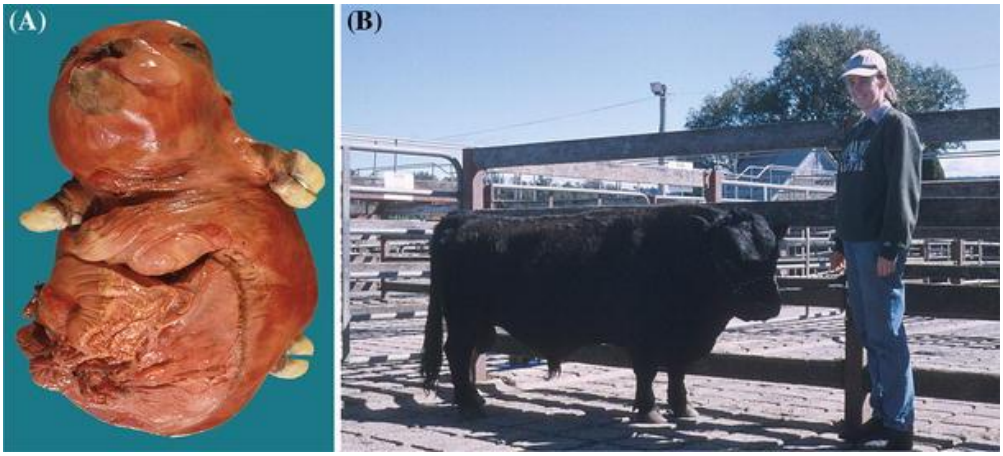
General: This disease is caused by one of two mutations (BD1 and BD2) in the ACAN gene. Affected animals display extreme dwarfism, die around the seventh month of gestation and are aborted. Heterozygous animals are born alive and live but have a mild form of dwarfism.

Being homozygous for either mutation or heterozygous for both will cause bulldog dwarfism.

Common Ancestor: None identified

Clinical: Affected foetuses display extreme dwarfism, a short vertebral column, abnormal cartilage development, marked micromelia, large abdominal hernia, large head, retruded muzzle, and cleft palate. The mutations cause aggrecan protein to be absent from the cartilage extra cellular matrix causing it to be structurally compromised. Thus the cartilage fails to expand which compromises the growth of long bones.

The BD1 allele results in a premature stop codon in exon 11. The BD2 allele introduces a start codon 199 base pairs upstream and in a different frame, the resulting protein does not resemble the normal aggrecan protein.



A) BD affected embryo, B) Heterozygous animal exhibiting dwarfism from Cavangh et al., 2007

OMIA: 001271-9913

Gene: ACAN (Aggrecan)

Genetic: Two mutations in ACAN that being homozygous for either mutation or heterozygous for both will cause the bulldog dwarfism.

BD1

Genetic: 21:g.20844570insGGCA, c.2266insGGCA

Flanking Sequence:

ATCGGGGAGGAGACGACTGCAATCCCAGGCTTCACCGTTGAGCCAGAAAACAAGACGGAATGGGAACTTGCCTACA
CCCCAGCGGGCACTTTGCCACTAC**[-/GGCA]**CAGGTCCGTCCGGGCTCTCCTGCATGTCCTGCTGCCTCCCTGGGCCAG
GGTGTGGCCTGGAAGGGGGGAGGAGGAAGTGTTCTCTCCCTGGGACCCGTGA

BD2

Genetic: 21:g.20800319C>T, c.-198C>T

Flanking Sequence:

CTCAGCACCCTCGCCGGCCGGCATCTGACACGGGTGTCAGGGGGCTCCGGGCGCCTTTCAGCATCCCTTCCCCAGGCC
GGCCGGGACTCCGCTACCCAGA**[C/T]**GCCGCCACTGCGGCCACCGCCCGAGGGGACCTGCGGACAGGACGCCGGCA
GGAGGAGGGGTGCGCAGCGCCCGCCCAGAGCGTCTCCCCCGCGGCGCGGC

CAVANAGH, J. A., TAMMEN, I., WINDSOR, P. A., BATEMAN, J. F., SAVARIRAYAN, R., NICHOLAS, F. W. & RAADSMA, H. W. 2007. Bulldog dwarfism in Dexter cattle is caused by mutations in ACAN. *Mamm Genome,* 18, 808-14.

Cardiomyopathy and Woolly Haircoat Syndrome

Abbreviations: CWH **Genetic Mode: Recessive**

Royalty Fee: No **Trait Type: Lethal**

Breeds found in: Hereford

General: Animals have heart problems and a woolly hair coat. Some have protruding eyeballs and a prominent forehead. Death usually occurs within the first 12 weeks of life.

Common Ancestor: None identified

Clinical: Affected calves have signs so cardiac dysfunction, including arrhythmias. A number will develop a severe, ulcerative ocular keratitis. A spectrum of myocardial changes are observed in both ventricles, including multifocal to locally extensive myolysis or myocyte necrosis, and replacement fibrosis, with calcification in some cases; subepicardial fibrosis of the right ventricular free wall is often the predominant change.

CWH affected calf (left) versus unaffected calf (right) from Simpson et. al., 2009

OMIA: 000161-9913

Gene: PPP1R13L (Protein Phosphatase 1 Regulatory Subunit 13 Like)

Genetic: 18:g.53440861-53440867dupACAGGCG, c.956_962dupACAGGCG, p.Gly335GlufsX36

Flanking Sequence:

TTTCTATCTTCCTTCCTTCCCTCTTTCTCCCCCAGGACAACTTCACCAGCGCCACTCTGCCCCGCAATTACAAGGTCTCCC
CTCTGGCCAACGACAGGCG**[-/ACAGGCG]**TTCTGATGTGGGCAGCTACCGCCGATCACTGGGCTCCACGGGGC
CGTCAGGCACTTTGCCCCGAAGCTGGCAGCCTGTCAGTCGCATCCCCATGCCTCCT

SIMPSON, M. A., COOK, R. W., SOLANKI, P., PATTON, M. A., DENNIS, J. A. & CROSBY, A. H. 2009. A mutation in NFkappaB interacting protein 1 causes cardiomyopathy and woolly haircoat syndrome of Poll Hereford cattle. *Anim Genet,* 40**,** 42-6.

Citrullinaemia

Abbreviations: CT

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Lethal

Breeds found in: Friesian, Holstein

General: Affected calves are born normal and become depressed within 24 hours. In 3-5 days they develop tongue protrusion, unsteady gait, wander aimlessly, froth at the mouth, will press their head against something solid, develop convulsions, and die.

Common Ancestor: None identified

Clinical: Upon dissection they will have a histological lesion in the brain. The clinical signs are the same as ammonia poisoning as the defective ASS1 gene causes a fault in the urea cycle which leads to a build-up of ammonia in the body.

OMIA: 000194-9913

Gene: ASS1 (Argininosuccinate Synthase 1)

Genetic: 11:g.100802781C>T, c.256C>T, p.A86X

Flanking Sequence:

ATGGGCTGCTCTCCCACAGGTGTTCATTGAGGACATCAGCAAGGAGTTTGTGGAGGAGTTCATCTGGCCGGCCATCC
AGTCCAGCGCACTGTACGAGGAC**[C/T]**GATACCTCCTGGGCACCTCTCTCGCCAGGCCCTGCATCGCCCGCAAGCAGG
TGGAGATCGCCCAGCGAGAAGGAGCCAAGTATGTGTCTCACGG

DENNIS, J. A., HEALY, P. J., BEAUDET, A. L. & O'BRIEN, W. E. 1989. Molecular definition of bovine argininosuccinate synthetase deficiency. *Proceedings of the National Academy of Sciences of the United States of America,* 86**,** 7947-51.

Congenital Muscular Dystonia 1

Abbreviations: CMD1 **Genetic Mode: Recessive**

Royalty Fee: No **Trait Type: Lethal**

Breeds found in: Belgian Blue, Dutch Improved Red and White

General: Affected calves have episodes of generalized muscle contractures, impaired swallowing, and falling. CMD1 calves usually die within a few weeks as a result of respiratory complications.

Common Ancestor: None identified

Clinical: Animals have muscle myotonia which results in an inability to flex limbs and injurious falling. They also experience fatigue upon stimulation. The mutation causes a disorder in muscle function due to a defect in the Ca^2 pump**.**

OMIA: 001450-9913

Gene: ATP2A1 (ATPase, Ca++ Transporting, Cardiac Muscle, Fast Twitch 1)

Genetic: 25:g.26191380C>T, c.1675C>T, p.Arg559Cys

Flanking Sequence:

GCGAGTGGGCACCACCCGGGTGCCCATGACAGGGCCGGTGAAGGAGAAGATTCTGTCGGTGATCAAAGAGTGGGG
TACTGGCCGGGACACCCTG**[C/T]**GCTGCCTGGCGCTGGCCACTCGGGACACCCCCCCCAAGCGAGAGGAGATGGTCC
TGGATGACTCTACCAAGTTCATGGAGTACGAG

CHARLIER, C., COPPIETERS, W., ROLLIN, F., DESMECHT, D., AGERHOLM, J. S., CAMBISANO, N., CARTA, E., DARDANO, S., DIVE, M., FASQUELLE, C., FRENNET, J. C., HANSET, R., HUBIN, X., JORGENSEN, C., KARIM, L., KENT, M., HARVEY, K., PEARCE, B. R., SIMON, P., TAMA, N., NIE, H., VANDEPUTTE, S., LIEN, S., LONGERI, M., FREDHOLM, M., HARVEY, R. J. & GEORGES, M. 2008. Highly effective SNP-based association mapping and management of recessive defects in livestock. *Nature Genetics,* 40**,** 449-54.

GRUNBERG, W., SACCHETTO, R., WIJNBERG, I., NEIJENHUIS, K., MASCARELLO, F., DAMIANI, E. & DROGEMULLER, C. 2010. Pseudomyotonia, a muscle function disorder associated with an inherited ATP2A1 (SERCA1) defect in a Dutch Improved Red and White cross-breed calf. *Neuromuscul Disord,* 20**,** 467-70.

Congenital Muscular Dystonia 2

Abbreviations: CMD2, Startle Disease

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Lethal

Breeds found in: Belgian Blue

General: Affected calves show episodes of generalized muscle contractures and sever muscle twitching. Affected calves typically die within a few hours to days after birth.

Common Ancestor: None identified

Clinical: Affected calves present with lateral recumbency. They have a low head carriage when made to walk. Stimulation often triggers transient muscle spasms which regress when left alone. Calves are typically alert and able to suckle between spasms.

CMD2 affected calf from Harvey et al., 2008.

OMIA: 001451-9913

Gene: SLC6A5 (Solute Carrier Family 6 (Neurotransmitter Transporter), Member 5)

Genetic: 29:g.24610495T>C, c.809T>C, p.Leu270Pro

Flanking Sequence:

ATGCTGGCTCTGGCAGGGTTGCCCATCTTCTTCCTAGAGGTGTCCCTGGGCCAGTTTGCCAGCCAGGGGCCGGTGTCT
GTGTGGAAGGCCATCCCAGCCC**[T/C]**GCAAGGTGAGTGCTTCCTGCTTCCCAGCTGCCTCAGCCCTTCCCTGCCCTCTC
TGGCACCAAAGGGCCCCAGGGAGTGAGACCTGCTTCTGTGATTGGGA

CHARLIER, C., COPPIETERS, W., ROLLIN, F., DESMECHT, D., AGERHOLM, J. S., CAMBISANO, N., CARTA, E., DARDANO, S., DIVE, M., FASQUELLE, C., FRENNET, J. C., HANSET, R., HUBIN, X., JORGENSEN, C., KARIM, L., KENT, M., HARVEY, K., PEARCE, B. R., SIMON, P., TAMA, N., NIE, H., VANDEPUTTE, S., LIEN, S., LONGERI, M., FREDHOLM, M., HARVEY, R. J. & GEORGES, M. 2008. Highly effective SNP-based association mapping and management of recessive defects in livestock. *Nature Genetics,* 40**,** 449-54.

HARVEY, R. J., TOPF, M., HARVEY, K. & REES, M. I. 2008. The genetics of hyperekplexia: more than startle! *Trends in genetics,* 24**,** 439-447.

Complex Vertebral Malformation

Abbreviations: CVM

Genetic Mode: Recessive

Royalty Fee: Yes

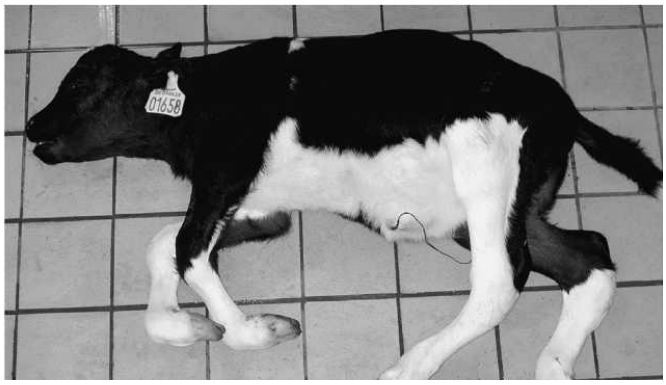
Trait Type: Lethal

Breeds found in: Friesian, Holstein

General: Affected calves are usually aborted during gestation; some are born alive but die soon after. Animals have a shortened neck and curved spine, they can have abnormal ribs, contracted joints, and contracted and rotated fetlocks.

Common Ancestor: Carlin-M Ivanhoe Bell and Pennstate Ivanhoe

Clinical: CVM diagnosis is often difficult due to significant clinical heterogeneity in affected calves. Affected animals are characterized by anomalies of the spinal column and limbs, a shortening of the cervical and thoracic parts of the vertebral column and symmetrical arthrogryphosis in the front and occasionally in the hind legs. Animals can have axial skeletal deformities, misshaped vertebrae, scoliosis, joint contractures of the lower limb joints, and cardiac anomalies. Pedigree plus necropsy can provide a presumptive diagnosis with DNA testing providing the definitive diagnosis.



CVM affected calf from Thomsen et al., 2006

OMIA: 001340-9913

Gene: SLC35A3 [SOLUTE CARRIER FAMILY 35 (UDP-N-ACETYLGLUCOSAMINE TRANSPORTER), MEMBER 3]

Genetic: 3:g.43412427, c.559G>T, p.Val180Phe, rs438228855

Flanking Sequence:

TAAACTTGTGTTGTTTCTTTTTGTTCAGTGGCCCTCAGATTCTCAAGAGCTTAATTCTAAGGAACTTTCAGCTGGCTCAC
AATTTGTAGGTCTCATGGCA**[G/T]**TTCTCACAGCATGTTTTTCCAGTGGCTTTGCTGGGGTTTACTTTGAGAAAATCTT
AAAAGAAACCAAACAATCAGTGTGGATAAGAAACATTCAACTTGG

THOMSEN, B., HORN, P., PANITZ, F., BENDIXEN, E., PETERSEN, A. H., HOLM, L. E., NIELSEN, V. H., AGERHOLM, J. S., ARNBJERG, J. & BENDIXEN, C. 2006. A missense mutation in the bovine SLC35A3 gene, encoding a UDP-N-acetylglucosamine transporter, causes complex vertebral malformation. *Genome Res,* 16**,** 97-105.

Deficiency of Uridine Monophosphate Synthase

Abbreviations: DUMPS **Genetic Mode: Recessive**

Royalty Fee: No **Trait Type: Lethal**

Breeds found in: Friesian, Holstein, Wagyu

General: Affected calves are aborted around day 40 of pregnancy. The affected embryos often are resorbed during the first two-month of gestation, leading to more services per calving and longer than normal calving intervals.

Common Ancestor: None identified

Clinical: The DUMPS mutation is lethal as it results in pyrimidine deficiencies. Heterozygous animals appear phenotypically normal they do have reduced Uridine Monophosphate Synthetase levels that cause an increase of orotic acid in the milk and urine.

OMIA: 000262-9913

Gene: UMPS (Uridine Monophosphate Synthetase)

Genetic: 1:g.69756880C>T, c.1213C>T, p.Arg405X

Flanking Sequence:

TGTGGTTAACTGCTGTCTTGTCATCTGTTGATTACATTCCATTCAGGTGCAAATGGCTGAAGAACATTCTGAATTTGTG
ATTGGTTTTATTTCTGGCTCC**[C/T]**GAGTAAGCATGAAACCAGAATTTCTTCACTTGACTCCAGGAGTTCAGTTAGAAG
CAGGAGGTAAGCCTATTGATTGGTAATGATTCCTCTAAAATGCTGC

KUMAR, V., SINGH, R. K. & SHARMA, A. 2010. Deficiency of Uridine Monophosphate Synthase: A Recessive Disorder in Holstein Friesian Cattle. *Veterinary World,* 3**,** 523-525.

SCHWENGER, B., SCHOBER, S. & SIMON, D. 1993. DUMPS cattle carry a point mutation in the uridine monophosphate synthase gene. *Genomics,* 16**,** 241-4.

SCHWENGER, B., TAMMEN, I. & AURICH, C. 1994. Detection of the homozygous recessive genotype for deficiency of uridine monophosphate synthase by DNA typing among bovine embryos produced in vitro. *J Reprod Fertil,* 100**,** 511-4.

Holstein Haplotype 1

Abbreviations: HH1

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Lethal

Breeds found in: Friesian, Holstein

General: Affected calves are aborted after the first trimester.

Common Ancestor: Pawnee Farm Arlinda Chief

Clinical: APAF1 is necessary for normal neural tube development. In mice, knockout of the APAF1 gene leads to embryonic lethality, and APAF1 mutations result in malformed embryos.

OMIA: 000001-9913

Gene: APAF1 (Apoptotic Peptidase Activating Factor 1)

Genetic: 5:g.6315040C>T, c.1741C>T, p.Gln579X, rs448942533

Flanking Sequence:

GGAGTTTTTATCTTTAAATGGACATCTTCTTGGACGACAGCCATTTCCTAATATTGTGCAACTGGGCCTCTGTGAACTG
GAAACTTCAGAGGTTTATCGG**[C/T]**AAGCTAAGCTGCAGGCCAAGCAGGAGGTCGATAACGGAATGCTTTACCTGGA
GTGGGTGTAAGTAGGTTAGGAGAGAAACCAGAGGGAGCAGAGCGCTGA

ADAMS, H. A., SONSTEGARD, T., VANRADEN, P. M., NULL, D. J., VAN TASSELL, C. P. & LEWIN, H. 2012. Identification of a nonsense mutation in APAF1 that is causal for a decrease in reproductive efficiency in dairy cattle. *Plant Anim. Genome XX Conf.* San Diego, CA: Abstr. P0555.

ADAMS, H. A., SONSTEGARD, T. S., VANRADEN, P. M., NULL, D. J., VAN TASSELL, C. P., LARKIN, D. M. & LEWIN, H. A. 2016. Identification of a nonsense mutation in APAF1 that is likely causal for a decrease in reproductive efficiency in Holstein dairy cattle. *Journal of Dairy Science,* 99**,** 6693-701.

FRITZ, S., CAPITAN, A., DJARI, A., RODRIGUEZ, S. C., BARBAT, A., BAUR, A., GROHS, C., WEISS, B., BOUSSAHA, M., ESQUERRE, D., KLOPP, C., ROCHA, D. & BOICHARD, D. 2013. Detection of Haplotypes Associated with Prenatal Death in Dairy Cattle and Identification of Deleterious Mutations in GART, SHBG and SLC37A2. *PLoS one,* 8**,** e65550.

Holstein Haplotype 3

Abbreviations: HH3

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Lethal

Breeds found in: Friesian, Holstein

General: Affected calves are aborted before day 60 of gestation.

Common Ancestor: Glendell Arlinda Chief, Gray View Skyliner, Oman

Clinical: SMC2 is required for the structural maintenance of chromosomes and DNA repair in mammals and for the formation of condensing complexes to convert interphase chromatin into mitotic-like condensed chromosomes. It's hypothesized that the mutation causes reduced ability to hydrolyse ATP which results in compromised condensin activity.

