

AUSTRALIAN WAGYU ASSOCIATION

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IARS Disorder – also known as perinatal weak calf syndrome

IARS Disorder results in a high frequency of death in affected calves within the last few weeks of gestation or first few days of life. DNA testing can now be performed for Japanese Black Wagyu through the Australian Wagyu Association to enable management of the IARS genetic condition.

A scientific article published by Japanese authors in 2013 (*Hirano et al., PlosOne, 5: e64036*) indicated that of 538,111 Japanese Black calves born in 2010, the number of calves that died before three months was 22,020 (4.1%). The incidence of perinatal mortality was slightly higher at 4.5%, with 27.7% of the cases caused by neonatal weakness and 72% of these deaths were associated with normal gestation periods and low birth weights which suggests intrauterine growth retardation.

The calf shown in Figure 1 had a birth weight of 16 kg (normal average; 28.5kg). The gestation period was 296 days (normal average; 288.9 days). The affected calf was weak and had difficulty nursing. The calf died at two days old.



**Figure 1. (Hirano et al., PlosOne, 5: e64036)
A calf born in Japan with perinatal weak calf syndrome.**

Hirano et al. (2013) identified a mutation in the IARS gene (isoleucyl-tRNA synthetase) as being the causative mutation. The mutation results in a reduction in activity of a key enzyme that is important for the protein synthesis process in the developing embryo and newborn. Calves affected by this disorder exhibit anaemia, depression, weakness, variable body temperature, difficulty nursing, growth retardation, and increased susceptibility to infection.

A further publication by Hirano (*Hirano et al. Journal of Animal Science, 87: 1178-1181*) identified that in addition to deaths associated with weak calf syndrome, more than half of affected embryos – those carrying two copies of the IARS gene mutation – died prenatally. When rates of artificial insemination were examined on 11,580 individuals, the frequency of re-insemination in IARS carrier x IARS carrier matings was also significantly higher at 61-140 days gestation.

These findings strongly suggest that the homozygous IARS mutation not only contributes to perinatal calf death, but also embryonic or fetal death.

IARS in the Australian Wagyu population

The SNP information that allows identification of the IARS mutation has now been validated on chips used for genomic testing for the Australian Wagyu Association. Using this SNP information for 44,839 anonymous registered animals, 36,991 were identified as Free (not carriers), 7,701 as Carrier (carrying one copy of the mutation) and 147 as Affected (having two copies of the mutation).

The prevalence of IARS mutation in the registered Australian Wagyu Association Herdbook population was plotted against year of birth so that trends in frequency of the mutation over time could be determined (See Figure 2).

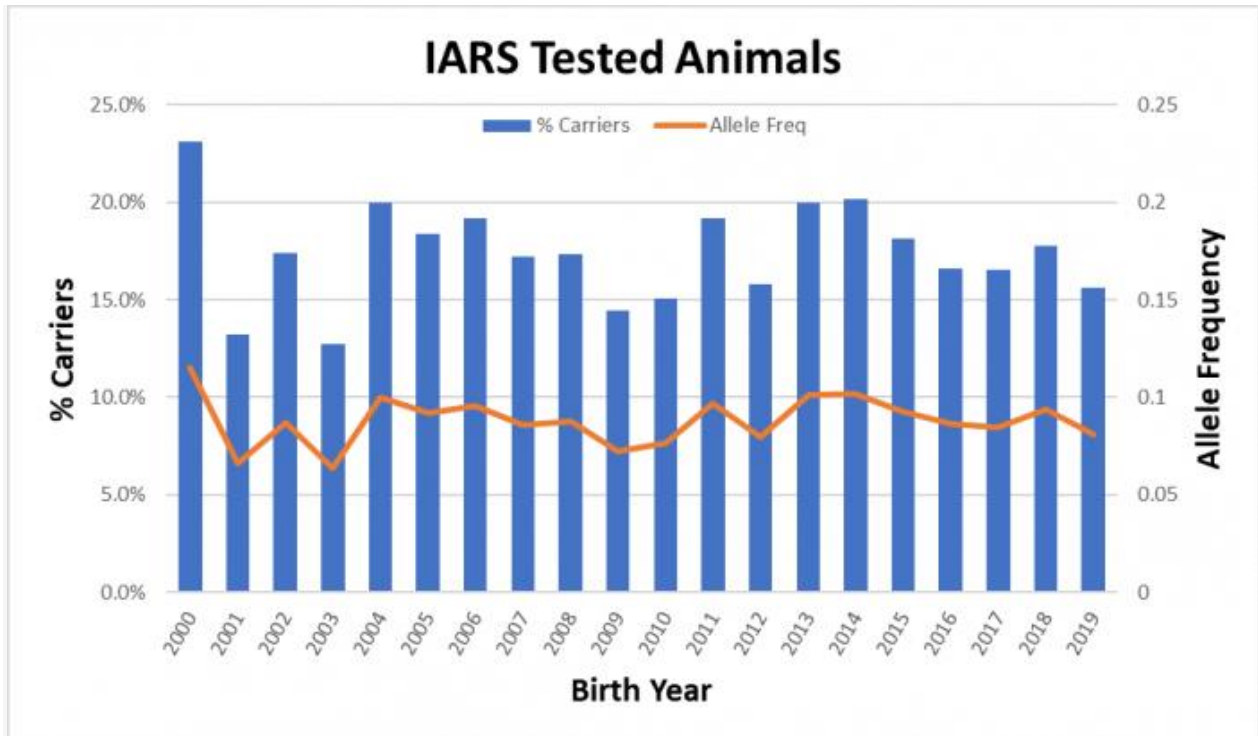


Figure 2. IARS mutation carriers (blue bars) expressed as a percentage of animals tested for animals born from 2000 to 2019. The orange line represents the allele frequency of the mutation.

