Understanding Genetics

and

Complete Genetic Disease and Trait Definition

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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).

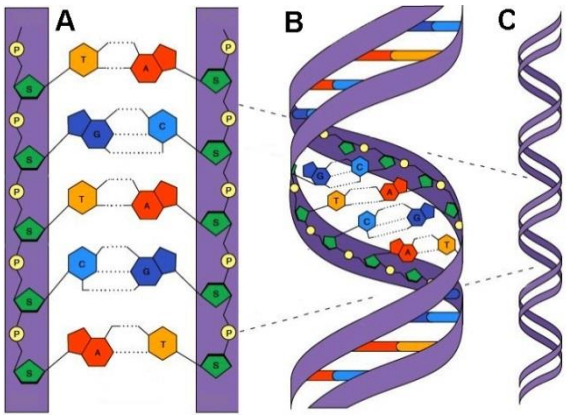


Figure 1:
A- If you were to zoom in, untwist the double helix, and flatten it out, it would look like this. Notice that the nucleotides in the centre are paired up, and the sugar and phosphate backbone, highlighted in purple, are on either side. This is what makes up every part of all living things.
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 and 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.

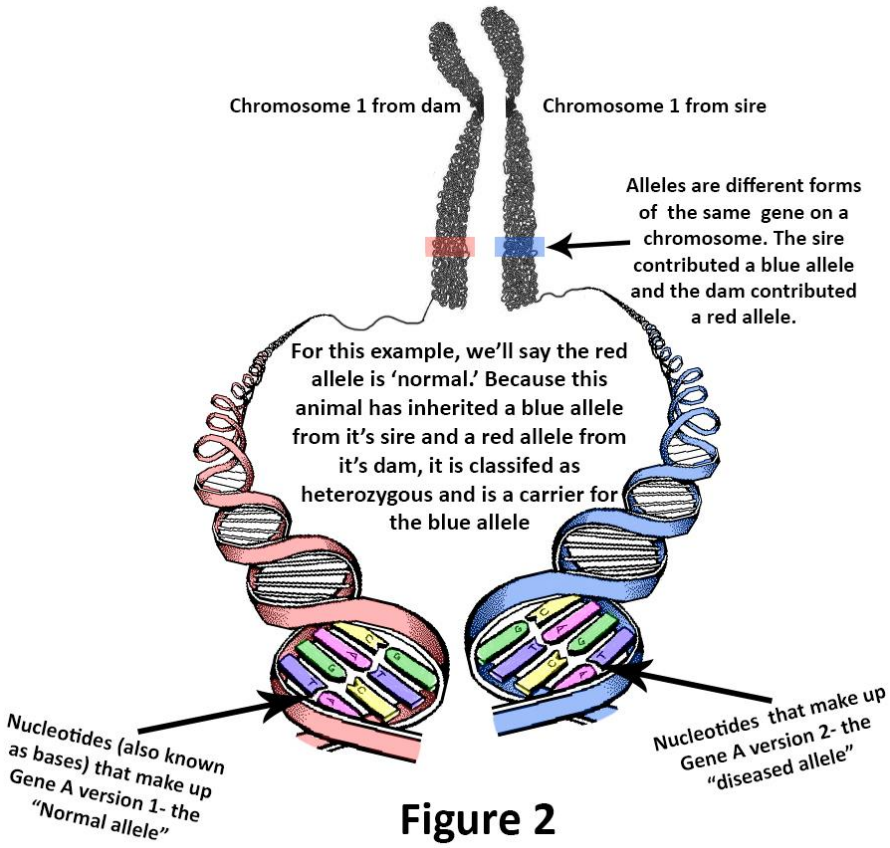


Figure 2

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

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

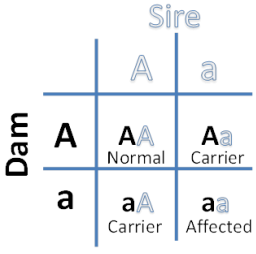
4. Mating a **carrier** to **carrier** results in a 25% chance of having an affected calf, a 50% chance of having a carrier calf, and a 25% chance of having a normal calf born.

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

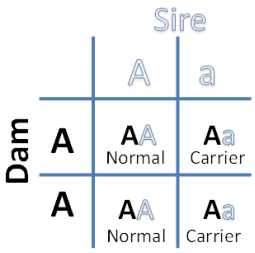
6. Mating a **homozygous** to **homozygous** results in a 100% chance of having an affected calf born

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:

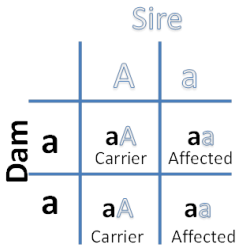
Carrier sire X Carrier dam. How do we know they are both carriers? When looking at the gene designations at the top of the squares, they have one copy of the normal allele (**A**) and one copy of the affected allele (**a**).



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

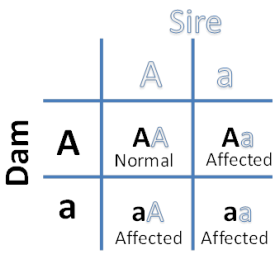
4. Mating a **carrier** to **carrier** results in a 75% chance that the calf born will be affected and a 25% chance that it will be normal.

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

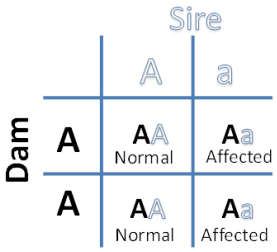
6. Mating a **homozygous** to **homozygous** results in a 100% chance of having an affected homozygous calf born

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

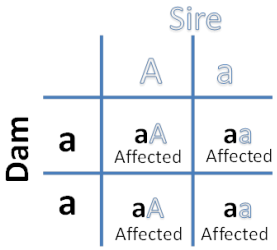
Carrier sire (Aa) X Carrier dam (Aa)



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.

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. Breed specific alleles will be in parentheses.

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

Gene: The gene symbol and name where the mutation lies in

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: g.X:Y R>A where 'g' denotes genome, 'X' is the chromosome, '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

IDB Probe: The probe ID for the trait on the IDB chip. Multiple IDB probes are designed for each trait allele. Probe IDs for other chips are included as well

Flanking Seq: Flanking DNA sequence around the alleles in brackets. 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**, **IDB Probe**, **Flanking Sequence**, and **Reference** information might not be provided or be minimal

Traits are grouped by the following:

1) Lethal or Unwanted: Alleles that either result in mortality or have a negative economic effect

2) Beneficial: Alleles that are economically beneficial

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

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

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

Traits on the IDB

LETHAL

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

UNWANTED

1. Bovine Leukocyte Adhesion Deficiency
2. Congenital Myoclonus
3. Crooked Tail Syndrome
4. Dystrophic Epidermolysis Bullosa
5. Hypotrichosis KRT71
6. Mulefoot
7. Rat-tail Syndrome
8. Protoporphyria
9. Pseudomyotonia
10. RNF11 Growth Retardation
11. Stat1
12. Stat5A

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 967 **Genetic Mode: Recessive**

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

Breeds found in: Angus (AM_961), Murray Grey (AM_961), Galloway (AM_662)

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.

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

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

AM_662

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

IDB probe: IDBv20700001524, IDBv20700001525, IDBv20700001526, IDBv20700001527, IDBv207000015248

Flanking Sequence (AM_662)**:**

CCGGTCCCTTATGCATCCTGCCCTCTCTTGTTCTCCCATCCCACTCGTCATCCCTCCCCATCTCCAGATGGGTTTTGA
CGGCTTCTTCTTTGGAC[G/A]CCTGGATTATCAAGACAAGAAGGTGCGGAAAAAGACGCTGCAGATGGAGCAGG
TGTGGCGGGCCAGCACCAGCCTGAAACCTCCCACTGCCGACC

AM_961

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

IDB probe: IDBv20700001529, IDBv20700001530 , IDBv20700001531, IDBv20700001532, IDBv20700001533

Flanking Sequence (AM_961)**:**

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.

Beta Mannosidosis

Abbreviations: BM

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Lethal

Breeds found in: Salers

General: Affected calves are hypothyroid, 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.

Gene: MANBA (Mannosidase Beta A)

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

IDB probe: IDBv20600001131, IDBv20600001132, IDBv20600001133, IDBv20600001134, IDBv20600001135

Flanking Sequence:

CCATCCCCATGGAAAAGAAATGCAAAAAAGCAAAATGGCTGTCTGAGGAGGACTTACAAATAGCTGTGAAAAGAAG
AGAAGTGAAAAGCAAAGGAGAAAA[G/A]GAAAGATATAAGCATCTGAATACAGAGTTCCAAAGAATAGCAAGGAGA
GATAAGAAAGCCTTCCTCAGCAATCGATGCAAAGAAATAAAGGAAAACAACA

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: Holstein-Friesian

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

Gene: FANCI (Fanconi anemia complementation group I)

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

IDB Probe: IDBv22100003530, IDBv22100003531, IDBv22100003532, IDBv22100003533, IDBv22100003534

Flanking Sequence:

TGTCACATACATAAATGTAAAATGGTGCAGCCACTTTGGAAAATAATTTGTCAGTTTCTTAAAAAGTTAAGCACACACC
TATCTTACGGTACACCCATTC[CACTCTTAGGTATTTAC…3,329bp….AAATTTGCAGGAAATGGT/-]CACCTTTCTATCC
GTGTCCTCCATCTGTTCAGTTCTTCTCCCCCAGTAGCTAAATATCTTTTAGTGTCTTGTGTAAAGAATTCTTTTATTCCTG
TACAGC

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

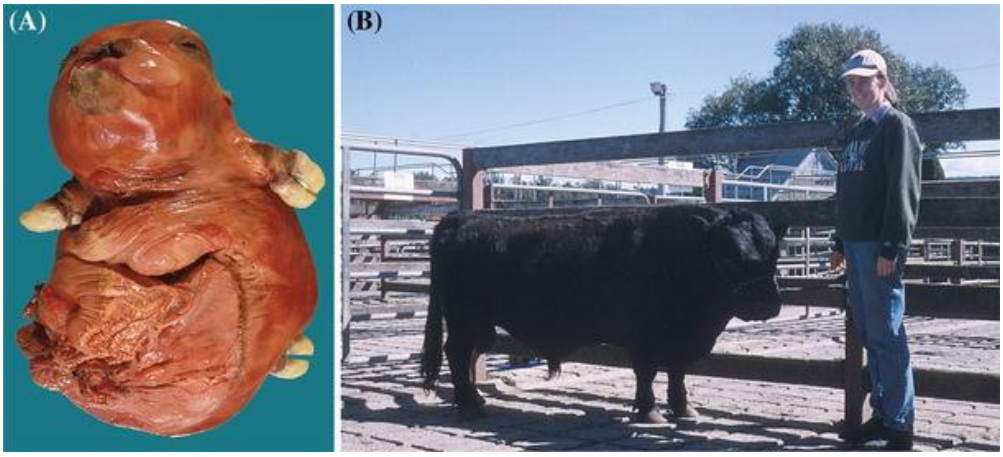
Breeds found in: Dexter

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

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

IDB Probe: IDBv22100003525, IDBv22100003526, IDBv22100003527, IDBv22100003528, IDBv22100003529

Flanking Sequence:

ATCGGGGAGGAGACGACTGCAATCCCAGGCTTCACCGTTGAGCCAGAAAACAAGACGGAATGGGAACTTGCCTACA
CCCCAGCGGGCACTTTGCCACTAC[-/GGCA]CAGGTCCGTCCGGGCTCTCCTGCATGTCCTGCTGCCTCCCTGGG
CCAGGGTGTGGCCTGGAAGGGGGGAGGAGGAAGTGTTCTCTCCCTGGGACCCGTGA

BD2

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

IDB Probe: IDBv22100003521, IDBv22100003522, IDBv22100003523, IDBv22100003524

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.