OMIA: 001824-9913

Gene: SMC2 (Structural Maintenance of Chromosomes 2)

Genetic: 8:g.95410507, c.3404T>C, p.Phe1135Ser, rs456206907

Flanking Sequence:

CTCCTTTTCAAACCTGCCCCAATCTACATCCTGGATGAGGTCGATGCAGCCCTGGATCTTTCTCATACTCAGAATATTG
GACATATGCTACGTACTCATT**[T/C]**CACACATTCTCAGGTAAGAACCAAAAAGAGCCTCAGAATAGTTCTAGGATTTGT
TTTTCTAAAACTATTCTTTAGTAATGGTCAGTATATATAAGGAATT

MCCLURE, M. C., BICKHART, D., NULL, D., VANRADEN, P., XU, L., WIGGANS, G., LIU, G., SCHROEDER, S., GLASSCOCK, J., ARMSTRONG, J., COLE, J. B., VAN TASSELL, C. P. & SONSTEGARD, T. S. 2014. Bovine Exome Sequence Analysis and Targeted SNP Genotyping of Recessive Fertility Defects BH1, HH2, and HH3 Reveal a Putative Causative Mutation in *SMC2* for HH3. *PLoS one,* 9**,** e92769.

Holstein Haplotype 4

Abbreviations: HH4

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Lethal

Breeds found in: Friesian, Holstein

General: Affected calves are aborted very early in pregnancy, often in the first month.

Common Ancestor: Besne Buck

Clinical: GART is required for de novo biosynthesis of purines, which are key components of DNA, RNA, and ATP. Therefore the loss of GART function is predicted to cause the death of the embryo soon after fertilization.

OMIA: 001826-9913

Gene: GART (Phosphoribosylglycinamide Formyltransferase)

Genetic: 1:g.1277227, c.869A>C, p.Asn290Thr

Flanking Sequence:

TACAATGTCTGCATTAACGATTTTTTTTTCTTTTTTAATGAAGGTGTCCTCTATGCTGGTATAATGCTGACCAAGAACGG
CCCCAAAGTTCTGGAATTTA**[A/C]**TTGCCGTTTCGGTGATCCAGAGTGCCAAGTGAGTAAAAAAAGATGCGTGCTATT
TTAATCTTAGGATTTTTCAGCCTTGAAATAATTATTACCTTTGAGA

FRITZ, S., CAPITAN, A., DJARI, A., RODRIGUEZ, S. C., BARBAT, A., BAUR, A., GROHS, C., WEISS, B., BOUSSAHA, M., ESQUERRE, D., KLOPP, C., ROCHA, D. & BOICHARD, D. 2013. Detection of Haplotypes Associated with Prenatal Death in Dairy Cattle and Identification of Deleterious Mutations in GART, SHBG and SLC37A2. *PLoS one,* 8**,** e65550.

Idiopathic Epilepsy

Abbreviations: IE

Genetic Mode: Recessive

Royalty Fee: Yes

Trait Type: Lethal

Breeds found in: Hereford

General: Affected calves are born normal and have no outward appearance of the disorder until they start having seizures. The initial seizure can occur from birth up to several months of age. When seizing the animal will lay on its side with legs straight out, episodes may last from several minutes to over an hour.

Common Ancestor: None identified

Clinical: This disease causes a generalized seizure disorder and Parkinson's like locking up syndrome. Environmental stresses such as temperature or increased physical handling can bring out the seizures. During seizures manual flexing of the limbs is possible, but upon release they return to the extended position. Animals will not have anatomic abnormalities or histologic lesions upon post mortem examination.

Idiopathic Epilepsy affected cows appear normal unless having a seizure from Kaiser, 2010

OMIA: 000344-9913

Gene: Confidential genomic defect

Genetic: Confidential genomic defect

Flanking Sequence: Confidential genomic defect

JOHNANTHAN BEEVER, UNIVERSITY OF ILLINOIS, 2012. PERSONAL COMMUNCIATION. CONFIDENTIAL GENOMIC DEFECT.

KAISER, L. 2010. *Dead Cows Don't Lie!! Moo News Tells you Why!* [Online]. Kaisercattle.com. Available: http://kaisercattle.com/pdf/MCA%20Defects%20combined.pdf [Accessed 28/08/2015].

Jersey Haplotype 1

Abbreviations: JH1

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Lethal

Breeds found in: Jersey

General: Calves homozygous for the mutation are aborted before day 60.

Common Ancestor: Observer Chocolate Soldier

Clinical: CWC15 is expressed during early embryo development and is an essential gene for cell function.

OMIA: 001697-9913

Gene: CWC15 (Spliceosome-Associated Protein CWC15 Homolog)

Genetic: 15:g.15707169C>T, c.163C>T, p.Arg55X

Flanking Sequence:

AATTGTCTTCCATTACTACAGCTGTGTGTTTTTTAGAAGTGACTTTGCCTTGTCTTGTTTCTACTTTAGACAGACCACTCA
GGATGCCCCTGAAGAGGTT**[C/T]**GAAACCGTGACTTCAGGAGAGAGTTGGAGGAGAGAGAGAGAGCTGCTGCAAG
AGAAAAAAACAGAGATCGGCCAACCCGAGGTACCAATACTATCTTAGA

SONSTEGARD, T. S., COLE, J. B., VANRADEN, P. M., VAN TASSELL, C. P., NULL, D. J., SCHROEDER, S. G., BICKHART, D. & MCCLURE, M. C. 2013. Identification of a nonsense mutation in CWC15 associated with decreased reproductive efficiency in Jersey cattle. *PLoS One,* 8**,** e54872.

Maple Syrup Urine

Abbreviations: MSU_HER, MSU_SH

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Lethal

Breeds found in: Hereford, Shorthorn

General: Some affected calves are stillborn, those born alive look normal but exhibit neurological symptoms within 24 hours. Their condition will rapidly deteriorate with ataxia, an inability to walk, and death within 96 hours after birth. The most telling symptom and how the disorder got its name is that the animals will have sweet-smelling urine.

Common Ancestor: None identified

Clinical: The disease is caused by a deficiency of activity of the mitochondrial BCKDHA enzyme. This deficiency causes neurological disease due to elevated concentrations of branched chain α-keto acids and their precursors: valine, leucine and isoleucine.

OMIA: 000627-9913

Gene: BCKDHA (Branched Chain Keto Acid Dehydrogenase E1, Alpha Polypeptide)

MSU_HER:

Genetic: 18:g.50828853C>T, c.148C>T, p.Gln50X

Flanking Sequence:

CTGCATCACCAGCAATGCTGCCTGTCAGCACAGGGAACCTCTGCTGCTCCTGACCTGGGTGTTCCCCTCCACCCTCCCT
CCCCAGCACCCCCACAGGTGG**[C/T]**AGCAACAGCAGCACTTCTCGTCCCTGGATGACAAGCCGCAGTTCCCAGGGGC
CTCAGCGGAGTTCATAGACAAGCTCGAATTCATCCAGCCCAATGTCAT

MSU_SH:

Genetic: 18:g.50837932C>T, c.1380C>T, p.Pro372Leu

Flanking Sequence:

GTAATGGAGGCCTTTGAGCAGGCTGAGCGGAAGCTGAAGCCCAACCCCAGCTTGATCTTCTCGGACGTGTATCAGGA
GATGC**[T/C]**TGCCCAGCTCCGCAAGCAGCAGGAGTCTCTGGCACGTCACCTCCAGACCTATGGTGAACACTACCCGCT
GGACCACTTCGAGAAG

DENNIS, J. A. & HEALY, P. J. 1999. Definition of the mutation responsible for maple syrup urine disease in Poll Shorthorns and genotyping Poll Shorthorns and Poll Herefords for maple syrup urine disease alleles. *Res Vet Sci,* 67, 1-6.

ZHANG, B., HEALY, P. J., ZHAO, Y., CRABB, D. W. & HARRIS, R. A. 1990. Premature translation termination of the pre-E1 alpha subunit of the branched chain alpha-ketoacid dehydrogenase as a cause of maple syrup urine disease in Polled Hereford calves. *J Biol Chem,* 265**,** 2425-7.

Montbeliarde Haplotype 2

Abbreviations: MH2

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Lethal

Breeds found in: Montbeliarde

General: Affected animals are aborted early in gestation.

Common Ancestor: None identified

Clinical: The SLC37A2 protein is a cell membrane transporter protein for glucose-6-phosphate, a key molecule in cellular energy metabolism.

OMIA: 001828-9913

Gene: SLC37A2 (Solute Carrier Family 37 (Glucose-6-Phosphate Transporter), Member 2)

Genetic: 29:g.28879810, c.34C>T, p.Arg12X

Flanking Sequence:

GCTGCCAGAACGAGCACAGGTGGACTGCTTCCTGGACACAGTGGAGACGGTAGGCCTGGACTCTCTGCTAACCCAGA TGCCCACCTTCCCCTGCAGGTAC**[C/T]**GAGCCTTCATCCTGCTCATCACCTTCTTAATCTACACCTGCTATCACATGTCCC GGAAGCCCATCAGTGTCGTCAAGGTGAGTCTGGCCCGGGGGTAAGG

FRITZ, S., CAPITAN, A., DJARI, A., RODRIGUEZ, S. C., BARBAT, A., BAUR, A., GROHS, C., WEISS, B., BOUSSAHA, M., ESQUERRE, D., KLOPP, C., ROCHA, D. & BOICHARD, D. 2013. Detection of Haplotypes Associated with Prenatal Death in Dairy Cattle and Identification of Deleterious Mutations in GART, SHBG and SLC37A2. *PLoS one,* 8, e65550.

Neuropathic Hydrocephalus

Abbreviations: NH, Water Head

Genetic Mode: Recessive

Royalty Fee: Yes

Trait Type: Lethal

Breeds found in: Angus

General: Affected calves are stillborn or aborted between 90 and 150 days of gestation. Those stillborn typically weigh between 11 - 16 kg and have an enlarged head that is fluid filled.

Common Ancestor: GAR Precision 1680

Clinical: The bones of the skull are malformed and loosely organized. The cranial cavity and spinal canal is fluid filled with no recognizable brain or spinal tissue. The mutation changes abnormal function in a gene that is involved in the development and maintenance of the central nervous system tissue.

Neuropathic hydrocephalus affected calf from Kaiser 2010

OMIA: 000487-9913

Gene: Confidential genomic defect

Genetic: Confidential genomic defect

Flanking Sequence: Confidential genomic defect

JOHNANTHAN BEEVER, UNIVERSITY OF ILLINOIS, 2012. PERSONAL COMMUNCIATION. CONFIDENTIAL GENOMIC DEFECT.

KAISER, L. 2010. *Dead Cows Don't Lie!! Moo News Tells you Why!* [Online]. Kaisercattle.com. Available: http://kaisercattle.com/pdf/MCA%20Defects%20combined.pdf [Accessed 28/08/2015].

Osteopetrosis

Abbreviations: OS, Marble Bone Disease **Genetic Mode: Recessive**

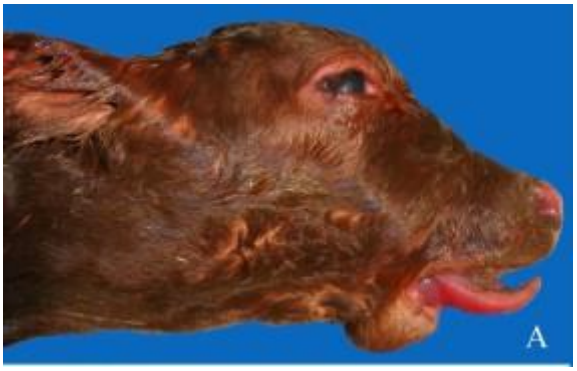
Royalty Fee: No **Trait Type: Lethal**

Breeds found in: Multiple including Angus, Friesian, Hereford, Holstein, Simmental

General: Affected calves are typically stillborn prematurely (250-275 days of gestation). They often have a small body size, flat skull, impacted molars, shortened lower jaw, protruding tongue; the leg bones are easily broken.

Common Ancestor: None identified

Clinical: The long bones contain no marrow cavity, are very dense, very fragile, and can be easily broken. They have lesions and mineralization in the brain.



Head of Osteopetrisis affected calf from Meyers et al., 2010

OMIA: 000755-9913

Gene: SLC4A2 (Solute Carrier Family 4 (Anion Exchanger), Member 2)

Genetic: 4:g.114437192_114439942del

Flanking Sequence:

CGTCAGCCCGGCCGCTCAGATTTTCCTGGCCGCGGGTTTGGGGAAGGGAAGCACTAAGACTGCCCCCAGGGCAGAA
CCTCGGGGTTTCTGTGCCCCCTCCT**[CCCCGGGCGTCACGTGCCCCTCCCCCAG…2784bp….GGAGGATGAACTCCAC
CGCA/-]**CCCTGGGCGTGGAGCGGTTTGAGGAGATCCTTCAGGAGGCGGGGTCCCGAGGAGGGGAGGAGC
TCGGCCGCAGCTACGGGGAGGAAGACTTTGAATGTGA

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. & SMITH, T. P. 2010. A deletion mutation in bovine SLC4A2 is associated with osteopetrosis in Red Angus cattle. *BMC Genomics,* 11, 337.

Paunch Calf Syndrome

Abbreviations: PCS

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Lethal

Breeds found in: Romagnola

General: Affected calves are usually stillborn, have abnormal development of multiple organs; facial deformities; and an enlarged distended fluid-filled stomach (hence the name 'Paunch Calf'). Some affected calves also have a protruding tongue and cleft palate.

Common Ancestor: None identified

Clinical: Affected calves have severe abdominal distension, subcutaneous oedema, ascites, a lobulated firm liver with two small (5 mm and 10 mm) blood-filled cysts, a small (1 cm) atrial septal defect, slight shortening of the face and bilateral exopthalmos.

Affected Paunch Calf Syndrome calf from Toolan et al., 2014

OMIA: 001722-9913

Gene: KDM2B (Lysine (K)-Specific Demethylase 2B)

Genetic: 17:g.56010031, c.2503G>A, p.Asp835Asn

Flanking Sequence:

TTCTTGGTGGGGCTGGGTGTGGAGGGGACCAAATCCCGCGACCCCTGGGAGCAAGCTTTGCATCTTTTCTTTCCCATG
ACAGCTAAAACCTGGCAAAGAA**[G/A]**ATAAGCTTTTCAGGAAAAAGGTACCATCTCCCACCCACCCCCTGCCCCTGTC
CCAGAACCTCTCTTGGGGCAGTAGTCTTAGGCTGGAGGGTAGGAGGCC

TESTONI, S., BARTOLONE, E., ROSSI, M., PATRIGNANI, A., BRUGGMANN, R., LICHTNER, P., TETENS, J., GENTILE, A. & DROGEMULLER, C. 2012. KDM2B is implicated in bovine lethal multi-organic developmental dysplasia. *PLoS one,* 7, e45634.

TOOLAN, D. P., MCELROY, M. C., FLYNN, P., WELD, R., MCCLURE, M. & SHEEHAN, M. 2014. Congenital Paunch Calf Syndrome in Ireland. *Cattle Association of Veterinary Ireland* Douglas, Co Cork, Ireland.

Pulmonary Hypoplasia with Anasarca 1

Abbreviations: PHA1, Waterbaby

Genetic Mode: Recessive

Royalty Fee: Yes

Trait Type: Lethal

Breeds found in: Chianina, Maine Anjou, Shorthorn

General: Some affected calves are aborted at 90 to 180 days; others are born dead with underdeveloped lungs and swelling caused by excessive fluid retention. PHA1 calves have a swollen appearance and this can make delivery very difficult for the cow, often a caesarean section is required.

Common Ancestor: Maine Anjou**:** Paramount, Draft Pick, Stinger
Chianina: Payback

Clinical: A dam carrying a PHA1 calf might have a swollen belly prior to calving due to an excess of amniotic fluid, and may need a caesarean section to remove the calf because it has swollen too large for vaginal delivery. Post-mortem results from affected calves will reveal small lungs and virtually no lymphatic system. The PHA1 foetuses are similar in appearance to the aborted "bulldog" calves of chondrodysplasia but can be identified by the longer legs and hooves.

Pulmonary Hypoplasia with Anasarca 1 affected calf from Kaiser 2010

OMIA: Not available

Gene: Confidential genomic defect

Genetic: Confidential genomic defect

Probes: Confidential genomic defect

Flanking Sequence: Confidential genomic defect

JOHNANTHAN BEEVER, UNIVERSITY OF ILLINOIS, 2012. PERSONAL COMMUNCIATION. CONFIDENTIAL GENOMIC DEFECT.

KAISER, L. 2010. *Dead Cows Don't Lie!! Moo News Tells you Why!* [Online]. Kaisercattle.com. Available: http://kaisercattle.com/pdf/MCA%20Defects%20combined.pdf [Accessed 28/08/2015].

Spinal Muscular Atrophy

Abbreviations: SMA

Genetic Mode: Recessive

Royalty Fee: No

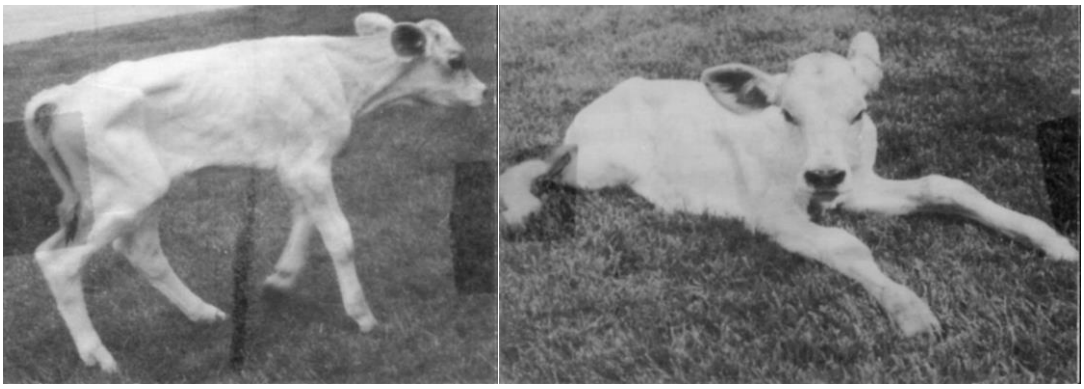
Trait Type: Lethal

Breeds found in: Brown Swiss

General: Calves often die of pneumonia by six to eight weeks of age. While born normal SMA affected calves start to show symptoms between three and six weeks of age when they show loss of strength and balance in the rear legs. As the disease progresses they will become weaker, lose flesh, and lose balance in the front legs. Once they show signs of laboured breathing death usually occurs within a couple of days. Usually the cause of death is pneumonia by six to eight weeks of age.

Common Ancestor: None identified

Clinical: This neurodegenerative disease causes loss of motor neurons, progressive weakness, decreased spinal reflexes, and loss of balance in the legs Terminal stages were characterized by severe muscular atrophy, quadriparesis, and sternal recumbence. Bronchopneumonia was a frequent complicating disease. Microscopic changes consisted mainly of degeneration, loss of motor neurons in the ventral horns of the spinal cord, and neurogenic atrophy of muscles.



SMA affected calves from Brown Swiss Association 2001

OMIA: 000939-9913

Gene: KDSR (3-Ketodihydrosphingosine Reductase)

Genetic: 24:g.62138835C>T, g.490C>T, p.Ala164Thr

Flanking Sequence:

GAAGACGCTCTTACCTCCATCTGCAAAGCCTCCGCAAGTCCCCTGAGGGCGAACTTGGATGAAGAGTATGCTGTGTAA
CCAAACAGGCCCAGCTGCCCGG**[T/C]**CTGGGAAGACACGAAGACGACCCTGCCCATGCGGCGTTCCTTCATGGTGGC
GATCACCGCCCGGCTGGGGTACACGCTGCCCAGGTAGTTGATGCTCATC

BROWN SWISS ASSOCIATION. 2011. *Genetic Abnormalities in the Brown Swiss Breed* [Online]. Available: http://www.brownswissusa.com/Portals/0/Documents/Abnormality%20Pamphlet.pdf [Accessed 6/12/2011 2011].

KREBS, S., MEDUGORAC, I., ROTHER, S., STRASSER, K. & FORSTER, M. 2007. A missense mutation in the 3-ketodihydrosphingosine reductase FVT1 as candidate causal mutation for bovine spinal muscular atrophy. *Proceedings of the National Academy of Sciences of the United States of America,* 104, 6746-51.

