AUSTRALIAN WAGYU ASSOCIATION™

WAGYU TECHNICAL
UPDATE

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# DIVERSITY BRINGS GENETIC STRENGTH

IT IS WIDELY ACCEPTED, THAT THE GENETIC DIVERSITY OF WAGYU OUTSIDE OF JAPAN REQUIRES GREATER VIGILANCE TO MANAGE INBREEDING AND RECESSIVE GENETIC CONDITIONS.

Inbreeding is essentially the mating of animals that are closely related – Sire with daughter, for example. Within Wagyu, it is not uncommon to have one or more progeny related through the mating of a Sire or Dam, resulting in a certain level of inbreeding. The level of inbreeding for the progeny is dependent on how closely related the parent animals are.

The attraction to mating closely related animals is to concentrate on desirable characteristics for the progeny, concentrating on the traits that may be strong within the Sire or Dam. For example, to enhance marbling traits, it is tempting to mate a Sire and Dam with high marbling EBVs, who may be closely related.

The potential production outcomes for enhanced traits in progeny are attractive, however, the risks associated with inbreeding need to be considered.

In general terms there are three main risk outcomes:

- Inbreeding depression in production traits
- Reduction in genetic diversity
- Increase homozygosity of recessive conditions

To calculate the level of inbreeding, a coefficient is derived as the probability percentage (%) for any allele (i.e. pair of genes at a specific location on the chromosome) to be identical by descent.

| RELATIONSHIP | INBREEDING COEFFICIENT (assuming no previous inbreeding) |
|---|---|
| **ANIMAL MATED TO ITS OWN PARENT** EG: SIRE to DAUGHTER | 25% |
| **FULL SIBLINGS** SIRE to DAM sharing the same SIRE and DAM as parents | 25% |
| **HALF SIBLINGS** SIRE to DAM with common SIRE and DAM | 12.5% |
| **HALF COUSINS** SIRE to DAM sharing a common grandparent | 3.1% |

The depth and accuracy of pedigree that is recorded will determine how true the level of inbreeding is. For animals with little or no pedigree recorded, the inbreeding coefficient may understate the true level, and be lower than it should, compared to full records for many generations.

A literature review undertaken by Burrow (1993) investigated the effects of inbreeding in beef cattle. The review, which did not include Wagyu, revealed that inbreeding of the individual has a consistent adverse effect on growth traits from birth to maturity and on maternal traits.

More specifically, for every 1% increase in the inbreeding coefficient a decrease of 0.06, 0.44, 0.69 and 1.30 kg in live weight at birth, weaning, yearling and maturity respectively was observed. Additionally, inbreeding in the dam decreased weaning and yearling weights by 0.30 and 0.21 kg respectively for every 1% increase in the inbreeding coefficient, probably as a result of decreasing milk yield and reduced maternal value of the inbred dams.

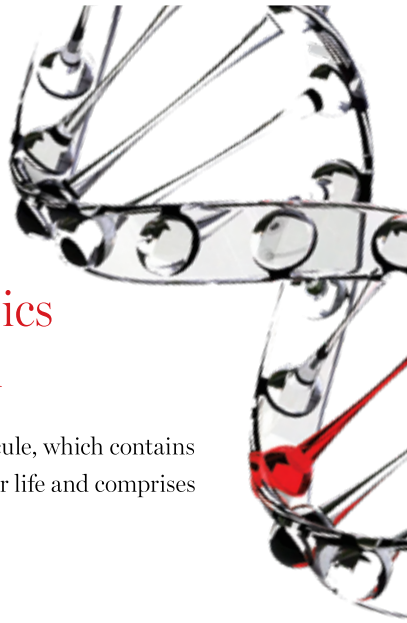
The depression caused by inbreeding tends to negatively affect the traits which are positively affected by heterosis (i.e. crossbreeding - the opposite of inbreeding), with these being fertility, survival, growth, and to a lesser extent, carcase traits.

The review also reported inbreeding as having a depressive effect (although the magnitudes of effect were small in some cases) on heifer conception rates, female fertility, conformation/structure, feed intake, feed conversion efficiency, carcase traits and male reproductive traits

Aiming to produce a single animal with the highest EBVs and BreedObject $Indexes, may seem an attractive proposition through selective inbreeding, but runs the risk of subsequent progeny exhibiting depressed traits or carrying higher levels of recessive genetic conditions.

By focusing on the overall average performance of the herd, the Wagyu breeder can lift the standards through objective selection and allocation of matings that suit their production goals – whether it is to enhance fertility, carcase or maternal traits, while maintaining genetic diversity.