An allele is a term given to describe a variant of a gene. This can be used to describe a mutation variant such as the IARS mutation. The relative allele frequency of the IARS mutation has stayed at approximately 8% for the past 20 years. Because each animal contains up to two variants of each allele (one maternal and one paternal), the relative level of carrier animals in the population is roughly twice the allele frequency. The relative level of carrier animals in the population is approximately 16%.

If mutations have no effect on survival and reproduction, the frequency of Free compared to Carrier and Affected animals would be predicted to conform to the expected population genetics ratios. In Figure 3, the expected and observed frequencies are compared for different IARS condition status. For Affected animals, only 41% (147) of the expected 356 were found in the genotyped population. This represents a highly significant difference (statistical significance $p < 0.001$). This is a clear indication that IARS affected animals are dying during pregnancy or shortly after birth.

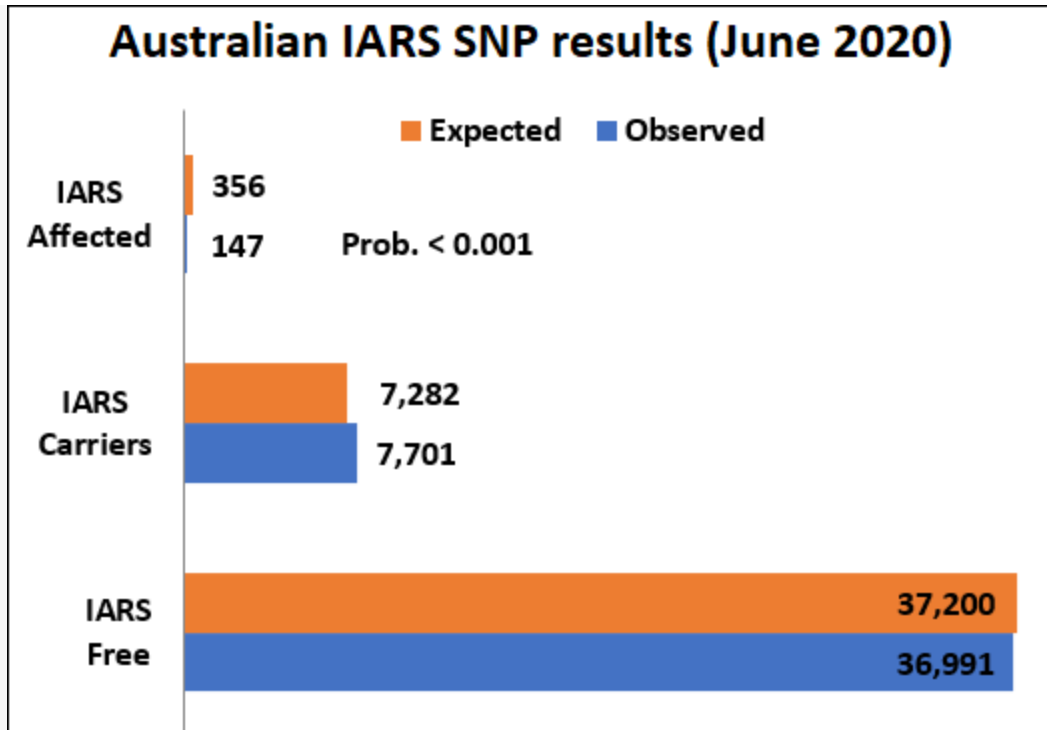


Figure 3. Based on SNP test results, the expected compared to observed number of affected, carrier and free animals show that 209 affected animals were unaccounted for and therefore “lost” before calving or registration.

The relative frequency of the IARS mutation in the Australian Wagyu Association registered population is approximately half of that seen for the F11 genetic condition. F11 was described in V74 of the [Wagyu Update Magazine](#) .

For F11, 83% of the expected number of Affected animals were observed in the Australian Wagyu Association registered population. The relative frequency of IARS affected animals (41%) indicates that the impact of IARS disorder on the viability of IARS affected animals is significant.

Australian Wagyu Association IARS DNA Testing now available

Neogen Australasia have supported the Australian Wagyu Associations analysis of 50K genotype information for the IARS mutation. This has enabled confirmation of the IARS mutation on the Neogen genomics chip.

The Australian Wagyu Association is now updating its DNA test request forms to allow IARS genetic condition testing as stand-alone tests and within Genomics Bundles. The Australian Wagyu Association will begin reporting IARS status of animals registered with the Australian Wagyu Association and will use GeneProb software to estimate probability of carrier animals within the registered Fullblood population – based on DNA tested animals.

Testing for IARS is available from Monday the 24 August 2020 for Australian Wagyu Association members through Neogen Australasia