Tibial Hemimelia

Abbreviations: TH-Improver

Genetic Mode: Recessive

Royalty Fee: Yes

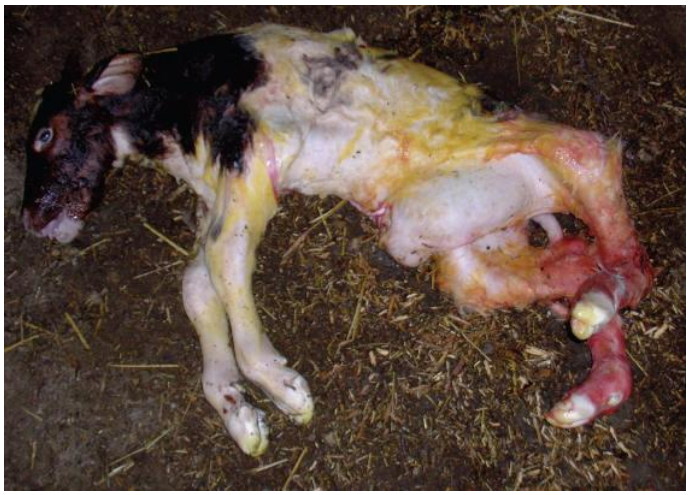
Trait Type: Lethal

Breeds found in: Galloway, Shorthorn

General: Affected animals are born with severe deformities including twisted rear legs with fused joints, large abdominal hernias and/or skull deformities. Affected calves are born dead or die (or are euthanized) shortly after birth.

Common Ancestor: Deerpark Improver

Clinical: The disease presents a constellation of abnormalities: abnormally twisted legs, fused joints, abdominal hernia, meningocele, and cryptorchidism.



Tibial Hemimelia affected calf from Kaiser 2010

OMIA: 001009-9913

Gene: ALX4 (Aristaless-Like Homeobox 4)

Genetic: Mutation is a deletion that removes approximate 1/3 of the gene

Flanking Sequence: Confidential genomic defect

JOHNANTHAN BEEVER, UNIVERSITY OF ILLINOIS, 2012. PERSONAL COMMUNCIATION. CONFIDENTIAL GENOMIC DEFECT.

KAISER, L. 2010. *Dead Cows Don't Lie!! Moo News Tells you Why!* [Online]. Kaisercattle.com. Available: http://kaisercattle.com/pdf/MCA%20Defects%20combined.pdf [Accessed 28/08/2015].

UNWANTED

Axonopathy

Abbreviations: AX, Demetz syndrome

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Unwanted

Breeds found in: Tyrolean Grey

General: Calves often have a wide stance and start losing control of hind legs at 1 month of age that progresses to them being unable to stand. While not lethal, affected calves are usually humanly euthanized by 10 months of age.

Common Ancestor: Gusti

Clinical: The C>T mutation in exon 20 causes a splicing defect that leads to partial retention of intron 19 and introduces a premature stop codon. Animals have spinal ataxia, mild ambulatory paraparesis with pelvic limb ataxia. They have prominent bilateral-symmetrical axonal degeneration/loss and astrogliosis targeting primarily the dorsal spinocerebellar tract and the gracile fascicle of the spinal cord. Scattered degenerating axons were observed in the remaining white matter tracts of the spinal cord, in the white matter of the brain and in the femoral nerve.

AX affected Tyrolean Grey from Drogemuller, et al., 2011

OMIA: 001106-9913

Gene: MFN2 (Mitofusin 2)

Genetic: 16:g.42562057C>T, c.2229C>T

Flanking Sequence:

CCGGTAGAACGCTTGGCAGGTTACGCCACGGCTAGTTATCAGCTCTTGCCACTACAAGGTAACCTTTTCTCTGCAGGA
ATAAAGCCGGCTGGTTGGACAG**[C/T]**GAACTCAACATGTTCACCCACCAGTACCTGCAGCCCAGCAGATAGTGGGCA
CCCGGAGCCGGACCCCCTGTGGGGAGGACAGTGCTGCGAGCGCGGGGGG

DROGEMULLER, C., REICHART, U., SEUBERLICH, T., OEVERMANN, A., BAUMGARTNER, M., KUHNI BOGHENBOR, K., STOFFEL, M.H., SYRING, C., MEYLAN, M., MULLER, S., *et al*: An unusual splice defect in the mitofusin 2 gene (MFN2) is associated with degenerative axonopathy in Tyrolean Grey cattle. *PLoS One* 2011, 6(4):e18931.

Bovine Leukocyte Adhesion Deficiency

Abbreviations: BLAD

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Unwanted

Breeds found in: Friesian, Holstein

General: Affected cattle often have severe ulcers on in the mouth, teeth loss, chronic pneumonia, and diarrhoea. Affected cattle often die at a young age due to infections.

Common Ancestor: Osborndale Ivanhoe

Clinical: Affected animals are characterized by recurrent bacterial infections, delayed wound healing, and stunted growth, along with persistent neutrophilia. There is a deficiency in $ß_2$-integrin of leukocytes. These glycoproteins - integrins - are vital to cell-cell and cell-substratum adhesion reactions in the body. Such adhesions are centre of anti-inflammatory reaction.

OMIA: 000595-9913

Gene: ITGB2 (Integrin Beta 2, also called CD18)

Genetic: 1:145114963, c.383A>C, p.Val128Ala, rs445709131

Flanking Sequence:

CCCCCCACCCCCAGACCAGGTGGTACACCCTGACTCTCTCCCAAATCCTGGCAGGTCAGGCAGTTGCGTTCAAAGTGA
CCTTCCGGAGGGCCAAGGGCTACCCCATCG**[A/G]**CCTGTACTACCTGATGGACCTCTCCTACTCCATGGTGGATGACC
TCGTCAACGTCAAGAAGCTGGGGGGTGACCTGCTCCGGGCCCTC

NAGAHATA, H. 2004. Bovine leukocyte adhesion deficiency (BLAD): a review. *J Vet Med Sci,* 66**,** 1475-82.

Bovine Progressive Degenerative Myeloencephalopathy

Abbreviations: Weaver **Genetic Mode: Recessive**

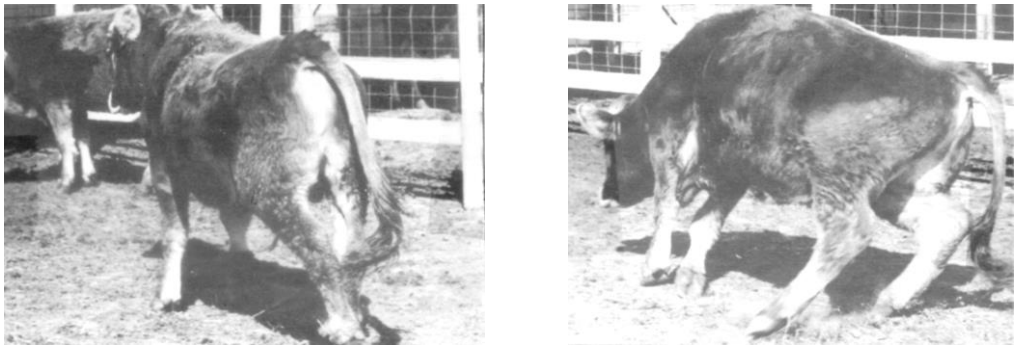
Royalty Fee: No **Trait Type: Unwanted**

Breeds found in: Brown Swiss, Corara

General: Affected animals appear fine until 6 to 18 months of age when they start losing control of their hind legs and appear to "Weave" when walking. While not fatal, as the disease progresses they eventually will become unable to move and are normally humanely euthanized.

Common Ancestor: Rolling View Modern Stretch

Clinical: Neurological disease that results in bilateral hind limb weakness and ataxia appear in afflicted animals at 6 to 18 months of age, which slowly progresses to total loss of hind limb control by 3 to 4 years of age. Once animals are recumbent they normally are humanely euthanized or else they will die from malnutrition or infection. Symptoms are caused from degeneration of nerve passages in the spinal cord and brain which prevents the transfer of nerve impulses from the brain to the leg muscles, this degeneration is comparable to Amyotrophic Lateral Sclerosis in humans.



Weaver affected animal from Brown Swiss Association USA, 2011

OMIA: 000827-9913

Gene: PNPLA8 (Patatin-Like Phospholipase Domain Containing 8)

Genetic: 4:g.49878773C>T, c.1703G>A, p.Ser568Asn, rs800397662

Flanking Sequence:

ATACTGACAGCCTCCCAAATAGTGAGAGTTGATTCCAGGAAAATGTCCATAGTTCCTGAACACAAAGGCTTTTGGCGT
TATCCCTCTGTTCACTATGGTA**[C/T]**TTACTGCAGCGACCTAGTCGATTAAAAAGTGGACAATACGCATTGTAAGCAGC
AATATTTGGGACTGTAAAAATTAAATATTTAGTGGTATGAATGAACA

BROWN SWISS ASSOCIATION USA. 2011. Genetic Abnormalities in the Brown Swiss Breed. http://www.brownswissusa.com/Portals/0/Documents/Abnormality%20Pamphlet.pdf

KUNZ, E., ROTHAMMER, S., PAUSCH, H., SCHWARZENBACHER, H., SEEFRIED, F. R., MATIASEK, K., SEICHTER, D., RUSS, I., FRIES, R. & MEDUGORAC, I. 2016. Confirmation of a non-synonymous SNP in PNPLA8 as a candidate causal mutation for Weaver syndrome in Brown Swiss cattle. *Genetics Selection Evolution,* 48**,** 1-14.

MCCLURE, M., KIM, E., BICKHART, D., NULL, D., COOPER, T., COLE, J., WIGGANS, G., AJMONE-MARSAN, P., COLLI, L., SANTUS, E., LIU, G. E., SCHROEDER, S., MATUKUMALLI, L., VAN TASSELL, C. & SONSTEGARD, T. 2013. Fine Mapping for Weaver Syndrome in Brown Swiss Cattle and the Identification of 41 Concordant Mutations across NRCAM, PNPLA8 and CTTNBP2. *PLoS One,* 8**,** e59251.

Chediak Higashi Syndrome

Abbreviations: CHS

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Unwanted

Breeds found in: Japanese Black

General: Animals have pink eyes, bruise easily, and bleed readily which cause economic loss.

Common Ancestor: None identified

Clinical: It is thought that the mutation causes malfunction of the lysosomal trafficking regulator protein, encoded by the Lyst gene, which leads to alterations in the size, structure and function of lysosomes.

OMIA: 000185-9913

Gene: LYST (Lysosomal Trafficking Regulator)

Genetic: 28:g.8508619A>G, c.6044A>G, p.His2015Arg

Flanking Sequence:

CACAAAGAGGGGCAGCTTATATCCATGCCCCAAGAGGTTTGTAGATCCTTTGTGAAAAATACAGCAGAACTCCTTGGA TCTCCTCCGGATTTGGAATTATTGACGATTATCTTCAATTTCCTTTTAGCAGTTC**[A/G]**TCCTCCTACTAATACTTATGTT TGTCACAACCCCACAAACTTCTATTTTTCTTTGCACATAGATGGCAAGATCTTTCAGGAAAAAGTACAATCAATCATGT ACTTG

ABDEEN, A., SONODA, H., KOBAYASHI, I., KITAHARA, G. & IKEDA, M. 2013. A New Method for Rapid Detection of the Mutant Allele for Chediak-Higashi Syndrome in Japanese Black Cattle. *J Vet Med Sci*.

Congenital Myoclonus

Abbreviations: CM

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Unwanted

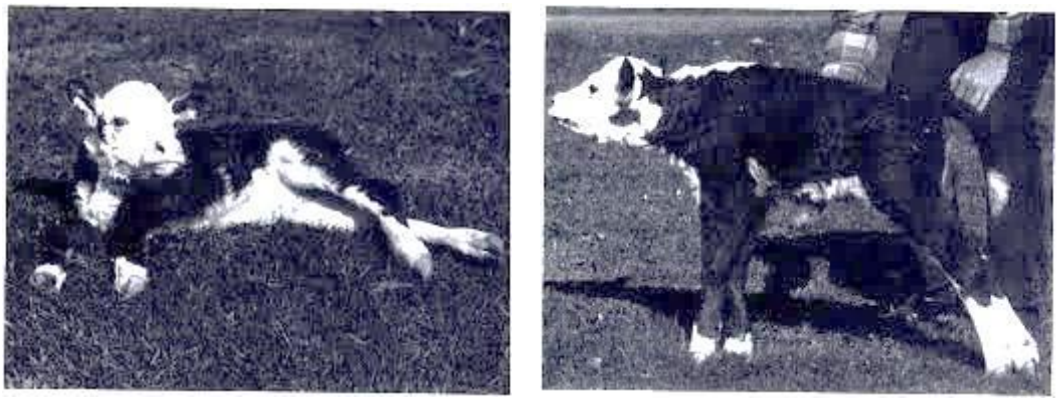
Breeds found in: Hereford

General: Affected animals often appear normal but have spontaneous muscle spasms and whole body rigidity in response to stimulation. When laying down the back legs are often crossed. When assisted to a standing position the handlers touch can cause full body rigidity and a sawhorse position.

While not lethal, affected calves are usually humanly euthanized.

Common Ancestor: None identified

Clinical: Animals are characterized by hyperesthesia and myoclonic jerks of the skeletal musculature from both spontaneously and from stimulation tactile, visual, and auditory. Affected animals do not have pathological lesions in the central nervous system and do not respond to anti-epileptic or anticonvulsive medication. Spinal cord and brain stem sections will show a marked deficit in [^{3}H]strychnine-binding sites. Musculoskeletal lesions of the hip joints can be observed.



Affected calf with crossed limbs (left) and sawhorse posture (right) from Gundlach, A.L, 1990.

OMIA: 000689-9913

Gene: GLRA1 (Glycine Receptor, Alpha 1)

Genetic: 7:g. 65080197C>A, c.156C>A, p.Tyr52X

Flanking Sequence:

AGTCTTGCTGCTTCCAAGGAGGCTGAAGCTGCTCGGTCTGCTTCCAAGCCCATGTCACCGTCCGATTTCCTGGATAAAC
TCATGGGGAGGACTTCTGGATA**[C/A]**GACGCCAGGATCAGGCCCAATTTCAAAGGTAGATAATCTTGCCTTTCAGAG
CCCCAGGGATCTGCTTTCCCAGATTGTGGCAGCAAGCCCACTGAATTGT

GUNDLACH, A. L. 1990. Disorder of the inhibitory glycine receptor: inherited myoclonus in Poll Hereford calves. *FASEB J,* 4**,** 2761-6.

PIERCE, K. D., HANDFORD, C. A., MORRIS, R., VAFA, B., DENNIS, J. A., HEALY, P. J. & SCHOFIELD, P. R. 2001. A nonsense mutation in the alpha1 subunit of the inhibitory glycine receptor associated with bovine myoclonus. *Mol Cell Neurosci,* 17**,** 354-63.

Crooked Tail Syndrome

Abbreviations: CTS_AG, CTS_T>C

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Unwanted

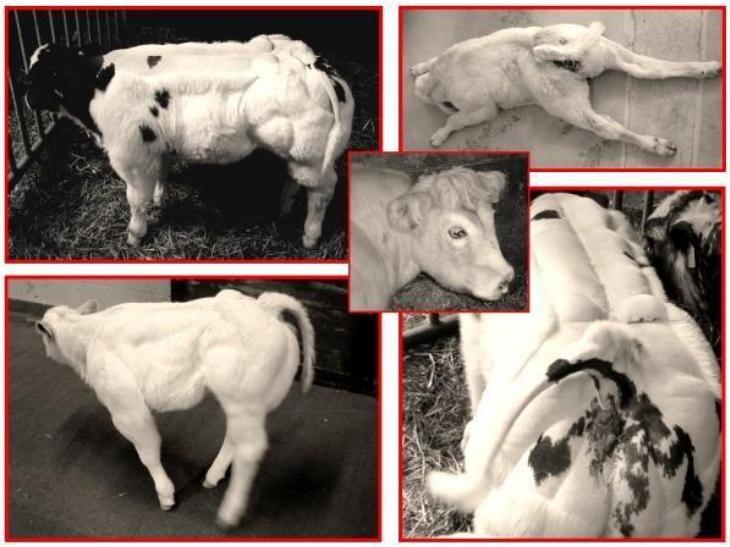
Breeds found in: Belgian Blue

General: CTS is not lethal but >25% of affected animals are euthanized due to welfare concerns. CTS causes substantial economic losses due to growth retardation and treatment costs. Affected animals have a crooked tail, abnormally shaped legs, stocky head, growth retardation, extreme muscularity, and straight hocks.

Heterozygous animals have enhanced muscular development, and are smaller, stockier, and toed-in front legs.

Common Ancestor: None identified

Clinical: Additional symptoms show variable penetrance: A) spastic paresis of the hind limbs, (B) short, straight and extended fore limbs, (C) pronounced scoliosis.



Affected CTS animals from Fasquelle et al., 2009.

OMIA: 001452-9913

Gene: MRC2 (Mannose Receptor, C Type 2)

Genetic: Two mutations in ACAN that being homozygous for either mutation or heterozygous for both will cause the disease.

CTA_AG

Genetic: 19:g.47740473delAG, p.Gly934X

Flanking Sequence:

TCACAGAGGACTGGGGGGACCAGAGGTGCACAACAGCCTTGCCTTACATCTGCAAGCGGCGCAACAGCACCAGAGA
GCAGCAGCCCCCAGACCTGCCGCCCAC**[AG/-]** GGGGCTGCCCCTCTGGCTGGAGCCAGTTCCTGAACA
AGGTAGGGAGTAGGGAGGGGGCCTGAGGGGAAGGCTGAGCTTCAGGAGTCCTGGCCCTCTGGCAA

CTS_C>T

Genetic: 19:g.47734925T>G,c.1801T>G,p.Cys601Gly, rs466131011

Flanking Sequence: (CTS_C>T):

TCAGTGTGTGGGTCCCCTCCTCCCTCCTCCAGGGTACAGCCGTGGGGGCTGCGTGGCCCTGGCCACAGGCAGTGCCA
TGGGGCTGTGGGAGGTGAAGAAC**[T/C]**GCACATCGTTCCGGGCTCGCTACATCTGCCGCCAGAGCCTGGGCACGCCC
GTGACGCCTGAGCTGCCTGGGCTAGACCCCACGCCCAGCCTCACCGGCGC

FASQUELLE, C., SARTELET, A., LI, W., DIVE, M., TAMMA, N., MICHAUX, C., DRUET, T., HUIJBERS, I. J., ISACKE, C. M., COPPIETERS, W., GEORGES, M. & CHARLIER, C. 2009. Balancing selection of a frame-shift mutation in the MRC2 gene accounts for the outbreak of the Crooked Tail Syndrome in Belgian Blue Cattle. *PLoS Genet,* 5**,** e1000666.

SARTELET, A., KLINGBEIL, P., FRANKLIN, C. K., FASQUELLE, C., GERON, S., ISACKE, C. M., GEORGES, M. & CHARLIER, C. 2012. Allelic heterogeneity of Crooked Tail Syndrome: result of balancing selection? *Anim Genet,* 43**,** 604-7.

Developmental Duplication

Abbreviations: DD, Polymelia

Genetic Mode: Recessive, Incomplete Penetrance

Royalty Fee: Yes

Trait Type: Unwanted

Breeds found in: Angus

General: There are a range of phenotypes associated with this disease that all represent extra body tissue. Not all DD homozygous animals will present visible deformities. Affected calves can be born with additional limb(s), extra skin flaps on the head or as "2 headed" calves. With the exception of mortality associated with calving difficulty, these calves can often thrive, particularly if the extra limbs are surgically removed.

Common Ancestor: Ken Caryl Mr Angus 8017, B/R New Design 036, Bon View New Design 1407, GAR Predestined

Clinical: While the phenotype can also be called polymelia, the DD mutation is transmitted with incomplete penetrance and variable expressivity. Penetrance of the DD phenotype is estimated to be 54%, with 46% of the expected number of homozygotes as apparently normal individuals, although some of these animals are likely to have sub-clinical DD lesions and develop clinical signs at a later time.

DD is a fundamental defect of embryonic neurulation involving both cranial and spinal dysraphism. Nothing is currently known about the function of the protein coded by the DD gene but it is likely to be a regulator of gene transcription in cell-cell signalling during neurulation.