While there is no ideal level of inbreeding for any cattle breed, with Wagyu, there is little choice but to manage the genetic diversity available. Indiscriminate breeding is unlikely to be economically sustainable in the long term. A good rule of thumb, according to Southern Beef Technology Services (SBTS), is to ensure inbreeding levels do not increase by more than 1% per generation.



# The basics of DNA

DNA is a molecule, which contains the blueprint for life and comprises the nucleotides
**Adenosine** (**A**),
**Thymine** (**T**),
**Guanosine** (**G**) and
**Cytosine** (**C**).

In mammals such as humans and cattle, the DNA is arranged in chromosomes, and each chromosome contains many genes, which provide the instructions to produce proteins. Proteins are vital to perform and maintain normal body functions.

In mammals each chromosome, and therefore each gene, is in duplicate because one full copy is inherited from the mother (maternal) and the other full copy is inherited from the father (paternal).

## DNA VARIATION

There can be many differences in the DNA sequence between individuals. These differences are often referred to as mutations or polymorphisms. Single nucleotide polymorphisms (SNP; pronounced “snips”) are a common form of variation in the DNA sequence.

SNP refers to a single nucleotide change in the DNA sequence between individuals. SNP can occur as frequently as 1 in every 1000 nucleotides, and the entire DNA sequence (genome) for cattle and humans is about 3 billion nucleotides in length.

## RECESSIVE CONDITIONS IN WAGYU

Our improved understanding of molecular and quantitative genetics has had a profound impact on the productiveness of livestock. The recent incorporation of genomics has also had a marked contribution towards genetic gain at a breed and herd level. Conversely, the use of favoured sires or sire lines presents a risk of concentrating and amplifying undesirable traits and inherited disease.

All breeds of cattle, including Wagyu, are prone to undesirable genetic conditions

Inherited diseases occur naturally in animals and can range from diseases with minor impact on animal welfare to lethal diseases. Inherited disease is the result of an abnormality in the normal DNA sequence of an individual. This abnormality may affect a single gene, an entire chromosome or it may be multifactorial compromising a complex combination of genetic, behavioural and environmental influences.

Mutations causing disease, disrupt the normal function of the gene, which prevents the formation of a protein that is able to perform its vital role; either adequately or at all. Disease causing mutations may exist as a SNP, where the "misspelling" of a single nucleotide cannot be tolerated, or if nucleotides have been lost (deletion) or gained (insertion), which changes the normal instructions in the gene to make the protein.

## INHERITED CONDITIONS IN LIVESTOCK

Online Mendelian Inheritance in Animals (Table 1) has 537 inherited conditions recorded for cattle. Of these, the mutation responsible has been described for 153 conditions, which means that the condition can be effectively managed through DNA testing.

The majority of inherited diseases in livestock that require management are single gene disorders that follow a recessive mode of inheritance.

"What this means is that the affected animals must inherit two copies (paternal and maternal) of the disruptive mutation," said Brendon O'Rourke, NSW DPI.

"It also means that both parents had one copy of the mutation, but did not show evidence of the disease. The success of management programs is reliant upon the accurate detection of these "carrier" animals. Unmanaged, there is high risk of an increased prevalence of the disease-causing mutation."

Like humans, cattle all carry lethal recessive mutations. Identification of these mutations and good breeding practices are central to proactive management of inherited disease.

TABLE ONE

## INHERITED TRAITS AND DISEASES IN ANIMAL SPECIES

| | DOG | CATTLE | CAT | PIG | SHEEP | HORSE | CHICKEN | RABBIT | GOAT | OTHER | TOTAL |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Total traits/disorders** | 756 | 537 | 353 | 275 | 252 | 239 | 221 | 97 | 86 | 659 | 3,564 |
| Mendelian trait/disorder | 335 | 247 | 104 | 82 | 109 | 58 | 129 | 58 | 17 | 251 | 1,455 |
| Mendelian trait/disorder; likely causal variant(s) known | 271 | 153 | 72 | 37 | 53 | 46 | 48 | 11 | 11 | 121 | 848 |
| Likely causal variants | 399 | 203 | 115 | 46 | 68 | 96 | 63 | 13 | 16 | 107 | 1,144 |
| Potential models for human disease | 445 | 211 | 218 | 122 | 112 | 132 | 50 | 53 | 38 | 361 | 1,774 |

*Online Mendelian Inheritance in Animals, OMIA. Sydney School of Veterinary Science, 14/02/2020.* omia.org

