Understanding Genetics

and

Complete Genetic Disease and Trait Definition

INDEX

Understanding Genetics:

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

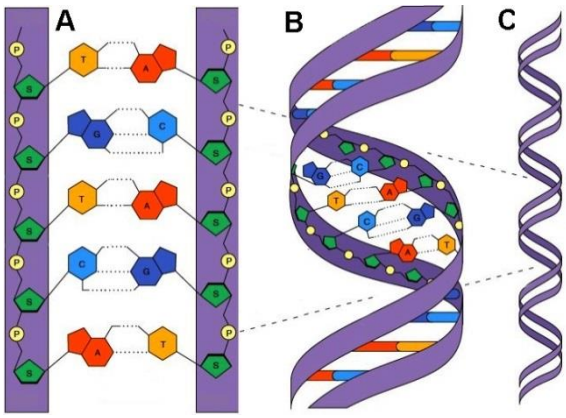


Figure 1:
A- If you were to zoom in, untwist the double helix, and flatten it out, it would look like this. Notice that the nucleotides in the centre are paired up, and the sugar and phosphate backbone, highlighted in purple, are on either side. This is what makes up every part of all living things.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

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

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

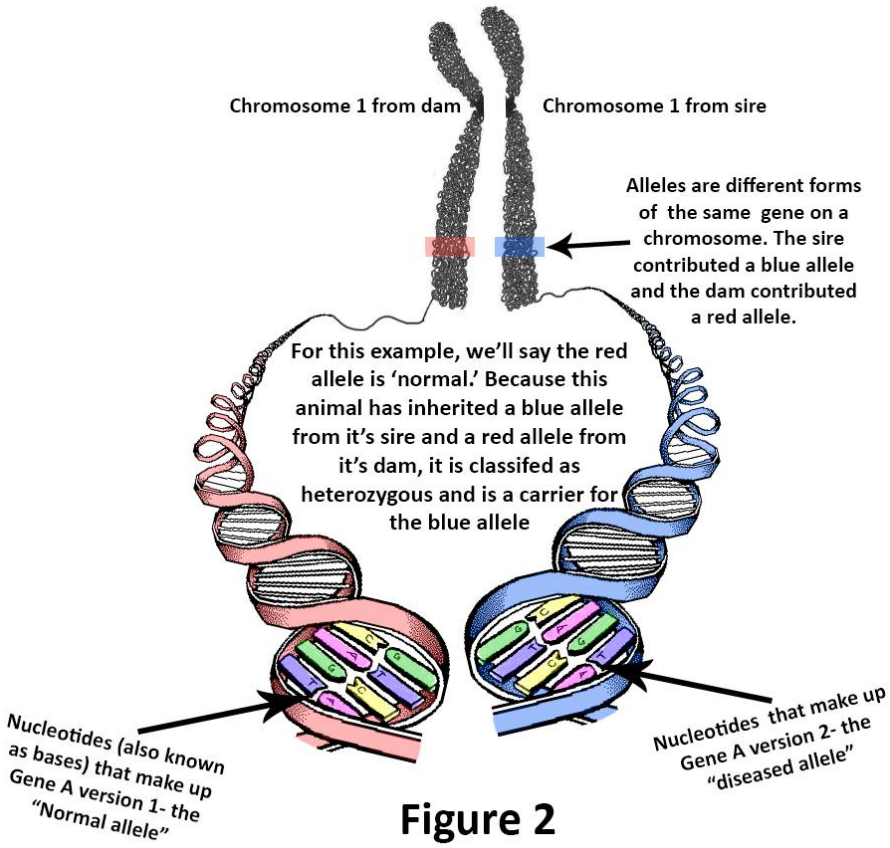


Figure 2

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

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

Normal= animal has 0 copies of the trait allele

Carrier = animal has 1 copy of the trait allele

Homozygous = animal has 2 copies of the trait allele

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

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

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

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

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

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

Recessive Disease Mating Risk

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

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

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

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

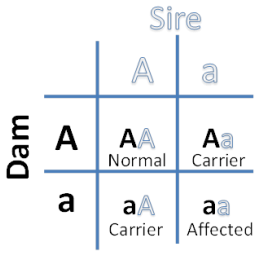
4. Mating a **carrier** to **carrier** results in a 25% chance of having an affected calf, a 50% chance of having a carrier calf, and a 25% chance of having a normal calf born