Mutation of the NHLRC2 gene causes neural tube defects in Angus cattle with multiple congenital malformation phenotypes that include axial and limb duplications, heteropagus conjoined twins, midbrain and forebrain malformations including pseudoholoprosencephalon, craniofacial dysmorphogenesis, micropthalmia, diprosopus, embryogenic teratomas, dermoid cysts, myolipomas, split cord malformation and cranial and spinal dysraphism. For more information on how DD can present please view Dr. Denholm's page at http://www.flockandherd.net.au/cattle/reader/developmental-duplication-angus.html

DD affected calf from http://www.flockandherd.net.au/cattle/reader/developmental-duplication-angus.html

OMIA: 001226-9913

Gene: NHLRC2 (NHL repeat containing 2)

Genetic: 26:g.34618072T>C, c.932T>C, p.Val311Ala

Flanking Sequence:

AAATAAAGCACATGTTTTCTATATGTTCTATTGTAAATAGATGCATTGTATAAAACCTGTATTAATTTCTATAGATTGAC
CTAGAAGCTGAGATGG**[T/C]**GAGCACTGTGGCTGGCATTGTAATTCAAGGTACAGATAAAGAAGGTGGAGCTAAAG
GAGATGAACAGCCCATTAGTTCC

http://www.angus.org/Pub/DD/DD_Update08122013.pdf

http://redangus.org/genetics/dna-tools/defects/DD

http://www.flockandherd.net.au/cattle/reader/developmental-duplication-angus.html

http://vetbook.org/wiki/cow/index.php?title=Polymelia

Dystrophic Epidermolysis Bullosa

Abbreviations: DEB

Genetic Mode: Recessive

Royalty Fee: No

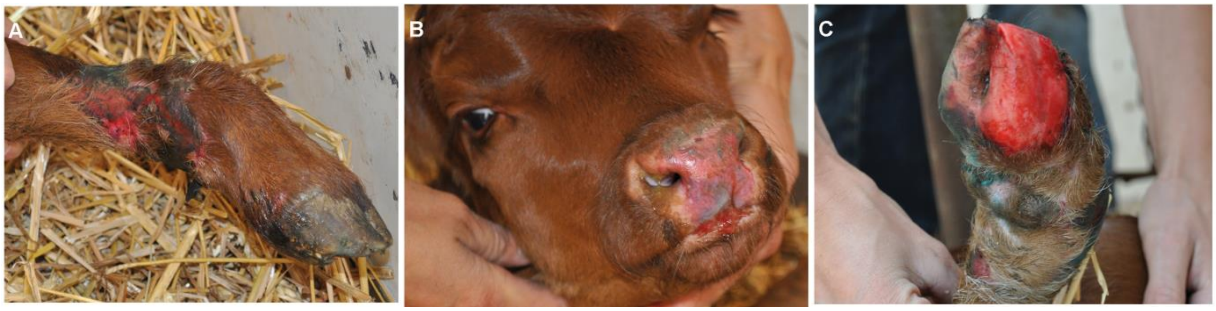
Trait Type: Unwanted

Breeds found in: Rotes Hohenvieh

General: The skin and mucus membranes of affected animals are very fragile making it easy to rip or tear, especially around the muzzle, mouth, fetlocks, and hooves. Some demonstrate a large loss of skin or blisters around the fetlocks and on the muzzle. While not fatal, affected animals are usually humanely euthanized due to the extent of the skin lesions.

Common Ancestor: None identified

Clinical: Affected skin regions have epidermis that is greatly or completely detached from the dermis. Additional phenotypes that can appear are missing dewclaws, closed ears, and skin lesions on the tail.



Images of lesions found on a DEB affected from Menoud et al., 2012

OMIA: 000341-9913

Gene: COL7A1 (Collagen Type VII Alpha 1)

Genetic: 22:g.51873390C>T, c.4756C>T, p.Arg1586X

Flanking Sequence:

GGTGACAGTTGTGTCCCCTGACTTCTGATCCTTCCTTCCACAGGGCTCACCTGGCTTGGCTCTTCCTGGAGACCCTGGC
CCCAAGGGAGACCCTGGAGGC**[C/T]**GAGTGCGTAAATGTGGGGAAGGGGAATGTGACAGAAAGAGATGGGATGGT
GCCTGGGAGCCCCAACTAAGTCCTGTCCCTCCTCCCCATGCCCTGCAGGG

MENOUD, A., WELLE, M., TETENS, J., LICHTNER, P. & DROGEMULLER, C. 2012. A COL7A1 mutation causes dystrophic epidermolysis bullosa in Rotes Hohenvieh cattle. *PLoS one,* 7**,** e38823.

Factor XI Deficiency

Abbreviations: FXI_WA

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Unwanted

Breeds found in: Wagyu

General: Affected animals have an increased blood clotting time, may express bloody milk, and be anaemic. Heterozygous and affected animals have reduced fertility, increased susceptibility to infections including mastitis.

Common Ancestor: Hikari, Itohana 2 TF38, Itoshigenami TF148, JVP Fukutsuru 06, Kimifuku TF726, Kitateruyasu 003, Shigemaru, TF601, and JVP Yasutanisakura 931

Clinical: Factor XI deficiency is encountered in Wagyu. There are similarities in the clinical symptoms in the breeds. The causative insertion mutations are on different locations of the F11 gene and these variations are considered to be responsible for the differences in severity between the breeds. The Factor XI protein is important in the coagulation cascade. Heterozygotes are usually subclinically affected with mild hemophilia-like disorders.

OMIA: 000363-9913

Gene: F11 (Coagulation Factor XI)

Genetic: 27:g. 15362363C>ATATGTGCAGAATATA, c.870insC>ATATGTGCAGAATATA, p.Phe290LeuTyrValGlnAsnIle

Flanking Sequence:

GAACAGAGCTTTTTCTGGTTTTAGTCTACAACACTGCCAGCACAGTGTCCCAGGTAATCAGTGCAAGCCCTTTCTTCTG
ATCAAGGTCAACAAATGGGCGGGAGGGTTTTGCCTTTCACATCTCAATATGTGCTTCTGCTGTGCAGTGTT**[C/ATATG
TGCAGAATATA]**TGCCATTCTTCATTCTATCGCAACACTGATTTCTTGGGAGAAGAACTGGACATCGTAGACGCGGAC
AGCCACGAAGCCTGCCAGAAAACATGTACCAACAGCATCCGCTGCCAGTTCTTTACCTATTCTCCATC

KUNIEDA, M., TSUJI, T., ABBASI, A. R., KHALAJ, M., IKEDA, M., MIYADERA, K., OGAWA, H. & KUNIEDA, T. 2005. An insertion mutation of the bovine Fii gene is responsible for factor XI deficiency in Japanese black cattle. *Mamm Genome,* 16**,** 383-9.

MEYDAN, H., YILDIZ, M. A., OZDIL, F., GEDIK, Y. & OZBEYAZ, C. 2009. Identification of factor XI deficiency in Holstein cattle in Turkey. *Acta Vet Scand,* 51**,** 5.

http://www.wagyuinternational.com/reference_recessives.php

http://vetbook.org/wiki/cow/index.php?title=Factor_XI_deficiency

Hypotrichosis

Abbreviations: HY_KRT71, HY_ERCC6L, HY_TSR2 **Genetic Mode: Recessive**

Royalty Fee: Yes: HY_KRT71 **Trait Type: Unwanted**
No: HY_ERCC6L and HY_TSR2

Breeds found in: Galway, Hereford, Holstein, Pezzata Rossa

General: Affected cattle have partial absence of hair at birth over all or parts of the body: often on the poll, brisket, neck and legs. The hair can be very short, fine, or kinky that may fall out leaving bare spots, and the tail switch can be underdeveloped. Affected animals are more vulnerable to environmental stress, skin infections, pests, sunburn, cold stress, and have a decreased economic value.

HY_ERCC6L and HY_TSR2 mutations are on the X chromosome so males only need 1 copy and females need 2 copies to be affected. They cause hairless streaks on the body.

Males and females need 2 copies of HY_KRT71 to be affected by this mutation.

Common Ancestor: None identified

Clinical: The condition may vary in expression as the animal matures, thus becoming less noticeable with age.

Calf with hypotrichosis affected legs. (Photo kindly provided by Dr. Johnathan Beever, University of Illinois)

OMIA: 000540-9913 (HY_KRT71), 000542-9913 (HY_ERCC6L, HY_TSR2)

HY_KRT71 (Found in Hereford lineages)

Gene: KRT71 (Keratin 71)

Genetic: 5:g.27505486delTGTGCCCA, c.334delTGTGCCCA, p.Met93AsnfsX14

Flanking Sequence:
TGTGGCCAGCGGCAGTGGGAAGAGTGGAGGTTATGGATTTGGCCGGGGCCGGGCCAGTGGTTTCGCCGGCAGCAT
GTTTGGCAGCGTGGCCCTGGGGCCCA**[TGTGCCCA/-]**ACTGTGTGCCCACCTGGAGGCATCCACCAGGTCACT
GTCAATGAGAGCCTCCTG GCCCCCCTCAACGTGGAGCTGGACCCCGAGATCCAGAAAGTGCGTGC

HY_ERCC6L (Found in Pezzata Rossa and Holstein lineages)

Gene: ERCC6L

Genetic: X:g.83572401G>A, c.52G>A, p.Ala17Thr

Flanking Sequence:

AAACGAGGGAAATTCAATCCCCGGCCGAGAGGAAACTCTCTGAGGCGTCATGGAGGTGTCCCGAGGATTTGCGGAA
GCTGGGGCCTTAAGCCCGGAGCAG**[G/A]**CTGCCAGTTACCTGAGGTATGTCTGGGACGATGGGCGGGTCTGGTTCA
CCGGCCCTGGCCGGGAGTGGGGATGAAGGTCCCTTGGACTCCCCCAGGGGCC

HY_TSR2 (Found in Pezzata Rossa and Holstein lineages)

Gene: TSR2

Genetic: X:g.97363937A>G, c.441+226A>G

Flanking Sequence:

TCCCAAGGTCTCATGGCCAGTCCTGGCAAAGCTAGGAGAGCCTGGGTCTCCATTGGCCATAGCTGGGGGTTTATTTAG
CTCTCTCTTGTATTTCTCCCCT**[A/G]**GGTTGCAGCTACGAATGATGGGGCAGCTACAGATGGGGTCTGCCCCCAGCCT
GAACCCTCTGGTCCAGACTCCCAGACTATTAAGGAAGAGGATATAGTG

MARKEY, A.D., TAYLOR, J.F., SCHNABEL, R.D., MCKAY, S.D., MCCLURE, M.C., BEEVER, J.E., A Deletion Mutation in Krt71 is Associated with Congenital Hypotrichosis in Hereford Cattle*. Plant & Animal Genomes* XVIII Conference, San Diego, 9-13 January 2010, p. 552.

MARRON, B. M. & BEEVER, J. E. 2012. A Mutation in Hephaestin-Like 1 (HEPHL1) is Responsible for Hypotrichosis in Belted Galloway Cattle. *Plant and Animal Genomes XX.* San Diego, CA, USA.

MURGIANO, L., SHIROKOVA, V., WELLE, M. M., JAGANNATHAN, V., PLATTET, P., OEVERMANN, A., PIENKOWSKA-SCHELLING, A., GALLO, D., GENTILE, A., MIKKOLA, M. & DROGEMULLER, C. 2015. Hairless Streaks in Cattle Implicate TSR2 in Early Hair Follicle Formation. *PLoS Genet,* 11**,** e1005427.

Mulefoot

Abbreviations: Syndactyly, MF_R1740X, MF_P1647L, MF_NG1621KC, MF_G1199S, MF_G907R, MF_G81S

Genetic Mode: Recessive

Trait Type: Unwanted

Royalty Fee: No

Breeds found in: Angus, Charolais, Holstein, and Simmental

General: Also called Syndactyly which means "joined finger, the cloven hoof is fused together. Affected cattle can have 1-4 fused hooves, show varying degrees of lameness, have a high-step gait, and may walk slowly.

Common Ancestor: None identified

Clinical: The LRP4 gene plays a critical role in limb development. This disease has incomplete penetrance so it is possible that an animal homozygous for the mutation does not have the disease. It is estimated that up to 20% of animals homozygous for the disease won't have fused hooves.

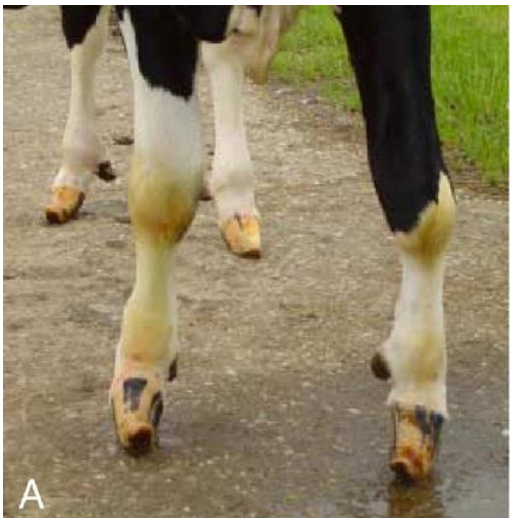


Photo of an affected Mulefoot animal from Duchesne et al., 2006

OMIA: 000963-9913

Gene: LRP4 (Low Density Lipoprotein Receptor-Related Protein 4)

MF_NG1621KC (Found in Holstein lineages)

Common Ancestor: Raven Burke Elsie

Genetic: 15:g.77675516CG>AT, c.4840CG>AT, p.AsnGly1614LysCys

Flanking Sequence:

CCTCCATTTGGAGAAGCGTCAAACTGGGAGACTTGATTCTGCCCCAGGCCAGATGTTCATTTGCTTTGCTCATAGGGA CCAACGCTTGTGGCGTGAACAA**[CG/AT]**GCGGATGCACTCACCTCTGCTTTGCCAGAACCTCGGACTTTGTGTGTGCC TGTCCTGATGAGCCCGACGGCCGGCCCTGCTCCCTCGGTGAGTTGGACTG

MF_G1199S (Found in a crossbred (Simmental x Charolais x Holstein) lineage)

Genetic: 15:g.77682052G>A, c.3571G>C, p.Gly1199Ser

Flanking Sequence:

AGGAACTGTGGGAGGAACCAGCTATTACCGTCTCTTGCCCAGGTTCATGTACTGGACGGACTGGGGGGAGCATGCCA
AGTTGGAGCGGTCTGGGATGGAC**[G/A]**GCTCCGACCGCGCCGTGCTCATCAACAGCAACCTCGGGTGGCCCAACGG
ACTGACTGTGGACAAGGCCAGCTCCCAGCTGCTCTGGGCTGACGCCCACAC

MF_G907R (Found in Simmental lineages)

Genetic: 15:g.77686731G>A, c.2719G>A, p.Gly907Arg

Flanking Sequence:

GCCTGCCTGAGTAAGTGCCCCAGACTGACCCCTGTTCCCCTCCCGTTCCCGGGGCTCAGAGTTGCCCACCTGCTCCCCT
CTCGACTTTCACTGTGACAAC**[G/A]**GCAAATGTATCCGCCGCTCCTGGGTGTGCGACGGGGACAACGACTGTGAGGA
TGACTCGGACGAGCAGGACTGTCGTGAGTGCTGGGCGGGGCTGGGCGG

MF_G81S (Found in Simmental lineages)

Genetic: 15:g.77699623G>A, c.217G>A, p.Gly73Ser rs453049317

Flanking Sequence:

GCCTGCCTGAGTAAGTGCCCCAGACTGACCCCTGTTCCCCTCCCGTTCCCGGGGCTCAGAGTTGCCCACCTGCTCCCCT
CTCGACTTTCACTGTGACAAC**[G/A]**GCAAATGTATCCGCCGCTCCTGGGTGTGCGACGGGGACAACGACTGTGAGGA
TGACTCGGACGAGCAGGACTGTCGTGAGTGCTGGGCGGGGCTGGGCGG

DROGEMULLER, C., LEEB, T., HARLIZIUS, B., TAMMEN, I., DISTL, O., HOLTERSHINKEN, M., GENTILE, A., DUCHESNE, A. & EGGEN, A. 2007. Congenital syndactyly in cattle: four novel mutations in the low density lipoprotein receptor-related protein 4 gene (LRP4). *BMC genetics,* 8**,** 5.

DUCHESNE, A., GAUTIER, M., CHADI, S., GROHS, C., FLORIOT, S., GALLARD, Y., CASTE, G., DUCOS, A. & EGGEN, A. 2006. Identification of a doublet missense substitution in the bovine LRP4 gene as a candidate causal mutation for syndactyly in Holstein cattle. *Genomics,* 88**,** 610-21.

KOUYOU AKIYAMA, TAKASHI HIRANO, ALI AKBAR MASOUDI, KAZUYUKI UCHIDA, TAKEHITO TSUJI, TAEKO KUMAGAI, KOUJI OHWADA & TETSUO KUNIEDA 2013. A Mutation of the GFRA1 Gene is Responsible for Forelimb-Girdle Muscular Anomaly (FMA) of Japanese Black Cattle *Plant and Animal Genome XXI.* San Diego, CA, USA.

Neuronal Ceroid Lipofuscinosis

Abbreviations: NCL

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Unwanted

Breeds found in: Devon

General: Affected cattle will walk in circles and repetitively tilt their head. They have visual impairment that progresses to blindness, ataxia, and seizures. Premature death of affected cattle occurs at approximately two years of age.

Common Ancestor: None identified

Clinical: Blindness is caused by the destruction of rod and cone photoreceptors within the eye. Neurological degradation occurs within the cerebrocortical gray matter of affected cattle and there is substantial atrophy of the cerebral cortex, thinning of the gyri in the occipital area, atrophy of the cerebellum and dilation of the lateral ventricles as well as atrophy of the hippocampus.

OMIA: 001482-9913

Gene: CLN5 (Ceroid-Lipofuscinosis, Neuronal 5)

Genetic: 12:g.52461241insG, c.662insG, p.Ala221GlyfsX6

Flanking Sequence:

TGGTTAGAATATTTTACTTAAAACTAACATGATCAGCTTTAATTATGTCCACGTAATTTTTGTCTTGTTTGTTTTTAACTA
GGAGGCATGTTTAACAGAATGGCAAAGTGGGTAAAACAGGACAATGAAACAGGGATTTATTATGAGACATGGACTG
TCCAAGCCAGCCCGGAAAGGGGGG**[-/G]**CAGAGAGATGGTTTGAATCCTACGACTGTTCCAAATTTGTGTT
AAGGACCTATGAGAAATTGGCTGAACTTGGAGCAGACTTCAAGAAGATAGAAACCAACTATACAAGGATATTTCTTTA
CAGTGGAGAACCTACTTATCTGGGAAATGAAACATCTGTTTTTGGGCCAACAGGAAAC

HOUWELING, P. J., CAVANAGH, J. A., PALMER, D. N., FRUGIER, T., MITCHELL, N. L., WINDSOR, P. A., RAADSMA, H. W. & TAMMEN, I. 2006. Neuronal ceroid lipofuscinosis in Devon cattle is caused by a single base duplication (c.662dupG) in the bovine CLN5 gene. *Biochim Biophys Acta,* 1762**,** 890-7.

Protoporphyria

Abbreviations: Proto

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Unwanted

Breeds found in: Limousin, Blond de'Aquitaine

General: Protoporphyria causes extreme photosensitivity. Affected animals have hair loss and ulcers develop on skin exposed to sunlight, especially the ears, lips, nose and udder. Soon after birth affected animals often lick their lips and nose due to the pain/itchiness of developing ulcers. Affected animals are very reluctant to leave shade. Their teeth, bones and urine can also have a reddish brown discoloration.

While not lethal affected animals often fail to thrive and are sold to slaughter before reaching optimal slaughter weight.

Common Ancestor: None identified

Clinical: This disease is sometimes referred to as Bovine Congenital Erythropoietic Protoporphyria (BCEPP). The disease is caused by a deficiency of the enzyme ferrochelatease. Some affected animals also have seizures, or suffer depression.

Examples of skin ulceration on a Protoporphyria affected calf from McAloon et al., 2015

OMIA: 000836-9913

Gene: FECH (Ferrochelatase)

Genetic: 24:g.57298882G>T, c.1250 G>T, p.Ter417CysfsX27

Flanking Sequence:

TCCAAGGAGCGCTGCTCCACACAGCTGACTCTGAGCTGTCCGCTCTGCGTGAACCCCACCTGCAGGGAGACCAAATCC
TTCTTCACCAGCCAGCAGCTGT**[G/T]**ACCCTGGCGGCACGCCGCTGGGAGGTGCGCGTGCCCGCCTCCCGACACCTCC
GAGGAGGAGGAGGGCGCATCCGGCCGTTAGGGAGGAGGTTACATCCGT

JENKINS, M. M., LEBOEUF, R. D., RUTH, G. R. & BLOOMER, J. R. 1998. A novel stop codon mutation (X417L) of the ferrochelatase gene in bovine protoporphyria, a natural animal model of the human disease. *Biochim Biophys Acta,* 1408**,** 18-24.