TABLE TWO

## INHERITED DISEASES IMPACTING WAGYU CATTLE

| DISEASE | TYPE | MUTATION | INHERITANCE |
|---|---|---|---|
| Chediak Higashi Syndrome (CHS) | Single gene | SNP | Recessive |
| Spherocytosis (B3) | Single gene | SNP | Recessive |
| Claudin 16 deficiency (CL16) Type 1 | Single gene | Deletion | Recessive |
| Claudin 16 deficiency (CL16) Type 2 | Single gene | Deletion | Recessive |
| Factor 13 deficiency (F13) | Single gene | SNP | Recessive |
| Factor 11 deficiency (F11) | Single gene | SNP | Recessive |
| Multiple Ocular defect | Single gene | Insertion | Recessive |

> "This proactive approach has resulted in a decline in prevalence of these disease-causing mutations ...

Six inherited diseases impacting animal welfare have been reported in the Wagyu breed (Table 2).

"The Australian Wagyu Association and its members have adopted a proactive approach to inherited disease with more than 100,000 cattle tested for the presence of these mutations to inform smarter breeding programs," said Brendon.

"Significant progress has been made to reduce the frequency of B3, CHS and CL16.

"This proactive approach has resulted in a decline in prevalence of these disease-causing mutations, which ultimately, is improving the genetic gain of the Wagyu breed through the avoidance of at-risk matings."

### INHERITED DISEASE RESEARCH

In collaboration with the University of Sydney, Brendon's team are investigating the molecular basis of several emerging inherited diseases impacting livestock industries. There are many reports about suspect emerging conditions from private and district veterinarians. In this collaboration, the collection of appropriate samples and data for biobanking and storage to assist with characterisation of the disease and facilitate future investigations is required. If breeders suspect inherited disease, because affected animals are descendants of a common sire(s) or because of observes affected individuals in multiple generations then independent and confidential collection of samples and data that can be used for future investigations.

## Genetic conditions in Wagyu

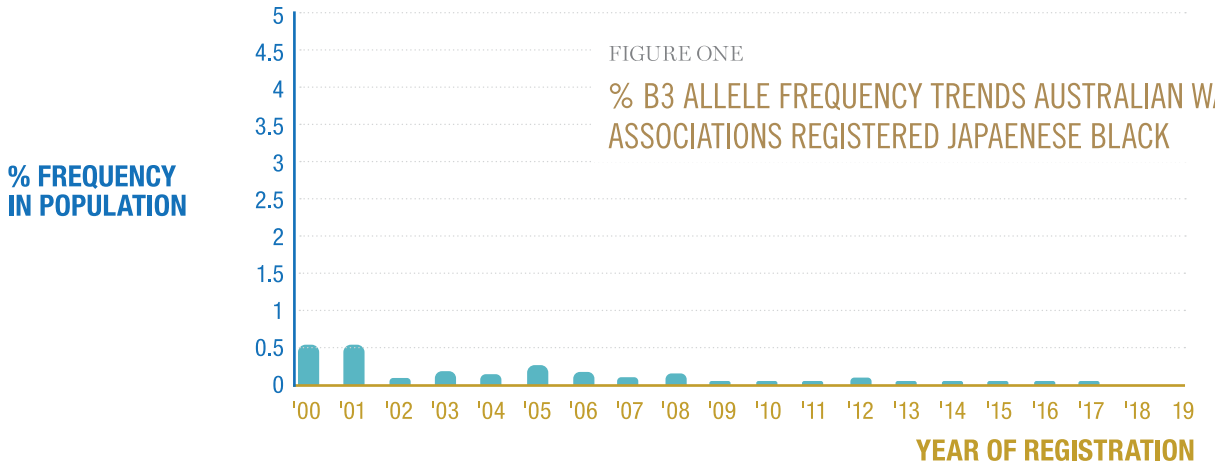
### SPHEROCYSTOSIS (B3)

This is a disorder of the surface membrane of the erythrocyte (red blood cells). The protein from the B3 gene makes up the basic structure of the erythrocyte. Cattle that are homozygous (have two copies of the recessive allele) have pernicious anaemia (bleeding caused by the abnormal red blood cells). Death normally occurs within the first 7 days after birth. Some cases live to adulthood but there is a severe retardation in growth.

As shown in Figure 1, the frequency of B3 in the Australian Japanese Black population was approximately 0.6% in 2000/2001. There is now a very low frequency of the B3 mutation with approximately 0.02% registered animals registered in 2019 having 1 copy of the mutated allele. Please note that the y-axis scale maximum is set at 5% in Figure 1 so that the declining trend in B3 frequency can be visualised.