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

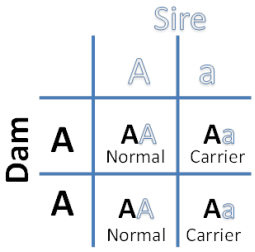
6. Mating a **homozygous** to **homozygous** results in a 100% chance of having an affected calf born

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

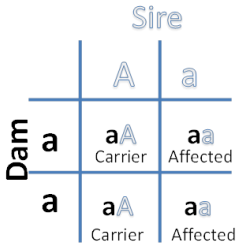
Carrier sire X Carrier dam. How do we know they are both carriers? When looking at the gene designations at the top of the squares, they have one copy of the normal allele (**A**) and one copy of the affected allele (**a**).



Carrier sire (Aa) X Normal dam (AA)



Carrier sire (Aa) X Homozygous dam (aa)



Dominant Disease Mating Risk

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

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

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

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

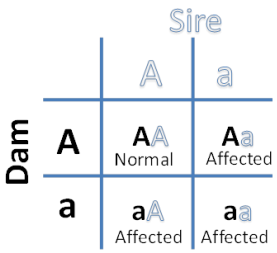
4. Mating a **carrier** to **carrier** results in a 75% chance that the calf born will be affected and a 25% chance that it will be normal

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

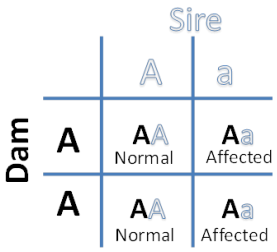
6. Mating a **homozygous** to **homozygous** results in a 100% chance of having an affected homozygous calf born

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

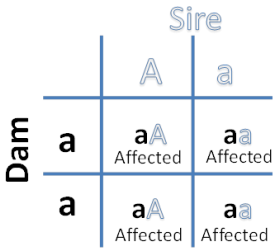
Carrier sire (Aa) X Carrier dam (Aa)



Carrier sire (Aa) X Normal dam (AA)



Carrier sire (Aa) X Homozygous dam (aa)



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

Trait definition layout:

Full Trait Name

Abbreviations: Abbreviations and alternative names for the trait

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

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

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

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

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

General: A general description of the trait

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

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

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

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

Gene: The gene symbol and name where the mutation lies

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

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

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

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

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

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

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

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

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

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

Traits are grouped by the following:

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

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

3) Beneficial: Alleles that are economically beneficial

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

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

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

DNA Allele and Amino Acid abbreviations

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

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

List of IDB reported diseases and traits

LETHAL

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

UNWANTED

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

BENEFICIAL

1. Infectious Bovine Keratoconjunctivitis (Pinkeye)
2. Poll

MEAT

1. Calpain1
2. Calpastatin
3. Myostatin

MILK

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

COLOUR

1. Dun
2. MC1R
3. PMEL17

LETHAL

Alpha Mannosidosis

Abbreviations: AM_662, AM _961

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Lethal

Breeds found in: Angus, Galloway, Murray Grey

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

Common Ancestor: None identified

Arachnomelia Syndrome

Abbreviations: SAA_SUOX

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Lethal

Breeds found in: Brown Swiss

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

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

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

Beta Mannosidosis

Abbreviations: BM

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Lethal

Breeds found in: Salers

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

Common Ancestor: None identified

Brachyspina

Abbreviations: BY

Genetic Mode: Recessive

Royalty Fee: Yes

Trait Type: Lethal

Breeds found in: Friesian, Holstein

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

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

Bulldog Dwarfism

Abbreviations: BD1, BD2, Dexter Chondrodysplasia

Genetic Mode: Recessive

Trait Type: Lethal

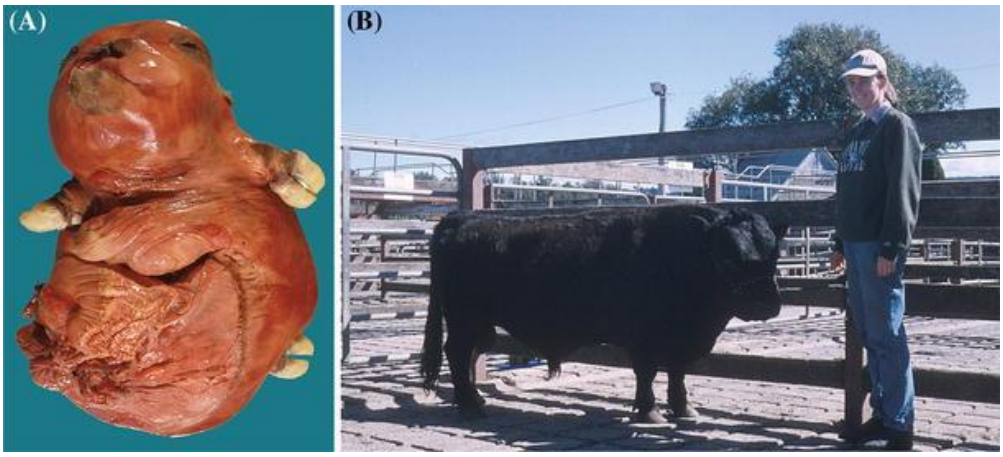
Royalty Fee: No

Breeds found in: Dexter

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

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

Common Ancestor: None identified



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

Cardiomyopathy and Woolly Haircoat Syndrome

Abbreviations: CWH

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Lethal

Breeds found in: Hereford

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

Common Ancestor: None identified

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

Citrullinaemia

Abbreviations: CT **Genetic Mode: Recessive**

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

Breeds found in: Friesian, Holstein

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

Common Ancestor: None identified

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

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

CMD2 affected calf from Harvey et al., 2008.

Complex Vertebral Malformation

Abbreviations: CVM

Genetic Mode: Recessive

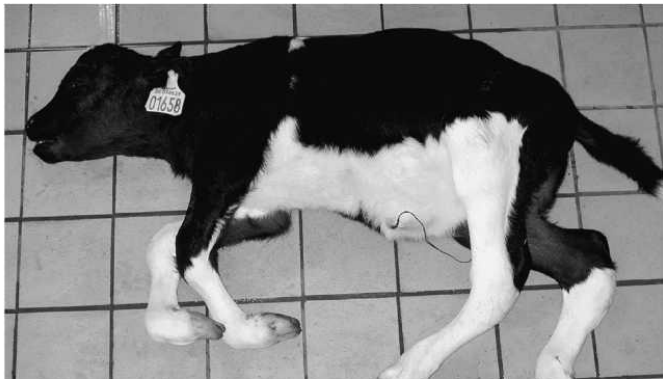
Royalty Fee: Yes

Trait Type: Lethal

Breeds found in: Friesian, Holstein

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

Common Ancestor: Carlin-M Ivanhoe Bell and Pennstate Ivanhoe



CVM affected calf from Thomsen et al., 2006

Deficiency of Uridine Monophosphate Synthase

Abbreviations: DUMPS

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Lethal

Breeds found in: 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

Holstein Haplotype 1

Abbreviations: HH1

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Lethal

Breeds found in: Friesian, Holstein

General: Affected calves are aborted after the first trimester.