Citrullinaemia

Abbreviations: CT

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Lethal

Breeds found in: Holstein-Friesian

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.

Gene: ASS1 (Argininosuccinate Synthase 1)

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

IDB Probe: IDBv21100001911, IDBv21100001912, IDBv21100001913, IDBv21100001914, IDBv21100001915

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**.**

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

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

IDB Probe: IDBv22500003750, IDBv22500003751, IDBv21100001916, IDBv21100001917, IDBv21100001918

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.

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

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

IDB Probe: IDBv22900003918, IDBv22900003919, IDBv21100001919, IDBv21100001920, IDBv21100001921

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

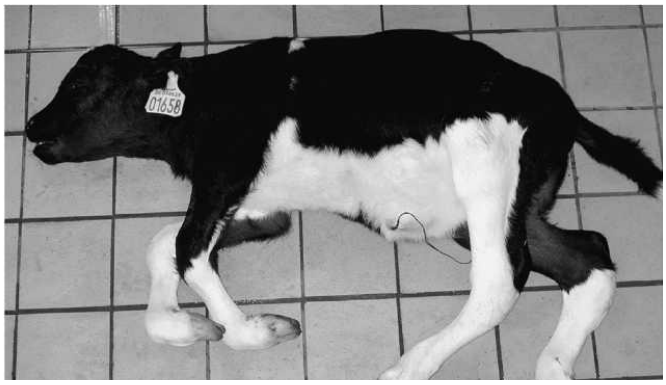
Trait Type: Lethal

Breeds found in: Holstein-Friesian

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 thoracici 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

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

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

IDB Probe: IDBv20300000706, IDBv20300000707, IDBv20300000708, IDBv20300000709, IDBv20300000710

Flanking Sequence:

TAAACTTGTGTTGTTTCTTTTTGTTCAGTGGCCCTCAGATTCTCAAGAGCTTAATTCTAAGGAACTTTCAGCTGGCTCAC
AATTTGTAGGTCTCATGGCA[G/T]TTCTCACAGCATGTTTTTCCAGTGGCTTTGCTGGGGTTTACTTTGAGAAAATCTTA
AAAGAAACCAAACAATCAGTGTGGATAAGAAACATTCAACTTGG

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: Holstein, Friesian, 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 UMPS levels that causes an increase of orotic acid in the milk and urine

Gene: UMPS (Uridine Monophosphate Synthetase)

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

IDB Probe: IDBv20100000193, IDBv20100000194, IDBv20100000195, IDBv20100000196, IDBv20100000197

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: Holstein-Friesian

General: Affected calves are aborted during in pregnancy.

Common Ancestor: Pawnee Farm Arlinda Chief,

Clinical:

Gene: APAF1 (Apoptotic Peptidase Activating Factor 1)

Genetic: g.5:6315040C>T, c.1741C>T, p.Gln581X, rs448942533

IDB Probe: IDBv20500000940, IDBv20500000941, IDBv20500000942, IDBv20500000943, IDBv20500000944

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.

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: Holstein-Friesian

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

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

Clinical:

Gene: SMC2 (Structural Maintenance Of Chromosomes 2)

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

IDB Probe: IDBv20800001678, IDBv20800001679, IDBv20800001680, IDBv2080000181, IDBv20800001682

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: Holstein-Friesian

General: Affected calves homozygous are aborted early in pregnancy.

Common Ancestor: Besne Buck

Clinical:

Gene: GART (Phosphoribosylglycinamide Formyltransferase)

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

IDB Probe: IDBv20100000001, IDBv20100000002, IDBv20100000003, IDBv20100000004, IDBv20100000005

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, Simmental

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

Common Ancestor: None identified

Clinical: This disease causes generalized seizure disorder, neurologic, Parkinson's like locking up syndrome. Environmental stresses such as temperature or increased physical handling can bring out the seizures.

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

Gene: Confidential genomic defect

Genetic: Confidential genomic defect

IDB Probe: 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.

Gene: CWC15 (Spliceosome-Associated Protein CWC15 Homolog)

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

IDB Probe: IDBv21500002145, IDBv21500002146, IDBv21500002147, IDBv21500002148, IDBv21500002149

Flanking Sequence:

AATTGTCTTCCATTACTACAGCTGTGTGTTTTTTAGAAGTGACTTTGCCTTGTCTTGTTTCTACTTTAGACAGACCACTCA
GGATGCCCCTGAAGAGGTT[C/T]GAAACCGTGACTTCAGGAGAGAGTTGGAGGAGAGAGAGAGAGCTGCTGCAAGA
GAAAAAAACAGAGATCGGCCAACCCGAGGTACCAATACTATCTTAGA

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_SH

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Lethal

Breeds found in: Shorthorn

General: Some affected calves are stillborn, those born alive look normal but exhibit mental disorders within 1 day. Their condition will rapidly deteriorate with ataxia, sweet smelling urine, an inability to walk , and death within 96 hours after birth.

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 a-keto acids and their precursors: valine, leucine and isoleucine.

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

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

IDB Probe: IDBv2UN00004128, IDBv2UN00004129, IDBv2UN00004130, IDBv2UN00004131, IDBv2UN00004132

Flanking Sequence:

GTAATGGAGGCCTTTGAGCAGGCTGAGCGGAAGCTGAAGCCCAACCCCAGCTTGATCTTCTCGGACGTGTATCAGGAGATGC[T/C]TGCCCAGCTCCGCAAGCAGCAGGAGTCTCTGGCACGTCACCTCCAGACCTATGGTGAACACTACCCGCTGGACCACTTCGAGAAG

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.

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.

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

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

IDB Probe: IDBv22900003925, IDBv22900003926, IDBv22900003927, IDBv22900003928, IDBv22900003929

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 may be stillborn or die soon after birth. Those born alive might have an enlarged head, they will likely show depression, weakness, poor suckle reflex, droopy ears and head, head tremors, and convulsions.

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.

Neuropathic hydrocephalus affected calf from Kaiser 2010

Gene: Confidential genomic defect

Genetic: Confidential genomic defect

IDB Probe: 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

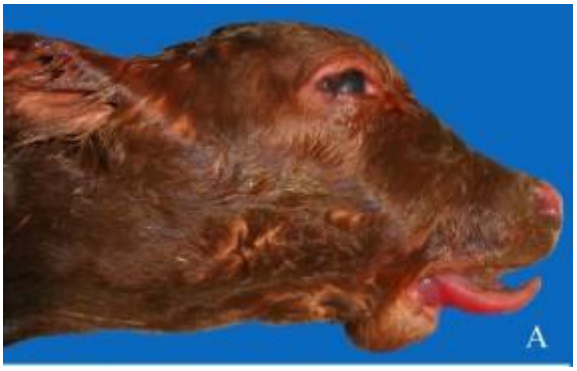
Trait Type: Lethal

Breeds found in: Angus

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

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

Genetic: g.4:114437192_114439942del

IDB Probe: IDBv20400000930, IDBv20400000931, IDBv20400000932, IDBv20400000933, IDBv20400000934

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

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

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

IDB Probe: IDBv21700002258, IDBv21700002259, IDBv21700002260, IDBv21700002261, IDBv21700002262

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.

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

Gene: KDSR (3-Ketodihydrosphingosine Reductase)

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

IDB Probe: IDBv22400003734, IDBv22400003735, IDBv22400003736, IDBv22400003737, IDBv22400003738

Flanking Sequence:

GAAGACGCTCTTACCTCCATCTGCAAAGCCTCCGCAAGTCCCCTGAGGGCGAACTTGGATGAAGAGTATGCTGTG
TAACCAAACAGGCCCAGCTGCCCGG[T/C]CTGGGAAGACACGAAGACGACCCTGCCCATGCGGCGTTCCTTCATG
GTGGCGATCACCGCCCGGCTGGGGTACACGCTGCCCAGGTAGTTGATGCTCATC

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 Improver

Abbreviations: TH-Improver

Genetic Mode: Recessive

Royalty Fee: YES

Trait Type: Lethal

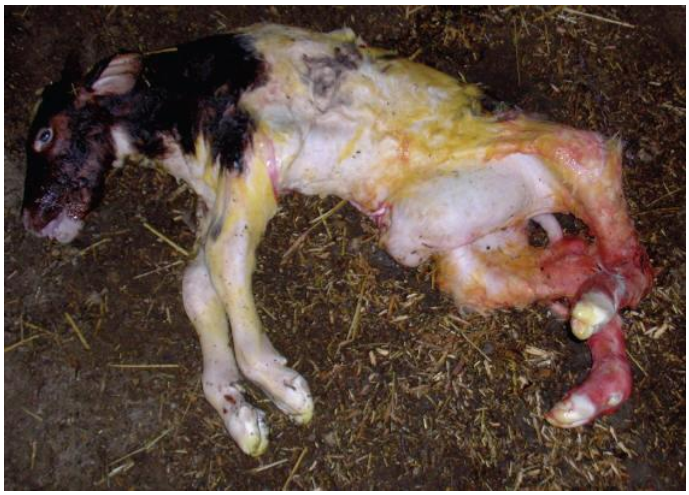
Breeds found in: Galloway, Shorthorn

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

Gene: ALX4 (Aristaless-Like Homeobox 4)

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

IDB Probe: 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].

UNWANTED

Bovine Leukocyte Adhesion Deficiency

Abbreviations: BLAD

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Unwanted

Breeds found in: Holstein-Friesian

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.

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

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

IDB Probe: IDBv20100000221, IDBv20100000222, IDBv20100000223, IDBv20100000224, IDBv20100000225

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.