MCALOON, C. G., DOHERTY, M. L., O'NEILL, H., BADMINTON, M. & RYAN, E. G. 2015. Bovine congenital erythropoietic protoporphyria in a crossbred limousin heifer in Ireland. *Ir Vet J,* 68**,** 15.

Pseudomyotonia

Abbreviations: PMT_164, **PMT_211, PMT_284**

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Unwanted

Breeds found in: Chiania, Romagnola

General: Affected animals are characterized by having muscle contractions when startled or move faster than a slow walk. When contractions occur the animals will have an uncoordinated gait, sometimes 'bunny hopping' on their back feet. Under prolonged stimulation the muscles become so stiff the animals can fall over. The contractions stop once the stimulation is removed and they are able to move normally again.

Common Ancestor: None identified

Clinical: Muscle biopsies taken from affected cattle after muscle exercise showed necrotic and regenerative fibres in type 2 muscle fibres. Muscle fibres might be enlarged with pale cytoplasm.

Pseudomyotonia affected animal from Drogemuller et al., 2008

OMIA: 001464-9913

Gene: ATP2A1 (ATPase, Ca++ Transporting, Cardiac Muscle, Fast Twitch 1)

PMT_164 (Found in Chininia lineages)

Genetic: 25:g.25:26198573G>A, c.491G>A, p.Arg164His

Flanking Sequence:

GGAGGGGTCTTCAGACAAAGATGGGGTTTTCTCCCTTCTCTGCTGACTTCATGCCCCTCTTCTCTCTCCACAGTGGGGG
ACAAGGTCCCGGCAGATATCC**[G/A]**CATCCTCACCATCAAGTCTACCACCCTCCGGGTCGACCAGTCCATCCTGACAG
GTCTACTGGCCAGAGGGCAGGGCGGGGGATGCATCACAGGAGGATTT

PMT_211 (Found in Romagnola lineages)

Genetic: 25:g.:26197429G>T, c.632G>T, p.Gly211Val

Flanking Sequence:

CAGGGGGCCCTGGTCTGGGAGAGATGTGACGGCAAGGGAAGAGATGAGGCCCACAGCTGGGGCCTCACCTGACTC
CCTGCCTCTTCTTCCCCTTCCCAGG**[G/T]**CACCAACATCGCAGCCGGCAAGGCCATCGGCATTGTGGCCACCACCGGT
GTGGGCACCGAGATTGGGAAGATCCGTGACCAAATGGCCGCCACAGAGCAG

PMT_284 (Found in Romagnola lineages)

Genetic: 25:g.26197204G>T, c.857G>T, p.Gal284Val

Flanking Sequence:

CTGGATGAGTTTGGGGAGCAGCTCTCCAAGGTCATCTCCCTCATCTGCGTGGCCGTCTGGCTCATCAACATTGGCCAC
TTCAACGACCCCGTGCATGGGG**[G/T]**CTCCTGGATCCGTGGTGCCATCTACTACTTTAAGATCGCCGTGGCCCTGGCT
GTGGCTGCCATCCCCGAGGGTAGGGCGACCTCTCTGTCTCCTCCCATT

DROGEMULLER, C., DROGEMULLER, M., LEEB, T., MASCARELLO, F., TESTONI, S., ROSSI, M., GENTILE, A., DAMIANI, E. & SACCHETTO, R. 2008. Identification of a missense mutation in the bovine ATP2A1 gene in congenital pseudomyotonia of Chianina cattle: an animal model of human Brody disease. *Genomics,* 92, 474-7.

GRUNBERG, W., SACCHETTO, R., WIJNBERG, I., NEIJENHUIS, K., MASCARELLO, F., DAMIANI, E. & DROGEMULLER, C. 2010. Pseudomyotonia, a muscle function disorder associated with an inherited ATP2A1 (SERCA1) defect in a Dutch Improved Red and White cross-breed calf. *Neuromuscul Disord,* 20**,** 467-70.

MURGIANO, L., SACCHETTO, R., TESTONI, S., DOROTEA, T., MASCARELLO, F., LIGUORI, R., GENTILE, A. & DROGEMULLER, C. 2012. Pseudomyotonia in Romagnola cattle caused by novel ATP2A1 mutations. *BMC Vet Res,* 8, 186.

RNF11 Growth Retardation

Abbreviations: RNF11

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Unwanted

Breeds found in: Belgian Blue

General: Affected animals appear normal at birth but suffer from severely stunted growth at 6 months; they have a narrow skull and very hairy head. Approximate one-third of affected animals will die from infections before 6 months of age due to a compromised resistance to pathogens.

Common Ancestor: Galopeur des Hayons

Clinical: Upon necropsy affected calves can have inflammation of the respiratory tract or polyarthritis. The allele affects the spice site and removes exon 2.

RNF11 affected (front) and normal (back) calf of the same age from Sartelet et al., 2012

OMIA: 001686-9913

Gene: RNF11 (Ring Finger Protein 11)

Genetic: 3:g.95601696A>G, c.124-2A>G

Flanking Sequence:

AGGTCCCCTCCTCAGCCCAAAAAGGAAGAAACAAAAGGAAAACATTACCTAGAAAACAGATTTTTTAAAAAATAATTA
ATTTCTCCATTTTAAAAAATTT**[A/G]**GGAACAAGTTCCAGTTCCGGTCTATCATCCAACACCTAGCCAGACTCGCCTAG
CAACTCAGCTGACTGAAGAGGAACAAATTAGGATAGCTCAAAGAATA

SARTELET, A., DRUET, T., MICHAUX, C., FASQUELLE, C., GERON, S., TAMMA, N., ZHANG, Z., COPPIETERS, W., GEORGES, M. & CHARLIER, C. 2012a. A splice site variant in the bovine RNF11 gene compromises growth and regulation of the inflammatory response. *PLoS Genet,* 8, e1002581.

STAT1

Abbreviations: STAT1

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Unwanted

Breeds found in: Multiple Breeds

General: Decreased embryo survival rate. Animals born alive will appear normal.

Common Ancestor: None identified

Clinical: Animals homozygous for the 'C' allele have a decreased embryo survival rate. Animals born alive and heterozygous or homozygous will appear normal.

OMIA: Not available

Gene: STAT1 (Signal Transducer and Activator of Transcription 1, 91kDa)

Genetic: 2:g.79888611G>A, c.*617C>T, rs43705173

Flanking Sequence:

AGAACTGTGAAGACAGTTTCATTTACTAACTTCAATTTCATGATGAAGGCAGAATATATTCAACTTTGGTATTAAAGCT
GAAATGGAAGATACTACTCAT**[G/A]**AATTTGTAAAGTTTACTTCCTTCTATTGATATTAGCCAGCATCATAAAGCCATA
CCAAAAGCTAATTCTCCCAAGAAAGAGAATCTTTAGTTTTCAATGG

COBANOGLU, O., ZAITOUN, I., CHANG, Y. M., SHOOK, G. E. & KHATIB, H. 2006. Effects of the signal transducer and activator of transcription 1 (STAT1) gene on milk production traits in Holstein dairy cattle. *Journal of dairy science,* 89, 4433-7.

KHATIB, H., HUANG, W., MIKHEIL, D., SCHUTZKUS, V. & MONSON, R. L. 2009. Effects of signal transducer and activator of transcription (STAT) genes STAT1 and STAT3 genotypic combinations on fertilization and embryonic survival rates in Holstein cattle. *Journal of Dairy Science,* 92, 6186-91.

STAT3

Abbreviations: STAT3_19069, STAT3_25402

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Unwanted

Breeds found in: Holstein

General: Decreased embryo survival rate.

Common Ancestor: None identified

Clinical: Embryos homozygous for either STAT3 mutation have a decreased survival rate. Embryos homozygous for both STAT3 mutations have a much lower survival rate

OMIA: Not available

Gene: STAT3 (Signal Transducer and Activator of Transcription 3)

STAT3_19069

Genetic Mode: Dominant

General: Animals heterozygous or homozygous for the 'T' allele have lower embryo survival rate.

Genetic: 19:g.43070296T>C, c.1215T>C, rs110942700

Flanking Sequence:

CCTCCGTCAGGTAAGGCTCTCCCCAAGTCCCTCCCCCTGCCAGAGGCCCTGCAGAAAGGGAGCCCAGGCTTCTCCCAT
GTACCAAGTGTTTGAACTCCGC**[T/C]**GAGAGGCTGCCATTGTTAGACTCTTCCATGTTCATCACTTTCGTGTTTGTGCCC
AGAATGTTAAATTTCCGGGACCTGAATCACAGGAGGAAAAGACCAA

STAT3_25402

Genetic Mode: Recessive

General: Animals homozygous for the **'**G' allele have a lower fertilization rate.

Genetic: 19:g.43063963T>G, c.1889-25T>G, rs134279188

Flanking Sequence:

ATGATTATTTCAGCAAATGACATGTTGTTCAGCTGCTGCTTGGTGTAAGGTTCCACTGACTGGATCTGGGTCTTGCCTG
TCATGGGATACAGAAAGAGAA**[T/G]**ACTCGGGTGATCTTAGAGAAGACTACCTGATTGATTTTCCCTTGAGGGGGAA
AGGCTTATGCCAACCTAGTGTTCGAGACCCTGAATATTCTGCCCAGTT

KHATIB, H., HUANG, W., MIKHEIL, D., SCHUTZKUS, V. & MONSON, R. L. 2009. Effects of signal transducer and activator of transcription (STAT) genes STAT1 and STAT3 genotypic combinations on fertilization and embryonic survival rates in Holstein cattle. *Journal of Dairy Science,* 92, 6186-91.

STAT5A

Abbreviations: STAT5A_13244, STAT5A_13319. STAT5A_13516

Genetic Mode: Recessive

Trait Type: Unwanted

Royalty Fee: No

Breeds found in: Multiple Breeds

General: Affected animals born alive appear normal, but they have an increased rate of unfertilized embryos and the fertilized embryos produced will have a decreased survival rate:

Animals born alive and heterozygous or homozygous for those alleles will appear normal.

Common Ancestor: None identified

Clinical: Mutations in the STAT5 gene family leads to infertility in mice due to small or absent corpora lutea

OMIA: Not available

Gene: STAT5A (Signal Transducer and Activator of Transcription 5A)

STAT5_13244. The 'A' allele is associated with reduced fertility

Genetic: 19:g.43046856A>G, c.1169+462A>G, rs109788842

Flanking Sequence:
ATGACAGCTAGTTTCAAGGCTGCGGGGTGACTAGGAGGAGATGGTGAACGGGCGTGGAGAGGGCAGACGTTCGGG
CAGAGAGAACACGGGCCTGTCTGGA**[A/G]**GAGGAGCAGACAAAGGGCGTGGTGGATGGAGAACCCGGGGTGAGG
TCCTGGGATTAGGCCAGGCCACCCGTGAAGGGCGTGGGAGTGAGTGAAGGAGGGC

STAT5_13319 The 'G' allele is associated with reduced fertility

Genetic: 19:g.43046931G>A, c.1169+537G>A, rs208753173

Flanking Sequence:
CAGAGAGAACACGGGCCTGTCTGGAAGAGGAGCAGACAAAGGGCGTGGTGGATGGAGAACCCGGGGTGAGGTCCT
GGGATTAGGCCAGGCCACCCGTGAA**[G/A]**GGCGTGGGAGTGAGTGAAGGAGGGCGGGAATGAGTGAGGGGAGAG
ACTGGGTCCTGAGTACTGAGGCCCACTGTGTGCTCTGGGGCTAGGATGACGAAGA

STAT5_13516 The 'T' allele is associated with reduced fertility

Genetic: 19:g.43047128T>G, c.1170-730T>G, rs110495396

Flanking Sequence:
AAGATGACGAAGAGTTCTCACTCTCTTAGAGCCTGCCTTTGGGCTGGGAACAAGACAGTCATATACTCTTAAAAATCA
GGCAGCGTCAGAAGGCAATAGA**[T/G]**TCTAGACAGAAAATTAAAGCCAAGCAATATCACAGCGCCTGGATAGATGTT
GCAACAGCACATGGATGGCCAAGGAGGGCCTTTCTGAGGATCTATTTGA

KHATIB, H., MONSON, R. L., SCHUTZKUS, V., KOHL, D. M., ROSA, G. J. & RUTLEDGE, J. J. 2008. Mutations in the STAT5A gene are associated with embryonic survival and milk composition in cattle. *Journal of Dairy Science,* 91**,** 784-93.

Thrombopathia

Abbreviations: THR, Simmental hereditary thrombopathy (SHT)

Genetic Mode: Recessive

Trait Type: Unwanted

Royalty Fee: No

Breeds found in: Fleckvieh, Simmental

General: Bleeding disorder characterised by impaired blood clotting. Bleeding can be mild to severe, even small injuries might cause life-threatening blood losses due to impaired blood coagulation.

Common Ancestor: None identified

Clinical: Affected cattle experienced mild to severe bleeding episodes, including epistaxis, gingival bleeding, and hematuria. Severe cases the animal can bleed to death from routine procedures: dehorning, tail bleed, and vaccinations. While the number of thrombocytes is normal, the platelet aggregation response to adenosine-diphosphate (ADP) or platelet activating factor (PAF16) is severely reduced.

Bleeding after an insect sting in a Thrombopathia affected calf from www.wsff.info

OMIA: 001003-9913

Gene: RASGRP2 (RAS Guanyl Releasing Protein 2)

Genetic: 29:g.43599204A>G, c.701A>G, p.Leu234Pro, rs385444696

Flanking Sequence:

TCTCCTTGAGGCGGGAGATGGAGCTGTGGCTCAGGCCCCCAACCACTGCCATCAGCGTGTTGAAATTCTGCAGGTGC AGG**[A/G]**GTTCCTGGGGGACAAATGGGGAGAGAGGAGGCAGTGAGTCACTGAGTGGGCCCAGAATTTGGCCCAGC TTTTCTGGGAA

BOUDREAUX, M. K., SCHMUTZ, S. M. & FRENCH, P. S. 2007. Calcium diacylglycerol guanine nucleotide exchange factor I (CalDAG-GEFI) gene mutations in a thrombopathic Simmental calf. *Vet Pathol,* 44**,** 932-5.

GENTRY, P. A., CHERYK, L. A., SHANKS, R. D. & HEALEY, R. 1997. An inherited platelet function defect in a Simmental crossbred herd. *Can J Vet Res,* 61**,** 128-33.

http://www.wsff.info/home-2/articles-evf/item/215-thrombopathia-in-fleckvieh-tp

BENEFICIAL

Infectious Bovine Keratoconjunctivitis

Abbreviations: IBK, Pinkeye

Genetic Mode: Additive

Royalty Fee: No

Trait Type: Beneficial

Breeds found in: Multiple Breeds

General: Pinkeye, also called Infectious Bovine Keratoconjunctivitis, is primarily caused by the bacterium Moraxella bovis. Flies, tall weeds, and tall grasses can act to irritate the eye and spread the disease from one animal to another. With each 'G' allele the animal reduces its risk of pinkeye infection by 8-13%. Thus an animal that is homozygous for the allele will have a 16-26% reduction in pinkeye infection risk.

Pinkeye can cause a decrease in weight gain. If both eyes are infected and untreated then the animal could become blind. Breeds which lack pigment on their eyelids, such as Herefords and Charolais, are more susceptible to pinkeye infection.

Common Ancestor: None identified

Clinical: The disease causes inflammation of the cornea (the clear outer layer) and conjunctiva (the pink membrane lining the eyelids) of the eye. If left untreated it will cause ulceration, which looks like a hole or depression in the cornea. After treatment they eye may appear a cloudy blue or have a white scar.

Left to Right: Examples of Stage 1, 2, 3, and 4 Pinkeye infections from Whitter et al., 2009

OIMA: 001533-9913

Gene: TLR4 (Toll-Like Receptor 4)

Genetic: 8:g.108833985A>G, c.94-24A>G, rs8193046

Flanking Sequence:

GGTTGACTGGTCTCTTTGCTCGTCCCAGTAGCCTCCAAGGCTGTAGTCTAGGAGAGGAGAGTTGCTTGGAAGTCTGCT
AAGGTGCATGCAGGAAGACACC**[A/G]**CATCTAATATCTAATCATTTCAGGTTGTTCCTAACATTAGTTACCAGTGCAT
GGAGCTGAATCTCTACAAAATCCCCGACAACATCCCCATATCAACCAA

KATARIA, R. S., TAIT, R. G., JR., KUMAR, D., ORTEGA, M. A., RODIGUEZ, J. & REECY, J. M. 2011. Association of toll-like receptor four single nucleotide polymorphisms with incidence of infectious bovine keratoconjunctivitis (IBK) in cattle. *Immunogenetics,* 63, 115-9.

WHITTIER, W. D., CURRIN, J. F. & CURRIN, N. 2009. Pinkeye in Beef Cattle. *Virginia Cooperative Extension,* Publication 400-750.

Polled

Abbreviations: Poll_C **Genetic Mode: Dominant**

Royalty Fee: No **Trait Type: Beneficial**

Breeds found in: Multiple breeds including Angus, Galloway, Speckle Park, Murray Grey, Senepol, and Holstein

General: The poll allele causes animals to have an absence of horns. Besides the lack of horns, genetically polled animals also have a narrower skull, especially noticeable at the poll. Horned and dehorned cattle typically have a flat-looking poll, while genetically polled cattle have more peaked-looking poll. The Poll_C allele is found in animals with Nordic and British lineages.

Common Ancestor: None identified

Clinical: Poll is an economically favourable trait due to human and animal safety, economic loss from horn injuries, animal welfare, and the cost of dehorning. Allele causes tissue-specific overexpression of LincRNA#1 in the fetus' horn bud which results in the Polled phenotype.

Angus with polled versus Aubrac with horn phenotype. (Photos provided by ICBF)

OMIA: 000483-9913

Gene: Not located in a known gene

Genetic: 1:g.1706051_1706060del-ins1705834_1706045dup

Flanking Sequence:

TGGATTACATTTAAGATACATATTTTTCTTTCTTGTCTGAAAGTCTTTGTAGTGAGAGCAGGCTGGAATTATGTCTGGG GTGAGATAGTTTTCTTGGTAG**[GCTGGTATTC/CTGTGAAATG..192bp..TAGTTTTCTT]**TTGCTCTTTAGATCAAAACT CTCTTTTCATTTTTAAGTCTATCCCAAAAGTTGCTCTTTAGATCAAAACTCTCTTTTCATTTTTAAGTCTATCCCAAAAGT GTGGGAGG

ALLAIS-BONNET, A., GROHS, C., MEDUGORAC, I., KREBS, S., DJARI, A., GRAF, A., FRITZ, S., SEICHTER, D., BAUR, A., RUSS, I., BOUET, S., ROTHAMMER, S., WAHLBERG, P., ESQUERRE, D., HOZE, C., BOUSSAHA, M., WEISS, B., THEPOT, D., FOUILLOUX, M. N., ROSSIGNOL, M. N., VAN MARLE-KOSTER, E., HREIETHARSDOTTIR, G. E., BARBEY, S., DOZIAS, D., COBO, E., REVERSE, P., CATROS, O., MARCHAND, J. L., SOULAS, P., ROY, P., MARQUANT-LEGUIENNE, B., LE BOURHIS, D., CLEMENT, L., SALAS-CORTES, L., VENOT, E., PANNETIER, M., PHOCAS, F., KLOPP, C., ROCHA, D., FOUCHET, M., JOURNAUX, L., BERNARD-CAPEL, C., PONSART, C., EGGEN, A., BLUM, H., GALLARD, Y., BOICHARD, D., PAILHOUX, E. & CAPITAN, A. 2013. Novel insights into the bovine polled phenotype and horn ontogenesis in Bovidae. *PLoS one,* 8, e63512.

MEAT

Calpain 1 (CAPN1)

Abbreviations: CAPN1_316, CAPN1_4751, CAPN1_530

Genetic Mode: Additive

Trait Type: Meat

Royalty Fee: No

Breeds found in: Multiple breeds

General: Calpain 1 breaks down muscle fibers and is associated with more tender meat.

Common Ancestor: None identified

Clinical: The Calpain1 protease breaks down myofibrillar (muscle fiber) proteins post-mortem. While not causative mutations they are predictors of tenderness in multiple cattle breeds, the alleles each explain from 0.4 to 2% of the phenotypic variation in tenderness, with the amount explained varying across breeds.