Common Ancestor: Pawnee Farm Arlinda Chief

Holstein Haplotype 3

Abbreviations: HH3

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Lethal

Breeds found in: Friesian, Holstein

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

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

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Holstein Haplotype 4

Abbreviations: HH4

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Lethal

Breeds found in: Friesian, Holstein

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

Common Ancestor: Besne Buck

Idiopathic Epilepsy

Abbreviations: IE

Genetic Mode: Recessive

Royalty Fee: Yes

Trait Type: Lethal

Breeds found in: Hereford

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

Common Ancestor: None identified

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

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

Maple Syrup Urine

Abbreviations: MSU_HER, MSU_SH

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Lethal

Breeds found in: Hereford, Shorthorn

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

Common Ancestor: None identified

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

Neuropathic Hydrocephalus

Abbreviations: NH, Water Head

Genetic Mode: Recessive

Royalty Fee: Yes

Trait Type: Lethal

Breeds found in: Angus

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

Common Ancestor: GAR Precision 1680

Neuropathic hydrocephalus affected calf from Kaiser 2010

Osteopetrosis

Abbreviations: OS, Marble Bone Disease

Genetic Mode: Recessive

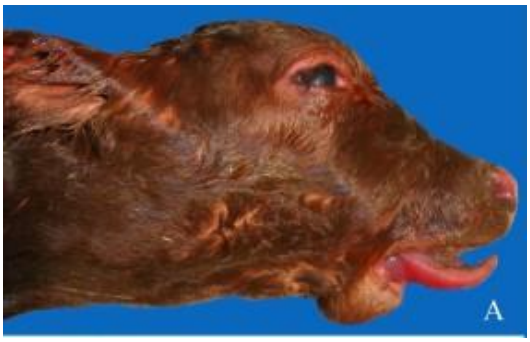
Royalty Fee: No

Trait Type: Lethal

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

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

Common Ancestor: None identified



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

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

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

Pulmonary Hypoplasia with Anasarca 1

Abbreviations: PHA1, Waterbaby

Genetic Mode: Recessive

Royalty Fee: Yes

Trait Type: Lethal

Breeds found in: Chianina, Maine Anjou, Shorthorn

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

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

Pulmonary Hypoplasia with Anasarca 1 affected calf from Kaiser 2010

Spinal Muscular Atrophy

Abbreviations: SMA

Genetic Mode: Recessive