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:

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 have no pathological lesions in the central nervous system and have no response to antiepileptic 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). Images from Gundlach, A.L, 1990.

Gene: GLRA1 (Glycine Receptor, Alpha 1)

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

IDB Probe: IDBv20700001605, IDBv20700001606, IDBv20700001607, IDBv20700001608, IDBv20700001609

Flanking Sequence:

AGTCTTGCTGCTTCCAAGGAGGCTGAAGCTGCTCGGTCTGCTTCCAAGCCCATGTCACCGTCCGATTTCCTGGATAAAC
TCATGGGGAGGACTTCTGGATA[C/A]GACGCCAGGATCAGGCCCAATTTCAAAGGTAGATAATCTTGCCTTTCAGAGC
CCCAGGGATCTGCTTTCCCAGATTGTGGCAGCAAGCCCACTGAATTGT

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 on welfare grounds. It causes substantial economic losses due to growth retardation and treatment. Affected animals have a crooked tail, abnormally shaped legs, stocky head, growth retardation, extreme muscularity, and straight hocks.

Heterozygous animals have enhanced muscular development, 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.

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: g.19:47740473delAG, p.Gly934X

IDB Probe: IDBv21900002544, IDBv21900002545, IDBv21900002546, IDBv21900002547, IDBv21900002548

Flanking Sequence:

TCACAGAGGACTGGGGGGACCAGAGGTGCACAACAGCCTTGCCTTACATCTGCAAGCGGCGCAACAGCACCAGA
GAGCAGCAGCCCCCAGACCTGCCGCCCAC[AG/-] GGGGCTGCCCCTCTGGCTGGAGCCAGTTCCTGAACA
AGGTAGGGAGTAGGGAGGGGGCCTGAGGGGAAGGCTGAGCTTCAGGAGTCCTGGCCCTCTGGCAA

CTS_C>T

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

IDB Probe: IDBv31900010186, IDBv31900010187, IDBv31900010188, IDBv31900010189, IDBv31900010190

Flanking Sequence: (CTS_C>T):

TCAGTGTGTGGGTCCCCTCCTCCCTCCTCCAGGGTACAGCCGTGGGGGCTGCGTGGCCCTGGCCACAGGCAGTGC
CATGGGGCTGTGGGAGGTGAAGAAC[T/C]GCACATCGTTCCGGGCTCGCTACATCTGCCGCCAGAGCCTGGGCAC
GCCCGTGACGCCTGAGCTGCCTGGGCTAGACCCCACGCCCAGCCTCACCGGCGC

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.

Dystrophic Epidermolysis Bullosa

Abbreviations: DEB

Genetic Mode: Recessive

Royalty Fee: No

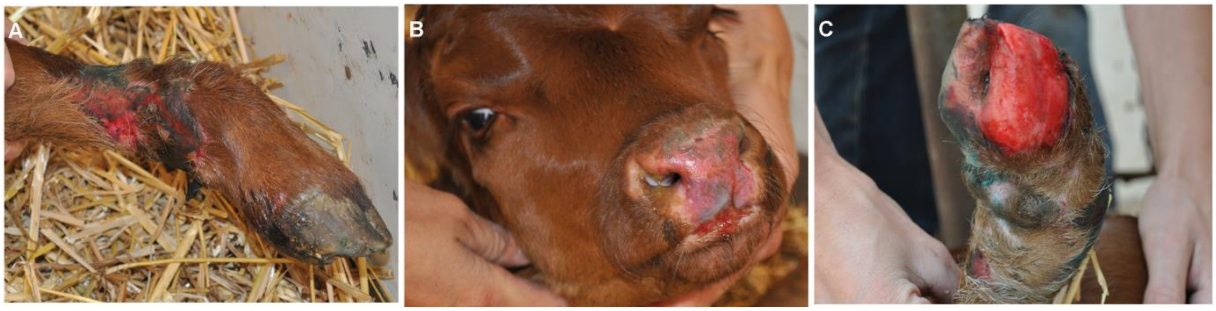
Trait Type: Unwanted

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

Gene: COL7A1

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

IDB Probe: IDBv22200003611, IDBv22200003612, IDBv22200003613, IDBv22200003614, IDBv22200003615

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.

Hypotrichosis KRT71

Abbreviations: HY_KRT71

Genetic Mode: Recessive

Royalty Fee: YES

Trait Type: Unwanted

Breeds found in: Hereford

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.

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)

Gene: Confidential genomic defect

Genetic: Confidential genomic defect

IDB Probe: Confidential genomic defect

Flanking Sequence: Confidential genomic defect

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

Mulefoot

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

Royalty Fee: No

Genetic Mode: Recessive

Trait Type: Unwanted

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.

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 hoofs.

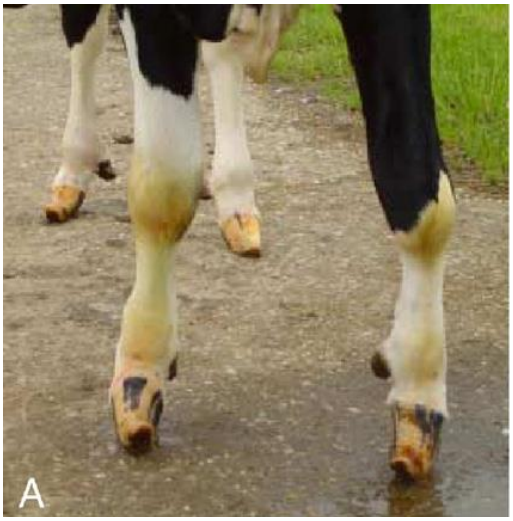


Photo of an affected Mulefoot animal from Duchesne et al., 2006

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

MF_R1740X: Found in Angus lineages.

Genetic: g.15:77667135G>A, c.5361+1G>A, p.His1782SerfsX17

IDB Probe: IDBv21500002186, IDBv21500002187, IDBv21500002188, IDBv21500002189, IDBv21500002190

Flanking Sequence:

GACCTACAGCAACCCCTCCTACCGAACTTCCACTCAGGAAGTGAAGATCGAAGCGACCCCCAAACCGGCCATGTA
CAATCAACTGTGCTATAAGAAAGAG[G/A]TGAGCGTGAAGACTTGCATCTGAGAGTTTGTTTCTGGGGCGGGCGG
GGGATCACGCTCCAGTCACCTGAGCAGGGAGGCCGCAGGGAGGGGTGTGATGTG

MF_P1647L: Found in Holstein lineages.

Genetic: g.15:77675440C>T, c.4916C>T, p.Pro1639Leu, rs109636878

IDB Probe: IDBv21500002191, IDBv21500002192, IDBv21500002193, IDBv21500002194, IDBv21500002195

Flanking Sequence:

ACCAACGCTTGTGGCGTGAACAACGGCGGATGCACTCACCTCTGCTTTGCCAGAACCTCGGACTTTGTGTGTGCCT

GTCCTGATGAGCCCGACGGCCGGC[C/T]CTGCTCCCTCGGTGAGTTGGACTGACGGGCCCCCCTGCAACAGCGGA
GCCCTTGCAAGGGCAGGGGATCAGCAGCTTTTTCCATCTGGGTGAGACTGTCC

MF_NG1621KC: Found in Holstein lineages.

Common Ancestor: Raven Burke Elsie.

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

IDB Probe: IDBv21500002196, IDBv21500002197, IDBv21500002198, IDBv21500002199, IDBv21500002200

Flanking Sequence:

CCTCCATTTGGAGAAGCGTCAAACTGGGAGACTTGATTCTGCCCCAGGCCAGATGTTCATTTGCTTTGCTCATAGG
GACCAACGCTTGTGGCGTGAACAA[CG/AT]GCGGATGCACTCACCTCTGCTTTGCCAGAACCTCGGACTTTGTGTG
TGCCTGTCCTGATGAGCCCGACGGCCGGCCCTGCTCCCTCGGTGAGTTGGACTG

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

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

IDB Probe: IDBv21500002206, IDBv21500002207, IDBv21500002208, IDBv21500002209, IDBv21500002210

Flanking Sequence:

AGGAACTGTGGGAGGAACCAGCTATTACCGTCTCTTGCCCAGGTTCATGTACTGGACGGACTGGGGGGAGCATG
CCAAGTTGGAGCGGTCTGGGATGGAC[G/A]GCTCCGACCGCGCCGTGCTCATCAACAGCAACCTCGGGTGGCCCA
ACGGACTGACTGTGGACAAGGCCAGCTCCCAGCTGCTCTGGGCTGACGCCCACAC

MF_G907R: Found in Simmental lineages

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

IDB Probe: IDBv21500002211, IDBv21500002212, IDBv21500002213, IDBv21500002214, IDBv21500002215

Flanking Sequence:

GCCTGCCTGAGTAAGTGCCCCAGACTGACCCCTGTTCCCCTCCCGTTCCCGGGGCTCAGAGTTGCCCACCTGCTCC
CCTCTCGACTTTCACTGTGACAAC[G/A]GCAAATGTATCCGCCGCTCCTGGGTGTGCGACGGGGACAACGACTGT
GAGGATGACTCGGACGAGCAGGACTGTCGTGAGTGCTGGGCGGGGCTGGGCGG

MF_G81S: Found in Simmental lineages.

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

IDB Probe: IDBv21500002216, IDBv21500002217, IDBv21500002218, IDBv21500002219, IDBv21500002220

Flanking Sequence:

GCCTGCCTGAGTAAGTGCCCCAGACTGACCCCTGTTCCCCTCCCGTTCCCGGGGCTCAGAGTTGCCCACCTGCTCC
CCTCTCGACTTTCACTGTGACAAC[G/A]GCAAATGTATCCGCCGCTCCTGGGTGTGCGACGGGGACAACGACTGT
GAGGATGACTCGGACGAGCAGGACTGTCGTGAGTGCTGGGCGGGGCTGGGCGG

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.