FIGURE ONE

% B3 ALLELE FREQUENCY TRENDS AUSTRALIAN WAGYU ASSOCIATIONS REGISTERED JAPAENESE BLACK



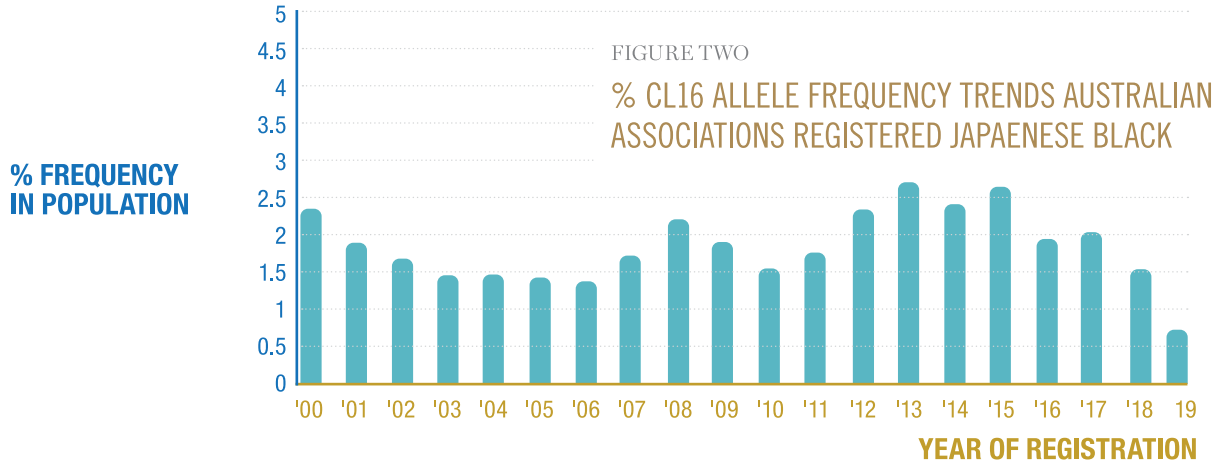
## CLAUDIN 16 DEFICIENCY (CL16)

CL16 (also known as RTD or Renal tubular dysplasia) is a gene disorder on chromosome 1 and causes kidney failure (chronic interstitial nephritis often with zonal fibrosis or excess of fibrous connective tissue). This disorder results in terminal kidney failure and the onset can occur anytime from late adolescence. Cattle are unlikely to live more than 6 years.

As shown in Figure 2, there is now a low frequency of the CL16 mutation in the Australian Japanese Black Wagyu population. Since 2014/15, the frequency of CL16 in newly registered animals has declined from approximately 2.5% to less than 1% of animals registered in 2019. Please note that the y-axis scale maximum is set at 5% in Figure 2 so that the declining trend in B3 frequency since 2015 can be observed.