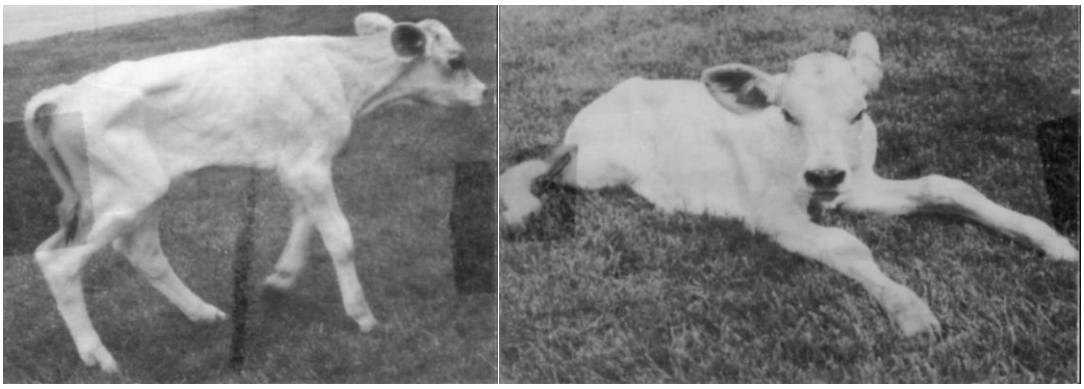
Royalty Fee: No

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



SMA affected calves from Brown Swiss Association 2001

Tibial Hemimelia

Abbreviations: TH-Improver

Genetic Mode: Recessive

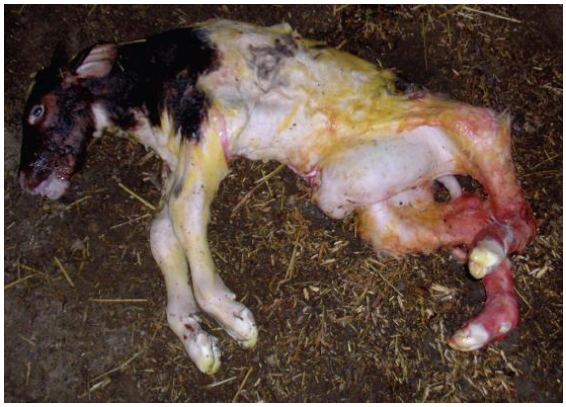
Royalty Fee: Yes

Trait Type: Lethal

Breeds found in: Galloway, Shorthorn

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

Common Ancestor: Deerpark Improver



Tibial Hemimelia affected calf from Kaiser 2010

UNWANTED

Axonopathy

Abbreviations: AX, Demetz syndrome

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Unwanted

Breeds found in: Tyrolean Grey

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

Common Ancestor: Gusti

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

Bovine Leukocyte Adhesion Deficiency

Abbreviations: BLAD

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Unwanted

Breeds found in: Friesian, Holstein

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

Common Ancestor: Osborndale Ivanhoe

Bovine Progressive Degenerative Myeloencephalopathy

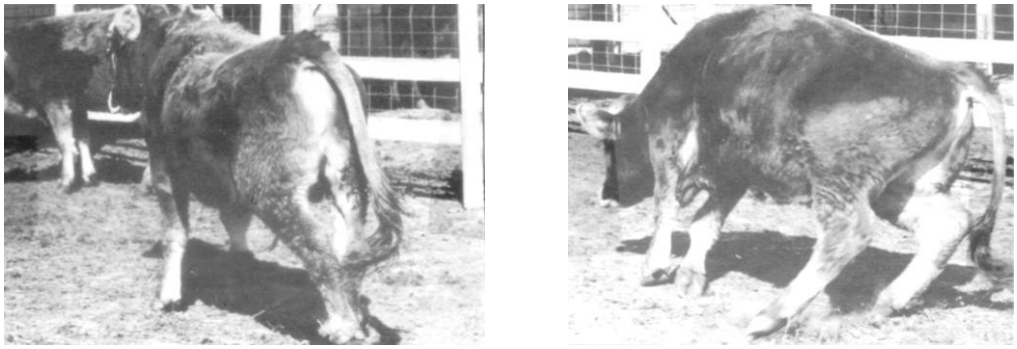
Abbreviations: Weaver **Genetic Mode: Recessive**

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

Breeds found in: Brown Swiss, Corara

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

Common Ancestor: Rolling View Modern Stretch



Weaver affected animal from Brown Swiss Association USA, 2011

Chediak Higashi Syndrome

Abbreviations: CHS **Genetic Mode: Recessive**

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

Breeds found in: Japanese Black

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

Common Ancestor: None identified

Congenital Myoclonus

Abbreviations: CM

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Unwanted

Breeds found in: Hereford

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

While not lethal, affected calves are usually humanly euthanized.

Common Ancestor: None identified

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

Crooked Tail Syndrome

Abbreviations: CTS_AG, CTS_T>C

Genetic Mode: Recessive

Royalty Fee: No

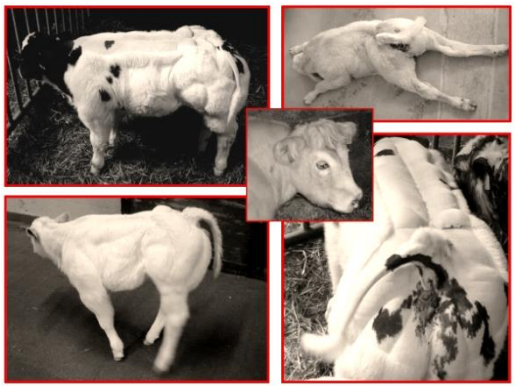
Trait Type: Unwanted

Breeds found in: Belgian Blue

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

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

Common Ancestor: None identified



Affected CTS animals from Fasquelle et al., 2009.