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

Gene: FECH (Ferrochelatase)

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

IDB Probe: IDBv22400003704, IDBv22400003705, IDBv22400003706, IDBv22400003707, IDBv22400003708

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: Chininia, Romagnola

General: Affected animals are characterized by having muscle contractions when startled or move faster thank a slow walk. When contractions occur the animals will have an uncoordinated gait, sometimes 'bunny hopping' on their back feet. a lifelong history of exercise-induced (more intense than a walk) muscle contractions. 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

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

PMT_164: Found in Chininia lineages

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

IDB Probe: IDBv22500003762, IDBv22500003763, IDBv22500003764, IDBv22500003765, IDBv22500003766

Flanking Sequence:

GGAGGGGTCTTCAGACAAAGATGGGGTTTTCTCCCTTCTCTGCTGACTTCATGCCCCTCTTCTCTCTCCACAGTGGG
GGACAAGGTCCCGGCAGATATCC[G/A]CATCCTCACCATCAAGTCTACCACCCTCCGGGTCGACCAGTCCATCCTG
ACAGGTCTACTGGCCAGAGGGCAGGGCGGGGGATGCATCACAGGAGGATTT

PMT_211: Found in Romagnola lineages

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

IDB Probe: IDBv22500003757, IDBv22500003758, IDBv22500003759, IDBv22500003760, IDBv22500003761

Flanking Sequence:

CAGGGGGCCCTGGTCTGGGAGAGATGTGACGGCAAGGGAAGAGATGAGGCCCACAGCTGGGGCCTCACCTGAC
TCCCTGCCTCTTCTTCCCCTTCCCAGG[G/T]CACCAACATCGCAGCCGGCAAGGCCATCGGCATTGTGGCCACCACC
GGTGTGGGCACCGAGATTGGGAAGATCCGTGACCAAATGGCCGCCACAGAGCAG

PMT_284: Found in Romagnola lineages.

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

IDB Probe: IDBv22500003752, IDBv22500003753, IDBv22500003754, IDBv22500003755, IDBv22500003756

Flanking Sequence:

CTGGATGAGTTTGGGGAGCAGCTCTCCAAGGTCATCTCCCTCATCTGCGTGGCCGTCTGGCTCATCAACATTGGCC
ACTTCAACGACCCCGTGCATGGGG[G/T]CTCCTGGATCCGTGGTGCCATCTACTACTTTAAGATCGCCGTGGCCCT
GGCTGTGGCTGCCATCCCCGAGGGTAGGGCGACCTCTCTGTCTCCTCCCATT

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.

Rat-tail Syndrome

Abbreviations: PMEL17_50_52delTTC, PMEL17_3del

Genetic Mode: Semi-Dominant

Trait Type: Unwanted

Royalty Fee: No

Breeds found in: Crossbred: Red Colour x Black Colour. Often 1 Simmental parent

General: Rat-Tail refers to a phenotype that has is deficient of hair on the tail switch and other parts of the body has short, curled, and crimped hair. Rat-tail animals have lower average daily gain in the winter months. This trait can occur from the mating of a black or black pied parent with a red coloured parent, particularly Simmental, when the red coloured parent carries the PMEL_3del allele.

If a calf from such a cross inherits **only 1** PMEL1_3del allele it will be rat-tailed. If the animal is homozygous for the PMEL17 3bp deletion then it will be light grey coloured and not rat-tailed. If it inherits no PMEL17_3del alleles it will be black and not rat-tailed

Common Ancestor: None identified

Clinical: Hair shafts are enlarged, irregularly distributed, and clumped melanin granules in the hair shafts, which are asymmetrical, short, curled, and small.

Left is a heterozygous PMEL17_3del calf with Rat-Tail. Centre is a homozygous PMEL17_3del calf. Right is a normal (no PMEL17_3del alleles) calf. Images from HECHT, B. C. 2006

Gene: PMEL17 (Premelanosome Protein)

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

IDB Probe: IDBv20500001008, IDBv20500001009, IDBv20500001010, IDBv20500001011, IDBv20500001012

Flanking Sequence:

TTTTAGGGAGAGAAAAACCAGAGCAGGTGTGCAACCCCAAATTCACACTTGTTCATGTCCAACATCCCACACTCACCTT
CTGTGGTCCCTMCAGCCAG[-/CTT]AACACCCATCAGAGCCACATGGAGAAGGTATTTTCTCAGCACCAGATC
CATCCTGTTCTTCCTTCCAGCAACCAAAGACTCTGGGGCATTGGACAA

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

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 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

Gene: RNF11 (Ring Finger Protein 11)

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

IDB Probe: IDBv20300000712, IDBv20300000713, IDBv20300000714, IDBv20300000715, IDBv20300000716

Flanking Sequence:

AGGTCCCCTCCTCAGCCCAAAAAGGAAGAAACAAAAGGAAAACATTACCTAGAAAACAGATTTTTTAAAAAATAATTA
ATTTCTCCATTTTAAAAAATTT[A/G]GGAACAAGTTCCAGTTCCGGTCTATCATCCAACACCTAGCCAGACTCGCCTAGC
AACTCAGCTGACTGAAGAGGAACAAATTAGGATAGCTCAAAGAATA

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

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.

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

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

IDB Probe: IDBv20200000628, IDBv20200000629, IDBv20200000630, IDBv20200000631, IDBv20200000632

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.

STAT5A_13319

Abbreviations: STAT5A_13319

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Unwanted

Breeds found in: Multiple Breeds

General: Animals can be heterozygous or homozygous for the unwanted 'G' allele, but there is an increased rate of unfertilized embryos and the fertilized embryos produced have a decreased survival rate:

Animals born alive and heterozygous or homozygous 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

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

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

IDB Probe: IDBv21900002510, IDBv21900002511, IDBv21900002512, IDBv21900002513, IDBv21900002514

Flanking Sequence:

CAGAGAGAACACGGGCCTGTCTGGAAGAGGAGCAGACAAAGGGCGTGGTGGATGGAGAACCCGGGGTGAGGT
CCTGGGATTAGGCCAGGCCACCCGTGAA[G/A]GGCGTGGGAGTGAGTGAAGGAGGGCGGGAATGAGTGAGGG
GAGAGACTGGGTCCTGAGTACTGAGGCCCACTGTGTGCTCTGGGGCTAGGATGACGAAGA

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.

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 GG for this gene 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

Gene: TLR4 (Toll-Like Receptor 4)

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

IDB Probe: BovineHD0800032700, AX-27654544, IDBv20800001683, IDBv20800001684, IDBv20800001685, IDBv20800001686, IDBv20800001687

Flanking Sequence:

GGTTGACTGGTCTCTTTGCTCGTCCCAGTAGCCTCCAAGGCTGTAGTCTAGGAGAGGAGAGTTGCTTGGAAGTCTGCTA
AGGTGCATGCAGGAAGACACC[A/G]CATCTAATATCTAATCATTTCAGGTTGTTCCTAACATTAGTTACCAGTGCATGGA
GCTGAATCTCTACAAAATCCCCGACAACATCCCCATATCAACCAA

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)

Gene:

Genetic: g.1706051_1706060del-ins1705834_1706045dup,

IDB Probe: IDBv20100000067, IDBv20100000068, IDBv20100000069, IDBv20100000070, IDBv20100000071

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) and Calpastain (CAST)

Abbreviations: CAPN1_316, CAPN1_4751, CAPN1_530, CAST_282, CAST_2870, CAST_2959

Genetic Mode: Additive

Trait Type: Meat

Breeds found in: Multiple breeds

Royalty Fee: No

General The Calpain 1 and Calpastain genes have alleles that 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.

Gene: CAPN1 (Calpain 1), CAST (Calpastain)

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

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

IDB Probe: IDBv22900003942, IDBv22900003943, IDBv22900003944, IDBv22900003945

Flanking Sequence:

TGGGCCAGGGAAGGACAGGCCCCAGGGATAGAGGCTGGGCAGGTCAGTGGCCGCCAGCCCCTGGCAGTGCCCT
TTTCCTGCAGCTCCTCGGAGTGGAACG[G/C]CGTGGACCCTTACATGCGGGAGCAGCTCCGGGTCAAGATGGAGG
ATGGGGAGTTCTGGTGAGCAGCCCCCTCCTCAGTCTGAGTGGGCACCCCAGCTCCCA

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

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

IDB Probe: IDBv22900003946, IDBv22900003947, IDBv22900003948, IDBv22900003949, IDBv22900003950

Flanking Sequence:

CCCCTGTCTCCCCCTTTCCTCCCACCACACCCTTGCTGCCCCAACCCCCGTTGACTGGCCCCTCTCTCTCCCCACCCTC
TGCAGAGAGCTGGATGACCAG[A/G]TCCAGGCCAATCTCCCCGACGAGGTACGTGCCCTGCCCCCACCCTGGGTG
CACGACGGGGACCCGGGTGTCCTGTGTCTTGGTCTCTAGCCAGCAAGGCAGAGCC

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

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

IDB Probe: IDBv22900003955, IDBv22900003956, IDBv22900003957, IDBv22900003958, IDBv22900003959

Flanking Sequence:

GAGGAAGGGCTCTGGGTGACCTGTCCCAAGAGCAGGGAAAGGGACAGATGTGGACAGGCCAGTTCCTTCCTGGC
ATCCTCCCCTTGACTGGGGGGAAAAC[C/T]GAGGCGCAGGGCTGTGTCAAGTGACGGGGGAGGGCCTCGTCTAC
AGGTGACCCTAAGGCTGGCACTCAGAGAACACCCCTCCCAGCCTACCCCAATTCAGGCCTG

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

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

IDB Probe: IDBv20700001611, IDBv20700001612, IDBv20700001613, IDBv20700001614

Flanking Sequence:

TGTTAAAACGGCACCTCTGTGTGGCATCAGCAGGTATTGCAATTTGCTTGTGTGATTCTTGCTGAATTTGGAGGGA
AGGAATTGCATTGTTTCAAATTTT[C/G]TACCCAAAGTGAAATTTGTCACATGTAAATCATACTAATTTAAATTCTCA
CAATTGACTACATAAAACACAAGTGTTATGAATTGCTTTCTACTCCTCAG

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

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

IDB Probe: IDBv20700001615, IDBv20700001616, IDBv20700001617, IDBv20700001618, IDBv20700001619

Flanking Sequence:

ACATTTGATAGTTTCTTAAAGCAGCACACAAAAAAGGAAAAACCTTTGCAAACTTTTGCACATTCTCCCCACAGTGC
CTGTAAATCTCATTAGTATTTTC[G/A]ATTTGCACTTATTTTTGTTGTTAGCATTTGGAAAACGATGCCTCACGTGTT
CTTCAGTGTTCTGATTTCTCATGACCCCTTTCCTCTTAGACTTGTGGAC

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

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

IDB Probe: IDBv20700001620, IDBv20700001621, IDBv20700001622, IDBv20700001623, IDBv20700001624

Flanking Sequence:

TTAGTATTTTCGATTTGCACTTATTTTTGTTGTTAGCATTTGGAAAACGATGCCTCACGTGTTCTTCAGTGTTCTGAT
TTCTCATGACCCCTTTCCTCTT[A/G]GACTTGTGGACTGTGTTTGATGTTTCTTTGGGTTGTTGTTTATAAGTCAGTC
ATAAAATACTGTGCATTGGGCACATGTCTCCTCTTGAGCTGCTAATCG