OMIA: Not available

Gene: CAPN1 (Calpain 1)

CAPN1_316 The 'C' allele is associated with more tender meat

Genetic: 29:g.44069063C>G, c.947G>C, p.Gly316Ala, rs17872000

Flanking Sequence:
TGGGCCAGGGAAGGACAGGCCCCAGGGATAGAGGCTGGGCAGGTCAGTGGCCGCCAGCCCCTGGCAGTGCCCTTTT
CCTGCAGCTCCTCGGAGTGGAACG**[G/C]**CGTGGACCCTTACATGCGGGAGCAGCTCCGGGTCAAGATGGAGGATGG
GGAGTTCTGGTGAGCAGCCCCCTCCTCAGTCTGAGTGGGCACCCCAGCTCCCA

CAPN1_530 The 'G' allele is associated with more tender meat

Genetic: 29:g.44085642G>A, c.1588G>A, p.Val530Ile, rs17871051

Flanking Sequence:
CCCCTGTCTCCCCCTTTCCTCCCACCACACCCTTGCTGCCCCAACCCCCGTTGACTGGCCCCTCTCTCTCCCCACCCTCTG
CAGAGAGCTGGATGACCAG**[A/G]**TCCAGGCCAATCTCCCCGACGAGGTACGTGCCCTGCCCCCACCCTGGGTGCACG
ACGGGGACCCGGGTGTCCTGTGTCTTGGTCTCTAGCCAGCAAGGCAGAGCC

CAPN1_4751 The 'C' allele is associated with more tender meat

Genetic: 29:g.44087629C>T, c.1800+169C>T, rs17872050

Flanking Sequence:
GAGGAAGGGCTCTGGGTGACCTGTCCCAAGAGCAGGGAAAGGGACAGATGTGGACAGGCCAGTTCCTTCCTGGCAT
CCTCCCCTTGACTGGGGGGAAAAC**[C/T]**GAGGCGCAGGGCTGTGTCAAGTGACGGGGGAGGGCCTCGTCTACAGGT
GACCCTAAGGCTGGCACTCAGAGAACACCCCTCCCAGCCTACCCCAATTCAGGCCTG

CASAS, E., WHITE, S. N., WHEELER, T. L., SHACKELFORD, S. D., KOOHMARAIE, M., RILEY, D. G., CHASE, C. C., JR., JOHNSON, D. D. & SMITH, T. P. 2006. Effects of calpastatin and micro-calpain markers in beef cattle on tenderness traits. *J Anim Sci,* 84, 520-5.

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WHITE, S. N., CASAS, E., WHEELER, T. L., SHACKELFORD, S. D., KOOHMARAIE, M., RILEY, D. G., CHASE, C. C., JR., JOHNSON, D. D., KEELE, J. W. & SMITH, T. P. 2005. A new single nucleotide polymorphism in CAPN1 extends the current tenderness marker test to include cattle of Bos indicus, Bos taurus, and crossbred descent. *J Anim Sci,* 83, 2001-8.

Calpastain (CAST)

Abbreviations: CAST_282, CAST_2870, CAST_2959 **Trait Type: Meat**

Royalty Fee: No **Breeds found in: Multiple breeds**

Genetic Mode: Additive

General: Calpastain alleles are associated with more tender meat.

Common Ancestor: None identified

Clinical: Calpain1 works to break down muscle fibre and Calpastatin is an inhibitor of Calpain 1. While not causative mutations they are predictors of tenderness in multiple cattle breeds, the alleles each explain from 0.4 to 2% of the phenotypic variation in tenderness, with the amount explained varying across breeds.

OMIA: Not available

Gene: CAST (Calpastain)

CAST_282 The 'C' allele is associated with more tender meat

Genetic: 7:g.98533961C>G, c.391-159C>G, rs110955059

Flanking Sequence:

TGTTAAAACGGCACCTCTGTGTGGCATCAGCAGGTATTGCAATTTGCTTGTGTGATTCTTGCTGAATTTGGAGGGAAG
GAATTGCATTGTTTCAAATTTT**[C/G]**TACCCAAAGTGAAATTTGTCACATGTAAATCATACTAATTTAAATTCTCACAAT
TGACTACATAAAACACAAGTGTTATGAATTGCTTTCTACTCCTCAG

CAST_2870 The 'G' allele is associated with more tender meat

Genetic: 7:g.98579574A>G, c.*382G>A, rs41255587

Flanking Sequence:

ACATTTGATAGTTTCTTAAAGCAGCACACAAAAAAGGAAAAACCTTTGCAAACTTTTGCACATTCTCCCCACAGTGCCT
GTAAATCTCATTAGTATTTTC**[G/A]**ATTTGCACTTATTTTTGTTGTTAGCATTTGGAAAACGATGCCTCACGTGTTCTTC
AGTGTTCTGATTTCTCATGACCCCTTTCCTCTTAGACTTGTGGAC

CAST_2959 The 'A' allele is associated with more tender meat

Genetic: 7:g.98579663A>G, c.*471A>G, rs109221039

Flanking Sequence:

TTAGTATTTTCGATTTGCACTTATTTTTGTTGTTAGCATTTGGAAAACGATGCCTCACGTGTTCTTCAGTGTTCTGATTTC
TCATGACCCCTTTCCTCTT**[A/G]**GACTTGTGGACTGTGTTTGATGTTTCTTTGGGTTGTTGTTTATAAGTCAGTCATAAA
ATACTGTGCATTGGGCACATGTCTCCTCTTGAGCTGCTAATCG

CASAS, E., WHITE, S. N., WHEELER, T. L., SHACKELFORD, S. D., KOOHMARAIE, M., RILEY, D. G., CHASE, C. C., JR., JOHNSON, D. D. & SMITH, T. P. 2006. Effects of calpastatin and micro-calpain markers in beef cattle on tenderness traits. *J Anim Sci,* 84, 520-5.

LI, J., ZHANG, L.-P., GAN, Q.-F., LI, J.-Y., GAO, H.-J., YUAN, Z.-R., GAO, X., CHEN, J.-B. & XU, S.-Z. 2010. Association of CAST gene polymorphisms with carcass and meat quality traits in Chinese Commercial Cattle Herds. *Asian-Australasian Journal of Animal Sciences,* 23**,** 1405-1411.

MCCLURE, M. C., RAMEY, H. R., ROLF, M. M., MCKAY, S. D., DECKER, J. E., CHAPPLE, R. H., KIM, J. W., TAXIS, T. M., WEABER, R. L., SCHNABEL, R. D. & TAYLOR, J. F. 2012. Genome-wide association analysis for quantitative trait loci influencing Warner-Bratzler shear force in five taurine cattle breeds. *Animal Genetics,* 43, 662-73.

VAN EENENNAAM, A. L., LI, J., THALLMAN, R. M., QUAAS, R. L., DIKEMAN, M. E., GILL, C. A., FRANKE, D. E. & THOMAS, M. G. 2007. Validation of commercial DNA tests for quantitative beef quality traits. *J Anim Sci,* 85**,** 891-900.

WHITE, S. N., CASAS, E., WHEELER, T. L., SHACKELFORD, S. D., KOOHMARAIE, M., RILEY, D. G., CHASE, C. C., JR., JOHNSON, D. D., KEELE, J. W. & SMITH, T. P. 2005. A new single nucleotide polymorphism in CAPN1 extends the current tenderness marker test to include cattle of Bos indicus, Bos taurus, and crossbred descent. *J Anim Sci,* 83, 2001-8.

Myostatin

Abbreviations: See below

Genetic Mode: Recessive

Royalty Fee: Yes

Trait Type: Meat

Breeds found in: Multiple, breed specific mutations listed below

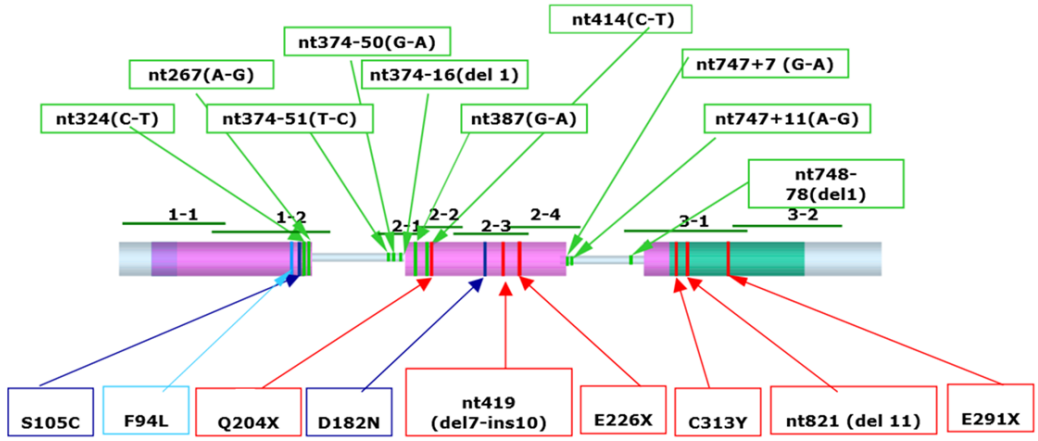
General: Multiple alleles in the Myostatin gene affect muscle mass, some effect calving difficulty.

Q204X, E226X, E291X, C313Y, nt419, and 821del11, result in double muscling (hyperplasia), larger birth weights, increased dystocia and meat tenderness.

F94L, S105C, and D182N increase muscularity and reduce external and intramuscular fat, with no change in birth weight.

Common Ancestor: None identified

Clinical: Myostatin is essential for proper regulation of skeletal muscle development. Hyperplasia (double-muscled) is a result of a defective myostatin protein.



Location of alleles in the Myostatin gene. Image from Dunner et al.,2003

Homozygous MYO_nt821 Belgian Blue (left) and homozygous MYO_F94L Limousine (right). (Photos provided by ICBF)

OMIA: 000683-9913

Gene: MSTN (Myostatin)

MYO_821del11 (Found in Asturiana, Belgian Blue, Blonde d' Aquitaine, Limousine, Parthenise, Asturiana, South Devon, Santa Gertrudis, Braford, Murray Grey, and Angus lineages)

Genetic: 2:g.6218379delATGAACACTCC,c.821-831delTGAACACTCCA,p.Glu275ArgfsX14

Flanking Sequence:

ATTATTAACTCTTCTTTCCTTTCCATACAGACTCCTTTTTTAGAAGTCAAGGTAACAGACACACCAAAAAGATCTAGGA
GAGATTTTGGGCTTGATTGTG**[ATGAACACTCC/-]**ACAGAATCTCGATGCTGTCGTTACCCTCTAA
CTGTGGATTTTGAAGCTTTTGGATGGGATTGGATTATTGCACCTAAAAGATATAAGGCCAATTACTGCTC

MYO_C313Y (Found in Gasconne, Piedmontese and Parthenise lineages)

Genetic: 2:g.6218499G>A, c.938G>A, p.Cyc313Tyr

Flanking Sequence:

CGATGCTGTCGTTACCCTCTAACTGTGGATTTTGAAGCTTTTGGATGGGATTGGATTATTGCACCTAAAAGATATAAG
GCCAATTACTGCTCTGGAGAAT**[A/G]**TGAATTTGTATTTTTGCAAAAGTATCCTCATACCCATCTTGTGCACCAAGCAA
ACCCCAGAGGTTCAGCCGGCCCCTGCTGTACTCCTACAAAGATGTCT

MYO_E226X (Found in Maine-Anjou and Marchingina lineages)

Genetic: 2:g.6216204G>T, c.610G>T, p.Glu226X

Flanking Sequence:

GAAACTTGACATGAACCCAGGCACTGGTATTTGGCAGAGCATTGATGTGAAGACAGTGTTGCAGAACTGGCTCAAAC
AACCTGAATCCAACTTAGGCATT**[G/T]**AAATCAAAGCTTTAGATGAGAATGGCCATGATCTTGCTGTAACCTTCCCAGA
ACCAGGAGAAGATGGACTGGTAAGTGATTACTGAAAATAACATGCTAA

MYO_E291X (Found in Maine-Anjou and Marchingina lineages)

Genetic: 2:g.6218432G>T, c.871G>T, p.Glu291X

Flanking Sequence:

AACAGACACACCAAAAAGATCTAGGAGAGATTTTGGGCTTGATTGTGATGAACACTCCACAGAATCTCGATGCTGTCG
TTACCCTCTAACTGTGGATTTT**[G/T]**AAGCTTTTGGATGGGATTGGATTATTGCACCTAAAAGATATAAGGCCAATTAC
TGCTCTGGAGAATGTGAATTTGTATTTTTGCAAAAGTATCCTCATAC

MYO_F94L (Found in Angus and Limousin lineages)

Genetic: 2:g.6213980A>C, c.282C>A, p.Phe94Leu, rs110065568

Flanking Sequence:

TCAGTAAACTTCGCCTGGAAACAGCTCCTAACATCAGCAAAGATGCTATCAGACAACTTTTGCCCAAGGCTCCTCCACT
CCTGGAACTGATTGATCAGTT**[C/A]**GATGTCCAGAGAGATGCCAGCAGTGACGGCTCCTTGGAAGACGATGACTACC
ACGCCAGGACGGAAACGGTCATTACCATGCCCACGGAGTGTGAGTAGT

MYO_Q204X (Found in Blonde d'Aquitaine, Charolaise, Charolais and Limousin lineages)

Genetic: 2:g.6216138C>T, c.610C>T, p.Gln204X, rs110344317

Flanking Sequence:

TGTGCAAATCCTGAGACTCATCAAACCCATGAAAGACGGTACAAGGTATACTGGAATCCGATCTCTGAAACTTGACAT
GAACCCAGGCACTGGTATTTGG**[C/T]**AGAGCATTGATGTGAAGACAGTGTTGCAGAACTGGCTCAAACAACCTGAAT
CCAACTTAGGCATTGAAATCAAAGCTTTAGATGAGAATGGCCATGATCT

MYO_S105C (Found in Parthenaise lineages)

Genetic: 2:g.6214012C>G, c.314C>G, p.Ser105Cys

Flanking Sequence:

ATCAGCAAAGATGCTATCAGACAACTTTTGCCCAAGGCTCCTCCACTCCTGGAACTGATTGATCAGTTCGATGTCCAGA
GAGATGCCAGCAGTGACGGCT**[C/G]**CTTGGAAGACGATGACTACCACGCCAGGACGGAAACGGTCATTACCATGCCC
ACGGAGTGTGAGTAGTCCTGCTGGTGCAGAGCAACGACTCTGCTGACT

CASAS, E., STONE, R. T., KEELE, J. W., SHACKELFORD, S. D., KAPPES, S. M. & KOOHMARAIE, M. 2001. A comprehensive search for quantitative trait loci affecting growth and carcass composition of cattle segregating alternative forms of the myostatin gene. *J Anim Sci,* 79**,** 854-60.

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KAMBADUR, R., SHARMA, M., SMITH, T. P. & BASS, J. J. 1997. Mutations in myostatin (GDF8) in double-muscled Belgian Blue and Piedmontese cattle. *Genome Res,* 7**,** 910-916.

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MARCHITELLI, C., SAVARESE, M. C., CRISA, A., NARDONE, A., MARSAN, P. A. & VALENTINI, A. 2003. Double muscling in Marchigiana beef breed is caused by a stop codon in the third exon of myostatin gene. *Mammalian Genome,* 14**,** 392-5.

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MILK

ATP-Binding Cassette, Sub-Family G, Member 2

Abbreviations: ABCG2

Genetic Mode: Additive

Royalty Fee: No

Trait Type: Milk

Breeds found in: Multiple beef and dairy breeds

General: Decreases milk fat (kg and %), protein (kg and %), and increases milk volume.

Common Ancestor: None identified

Clinical: Increase in milk fat, protein, and decrease in milk volume.

OMIA: Not available

Gene: ABCG2 (ATP-Binding Cassette, Sub-Family G, Member 2)

Genetic: 6:g.38027010A>C, c.1742A>C, p.Tyr581Ser, rs43702337

Flanking Sequence:

ATTTGTTTTTTGTAGATATTTTCAGGGCTGTTGGTAAATCTCAAAACCGTCGTGCCTTGGTTGTCATGGCTTCAATACTT
GAGCATTCCTCGATACGGCT**[A/C]**TGCGGTATGTTCTCCTTATCTGTCACCGTGCTGGTTCATTGTCCCCATGCTGGAA
ACAGCCAGAATAAAGCCTCTCATATCCTTGGCCATGAGCTGTGCA

COHEN-ZINDER, M., SEROUSSI, E., LARKIN, D. M., LOOR, J. J., EVERTS-VAN DER WIND, A., LEE, J. H., DRACKLEY, J. K., BAND, M. R., HERNANDEZ, A. G., SHANI, M., LEWIN, H. A., WELLER, J. I. & RON, M. 2005. Identification of a missense mutation in the bovine ABCG2 gene with a major effect on the QTL on chromosome 6 affecting milk yield and composition in Holstein cattle. *Genome Res,* 15, 936-44.

AcylCoA:Diacylglycerol Acyltransferase

Abbreviations: DGAT1 **Genetic Mode: Additive**

Royalty Fee: No **Trait Type: Milk**

Breeds found in: Multiple beef and dairy breeds

General: Increases fat yield, fat percentage, and protein percentage, while reducing milk yield and protein yield.

Common Ancestor: None identified

Clinical: The DGAT1 enzyme catalyzes the terminal step in triacylglycerol synthesis by conversion of diacylglycerol and fatty acyl CoA to triacylglycerol. The Lysine allele (K) affects the enzymatic activity of DGAT1 which results in an increase in this last step in triglyceride synthesis.

OMIA: Not available

Gene: DGAT1 (Diacylglycerol O-Acyltransferase 1)

Genetic: 14:g.11802265GC>AA, c.694GC>AA, p.Ala232Lys, rs473009810 and rs109326957

Flanking Sequence:

GGGCTGGGGCCACTGGGCTGCCACTTGCCTCGGGACCGGCAGGGGCTCGGCTCACCCCCGACCCGCCCCCTGCCGCT TGCTCGTAGCTTTGGCAGGTAAG**[GC/AA]**GGCCAACGGGGGAGCTGCCCAGCGCACCGTGAGCTACCCCGACAACCT GACCTACCGCGGTGAGGATCCTGCCGGGGGCTGGGGGGACTGCCCGGCGGC

GRISART, B., COPPIETERS, W., FARNIR, F., KARIM, L., FORD, C., BERZI, P., CAMBISANO, N., MNI, M., REID, S., SIMON, P., SPELMAN, R., GEORGES, M. & SNELL, R. 2002. Positional candidate cloning of a QTL in dairy cattle: identification of a missense mutation in the bovine DGAT1 gene with major effect on milk yield and composition. *Genome Res,* 12, 222-31.

Growth Hormone

Abbreviations: GH_2141, GH_2291, **Genetic Mode: Recessive**

Royalty Fee: No **Trait Type: Milk**

Breeds found in: Multiple beef and dairy breeds

General: Two alleles in the Growth Hormone gene have an effect on milk traits.

GH_2141: 'G' allele is associated with decreased milk protein yield and fat yield.

GH_2291: 'C' allele is associated with increased milk fat yield, fat percent, and protein percent.

Common Ancestor: None identified

Clinical: Growth Hormone is produced in the anterior pituitary gland and plays a critical role in the control of nutrient utilization, metabolism, lactation, fertility, and growth.

OMIA: Not available

Gene: GH1 (Growth Hormone 1)

GH_2141

Genetic: 19:g.48768916C>G, c.457C>G, p.Leu153Val, rs41923484

Flanking Sequence:

CCGTAGTTCTTGAGCAGCGCGTCGTCACTGCGCATGTTTGTGTCAAATTTGTCATAGGTCTGCTTGAGGATCTGCCCA
GCCCGGGGGGTGCCATCTTCCA**[C/G]**CTCCTGCCAAGGGAGGGAGAGACAGAGAGGCCGAAGGGCCCTCAGGAGC
AGCTCCCTCCTGCCCGCTCCATTTTCCACCCTCCCCTACAGGCTTGGAGAA

GH_2291

Genetic: 19:g.48768766A>C, c.607A>C, rs109191047

Flanking Sequence:

CAAATTTGACACAAACATGCGCAGTGACGACGCGCTGCTCAAGAACTACGGTCTGCTCTCCTGCTTCCGGAAGGACCT
GCATAAGACGGAGACGTACCTG**[A/C]**GGGTCATGAAGTGCCGCCGCTTCGGGGAGGCCAGCTGTGCCTTCTAGTTGC
CAGCCATCTGTTGTTTGCCCCTCCCCCGTGCCTTCCTTGACCCTGGAAG

MULLEN, M., BERRY, D., HOWARD, D., DISKIN, M., LYNCH, C., BERKOWICZ, E., MAGEE, D., MACHUGH, D. & WATERS, S. 2010. Associations between novel single nucleotide polymorphisms in the Bos taurus growth hormone gene and performance traits in Holstein-Friesian dairy cattle. *Journal of dairy science,* 93, 5959-5969.