Developmental Duplication

Abbreviations: DD, Polymelia

Genetic Mode: Recessive, Incomplete Penetrance

Royalty Fee: Yes

Trait Type: Unwanted

Breeds found in: Angus

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

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

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

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

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

Factor XI Deficiency

Abbreviations: FXI_WA

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Unwanted

Breeds found in: Wagyu

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

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

Hypotrichosis

Abbreviations: HY_KRT71, HY_ERCC6L, HY_TSR2

Genetic Mode: Recessive

Royalty Fee: Yes: HY_KRT71
No: HY_ERCC6L and HY_TSR2

Trait Type: Unwanted

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

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

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

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

Common Ancestor: None identified

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

Mulefoot

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

Genetic Mode: Recessive

Trait Type: Unwanted

Royalty Fee: No

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

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

Common Ancestor: None identified

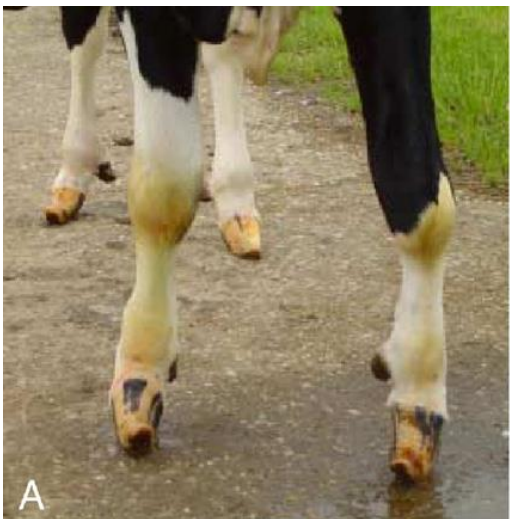


Photo of an affected Mulefoot animal from Duchesne et al., 2006

Neuronal Ceroid Lipofuscinosis

Abbreviations: NCL

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Unwanted

Breeds found in: Devon

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

Common Ancestor: None identified

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

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

Pseudomyotonia

Abbreviations: PMT_164, PMT_211, PMT_284

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Unwanted

Breeds found in: Chiania, Romagnola

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

Common Ancestor: None identified

Pseudomyotonia affected animal from Drogemuller et al., 2008

RNF11 Growth Retardation

Abbreviations: RNF11

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Unwanted

Breeds found in: Belgian Blue

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

Common Ancestor: Galopeur des Hayons

STAT1

Abbreviations: STAT1

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Unwanted

Breeds found in: Multiple Breeds

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

Common Ancestor: None identified

STAT3

Abbreviations: STAT3_19069, STAT3_25402

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Unwanted

Breeds found in: Holstein

General: Decreased embryo survival rate.

Common Ancestor: None identified

STAT5A

Abbreviations: STAT5A_13244, STAT5A_13319. STAT5A_13516

Genetic Mode: Recessive

Trait Type: Unwanted

Royalty Fee: No

Breeds found in: Multiple Breeds

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

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

Common Ancestor: None identified

Thrombopathia

Abbreviations: THR, Simmental hereditary thrombopathy (SHT)

Genetic Mode: Recessive

Trait Type: Unwanted

Royalty Fee: No

Breeds found in: Fleckvieh, Simmental

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

Common Ancestor: None identified

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

BENEFICIAL

Infectious Bovine Keratoconjunctivitis

Abbreviations: IBK, Pinkeye

Genetic Mode: Additive

Royalty Fee: No

Trait Type: Beneficial

Breeds found in: Multiple Breeds

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

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

Common Ancestor: None identified

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

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

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

MEAT

Calpain 1 (CAPN1)

Abbreviations: **CAPN1_316, CAPN1_4751, CAPN1_530**

Royalty Fee: No

Genetic Mode: Additive

Trait Type: Meat

Breeds found in: Multiple breeds

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

Common Ancestor: None identified

Calpastain (CAST)

Abbreviations: CAST_282, CAST_2870, CAST_2959

Royalty Fee: No

Genetic Mode: Additive

Trait Type: Meat

Breeds found in: Multiple breeds

General: Calpastain alleles are associated with more tender meat.