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Myostatin

Abbreviations: See below **Genetic Mode: Recessive**

Royalty Fee: YES **Trait Type: Meat**

Breeds found in: Multiple, breed specific mutations listed below

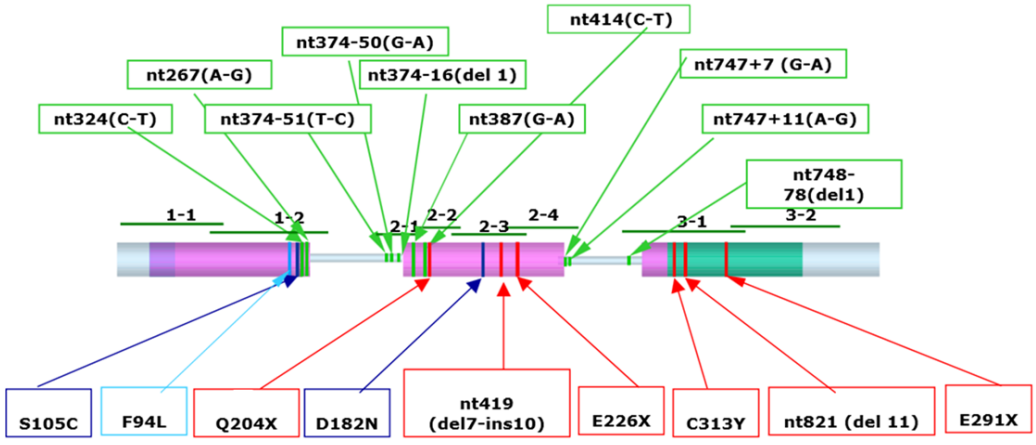
General:. Multiple alleles in the Myostain gene affect muscle mass. The effect on calving difficulty depends on the allele.

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

Alleles 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). Images from ICBF

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. Results in double muscling (hyperplasia), larger birth weights, increased dystocia and meat tenderness

Genetic: g.2:6218379delATGAACACTCC c.821_831delTGAACACTCCA p.Glu275ArgfsX14

Probe: IDBv20200000591, IDBv20200000592, IDBv20200000593, IDBv20200000594, IDBv20200000595

Flanking Sequence:

ATTATTAACTCTTCTTTCCTTTCCATACAGACTCCTTTTTTAGAAGTCAAGGTAACAGACACACCAAAAAGATCTAG
GAGAGATTTTGGGCTTGATTGTG[ATGAACACTCC/-]ACAGAATCTCGATGCTGTCGTTACCCTCTAA
CTGTGGATTTTGAAGCTTTTGGATGGGATTGGATTATTGCACCTAAAAGATATAAGGCCAATTACTGCTC

MYO_C313Y: Found in Gasconne, Piedmontese and Parthenise lineages. Results in double muscling (hyperplasia), larger birth weights, increased dystocia and meat tenderness

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

IDB Probe: IDBv20200000603, IDBv20200000604, IDBv20200000605, IDBv20200000606, IDBv20200000607

Flanking Sequence:

CGATGCTGTCGTTACCCTCTAACTGTGGATTTTGAAGCTTTTGGATGGGATTGGATTATTGCACCTAAAAGATATA
AGGCCAATTACTGCTCTGGAGAAT[A/G]TGAATTTGTATTTTTGCAAAAGTATCCTCATACCCATCTTGTGCACCAA
GCAAACCCCAGAGGTTCAGCCGGCCCCTGCTGTACTCCTACAAAGATGTCT

MYO_E226X: Found in Marchigiana and Maine-Anjou lineages. Results in double muscling (hyperplasia), larger birth weights, increased dystocia and meat tenderness

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

IDB Probe: IDBv20200000566, IDBv20200000567, IDBv20200000568, IDBv20200000569, IDBv20200000570

Flanking Sequence:

GAAACTTGACATGAACCCAGGCACTGGTATTTGGCAGAGCATTGATGTGAAGACAGTGTTGCAGAACTGGCTCAA
ACAACCTGAATCCAACTTAGGCATT[G/T]AAATCAAAGCTTTAGATGAGAATGGCCATGATCTTGCTGTAACCTTCC
CAGAACCAGGAGAAGATGGACTGGTAAGTGATTACTGAAAATAACATGCTAA

MYO_E291X: Found in Maine-Anjou and Marchingina lineages. Results in double muscling (hyperplasia), larger birth weights, increased dystocia and meat tenderness

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

IDB Probe: IDBv20200000600, IDBv20200000601, IDBv20200000602

Flanking Sequence:

AACAGACACACCAAAAAGATCTAGGAGAGATTTTGGGCTTGATTGTGATGAACACTCCACAGAATCTCGATGCTG
TCGTTACCCTCTAACTGTGGATTTT[G/T]AAGCTTTTGGATGGGATTGGATTATTGCACCTAAAAGATATAAGGCCA
ATTACTGCTCTGGAGAATGTGAATTTGTATTTTTGCAAAAGTATCCTCATAC

MYO_F94L: Found in Angus and Limousin lineages. Results in an increase muscularity and reduce external and intramuscular fat, with no change in birth weight

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

IDB Probe: IDBv20200000254, IDBv20200000255, IDBv20200000256, IDBv20200000257, IDBv20200000258

Flanking Sequence:

TCAGTAAACTTCGCCTGGAAACAGCTCCTAACATCAGCAAAGATGCTATCAGACAACTTTTGCCCAAGGCTCCTCC
ACTCCTGGAACTGATTGATCAGTT[C/A]GATGTCCAGAGAGATGCCAGCAGTGACGGCTCCTTGGAAGACGATGA
CTACCACGCCAGGACGGAAACGGTCATTACCATGCCCACGGAGTGTGAGTAGT

MYO_Q204X: Found in Blonde d'Aquitaine, Charolaise, Charolais and Limousin lineages. Results in double muscling (hyperplasia), larger birth weights, increased dystocia and meat tenderness

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

IDB Probe: IDBv20200000559, IDBv20200000560, IDBv20200000561, IDBv20200000562, IDBv20200000563

Flanking Sequence:

TGTGCAAATCCTGAGACTCATCAAACCCATGAAAGACGGTACAAGGTATACTGGAATCCGATCTCTGAAACTTGAC
ATGAACCCAGGCACTGGTATTTGG[C/T]AGAGCATTGATGTGAAGACAGTGTTGCAGAACTGGCTCAAACAACCT
GAATCCAACTTAGGCATTGAAATCAAAGCTTTAGATGAGAATGGCCATGATCT

MYO_S105C: Found in Parthenaise lineages. Results in an increase in muscularity and reduction of external and intramuscular fat, with no change in birth weight

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

IDB Probe: IDBv20200000310, IDBv20200000311, IDBv20200000312, IDBv20200000313, IDBv20200000314

Flanking Sequence:

ATCAGCAAAGATGCTATCAGACAACTTTTGCCCAAGGCTCCTCCACTCCTGGAACTGATTGATCAGTTCGATGTCC
AGAGAGATGCCAGCAGTGACGGCT[C/G]CTTGGAAGACGATGACTACCACGCCAGGACGGAAACGGTCATTACC
ATGCCCACGGAGTGTGAGTAGTCCTGCTGGTGCAGAGCAACGACTCTGCTGACT

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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: Holstein, Friesian, Jersey, Brown Swiss, Simmental, and multiple beef breeds

General: Each copy of the A allele (Tyrosine) increases milk fat (kg and %), protein (kg and %), and decreases milk volume.

Common Ancestor: None identified

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

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

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

IDB Probe: IDBv20600001147, IDBv20600001148, IDBv20600001149, IDBv20600001150, IDBv20600001151

Flanking Sequence:

ATTTGTTTTTTGTAGATATTTTCAGGGCTGTTGGTAAATCTCAAAACCGTCGTGCCTTGGTTGTCATGGCTTCAATACTT
GAGCATTCCTCGATACGGCT[A/C]TGCGGTATGTTCTCCTTATCTGTCACCGTGCTGGTTCATTGTCCCCATGCTGGAA
ACAGCCAGAATAAAGCCTCTCATATCCTTGGCCATGAGCTGTGCA

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AcylCoA:Diacylglycerol Acyltransferase

Abbreviations: DGAT1 **Genetic Mode: Additive**

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

Breeds found in: Holstein, Friesian, Jersey, Brown Swiss, Simmental, and multiple beef breeds

General: The Lysine allele 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.

Gene: DGAT1 (Diacylglycerol O-Acyltransferase 1)

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

IDB Probe: IDBv21400002069, IDBv21400002070, IDBv21400002071, IDBv21400002072, IDBv21400002073

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: Holstein, Friesian, Jersey, Brown Swiss, Simmental, and multiple beef 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

Gene: GH1 (Growth Hormone 1)

GH_2141

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

IDB Probe: IDBv21900002573, IDBv21900002574, IDBv21900002575, IDBv21900002576, IDBv21900002577

Flanking Sequence:

CCGTAGTTCTTGAGCAGCGCGTCGTCACTGCGCATGTTTGTGTCAAATTTGTCATAGGTCTGCTTGAGGATCTGCC
CAGCCCGGGGGGTGCCATCTTCCA[C/G]CTCCTGCCAAGGGAGGGAGAGACAGAGAGGCCGAAGGGCCCTCAG
GAGCAGCTCCCTCCTGCCCGCTCCATTTTCCACCCTCCCCTACAGGCTTGGAGAA

GH_2291

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

IDB Probe: BovineHD1900019005, IDBv21900002560, IDBv21900002561, IDBv21900002562, IDBv21900002563, IDBv21900002564

Flanking Sequence:

CAAATTTGACACAAACATGCGCAGTGACGACGCGCTGCTCAAGAACTACGGTCTGCTCTCCTGCTTCCGGAAGGA
CCTGCATAAGACGGAGACGTACCTG[A/C]GGGTCATGAAGTGCCGCCGCTTCGGGGAGGCCAGCTGTGCCTTCTA
GTTGCCAGCCATCTGTTGTTTGCCCCTCCCCCGTGCCTTCCTTGACCCTGGAAG

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Growth Hormone Receptor

Abbreviations: GHR_F279Y **Genetic Mode: Additive**

Royalty Fee: YES **Trait Type: Milk**

Breeds found in: Holstein, Friesian, Ayrshire, Jersey, Brown Swiss, Simmental, and multiple beef breeds

General: Animals with the Tyrosine allele have an increase in 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

Gene: GHR (Growth Hormone Receptor)

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

IDB Probe: IDBv22000003375, IDBv22000003376, IDBv22000003377, IDBv22000003378, IDBv22000003379

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.

Beta Casein

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

Genetic Mode: Additive

Trait Type: Milk

Royalty Fee: A2 YES, others No

Breeds found in: Multiple dairy and beef breeds

General: Approximately 25-30% of cow's milk is beta-casein (ß-casein). There are several ß-casein alleles, 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 fat percent and protein percent. 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. ß-casein does have an interaction effect with Kappa Casein. 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.