Growth Hormone Receptor

Abbreviations: GHR_F279Y **Genetic Mode: Additive**

Royalty Fee: Yes **Trait Type: Milk**

Breeds found in: Multiple beef and dairy breeds

General: Increases milk, casein, and lactose yield and a decrease in protein yield and in fat yield.

Common Ancestor: None identified

Clinical: GHR plays a major role in the initiation and maintenance of lactation.

OMIA: Not available

Gene: GHR (Growth Hormone Receptor)

Genetic: 20:g.31909478T>A, c.836T>A, p.Phe279Tyr, rs385640152

Flanking Sequence:

AACAAAAAATGGAAACATGGACATTTGCTAAATAACTGGCAAAACATATCAGAGTAGGTTATATCACACTTACCTTTG
CTGTTTAGAAAATATGAGTAAA**[T/A]**ATAATGTCACTGCTAGCCCAAGTATTCCAAAGATAATAATTAAGAACCATGG
AAACTGGAAATCTGAAAAACACAAAAATAATATCTCACAGAACTATGA

BLOTT, S., KIM, J. J., MOISIO, S., SCHMIDT-KUNTZEL, A., CORNET, A., BERZI, P., CAMBISANO, N., FORD, C., GRISART, B., JOHNSON, D., KARIM, L., SIMON, P., SNELL, R., SPELMAN, R., WONG, J., VILKKI, J., GEORGES, M., FARNIR, F. & COPPIETERS, W. 2003. Molecular dissection of a quantitative trait locus: a phenylalanine-to-tyrosine substitution in the transmembrane domain of the bovine growth hormone receptor is associated with a major effect on milk yield and composition. *Genetics,* 163, 253-66.

Casein Beta

Abbreviations: CSN2_A1, A2, A3, B, C, E, F, G, H1, H2, I

Genetic Mode: Additive

Trait Type: Milk

Royalty Fee: Yes: A2

No: A1, A3, B, C, D, E, F, G, H1, H2, I

Breeds found in: Multiple dairy and beef breeds

General: Approximately 25-30% of cow's milk is beta-casein (ß-casein). There are several alleles of ß-casein, the most common of which are A1 and A2 – other types include A3, B, C, D, E, F, G, H1, H2, and I are rarer. The A1 allele is associated with increased percent fat and protein. The A2 allele has a positive impact milk yield and protein yield and some hypothesize A2 milk is heathier than A1 milk. The B allele is more favourable for rennet coagulation and cheese making. Casein Beta does have an interaction effect with Casein Kappa. For coagulation time and curd firmness having one 'B' allele for each gene produces the best result

Common Ancestor: None identified

Clinical: Some CSN2 alleles are determined by a single SNP, such as H1, while others are determined by multiple SNP, such as H2. It is thought that the A2 variant was the original variant with the A1 mutation originating approximately 5,000 to 10,000 years ago.

CSN2 Gene Position	Allele Variants and Amino Acid										
	A1	**A2**	**A3**	**B**	**C**	**E**	**F**	**G**	**H1**	**H2**	**I**
c.41	Arg								Cys		
c.52	Glu					Lys					
c.51	Glu				Lys						
c.82	His	Pro	Pro			Pro				Pro	Pro
c.87	Gln									Glu	
c.103	Leu								Ile		
c.108	Met									Leu	Leu
c.121	His		Gln								
c.137	Ser			Arg							
c.167	Pro						Leu				

CSN2 Protein Position	Allele Variants and SNP										
	A1	**A2**	**A3**	**B**	**C**	**E**	**F**	**G**	**H1**	**H2**	**I**
p.118	C								T		
p.154	G					A					
p.151	G				C						
p.245	A	C	C			C				C	C
p.259	C									G	
p.307	C								A		
p.322	A									C	C
p.363	C		A								
p.411	C			G							
p.500	C						T				

Tables adapted from Caroli et al., 2009

OMIA: Not available

Gene: CSN2 (Casein Beta)

Genetic: 6:G.87183158C>T, c.118C>T, p.Arg41Cys

Flanking Sequence:

CTATTAAATTTCTTCATTTTCTGATTTATGTTGACAAATAAGAATTTTTTTTAAAGCTAGACCTGATTTTATTTTTATTTTT
CCAAAGGAATCTATTACA**[C/T]**GCATCAATAAGGTAAAACCCTCATATTTAAATGTACATTTTTTTTAATTTCATGTTTG
ATTTTTATAAACAGCATTTCTTTATGTATTTTTTTTTTAACC

Genetic: 6:g.87183034A>G, c.151G>C, p.Glu51Lys

Flanking Sequence:

CCCTCATATTTAAATGTACATTTTTTTAAATTTCATGTTTGATTTTTATAAACAGCATTTCTTTATGTATTTTTTTTTTAACC
AGAAAATTGAGAAGTTTCAGAGT**[A/G]**AGGAACAGCAGCAAACAGAGGTAATTTGTTCACTATGAGTATATTTTGAG
AAGTATTATGAAACATAACACATAAAAAGATTTATAATAATTATGTTCAGTCT

Genetic: 6:g.87183031G>A, c.154G>A, p.Glu52Lys, rs721259074

Flanking Sequence:

TTAAATGTACATTTTTTTTAATTTCATGTTTGATTTTTATAAACAGCATTTCTTTATGTATTTTTTTTTTAACCAGAAAATT
GAGAAGTTTCAGAGTGAG**[G/A]**AACAGCAGCAAACAGAGGTAATTTGTTCACTATGAGTATATTTTGAGAAGTATTA
TGAAACATAACACATAAAAAGATTTATAATAATTATGTTCAGTCT

Genetic: 6:g.87181619C.A, c.245C>A, p.Pro82His, rs43703011

Flanking Sequence:

TCAAAGATTTGTTTTCCTTCTTTCCAGGATGAACTCCAGGATAAAATCCACCCCTTTGCCCAGACACAGTCTCTAGTCTA
TCCCTTCCCTGGGCCCATCC**[C/A]**TAACAGCCTCCCACAAAACATCCCTCCTCTTACTCAAACCCCTGTGGTGGTGCCGC
CTTTCCTTCAGCCTGAAGTAATGGGAGTCTCCAAAGTGAAGGAG

Genetic: 6:g.87181605C>G, C.259C>G, p.Gln87Glu

Flanking Sequence:

TCCTTCTTTCCAGGATGAACTCCAGGATAAAATCCACCCCTTTGCCCAGACACAGTCTCTAGTCTATCCCTTCCCTGGGC
CCATCCCTAACAGCCTCCCA**[C/G]**AAAACATCCCTCCTCTTACTCAAACCCCTGTGGTGGTGCCGCCTTTCCTTCAGCCT
GAAGTAATGGGAGTCTCCAAAGTGAAGGAGGCTATGGCTCCTAA

Genetic: 6:g.87181557C>A, c.307C>A, p.Leu103Ile

Flanking Sequence:

GACACAGTCTCTAGTCTATCCCTTCCCTGGGCCCATCCCTAACAGCCTCCCACAAAACATCCCTCCTCTTACTCAAACCC
CTGTGGTGGTGCCGCCTTTC**[C/A]**TTCAGCCTGAAGTAATGGGAGTCTCCAAAGTGAAGGAGGCTATGGCTCCTAAG
CACAAAGAAATGCCCTTCCCTAAATATCCAGTTGAGCCCTTTACTGA

Genetic: 6:g.87181542A>C, c.322A>C, p.Met108Leu, rs109299401

Flanking Sequence:

CTATCCCTTCCCTGGGCCCATCCCTAACAGCCTCCCACAAAACATCCCTCCTCTTACTCAAACCCCTGTGGTGGTGCCGC
CTTTCCTTCAGCCTGAAGTA**[A/C]**TGGGAGTCTCCAAAGTGAAGGAGGCTATGGCTCCTAAGCACAAAGAAATGCCCT
TCCCTAAATATCCAGTTGAGCCCTTTACTGAAAGCCAGAGCCTGAC

Genetic: 6:g.87181501C>A, c.363C>A, p.His121Gln, rs43703012

Flanking Sequence:

ACATCCCTCCTCTTACTCAAACCCCTGTGGTGGTGCCGCCTTTCCTTCAGCCTGAAGTAATGGGAGTCTCCAAAGTGAA
GGAGGCTATGGCTCCTAAGCA**[C/A]**AAAGAAATGCCCTTCCCTAAATATCCAGTTGAGCCCTTTACTGAAAGCCAGAG
CCTGACTCTCACTGATGTTGAAAATCTGCACCTTCCTCTGCCTCTGC

Genetic: 6:g.87181453C>G, c.411C>G, p.Ser137Arg

Flanking Sequence:

AGCCTGAAGTAATGGGAGTCTCCAAAGTGAAGGAGGCTATGGCTCCTAAGCACAAAGAAATGCCCTTCCCTAAATAT
CCAGTTGAGCCCTTTACTGAAAG**[C/G]**CAGAGCCTGACTCTCACTGATGTTGAAAATCTGCACCTTCCTCTGCCTCTGC
TCCAGTCTTGGATGCACCAGCCTCACCAGCCTCTTCCTCCAACTGTCA

Genetic: 6:g.87181364C>T, c.500C>T, p.Pro167Leu

Flanking Sequence:

TTTACTGAAAGCCAGAGCCTGACTCTCACTGATGTTGAAAATCTGCACCTTCCTCTGCCTCTGCTCCAGTCTTGGATGC
ACCAGCCTCACCAGCCTCTTC**[C/T]**TCCAACTGTCATGTTTCCTCCTCAGTCCGTGCTGTCCCTTTCTCAGTCCAAAGTCC
TGCCTGTTCCCCAGAAAGCAGTGCCCTATCCCCAGAGAGATATG

KEATING, A., SMITH, T., ROSS, R. P. & CAIRNS, M. 2008. A note on the evaluation of a beta-casein variant in bovine breeds by allele-specific PCR and relevance to β-casomorphin. *Irish Journal of Agricultural and Food Research***,** 99-104.

CAROLI, A., CHESSA, S. & ERHARDT, G. 2009. Invited review: Milk protein polymorphisms in cattle: Effect on animal breeding and human nutrition. *Journal of dairy science,* 92**,** 5335-5352.

Casein Kappa

Abbreviations: CSN3_A, A1, B, B2, C, D, E, F1, F2, G1, H, I, J

Genetic Mode: Additive

Trait Type: Milk

Royalty Fee: No

Breeds found in: Multiple beef and dairy breeds

General: The 'B' allele has a positive effect on coagulation time and cheese yield due to a firmer curd production. The 'G' and 'E' alleles are associated with less favourable coagulation properties. Kappa Casein does have an interaction effect with Beta Casein, for coagulation time and curd firmness having one 'B' allele for each gene produces the best result.

Common Ancestor: None identified

Clinical: The 'A' is the ancestral allele and other alleles are characterized by changes within the CSN3 gene in the table below.

CSN3 Gene Position	Allele Variants and SNP												
	A	**A1**	**B**	**B2**	**C**	**D**	**E**	**F1**	**F2**	**G1**	**H**	**I**	**J**
c.92	G								A				
c.342	T			C									
c.352	C									T			
c.353	G				A	A							
c.373	T											G	
c.467	C									T	T		
c.470	C		T	T	T								T
c.498	T							G					
c.506	A		C	C	C								C
c.506	A							T					
c.513	A	G											
c.521	T			C									
c.526	A						G						
c.564	T			C									
c.567	A		G	G	G								

Table adapted from Caroli et al., 2009

CSN3 Protein Position	Allele Variants and SNP												
	A	**A1**	**B**	**B2**	**C**	**D**	**E**	**F1**	**F2**	**G1**	**H**	**I**	**J**
p.31	Arg								His				
p.114	Thr			Thr									
p.118	Arg									Cys			
p.118	Arg				His	His							
p.125	Ser											Ala	
p.156	Thr									Ile	Ile		
p.157	Thr		Ile	Ile	Ile								Ile
p.166	Thr							Thr					
p.169	Asp		Ala	Ala	Ala								Ala
p.169	Asp							Val					
p.171	Pro	Pro											
p.174	Ile			Thr									
p.176	Ser						Gly						
p.188	Thr			Thr									
p.189	Ala		Ala	Ala	Ala								

Table adapted from Caroli et al., 2009

OMIA: Not available

Gene: CSN3 (Kappa Casein)

Genetic: 6:g.87390198G>A, c.92G>A, p.Arg31His

Flanking Sequence:

CTCTTGCGACCCCATAGATGGCAGCCCACTAGGCTCCCCAGTCCCTGGGATTCTCCAGGCAAGAAATAATACCATTCT
GCATAATTTATTTTTTTACAGC**[G/A]**CTGTGAGAAAGATGAAAGATTCTTCAGTGACAAAATAGCCAAATATATCCCAA
TTCAGTATGTGCTGAGTAGGTATCCTAGTTATGGACTCAATTACTAC

Genetic: 6:g.87390448T>C, c.342T>C, p.Thr114Thr

Flanking Sequence:

AATTATGCAAAGCCAGCTGCAGTTAGGTCACCTGCCCAAATTCTTCAATGGCAAGTTTTGTCAAATACTGTGCCTGCCA
AGTCCTGCCAAGCCCAGCCAAC**[T/C]**ACCATGGCACGTCACCCACACCCACATTTATCATTTATGGCCATTCCACCAAA
GAAAAATCAGGATAAAACAGAAATCCCTACCATCAATACCATTGCTA

Genetic: 6:g.87390458T>C, c.352C>T, p.Arg118Cys, rs110870535

Flanking Sequence:

GCCAGCTGCAGTTAGGTCACCTGCCCAAATTCTTCAATGGCAAGTTTTGTCAAATACTGTGCCTGCCAAGTCCTGCCAA
GCCCAGCCAACTACCATGGCA**[C/T]**GTCACCCACACCCACATTTATCATTTATGGCCATTCCACCAAAGAAAAATCAGG
ATAAAACAGAAATCCCTACCATCAATACCATTGCTAGTGGTGAGCC

Genetic: 6:g.87390459G>A , c.353G>A, p.Arg118His, rs716557965

Flanking Sequence:

CCAGCTGCAGTTAGGTCACCTGCCCAAATTCTTCAATGGCAAGTTTTGTCAAATACTGTGCCTGCCAAGTCCTGCCAAG
CCCAGCCAACTACCATGGCAC**[G/A]**TCACCCACACCCACATTTATCATTTATGGCCATTCCACCAAAGAAAAATCAGGA
TAAAACAGAAATCCCTACCATCAATACCATTGCTAGTGGTGAGCCT

Genetic: 6:g.87390479T>G, c.373T>G, p.Ser125Ala, rs43706475

Flanking Sequence:

TGCCCAAATTCTTCAATGGCAAGTTTTGTCAAATACTGTGCCTGCCAAGTCCTGCCAAGCCCAGCCAACTACCATGGCA
CGTCACCCACACCCACATTTA**[T/G]**CATTTATGGCCATTCCACCAAAGAAAAATCAGGATAAAACAGAAATCCCTACCA
TCAATACCATTGCTAGTGGTGAGCCTACAAGTACACCTACCATCGA

Genetic: 6:g.87390573C>T, c.467C>T, p.Thr156Ile, rs450402006

Flanking Sequence:

CATTTATCATTTATGGCCATTCCACCAAAGAAAAATCAGGATAAAACAGAAATCCCTACCATCAATACCATTGCTAGTG
GTGAGCCTACAAGTACACCTA**[T/C]**CATCGAAGCAGTAGAGAGCACTGTAGCTACTCTAGAAGCTTCTCCAGAAGTTA
TTGAGAGCCCACCTGAGATCAACACAGTCCAAGTTACTTCAACTGCG

Genetic: 6:g.87390576, c.470T>C, p.Ile157Thr, rs43703015

Flanking Sequence:

TTATCATTTATGGCCATTCCACCAAAGAAAAATCAGGATAAAACAGAAATCCCTACCATCAATACCATTGCTAGTGGTG
AGCCTACAAGTACACCTACCA**[T/C]**CGAAGCAGTAGAGAGCACTGTAGCTACTCTAGAAGCTTCTCCAGAAGTTATTG
AGAGCCCACCTGAGATCAACACAGTCCAAGTTACTTCAACTGCGGTC

Genetic: 6:g.87390604T>G, c.498T>G, p.Thr166Thr,

Flanking Sequence:

AAAATCAGGATAAAACAGAAATCCCTACCATCAATACCATTGCTAGTGGTGAGCCTACAAGTACACCTACCATCGAAG
CAGTAGAGAGCACTGTAGCTAC**[T/G]**CTAGAAGCTTCTCCAGAAGTTATTGAGAGCCCACCTGAGATCAACACAGTCC
AAGTTACTTCAACTGCGGTCTAAATACTCTAAGGAGACATCAAAGAAG

Genetic: 6:g.87390612C>A, c.506C>A, p.Ala169Asp, rs43703016

Flanking Sequence:

GATAAAACAGAAATCCCTACCATCAATACCATTGCTAGTGGTGAGCCTACAAGTACACCTACCATCGAAGCAGTAGAG
AGCACTGTAGCTACTCTAGAAG**[C/A]**TTCTCCAGAAGTTATTGAGAGCCCACCTGAGATCAACACAGTCCAAGTTACT
TCAACTGCGGTCTAAATACTCTAAGGAGACATCAAAGAAGACAACGCA

Genetic: 6:g.87390612C>A, c.506T>A, p.Val169Asp,

Flanking Sequence:

GATAAAACAGAAATCCCTACCATCAATACCATTGCTAGTGGTGAGCCTACAAGTACACCTACCATCGAAGCAGTAGAG
AGCACTGTAGCTACTCTAGAAG**[T/A]**TTCTCCAGAAGTTATTGAGAGCCCACCTGAGATCAACACAGTCCAAGTTACT
TCAACTGCGGTCTAAATACTCTAAGGAGACATCAAAGAAGACAACGCA

Genetic: 6:g.87390619A>G , c.513A>G, p.Pro171Pro, rs439304887

Flanking Sequence:

CAGAAATCCCTACCATCAATACCATTGCTAGTGGTGAGCCTACAAGTACACCTACCATCGAAGCAGTAGAGAGCACTG
TAGCTACTCTAGAAGCTTCTCC**[A/G]**GAAGTTATTGAGAGCCCACCTGAGATCAACACAGTCCAAGTTACTTCAACTG
CGGTCTAAATACTCTAAGGAGACATCAAAGAAGACAACGCAGGTAAAT

Genetic: 6:g.87390627T>C, c.521T>C, p.Ile174Thr

Flanking Sequence:

CCTACCATCAATACCATTGCTAGTGGTGAGCCTACAAGTACACCTACCATCGAAGCAGTAGAGAGCACTGTAGCTACT
CTAGAAGCTTCTCCAGAAGTTA**[T/C]**TGAGAGCCCACCTGAGATCAACACAGTCCAAGTTACTTCAACTGCGGTCTAA
ATACTCTAAGGAGACATCAAAGAAGACAACGCAGGTAAATAAGCAAAA

Genetic: 6:g.87390632A>G, c.526A>G, p.Ser176Gly, rs43703017

Flanking Sequence:

CATCAATACCATTGCTAGTGGTGAGCCTACAAGTACACCTACCATCGAAGCAGTAGAGAGCACTGTAGCTACTCTAGA
AGCTTCTCCAGAAGTTATTGAG**[A/C]**GCCCACCTGAGATCAACACAGTCCAAGTTACTTCAACTGCGGTCTAAATACTC
TAAGGAGACATCAAAGAAGACAACGCAGGTAAATAAGCAAAATGAAT

Genetic: 6:g.87390632A>G, c.564T>C, p.Thr188Thr

Flanking Sequence:

CTACCATCGAAGCAGTAGAGAGCACTGTAGCTACTCTAGAAGCTTCTCCAGAAGTTATTGAGAGCCCACCTGAGATCA
ACACAGTCCAAGTTACTTCAAC**[T/C]**GCGGTCTAAATACTCTAAGGAGACATCAAAGAAGACAACGCAGGTAAATAA
GCAAAATGAATAACAGCCAAGATTCATGGACTTATTAATAAAATCGTAA

Genetic: 6:g.87390673G>A, c.567G>A, p.Ala189Ala, rs110014544

Flanking Sequence:

CCATCGAAGCAGTAGAGAGCACTGTAGCTACTCTAGAAGCTTCTCCAGAAGTTATTGAGAGCCCACCTGAGATCAACA
CAGTCCAAGTTACTTCAACTGC**[G/A]**GTCTAAATACTCTAAGGAGACATCAAAGAAGACAACGCAGGTAAATAAGCA
AAATGAATAACAGCCAAGATTCATGGACTTATTAATAAAATCGTAACAT

CAROLI, A., CHESSA, S. & ERHARDT, G. 2009. Invited review: Milk protein polymorphisms in cattle: Effect on animal breeding and human nutrition. *Journal of dairy science,* 92**,** 5335-5352.