Common Ancestor: None identified

Myostatin

Abbreviations: See below

Genetic Mode: Recessive

Royalty Fee: Yes

Trait Type: Meat

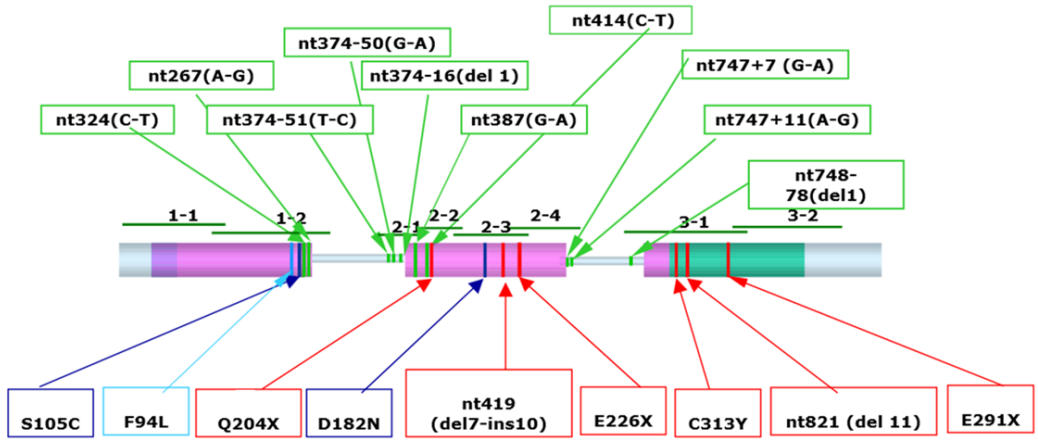
Breeds found in: Multiple, breed specific mutations listed below

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

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

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

Common Ancestor: None identified



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

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

MILK

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

Abbreviations: ABCG2

Genetic Mode: Additive

Royalty Fee: No

Trait Type: Milk

Breeds found in: Multiple beef and dairy breeds

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

Common Ancestor: None identified

AcylCoA:Diacylglycerol Acyltransferase

Abbreviations: DGAT1

Genetic Mode: Additive

Royalty Fee: No

Trait Type: Milk

Breeds found in: Multiple beef and dairy breeds

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

Common Ancestor: None identified

Growth Hormone

Abbreviations: GH_2141, GH_2291,

Genetic Mode: Recessive

Royalty Fee: No

Trait Type: Milk

Breeds found in: Multiple beef and dairy breeds

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

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

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

Common Ancestor: None identified

Growth Hormone Receptor

Abbreviations: GHR_F279Y

Genetic Mode: Additive

Royalty Fee: Yes

Trait Type: Milk

Breeds found in: Multiple beef and dairy breeds

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

Common Ancestor: None identified

Casein Beta

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

Genetic Mode: Additive

Trait Type: Milk

Royalty Fee: Yes: A2

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

Breeds found in: Multiple dairy and beef breeds

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

Common Ancestor: None identified

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

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

Tables adapted from Caroli et al., 2009

Casein Kappa

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

Genetic Mode: Additive

Trait Type: Milk

Royalty Fee: No

Breeds found in: Multiple beef and dairy breeds

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

Common Ancestor: None identified

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

Table adapted from Caroli et al., 2009

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

Table adapted from Caroli et al., 2009

Lactoglobulin Beta

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

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

Breeds found in: Multiple beef and dairy breeds

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

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

Common Ancestor: None identified

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

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

Tables adapted from Caroli et al., 2009

COLOUR

Dun

Abbreviations: DUN

Genetic Mode: Recessive and multi-gene interaction

Royalty Fee: No

Trait Type: Colour

Breeds found in: Dexter

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

Common Ancestor: None identified

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

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

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

PMEL17_delTTC

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

Genetic Mode: Semi-Dominant

Trait Type: Colour

Royalty Fee: No

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

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

Common Ancestor: None identified

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

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

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