Gene: CSN2 (Beta Casein)

IDB Probe	CSN2 Gene Position	Allele Variants and Amino Acid											
		A1	**A2**	**A3**	**B**	**C**	**D**	**E**	**F**	**G**	**H1**	**H2**	**I**
IDBv20600001264	c.41	Arg									Cys		
IDBv20600001252	c.52	Glu						Lys					
IDBv20600001258	c.51	Glu				Lys							
IDBv20600001247	c.82	His	Pro	Pro			Pro	Pro				Pro	Pro
IDBv20600001232	c.87	Gln										Glu	
IDBv20600001223	c.103	Leu									Ile		
IDBv20600001214	c.108	Met										Leu	Leu
IDBv20600001205	c.121	His		Gln									
IDBv20600001199	c.137	Ser			Arg								
IDBv20600001193	c.167	Pro							Leu				

IDB Probe	CSN2 Protein Position	Allele Variants and SNP											
		A1	**A2**	**A3**	**B**	**C**	**D**	**E**	**F**	**G**	**H1**	**H2**	**I**
IDBv20600001264	p.118	C									T		
IDBv20600001252	p.154	G						A					
IDBv20600001258	p.151	G				C							
IDBv20600001247	p.245	A	C	C			C	C				C	C
IDBv20600001232	p.259	C										G	
IDBv20600001223	p.307	C									A		
IDBv20600001214	p.322	A										C	C
IDBv20600001205	p.363	C		A									
IDBv20600001199	p.411	C			G								
IDBv20600001193	p.500	C							T				

Tables adapted from Caroli et al., 2009

IDB Probe: IDBv20600001264, IDBv20600001265, IDBv20600001266, IDBv20600001267, IDBv20600001268

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

Flanking Sequence:

CTATTAAATTTCTTCATTTTCTGATTTATGTTGACAAATAAGAATTTTTTTTAAAGCTAGACCTGATTTTATTTTTA
TTTTTCCAAAGGAATCTATTACA[C/T]GCATCAATAAGGTAAAACCCTCATATTTAAATGTACATTTTTTTTAATT
TCATGTTTGATTTTTATAAACAGCATTTCTTTATGTATTTTTTTTTTAACC

IDB Probe: IDBv20600001258, IDBv20600001259, IDBv20600001260 IDBv20600001261, IDBv20600001262

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

Flanking Sequence:

CCCTCATATTTAAATGTACATTTTTTTAAATTTCATGTTTGATTTTTATAAACAGCATTTCTTTATGTATTTTTTTTT
TAACCAGAAAATTGAGAAGTTTCAGAGT[A/G]AGGAACAGCAGCAAACAGAGGTAATTTGTTCACTATGAGTA
TATTTTGAGAAGTATTATGAAACATAACACATAAAAAGATTTATAATAATTATGTTCAGTCT

IDB Probe: IDBv20600001252, IDBv20600001253, IDBv20600001254, IDBv20600001255, IDBv20600001256

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

Flanking Sequence:

TTAAATGTACATTTTTTTTAATTTCATGTTTGATTTTTATAAACAGCATTTCTTTATGTATTTTTTTTTTAACCAGA
AAATTGAGAAGTTTCAGAGTGAG[G/A]AACAGCAGCAAACAGAGGTAATTTGTTCACTATGAGTATATTTTGA
GAAGTATTATGAAACATAACACATAAAAAGATTTATAATAATTATGTTCAGTCT

IDB Probe: IDBv20600001247, IDBv20600001248, IDBv20600001249, IDBv20600001250, IDBv20600001251

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

Flanking Sequence:

TCAAAGATTTGTTTTCCTTCTTTCCAGGATGAACTCCAGGATAAAATCCACCCCTTTGCCCAGACACAGTCTCTA
GTCTATCCCTTCCCTGGGCCCATCC[C/A]TAACAGCCTCCCACAAAACATCCCTCCTCTTACTCAAACCCCTGTG
GTGGTGCCGCCTTTCCTTCAGCCTGAAGTAATGGGAGTCTCCAAAGTGAAGGAG

IDB Probe: IDBv20600001232, IDBv20600001233, IDBv20600001234, IDBv20600001235, IDBv20600001236

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

Flanking Sequence:

TCCTTCTTTCCAGGATGAACTCCAGGATAAAATCCACCCCTTTGCCCAGACACAGTCTCTAGTCTATCCCTTCCC
TGGGCCCATCCCTAACAGCCTCCCA[C/G]AAAACATCCCTCCTCTTACTCAAACCCCTGTGGTGGTGCCGCCTTT
CCTTCAGCCTGAAGTAATGGGAGTCTCCAAAGTGAAGGAGGCTATGGCTCCTAA

IDB Probe: IDBv20600001223, IDBv20600001224, IDBv20600001225, IDBv20600001226, IDBv20600001227

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

Flanking Sequence:

GACACAGTCTCTAGTCTATCCCTTCCCTGGGCCCATCCCTAACAGCCTCCCACAAAACATCCCTCCTCTTACTCA
AACCCCTGTGGTGGTGCCGCCTTTC[C/A]TTCAGCCTGAAGTAATGGGAGTCTCCAAAGTGAAGGAGGCTATG
GCTCCTAAGCACAAAGAAATGCCCTTCCCTAAATATCCAGTTGAGCCCTTTACTGA

IDB Probe: IDBv20600001214, IDBv20600001215, IDBv20600001216, IDBv20600001217, IDBv20600001218

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

Flanking Sequence:

CTATCCCTTCCCTGGGCCCATCCCTAACAGCCTCCCACAAAACATCCCTCCTCTTACTCAAACCCCTGTGGTGGT
GCCGCCTTTCCTTCAGCCTGAAGTA[A/C]TGGGAGTCTCCAAAGTGAAGGAGGCTATGGCTCCTAAGCACAAA
GAAATGCCCTTCCCTAAATATCCAGTTGAGCCCTTTACTGAAAGCCAGAGCCTGAC

IDB Probe: IDBv20600001205, IDBv20600001206, IDBv20600001207, IDBv20600001208, IDBv20600001209

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

Flanking Sequence:

ACATCCCTCCTCTTACTCAAACCCCTGTGGTGGTGCCGCCTTTCCTTCAGCCTGAAGTAATGGGAGTCTCCAAA
GTGAAGGAGGCTATGGCTCCTAAGCA[C/A]AAAGAAATGCCCTTCCCTAAATATCCAGTTGAGCCCTTTACTGA
AAGCCAGAGCCTGACTCTCACTGATGTTGAAAATCTGCACCTTCCTCTGCCTCTGC

IDB Probe: IDBv20600001199, IDBv20600001200, IDBv20600001201, IDBv20600001202, IDBv20600001203

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

Flanking Sequence:

AGCCTGAAGTAATGGGAGTCTCCAAAGTGAAGGAGGCTATGGCTCCTAAGCACAAAGAAATGCCCTTCCCTA
AATATCCAGTTGAGCCCTTTACTGAAAG[C/G]CAGAGCCTGACTCTCACTGATGTTGAAAATCTGCACCTTCCT
CTGCCTCTGCTCCAGTCTTGGATGCACCAGCCTCACCAGCCTCTTCCTCCAACTGTCA

IDB Probe: IDBv20600001193, IDBv20600001194, IDBv20600001195, IDBv20600001196, IDBv20600001197

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

Flanking Sequence:

TTTACTGAAAGCCAGAGCCTGACTCTCACTGATGTTGAAAATCTGCACCTTCCTCTGCCTCTGCTCCAGTCTTGG
ATGCACCAGCCTCACCAGCCTCTTC[C/T]TCCAACTGTCATGTTTCCTCCTCAGTCCGTGCTGTCCCTTTCTCAGT
CCAAAGTCCTGCCTGTTCCCCAGAAAGCAGTGCCCTATCCCCAGAGAGATATG

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.

Kappa Casein

Abbreviations: CSN3_A, A1, B, B2, C, D, E, F1, F2, G1, G2, H, I, J

Genetic Mode: Additive

Trait Type: Milk

Royalty Fee: No

Breeds found in: Holstein, Friesian, Jersey, Brown Swiss, Simmental, and multiple beef 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.

Gene: CSN3 (Kappa Casein)

IDB Probe	CSN3 Gene Position	Allele Variants and SNP													
		A	**A1**	**B**	**B2**	**C**	**D**	**E**	**F1**	**F2**	**G1**	**G2**	**H**	**I**	**J**
IDBv20600001270	c.92	G								A					
IDBv20600001276	c.342	T			C										
IDBv20600001282	c.352	C									T				
IDBv20600001291	c.353	G				A	A								
IDBv20600001300	c.373	T												G	
IDBv20600001306	c.467	C									T		T		
IDBv20600001312	c.470	C		T	T	T									T
IDBv20600001321	c.498	T							G						
IDBv20600001336	c.506	A		C	C	C						C			C
IDBv20600001360	c.506	A							T						
IDBv20600001387	c.513	A	G												
IDBv20600001402	c.521	T			C										
IDBv20600001441	c.526	A						G							
IDBv20600001456	c.564	T			C							C			
IDBv20600001462	c.567	A		G	G	G						G			

Table adapted from Caroli et al., 2009

IDB Probe	CSN3 Protein Position	Allele Variants and SNP												
		A	A1	B	B2	C	D	E	F1	F2	G1	G2	H	I	J
IDBv20600001270	p.31	Arg								His					
IDBv20600001276	p.114	Thr			Thr										
IDBv20600001282	p.118	Arg									Cys				
IDBv20600001291	p.118	Arg				His	His								
IDBv20600001300	p.125	Ser												Ala	
IDBv20600001306	p.156	Thr									Ile		Ile		
IDBv20600001312	p.157	Thr		Ile	Ile	Ile									Ile
IDBv20600001321	p.166	Thr							Thr						
IDBv20600001336	p.169	Asp		Ala	Ala	Ala						Ala			Ala
IDBv20600001360	p.169	Asp							Val						
IDBv20600001387	p.171	Pro	Pro												
IDBv20600001402	p.174	Ile			Thr										
IDBv20600001441	p.176	Ser						Gly							
IDBv20600001456	p.188	Thr			Thr							Thr			
IDBv20600001462	p.189	Ala		Ala	Ala	Ala						Ala			

Table adapted from Caroli et al., 2009

IDB Probe: IDBv20600001270, IDBv20600001271, DBv20600001272, IDBv20600001273, IDBv20600001274

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

Flanking Sequence:

CTCTTGCGACCCCATAGATGGCAGCCCACTAGGCTCCCCAGTCCCTGGGATTCTCCAGGCAAGAAATAATACC
ATTCTGCATAATTTATTTTTTTACAGC[G/A]CTGTGAGAAAGATGAAAGATTCTTCAGTGACAAAATAGCCAAA
TATATCCCAATTCAGTATGTGCTGAGTAGGTATCCTAGTTATGGACTCAATTACTAC

IDB Probe: IDBv20600001276, IDBv20600001277, IDBv20600001278, IDBv20600001279, IDBv20600001280

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

Flanking Sequence:

AATTATGCAAAGCCAGCTGCAGTTAGGTCACCTGCCCAAATTCTTCAATGGCAAGTTTTGTCAAATACTGTGCC
TGCCAAGTCCTGCCAAGCCCAGCCAAC[T/C]ACCATGGCACGTCACCCACACCCACATTTATCATTTATGGCCAT
TCCACCAAAGAAAAATCAGGATAAAACAGAAATCCCTACCATCAATACCATTGCTA

IDB Probe: IDBv20600001282, IDBv20600001283, IDBv20600001284, IDBv20600001285, IDBv20600001286

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

Flanking Sequence:

GCCAGCTGCAGTTAGGTCACCTGCCCAAATTCTTCAATGGCAAGTTTTGTCAAATACTGTGCCTGCCAAGTCCT
GCCAAGCCCAGCCAACTACCATGGCA[C/T]GTCACCCACACCCACATTTATCATTTATGGCCATTCCACCAAAG
AAAAATCAGGATAAAACAGAAATCCCTACCATCAATACCATTGCTAGTGGTGAGCC

IDB Probe: IDBv20600001291, IDBv20600001292, IDBv20600001293, IDBv20600001294, IDBv20600001295

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

Flanking Sequence:

CCAGCTGCAGTTAGGTCACCTGCCCAAATTCTTCAATGGCAAGTTTTGTCAAATACTGTGCCTGCCAAGTCCTG
CCAAGCCCAGCCAACTACCATGGCAC[G/A]TCACCCACACCCACATTTATCATTTATGGCCATTCCACCAAAGA
AAAATCAGGATAAAACAGAAATCCCTACCATCAATACCATTGCTAGTGGTGAGCCT

IDB Probe: IDBv20600001300, IDBv20600001301, IDBv20600001302, IDBv20600001303, IDBv20600001304

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

Flanking Sequence:

TGCCCAAATTCTTCAATGGCAAGTTTTGTCAAATACTGTGCCTGCCAAGTCCTGCCAAGCCCAGCCAACTACCA
TGGCACGTCACCCACACCCACATTTA[T/G]CATTTATGGCCATTCCACCAAAGAAAAATCAGGATAAAACAGAA
ATCCCTACCATCAATACCATTGCTAGTGGTGAGCCTACAAGTACACCTACCATCGA

IDB Probe: IDBv20600001306, IDBv20600001307, IDBv20600001308, IDBv20600001309, IDBv20600001310

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

Flanking Sequence:

CATTTATCATTTATGGCCATTCCACCAAAGAAAAATCAGGATAAAACAGAAATCCCTACCATCAATACCATTGC
TAGTGGTGAGCCTACAAGTACACCTA[T/C]CATCGAAGCAGTAGAGAGCACTGTAGCTACTCTAGAAGCTTCTC
CAGAAGTTATTGAGAGCCCACCTGAGATCAACACAGTCCAAGTTACTTCAACTGCG

IDB Probe: IDBv20600001312, IDBv20600001313, IDBv20600001314, IDBv20600001315, IDBv20600001316

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

Flanking Sequence:

TTATCATTTATGGCCATTCCACCAAAGAAAAATCAGGATAAAACAGAAATCCCTACCATCAATACCATTGCTAG
TGGTGAGCCTACAAGTACACCTACCA[T/C]CGAAGCAGTAGAGAGCACTGTAGCTACTCTAGAAGCTTCTCCA
GAAGTTATTGAGAGCCCACCTGAGATCAACACAGTCCAAGTTACTTCAACTGCGGTC

IDB Probe: IDBv20600001321, IDBv20600001322, IDBv20600001323, IDBv20600001324, IDBv20600001325

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

Flanking Sequence:

AAAATCAGGATAAAACAGAAATCCCTACCATCAATACCATTGCTAGTGGTGAGCCTACAAGTACACCTACCATC
GAAGCAGTAGAGAGCACTGTAGCTAC[T/G]CTAGAAGCTTCTCCAGAAGTTATTGAGAGCCCACCTGAGATCA
ACACAGTCCAAGTTACTTCAACTGCGGTCTAAATACTCTAAGGAGACATCAAAGAAG

IDB Probe: IDBv20600001336, IDBv20600001337, IDBv20600001338, IDBv20600001339, IDBv20600001340

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

Flanking Sequence:

GATAAAACAGAAATCCCTACCATCAATACCATTGCTAGTGGTGAGCCTACAAGTACACCTACCATCGAAGCAG
TAGAGAGCACTGTAGCTACTCTAGAAG[C/A]TTCTCCAGAAGTTATTGAGAGCCCACCTGAGATCAACACAGT
CCAAGTTACTTCAACTGCGGTCTAAATACTCTAAGGAGACATCAAAGAAGACAACGCA

IDB Probe: IDBv20600001360, IDBv20600001361, IDBv20600001362, IDBv20600001363, IDBv20600001364

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

Flanking Sequence:

GATAAAACAGAAATCCCTACCATCAATACCATTGCTAGTGGTGAGCCTACAAGTACACCTACCATCGAAGCAG
TAGAGAGCACTGTAGCTACTCTAGAAG[T/A]TTCTCCAGAAGTTATTGAGAGCCCACCTGAGATCAACACAGTC
CAAGTTACTTCAACTGCGGTCTAAATACTCTAAGGAGACATCAAAGAAGACAACGCA

IDB Probe: IDBv20600001387, IDBv20600001388, IDBv20600001389, IDBv20600001390, IDBv20600001391

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

Flanking Sequence:

CAGAAATCCCTACCATCAATACCATTGCTAGTGGTGAGCCTACAAGTACACCTACCATCGAAGCAGTAGAGAG
CACTGTAGCTACTCTAGAAGCTTCTCC[A/G]GAAGTTATTGAGAGCCCACCTGAGATCAACACAGTCCAAGTTA
CTTCAACTGCGGTCTAAATACTCTAAGGAGACATCAAAGAAGACAACGCAGGTAAAT

IDB Probe: IDBv20600001402, IDBv20600001403, IDBv20600001404, IDBv20600001405, IDBv20600001406

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

Flanking Sequence:

CCTACCATCAATACCATTGCTAGTGGTGAGCCTACAAGTACACCTACCATCGAAGCAGTAGAGAGCACTGTAG
CTACTCTAGAAGCTTCTCCAGAAGTTA[T/C]TGAGAGCCCACCTGAGATCAACACAGTCCAAGTTACTTCAACT
GCGGTCTAAATACTCTAAGGAGACATCAAAGAAGACAACGCAGGTAAATAAGCAAAA

IDB Probe: IDBv20600001441, IDBv20600001442, IDBv20600001443, IDBv20600001444, IDBv20600001445

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

Flanking Sequence:

CATCAATACCATTGCTAGTGGTGAGCCTACAAGTACACCTACCATCGAAGCAGTAGAGAGCACTGTAGCTACT
CTAGAAGCTTCTCCAGAAGTTATTGAG[A/C]GCCCACCTGAGATCAACACAGTCCAAGTTACTTCAACTGCGGT
CTAAATACTCTAAGGAGACATCAAAGAAGACAACGCAGGTAAATAAGCAAAATGAAT

IDB Probe: IDBv20600001456, IDBv20600001457, IDBv20600001458, IDBv20600001459, IDBv20600001460

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

Flanking Sequence:

CTACCATCGAAGCAGTAGAGAGCACTGTAGCTACTCTAGAAGCTTCTCCAGAAGTTATTGAGAGCCCACCTGA
GATCAACACAGTCCAAGTTACTTCAAC[T/C]GCGGTCTAAATACTCTAAGGAGACATCAAAGAAGACAACGCA
GGTAAATAAGCAAAATGAATAACAGCCAAGATTCATGGACTTATTAATAAAATCGTAA

IDB Probe: IDBv20600001462, IDBv20600001463, IDBv20600001464, IDBv20600001465, IDBv20600001466

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

Flanking Sequence:

CCATCGAAGCAGTAGAGAGCACTGTAGCTACTCTAGAAGCTTCTCCAGAAGTTATTGAGAGCCCACCTGAGAT
CAACACAGTCCAAGTTACTTCAACTGC[G/A]GTCTAAATACTCTAAGGAGACATCAAAGAAGACAACGCAGGT
AAATAAGCAAAATGAATAACAGCCAAGATTCATGGACTTATTAATAAAATCGTAACAT

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.

Beta-Lactoglobulin

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

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

Breeds found in: Holstein, Friesian, Jersey, Brown Swiss, Simmental, and multiple beef breeds

General: Beta-Lactoglobulin 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.

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.

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

IDB Probe	LGB Gene Position	Allele Variants and SNP							
		B	A	C	D	H	I	J	W
IDBv21100001927	181	G			C				
IDBv21100001934	214	A							C
IDBv21100001943	225	G		T					
IDBv21100001946	237	C	T						
IDBv21100001952	239	G	A			A			
IDBv21100001958	258	G				C			
IDBv21100001975	312	T	C						
IDBv21100001984	371	A					G		
IDBv21100001990	401	C	T			T			
IDBv21100001998	425	C						T	

Table adapted from Caroli et al., 2009

IDB Probe	LGB Protein Position	Allele Variants and SNP							
		B	A	C	D	H	I	J	W
IDBv21100001927	61	Glu			Gln				
IDBv21100001934	72	Ile							Leu
IDBv21100001943	75	Gln		His					
IDBv21100001946	79	Asn	Asn						
IDBv21100001952	80	Gly	Asp			Asp			
IDBv21100001958	86	Lys				Asn			
IDBv21100001975	104	Asn	Asn						
IDBv21100001984	124	Glu					Gly		
IDBv21100001990	134	Ala				Val			
IDBv21100001998	142	Pro						Leu	

Table adapted from Caroli et al., 2009

IDB Probe: IDBv31100007221, IDBv31100007222, IDBv31100007223, IDBv31100007224, IDBv31100007225

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

Flanking Sequence:

TTCCTGGCGCTGGCAGCCAGCCTGGACCCAGAGCCTGGACACCCCCTGCGCCCCCACTTCTGGGGCGTACCAG
GAACCGTCCAGGCCCAGAGGGGGCCTT[C/A]CTGCTTGGCCTCGAATGGAAGAAGGCCTCCTATTGTCCTCGT
AGAGGAAGCAACCCCAGGGCCCAAGGATAGGCCAGGGGGGATTCGGGGAACCGCGTGG