MATĚJÍČEK, A., MATĚJÍČKOVÁ, J., ŠTÍPKOVÁ, M., HANUŠ, O., GENČUROVÁ, V., KYSEĽOVÁ, J., NĚMCOVÁ, E., KOTT, T., ŠEFROVÁ, J. & KREJČOVÁ, M. 2008. Joint effects of CSN3 and LGB genes on milk quality and coagulation properties in Czech Fleckvieh. *Czech J. Anim. Sci,* 53**,** 246-252.

Lactoglobulin Beta

Abbreviations: LBG_ A, B, C, D, H, I, J, W **Genetic Mode: Additive**

Royalty Fee: No **Trait Type: Milk**

Breeds found in: Multiple beef and dairy breeds

General: Lactoglobulin Beta is the major milk whey protein in cattle and has 8 alleles: A, B, C, D, H, I, J, and W. The 'B' allele is the ancestral allele, other alleles and their corresponding SNPs at various positions on the LGB gene are listed below. The 'B' allele is more favourable for rennet coagulation and the cheese making quality of milk.

An allele (-215C>A) 215 nucleotides upstream of the gene's translation initiation is associated with lower LGB content in milk which results in lower whey protein percent and casein number percent.

Common Ancestor: None identified

Clinical: Casein Kappa does have an interaction effect with Casein Beta. For coagulation time and curd firmness having one 'B' allele for each gene produces the best result. LGB does have alleles E, F, and G but those are present only in *Bos grunniens,* and *Bos javanicus* species.

LGB Gene Position	Allele Variants and SNP							
	B	**A**	**C**	**D**	**H**	**I**	**J**	**W**
181	G			C				
214	A							C
225	G		T					
237	C	T						
239	G	A			A			
258	G				C			
312	T	C						
371	A					G		
401	C	T			T			
425	C						T	

LGB Protein Position	Allele Variants and SNP							
	B	**A**	**C**	**D**	**H**	**I**	**J**	**W**
61	Glu			Gln				
72	Ile							Leu
75	Gln		His					
79	Asn	Asn						
80	Gly	Asp			Asp			
86	Lys				Asn			
104	Asn	Asn						
124	Glu					Gly		
134	Ala				Val			
142	Pro						Leu	

Tables adapted from Caroli et al., 2009

OMIA: Not available

Gene: LGB (Beta-Lactoglobulin) also referred to as PAEP (Progestagen-Associated Endometrial Protein)

Genetic: 11:g.103301489C>A. c.-215C>A

Flanking Sequence:

TTCCTGGCGCTGGCAGCCAGCCTGGACCCAGAGCCTGGACACCCCCTGCGCCCCCACTTCTGGGGCGTACCAGGAAC
CGTCCAGGCCCAGAGGGGGCCTT**[C/A]**CTGCTTGGCCTCGAATGGAAGAAGGCCTCCTATTGTCCTCGTAGAGGAAG
CAACCCCAGGGCCCAAGGATAGGCCAGGGGGGATTCGGGGAACCGCGTGG

Genetic: 11:g.103302553G>C, c.181G>C, p.Glu61Gln, rs211077340

Flanking Sequence:

CCCTCCCCAGGTGGCGGGGACTTGGTACTCCTTGGCCATGGCGGCCAGCGACATCTCCCTGCTGGACGCCCAGAGTG
CCCCCCTGAGAGTGTATGTGGAG**[G/C]**AGCTGAAGCCCACCCCTGAGGGCGACCTGGAGATCCTGCTGCAGAAATGG
TGGGCGTCCCCCCCAAAAAAAGCATGGAACCCCCACTCCCCAGGGATATG

Genetic: 11:g.103302586, c.214A>C, p.Ile72Leu, rs209252315

Flanking Sequence:

GGCCATGGCGGCCAGCGACATCTCCCTGCTGGACGCCCAGAGTGCCCCCCTGAGAGTGTATGTGGAGGAGCTGAAG
CCCACCCCTGAGGGCGACCTGGAG**[A/C]**TCCTGCTGCAGAAATGGTGGGCGTCCCCCCCAAAAAAAGCATGGAACCC
CCACTCCCCAGGGATATGGACCCCCCCGGGGTGGGGTGCAGGAGGGACCAG

Genetic: 11:g.103302597G>T, c.225G>T, p.Gln75His, rs210096472

Flanking Sequence:

CCAGCGACATCTCCCTGCTGGACGCCCAGAGTGCCCCCCTGAGAGTGTATGTGGAGGAGCTGAAGCCCACCCCTGAG
GGCGACCTGGAGATCCTGCTGCA**[G/T]**AAATGGTGGGCGTCCCCCCCAAAAAAAGCATGGAACCCCCACTCCCCAGG
GATATGGACCCCCCCGGGGTGGGGTGCAGGAGGGACCAGGGCCCCAGGGC

Genetic: 11:g.103303473C>T, c.237C>T, p.Asn79Asn, rs110180463

Flanking Sequence:

CAGCCCCTCCTGGGGCCGCCTTCTGCCCCTGGCCCTCAGTTCATCCTGATGAAAATGGTCCATGCCCGTGGCTCAGAA
AGCAGCTGTCTTTCAGGGAGAA**[C/T]**GGTGAGTGTGCTCAGAAGAAGATCATTGCAGAAAAAACCAAGATCCCTGCG
GTGTTCAAGATCGATGGTGAGTGCTGGGTCCCCAGGGGACGCCCACCAC

Genetic: 11:g.103303475G>A, c.239G>A, p.Gly80Asp, rs110180463

Flanking Sequence:

GCCCCTCCTGGGGCCGCCTTCTGCCCCTGGCCCTCAGTTCATCCTGATGAAAATGGTCCATGCCCGTGGCTCAGAAAG
CAGCTGTCTTTCAGGGAGAACG**[G/A]**TGAGTGTGCTCAGAAGAAGATCATTGCAGAAAAAACCAAGATCCCTGCGGT
GTTCAAGATCGATGGTGAGTGCTGGGTCCCCAGGGGACGCCCACCACCC

Genetic: 11:g.103303494G>C, c.258G>C, p.Lys86Asn

Flanking Sequence:

TCTGCCCCTGGCCCTCAGTTCATCCTGATGAAAATGGTCCATGCCCGTGGCTCAGAAAGCAGCTGTCTTTCAGGGAGA
ACGGTGAGTGTGCTCAGAAGAA**[G/C]**ATCATTGCAGAAAAAACCAAGATCCCTGCGGTGTTCAAGATCGATGGTGAG
TGCTGGGTCCCCAGGGGACGCCCACCACCCCCCAGGGACTGTGGGCAGG

Genetic: 11:g.103304668T>C, c.312C>T, p.Asn104Asn, rs110641366

Flanking Sequence:

GGGGAGCCCCGCTGGTTGTGGGGGGCGCTGGGGGCTGACCAGAAACCCCCCTCCTGCTGGAACTCACTTTCCTCCTG
TCTTGATCTCTACCAGCCTTGAA**[C/T]**GAGAACAAAGTCCTTGTGCTGGACACCGACTACAAAAAGTACCTGCTCTTCT
GCATGGAGAACAGTGCTGAGCCCGAGCAAAGCCTGGTCTGCCAGTGCC

Genetic: 11:g.103304727A>G, c.371A>G, p.Glu124Gly

Flanking Sequence:

GAACTCACTTTCCTCCTGTCTTGATCTCTACCAGCCTTGAACGAGAACAAAGTCCTTGTGCTGGACACCGACTACAAAA
AGTACCTGCTCTTCTGCATGG**[A/G]**GAACAGTGCTGAGCCCGAGCAAAGCCTGGTCTGCCAGTGCCTGGGTGGGTGC
CAACCCTGGCTGCCCAGGGAGACCAGCTGTGTGGTCCTCGCTGCAACG

Genetic: 11:g.103304757T>C, c.401T>C, p.Val134Ala, rs109625649

Flanking Sequence:

CCAGCCTTGAACGAGAACAAAGTCCTTGTGCTGGACACCGACTACAAAAAGTACCTGCTCTTCTGCATGGAGAACAGT
GCTGAGCCCGAGCAAAGCCTGG**[T/C]**CTGCCAGTGCCTGGGTGGGTGCCAACCCTGGCTGCCCAGGGAGACCAGCT
GTGTGGTCCTCGCTGCAACGGGGCCGGGGGGGACGGTGGGAGCAGGGAGC

Genetic: 11:g.103305456C>T, c.425C>T, p.Pro142Leu

Flanking Sequence:

GGCCAAGGGGGAAGGGCAGGTGTGCTGGAGGCCAAGGCAGACCTGCACACCACCCTGGAGAGCAGGGGTTGACCC
CGTCCCGGCCCCACAGTCAGGACCC**[C/T]**GGAGGTGGACGACGAGGCCCTGGAGAAATTCGACAAAGCCCTCAAGG
CCCTGCCCATGCACATCCGGCTGTCCTTCAACCCAACCCAGCTGGAGGGTGAG

BRAUNSCHWEIG, M. H. & LEEB, T. 2006. Aberrant low expression level of bovine beta-lactoglobulin is associated with a C to A transversion in the BLG promoter region. *Journal of dairy science,* 89**,** 4414-9.

CAROLI, A., CHESSA, S. & ERHARDT, G. 2009. Invited review: Milk protein polymorphisms in cattle: Effect on animal breeding and human nutrition. *Journal of dairy science,* 92**,** 5335-5352.

COLOUR

Dun

Abbreviations: DUN

Genetic Mode: Recessive and multi-gene interaction

Royalty Fee: No

Trait Type: Colour

Breeds found in: Dexter

General: The Dun coat colour allele (b) causes dilution of black hair pigment (eumelanin). The resulting hair colour is diluted to shades of dark brown to golden. Red hair pigment (phaeomelanin) is not diluted by this allele. There is an interaction with the MC1R gene as shown below

Common Ancestor: None identified

Clinical: In Dexter lineages the Dun has an interesting interplay with the MC1R black colour alleles as shown below. For a Dexter to be Dun coloured it must have one or two copies of the Black allele (E) at the MC1R gene and be homozygous 'b' at the TYRP1 gene. So an EE bb, EE+ bb, or Ee bb animal will be Dun. If the Dexter animal is E+e, or ee for MC1R it also be red coloured regardless of the Dun allele. MC1R E+E+ animals are usually red, but not always.

MC1R	TYRP1	Colour
EE	BB	**Black**
EE	Bb	**Black**
EE	bb	Dun
Ee	BB	**Black**
Ee	Bb	**Black**
Ee	bb	Dun
EE+	BB	**Black**
EE+	Bb	**Black**
EE+	bb	Dun
E+E+	BB	Usually Red
E+E+	Bb	Usually Red
E+E+	bb	Usually Red
E+e	BB	Red
E+e	Bb	Red
E+e	bb	Red
ee	BB	Red
ee	Bb	Red
ee	bb	Red

OMIA: 001249-9913

Gene: TYRP1 (Tyrosinase-Related Protein 1)

Genetic: g.8:31711945G>A, c.1300G>A, p.Asn434Asp

Flanking Sequence:

TGAACTTCGTAAGTATAGCCCAGGTTGTCTGGAGCAGTAACAAACATTTCTATGTTGGTAACTGGAGGCCAAAATGGT
ACCATATTGTATTGTCTGTTAT**[G/A]**TCCAATAGGGGCATTTTCCAGTGGATATGTGGATATATCTAAAATATGTCAAA
GACACCTTGTTAATAGACATAATCAGTTTGTATTAATATATTATTAT

BERRYERE, T. G., SCHMUTZ, S. M., SCHIMPF, R. J., COWAN, C. M. & POTTER, J. 2003. TYRP1 is associated with dun coat colour in Dexter cattle or how now brown cow? *Anim Genet,* 34, 169-75

MC1R

Abbreviations: MC1R_Ed, Ebr, E+, e **Genetic Mode: Recessive**

Royalty Fee: No **Trait Type: Colour**

Breeds found in: Multiple breeds including Angus, Brown Swiss, Holstein, Highland, and Jersey

General: The four alleles of the MC1R gene are dominant black (MC1R_Ed), Black/Red (MC1R_Ebr), wild type red (MC1R_E+) and recessive red (MC1R_e). Dominant black (Ed) is dominant to the other three alleles and animals with Ed are black and white. Black/Red, also known as Telstar, (Ebr) results in red colour at birth which changes to black at a young age. E+E+ cattle can be almost any colour since other genes take over dictating what coat colour pigments are produced. Two copies of the recessive red (e) allele result in red colour. The order of dominance is Ed>Ebr>E+>e.

Common Ancestor: None identified

Clinical: The MC1R gene controls black and red pigment production in cattle. Holstein cattle have another allele, Dominant Red, in the COPA gene, which overrides MC1R and produces dominant red pigment.

If an animal is homozygous for both the Ed and e alleles it is considered to be homozygous ee for its phenotype. This is because the e allele causes a loss of gene function via a deletion. This deletion causes a frameshift and a premature stop codon at amino acid 15.

OMIA: 001199-9913

Gene: MC1R (Melanocortin 1 Receptor (Alpha Melanocyte Stimulating Hormone Receptor))

MC1R_E+ is the ancestral/normal allele

MC1R_Ed

Genetic: g.18:14757910T>C, c.296T>C, p.Leu99Pro, rs109688013

Flanking Sequence:
AACCGCAACCTGCACTCCCCCATGTACTACTTTATCTGCTGCCTGGCTGTGTCTGACTTGCTGGTGAGCGTCAGCAACG
TGCTGGAGACGGCAGTCATGC**[T/C**]GCTGCTGGAGGCCGGTGTCCTGGCCACCCAGGCGGCCGTGGTGCAGCAGCT
GGACAATGTCATCGACGTGCTCATCTGCGGATCCATGGTGTCCAGCCTC

MC1R_e

Genetic: g.18:14757924delG, c.310delG, p.Gly104ValfsX53, rs110710422

Flanking Sequence:
CTCCCCCATGTACTACTTTATCTGCTGCCTGGCTGTGTCTGACTTGCTGGTGAGCGTCAGCAACGTGCTGGAGACGGC
AGTCATGCTGCTGCTGGAGGCC**[G/-]**GTGTCCTGGCCACCCAGGCGGCCGTGGTGCAGCAGCTG GACAATGTC
ATCGACGTGCTCATCTGCGGATCCATGGTGTCCAGCCTCTGCTTCCTGGGTGC

KLUNGLAND, H., VAGE, D. I., GOMEZ-RAYA, L., ADALSTEINSSON, S. & LIEN, S. 1995. The role of melanocyte-stimulating hormone (MSH) receptor in bovine coat color determination. *Mamm Genome,* 6**,** 636-9.

PMEL17 gene (Multiple mutations in the PMEL17 gene affect coat colour)

PMEL17_delTTC

Abbreviations: PMEL17_delTTC, PMEL17_3del, Dilutor 3, Silver Char Dilutor 2

Genetic Mode: Semi-Dominant

Trait Type: Colour

Royalty Fee: No

Breeds found in: Multiple breeds including Charolais, Hereford, Highland, Galloway, and Simmental

General: The PMEL17_delTTC allele causes dilution coat colours such as dun, silver dun, yellow, and cream based on an interaction with the MC1R gene. The resulting colour from the PMEL and MC1R interaction is listed below.

Common Ancestor: None identified

Clinical: Dilution may be caused by the inhibited production of the black pigment eumelanin. The affected offspring will have a red, charcoal, or chocolate coloured coat (depends on MC1R and other genes) and variable degrees of hypotrichosis. Any area of white hair colour will have normal hair patterns.

Coat colour	*MC1R*	*PMEL_delTTC*	Photo
Red	E^+/e	+/+	TR
	e/e	+/+	
Yellow	E^+/e	+/del	MR
	e/e	+/del	
White/cream	*e/e*	del/del	BR
	E^+/e	del/del	
Black	E^D/E^D	+/+	TL
	E^D/E^+	+/+	
	E^D/e	+/+	
Dun	E^D/E^D	+/del	ML
	E^D/E^+	+/del	
	E^D/e	+/del	
Silver dun	E^D/E^+	del/del	BL
	E^D/e	del/del	

Photographs, MC1R and PMEL17_delTTC genotypes of Highland cattle exhibiting distinct coat colours. The ancestral/normal allele is designated by '+'. Photo location: T=top, M=middle, B=bottom, L=left, R=right. Table and photos adapted from Schmutz & Dreger 2013

OMIA: 001545-9913

Gene: PMEL17 (Premelanosome Protein)

Genetic: 5:g.57669913_57669915delTTC, c.50_52delTTC,p.Leu19del, rs385468954

Flanking Sequence:

TTTTAGGGAGAGAAAAACCAGAGCAGGTGTGCAACCCCAAATTCACACTTGTTCATGTCCAACATCCCACACTCACCTT
CTGTGGTCCCTMCAGCCAG**[-/CTT]**AACACCCATCAGAGCCACATGGAGAAGGTATTTTCTCAGCACCAGATC
CATCCTGTTCTTCCTTCCAGCAACCAAAGACTCTGGGGCATTGGACAA

JOLLY, R. D., WILLS, J. L., KENNY, J. E., CAHILL, J. I. & HOWE, L. 2008. Coat-colour dilution and hypotrichosis in Hereford crossbred calves. *N Z Vet J,* 56, 74-7.

SCHMUTZ, S. M. & DREGER, D. L. 2013. Interaction of MC1R and PMEL alleles on solid coat colours in Highland cattle. *Anim Genet,* 44, 9-13.

PMEL17_64G_A

Abbreviations: PMEL17_64G_A, SD1, Silver Char Dilutor 1

Genetic Mode: Additive

Trait Type: Colour

Royalty Fee: No

Breeds found in: Charolais

General: This allele causes coat colour dilution. Animals that are homozygous 'A' for the PMEL17_64G>A allele are white coloured while heterozygous animals are an intermediate colour: light grey, dark grey, light red, or dark red, brown, or yellow depending on the animal's base coat colour.

Common Ancestor: None identified

Clinical: PMEL17_64G>A causes dilution of the eumelanin (black) and phaeomelanin (red) pigments in coat colour.

Examples of coat colour dilutions from PMEL17_64G>A from Gutierre-Gil et al., 2007.

OMIA: 001545-9913

Gene: PMEL17 (Premelanosome Protein)

Genetic: 5:g.57669926G>A, c.64G>A, p.Gly22Arg, rs718553050

Flanking Sequence:

TGCCCCAGAGTCTTTGGTTGCTGGAAGGAAGAACAGGATGGATCTGGTGCTGAGAAAATACCTTCTCCATGTGGCTCT
GATGGGTGTTCTTCTGGCTGTA**[G/A]**GGACCACAGAAGGTGAGTGTGGGATGTTGGACATGAACAAGTGTGAATTTG
GGGTTGCACACCTGCTCTGGTTTTTCTCTCCCTAAAATGGAAGATATCA

GUTIERREZ-GIL, B., WIENER, P. & WILLIAMS, J. L. 2007. Genetic effects on coat colour in cattle: dilution of eumelanin and phaeomelanin pigments in an F2-Backcross Charolais x Holstein population. *BMC Genet,* 8, 56.

HECHT, B. C. 2006. Sequence Analysis of PMEL17 as Candidate Gene for Causing Rat-Tail Syndrome in Cattle.

JOLLY, R. D., WILLS, J. L., KENNY, J. E., CAHILL, J. I. & HOWE, L. 2008. Coat-colour dilution and hypotrichosis in Hereford crossbred calves. *N Z Vet J,* 56, 74-7.