FIGURE TWO

% CL16 ALLELE FREQUENCY TRENDS AUSTRALIAN WAGYU ASSOCIATIONS REGISTERED JAPAENESE BLACK

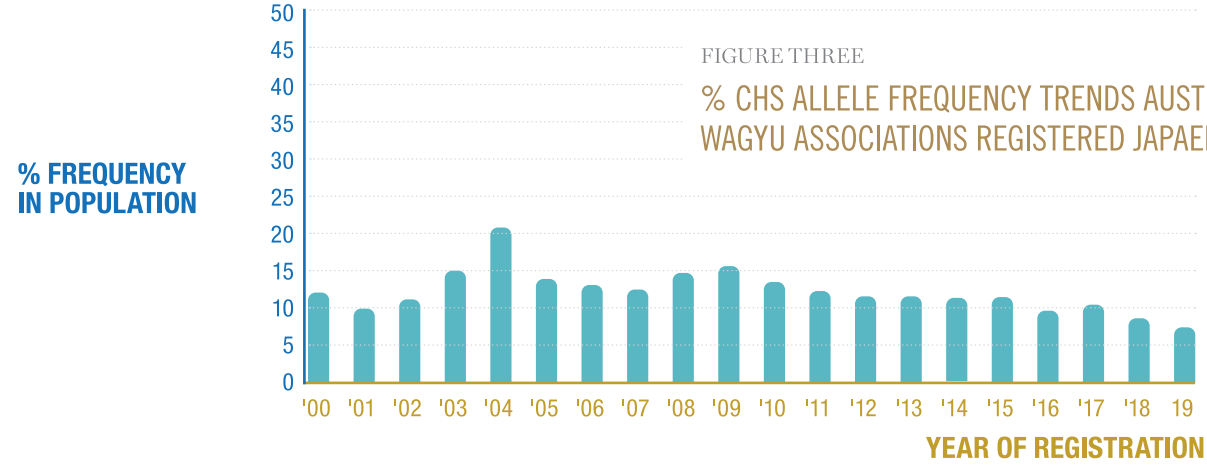



## CHEDIAK HIGASHI SYNDROME (CHS)

CHS is a macrophage disorder (a white blood cell that has an important role in the immune response to disease). If cattle have a malfunctioning immune system, this makes them unable to resist the bacterial challenge. Blood is slow to coagulate so often the first indicator is unusual umbilical cord haemorrhage at parturition (calving). Cattle with this syndrome often have an unusually pale coat colour. As shown in Figure 3, there is still a moderate frequency of the CHS mutation in the Australian Japanese Black Wagyu population with 7% of animals registered in 2019 having one copy of the mutated allele. Frequency of CHS has reduced significantly from 2009, where approximately 15% of animals registered in that year carried one copy of the mutated allele. Please note that the y-axis scale maximum is set at 50% in Figure 3 so that the recent declining trend in CHS frequency can be observed.

FIGURE THREE

% CHS ALLELE FREQUENCY TRENDS AUSTRALIAN WAGYU ASSOCIATIONS REGISTERED JAPAENESE BLACK

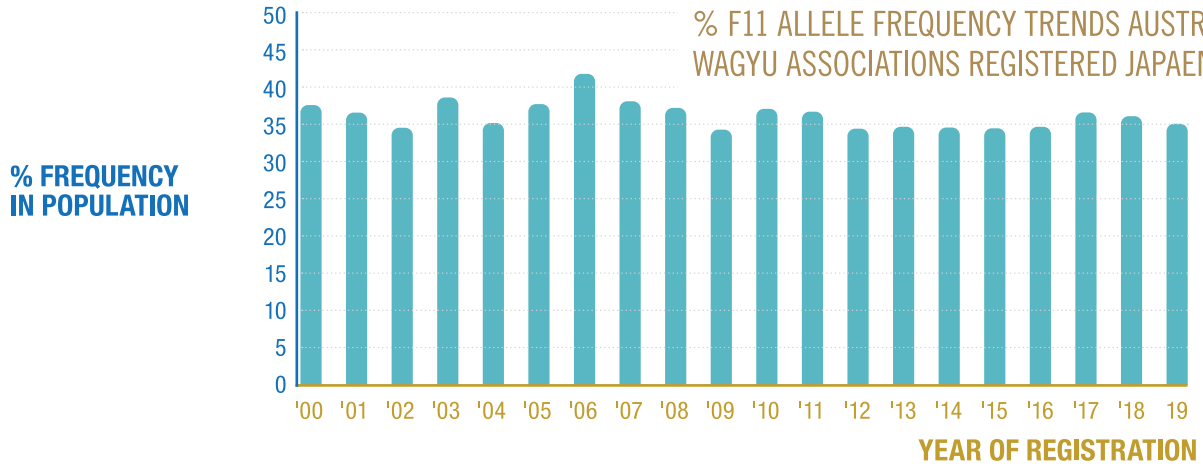


## FACTOR XI DEFICIENCY (F11)

F11 is a plasma protein that participates in the formation of blood clots. Factor XI deficiency is an autosomal disorder that is associated with mild bleeding in Wagyu. Affected animals show prolonged bleeding time and abnormal plasma coagulation after trauma or surgical procedures such as castration or dehorning. It is also possible that Carrier x Carrier matings have increased difficulty producing viable fertilised embryos or full-term pregnancies and are may be repeated (return to cycle) breeders. Note – this is generally a non-lethal recessive condition with affected animals being able to live and breed as normal. This condition also occurs in Holsteins. As shown in Figure 4, there is a high frequency of the F11 mutation in the Australian Japanese Black Wagyu population with approximately 35% of animals registered in 2019 having one copy of the mutated allele. Frequency of F11 has not reduced since 2000, suggesting that no selection pressure is being placed on decreasing its frequency in the population. Please note that the y-axis scale maximum is set at 50% in Figure 4.

FIGURE FOUR

% F11 ALLELE FREQUENCY TRENDS AUSTRALIAN WAGYU ASSOCIATIONS REGISTERED JAPAENESE BLACK

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MORE INFORMATION

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