IDB Probe: IDBv21100001923, IDBv21100001924, IDBv21100001925, IDBv21100001926, IDBv21100001927

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

Flanking Sequence:

CCCTCCCCAGGTGGCGGGGACTTGGTACTCCTTGGCCATGGCGGCCAGCGACATCTCCCTGCTGGACGCCCAG
AGTGCCCCCCTGAGAGTGTATGTGGAG[G/C]AGCTGAAGCCCACCCCTGAGGGCGACCTGGAGATCCTGCTG
CAGAAATGGTGGGCGTCCCCCCCAAAAAAAGCATGGAACCCCCACTCCCCAGGGATATG

IDB Probe: IDBv21100001934, IDBv21100001935, IDBv21100001936, IDBv21100001937, IDBv21100001938

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

Flanking Sequence:

GGCCATGGCGGCCAGCGACATCTCCCTGCTGGACGCCCAGAGTGCCCCCCTGAGAGTGTATGTGGAGGAGCT
GAAGCCCACCCCTGAGGGCGACCTGGAG[A/C]TCCTGCTGCAGAAATGGTGGGCGTCCCCCCCAAAAAAAGC
ATGGAACCCCCACTCCCCAGGGATATGGACCCCCCCGGGGTGGGGTGCAGGAGGGACCAG

IDB Probe: IDBv21100001940, IDBv21100001941, IDBv21100001942, IDBv21100001943

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

Flanking Sequence:

CCAGCGACATCTCCCTGCTGGACGCCCAGAGTGCCCCCCTGAGAGTGTATGTGGAGGAGCTGAAGCCCACCCC
TGAGGGCGACCTGGAGATCCTGCTGCA[G/T]AAATGGTGGGCGTCCCCCCCAAAAAAAGCATGGAACCCCCA
CTCCCCAGGGATATGGACCCCCCCGGGGTGGGGTGCAGGAGGGACCAGGGCCCCAGGGC

IDB Probe: IDBv21100001946, IDBv21100001947, IDBv21100001948, IDBv21100001949, IDBv21100001950

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

Flanking Sequence:

CAGCCCCTCCTGGGGCCGCCTTCTGCCCCTGGCCCTCAGTTCATCCTGATGAAAATGGTCCATGCCCGTGGCTC
AGAAAGCAGCTGTCTTTCAGGGAGAA[C/T]GGTGAGTGTGCTCAGAAGAAGATCATTGCAGAAAAAACCAAG
ATCCCTGCGGTGTTCAAGATCGATGGTGAGTGCTGGGTCCCCAGGGGACGCCCACCAC

IDB Probe: IDBv21100001952, IDBv21100001953, IDBv21100001954, IDBv21100001955, IDBv21100001956

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

Flanking Sequence:

GCCCCTCCTGGGGCCGCCTTCTGCCCCTGGCCCTCAGTTCATCCTGATGAAAATGGTCCATGCCCGTGGCTCAG

AAAGCAGCTGTCTTTCAGGGAGAACG[G/A]TGAGTGTGCTCAGAAGAAGATCATTGCAGAAAAAACCAAGAT
CCCTGCGGTGTTCAAGATCGATGGTGAGTGCTGGGTCCCCAGGGGACGCCCACCACCC

IDB Probe: IDBv21100001958, IDBv21100001959, IDBv21100001960, IDBv21100001961, IDBv21100001962

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

Flanking Sequence:

TCTGCCCCTGGCCCTCAGTTCATCCTGATGAAAATGGTCCATGCCCGTGGCTCAGAAAGCAGCTGTCTTTCAGG
GAGAACGGTGAGTGTGCTCAGAAGAA[G/C]ATCATTGCAGAAAAAACCAAGATCCCTGCGGTGTTCAAGATC
GATGGTGAGTGCTGGGTCCCCAGGGGACGCCCACCACCCCCCAGGGACTGTGGGCAGG

IDB Probe: IDBv21100001975, IDBv21100001976, IDBv21100001977, IDBv21100001978, IDBv21100001979

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

Flanking Sequence:

GGGGAGCCCCGCTGGTTGTGGGGGGCGCTGGGGGCTGACCAGAAACCCCCCTCCTGCTGGAACTCACTTTCC
TCCTGTCTTGATCTCTACCAGCCTTGAA[C/T]GAGAACAAAGTCCTTGTGCTGGACACCGACTACAAAAAGTAC
CTGCTCTTCTGCATGGAGAACAGTGCTGAGCCCGAGCAAAGCCTGGTCTGCCAGTGCC

IDB Probe: IDBv21100001981, IDBv21100001982, IDBv21100001983, IDBv21100001984, IDBv21100001985

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

Flanking Sequence:

GAACTCACTTTCCTCCTGTCTTGATCTCTACCAGCCTTGAACGAGAACAAAGTCCTTGTGCTGGACACCGACTA
CAAAAAGTACCTGCTCTTCTGCATGG[A/G]GAACAGTGCTGAGCCCGAGCAAAGCCTGGTCTGCCAGTGCCTG
GGTGGGTGCCAACCCTGGCTGCCCAGGGAGACCAGCTGTGTGGTCCTCGCTGCAACG

IDB Probe: IDBv21100001990, IDBv21100001991, IDBv21100001992

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

Flanking Sequence:

CCAGCCTTGAACGAGAACAAAGTCCTTGTGCTGGACACCGACTACAAAAAGTACCTGCTCTTCTGCATGGAGA
ACAGTGCTGAGCCCGAGCAAAGCCTGG[T/C]CTGCCAGTGCCTGGGTGGGTGCCAACCCTGGCTGCCCAGGG
AGACCAGCTGTGTGGTCCTCGCTGCAACGGGGCCGGGGGGGACGGTGGGAGCAGGGAGC

IDB Probe: IDBv21100001994, IDBv21100001995, IDBv21100001996, IDBv21100001997, IDBv21100001998

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

Flanking Sequence:

GGCCAAGGGGGAAGGGCAGGTGTGCTGGAGGCCAAGGCAGACCTGCACACCACCCTGGAGAGCAGGGGTT
GACCCCGTCCCGGCCCCACAGTCAGGACCC[C/T]GGAGGTGGACGACGAGGCCCTGGAGAAATTCGACAAAG
CCCTCAAGGCCCTGCCCATGCACATCCGGCTGTCCTTCAACCCAACCCAGCTGGAGGGTGAG

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.

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

Gene: TYRP1 (Tyrosinase-Related Protein 1)

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

IDB Probe: IDBv20800001630, IDBv20800001631, IDBv20800001632, IDBv20800001633, IDBv20800001634

Flanking Sequence:

TGAACTTCGTAAGTATAGCCCAGGTTGTCTGGAGCAGTAACAAACATTTCTATGTTGGTAACTGGAGGCCAAAAT
GGTACCATATTGTATTGTCTGTTAT[G/A]TCCAATAGGGGCATTTTCCAGTGGATATGTGGATATATCTAAAATATG
TCAAAGACACCTTGTTAATAGACATAATCAGTTTGTATTAATATATTATTAT

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.

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

MC1R_E+ is the ancestral allele

MC1R_Ed

IDB Probe: IDBv21800002345, IDBv21800002346, IDBv21800002347, IDBv21800002348, IDBv21800002349

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

Flanking Sequence:
AACCGCAACCTGCACTCCCCCATGTACTACTTTATCTGCTGCCTGGCTGTGTCTGACTTGCTGGTGAGCGTC
AGCAACGTGCTGGAGACGGCAGTCATGC[T/C]GCTGCTGGAGGCCGGTGTCCTGGCCACCCAGGCGGCCG
TGGTGCAGCAGCTGGACAATGTCATCGACGTGCTCATCTGCGGATCCATGGTGTCCAGCCTC

MC1R_e

IDB Probe: IDBv21800002364, IDBv21800002365, IDBv21800002366, IDBv21800002367, IDBv21800002368

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

Flanking Sequence:
CTCCCCCATGTACTACTTTATCTGCTGCCTGGCTGTGTCTGACTTGCTGGTGAGCGTCAGCAACGTGCTGGA
GACGGCAGTCATGCTGCTGCTGGAGGCC[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_50_52delTTC

Abbreviations: PMEL17_50_52delTTC, PMEL17_3del, Dilutor 3, Silver Char Dilutor 2,

Genetic Mode: Semi-Dominant

Trait Type: Colour and multi-gene interactions

Royalty Fee: No

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

General: The PMEL17_50_52delTTC 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. In Simmental and Hereford lineages this same mutation (PMEL17_50_52delTTC) acts in a dominant manner to cause hypotrichosis (thin hair) and colour dilution. 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*	*Photo*
Red	E^+/e	+/+	
	e/e	+/+	TR
Yellow	E^+/e	+/del	
	e/e	+/del	MR
White/cream	*e/e*	del/del	BR
	E^+/e	del/del	
Black	E^D/E^D	+/+	
	E^D/E^+	+/+	TL
	E^D/e	+/+	
Dun	E^D/E^D	+/del	
	E^D/E^+	+/del	ML
	E^D/e	+/del	
Silver dun	E^D/E^+	del/del	BL
	E^D/e	del/del	

Photographs, MC1R and PMEL17_50_52delTTC genotypes of Highland cattle exhibiting distinct coat colours. The wild type allele is desgniated by '+'. Photo location: T=top, M=middle, B=bottom, L=left, R=right. Table and photos adapted from Schmutz & Dreger 2013

Gene: PMEL17 (Premelanosome Protein)

IDB Probe: IDBv20500001008, IDBv20500001009, IDBv20500001010, IDBv20500001011, IDBv20500001012

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

Flanking Sequence:

TTTTAGGGAGAGAAAAACCAGAGCAGGTGTGCAACCCCAAATTCACACTTGTTCATGTCCAACATCCCACACTCAC
CTTCTGTGGTCCCTMCAGCCAG[-/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.

Gene: PMEL17 (Premelanosome Protein)

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

IDB Probe: IDBv20500001013, IDBv20500001014, IDBv20500001015, IDBv20500001016, IDBv20500001017

Flanking Sequence:

TGCCCCAGAGTCTTTGGTTGCTGGAAGGAAGAACAGGATGGATCTGGTGCTGAGAAAATACCTTCTCCATGTGGC
TCTGATGGGTGTTCTTCTGGCTGTA[G/A]GGACCACAGAAGGTGAGTGTGGGATGTTGGACATGAACAAGTGTGA
ATTTGGGGTTGCACACCTGCTCTGGTTTTTCTCTCCCTAAAATGGAAGATATCA

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.