Fertility haplotypes in dairy cattle

Technote 16

HIGHLIGHTS

- Genetic mutations that cause embryonic loss (and therefore affect fertility) have been identified in several breeds of dairy cattle.
- The mutations occur at such low frequency in the Australian population they account for a very small amount of variation in fertility.
- Fertility haplotypes are breed specific and those available are published on DataVat.com.au

The study of haplotypes is relatively new as it's been made possible by advances in genomic technologies in the past 15 years.

A haplotype is a stretch of DNA (containing one or more genes) that is inherited together from a single parent. Haplotypes may have desirable or undesirable effects on specific traits; for example, there is a haplotype for polledness.

In dairy cattle, fertility haplotypes have been identified that involve a recessive mutation. If an animal inherits the recessive mutation from both parents, the effect is lethal, causing early embryonic loss or stillbirth. This translates to reduced fertility of the parent that carries the haplotype.

At the end of this Tech Note is a quick overview of the principles of genetic inheritance which may be useful background for some readers.

Genes affecting fertility

Daughter Fertility is a very complex trait and is influenced by many genes, found on a variety of chromosomes. The Daughter Fertility Australian Breeding Value (ABV) accounts for all of the genes influencing dairy cow fertility.

Haplotype genes

Unlike daughter fertility, the genetics of lethal haplotypes is relatively simple, involving a short stretch of DNA located on the same chromosome. Although the actual mutation within each haplotype is not always known, gene markers can pick up the presence of the haplotype in the animal's genome.

Lethal haplotypes

The lethal effect of haplotypes is expressed only in homozygous recessive individuals. Because these individuals die as embryos, none are found in the live animals when genotyped.

Let's use the example of the Holstein haplotype HH1. The progeny from a mating between a carrier sire and a carrier dam will result in the following combinations (Figure 1):

- Homozygous non-carrier (HH): 25% of progeny
- Heterozygous carrier (Hh): 50% progeny
- Homozygous recessive – lethal (hh): 25% lost embryos.

Figure 1: Example mating between heterozygous haplotype carriers

		Carrier Sire Heterozygous	
		H	h
Carrrier Dam Heterozygous	H	HH	Hh
	h	Hh	hh (lethal)

Impact of haplotypes on fertility

Haplotypes explain a very small amount of the variation in dairy cattle fertility. They occur at such a low frequency in Australian dairy cattle that their impact on overall conception rates is minor.

A carrier (sire or dam) can still have daughters that are more fertile than the national average because they carry other good genes that affect fertility. A good example of this is the Holstein bull 7H6417 commonly known as "Oman". This bull had an enormous effect on daughter fertility globally and still has an ABV for daughter fertility of 115. He is also a carrier of the HH1 haplotype.

Overall, the effect of the haplotype at a population level will depend on the frequency of the carriers in the population.

Semen fertility

The impact of the fertility haplotypes on a carrier bull's semen fertility rating will be determined by the frequency of the haplotype in the general population. In general, bulls carrying haplotypes will have slightly lower semen fertility because half the embryos produced will inherit the lethal mutation from the bull and, if they inherit another copy from their dam, the embryo will die, and the mating will be recorded as a failure.

Breed differences

Lethal haplotypes affecting fertility are breed specific. They have been identified in many dairy breeds, including Holsteins, Jerseys, Ayrshires and Brown Swiss.

The table below lists fertility haplotypes most relevant to Australian dairy herds.

Haplotypes affecting fertility of relevance to Australia	
Holstein	HH1, HH2, HH3, HH4, HH5, HH6
Jersey	JH1
Ayrshire	AH1, AH2
Brown Swiss	BH2

Haplotype frequency

Cole, et.al (2018) published an extensive list of haplotypes and their corresponding frequencies in the US population. While we expect that the frequencies of these haplotypes in Australia will not be exactly the same, the influence of North American genetics on the global population and previous studies in this area by DataGene staff suggest that the frequencies in Australia will be similar. The following table summarises Cole's results.

Breed	Haplotype	Chromosome	Frequency %
Red Breeds	AH1	17	13.0
	AH2	3	9.8
Brown Swiss	BH2	19	7.78
Holstein	HH1	5	1.92
	HH2	1	1.66
	HH3	8	2.95
	HH4	1	0.37
	HH5	9	2.22
	HH6	3	0.50
Jersey	JH1	15	12.1

Impact on actual fertility

The impact of haplotypes on fertility depends on the frequency of the particular haplotype within the dairy population.

Where the frequency is low (for example 1%), the semen fertility of carrier bulls is predicted to be reduced by about 0.13% (see box). The conception rate of the daughters of carrier bulls is predicted to be reduced by half this (0.07%) because about half the daughters would themselves be carriers.

In cases where the frequency is higher, say 6.5% the semen fertility of carrier bulls is predicted to be reduced by 0.8% and the conception rate of the daughters of carrier bulls was predicted to be reduced by 0.4%.

Calculating impact of haplotypes on semen fertility

The impact of a haplotype on semen fertility is influenced by the frequency of the haplotype, conception rate (assume 50%) and the chance of inheriting the haplotype (one in four).

$$\frac{\text{Haploytpe frequency } \times 0.5}{4}$$

Example low frequency

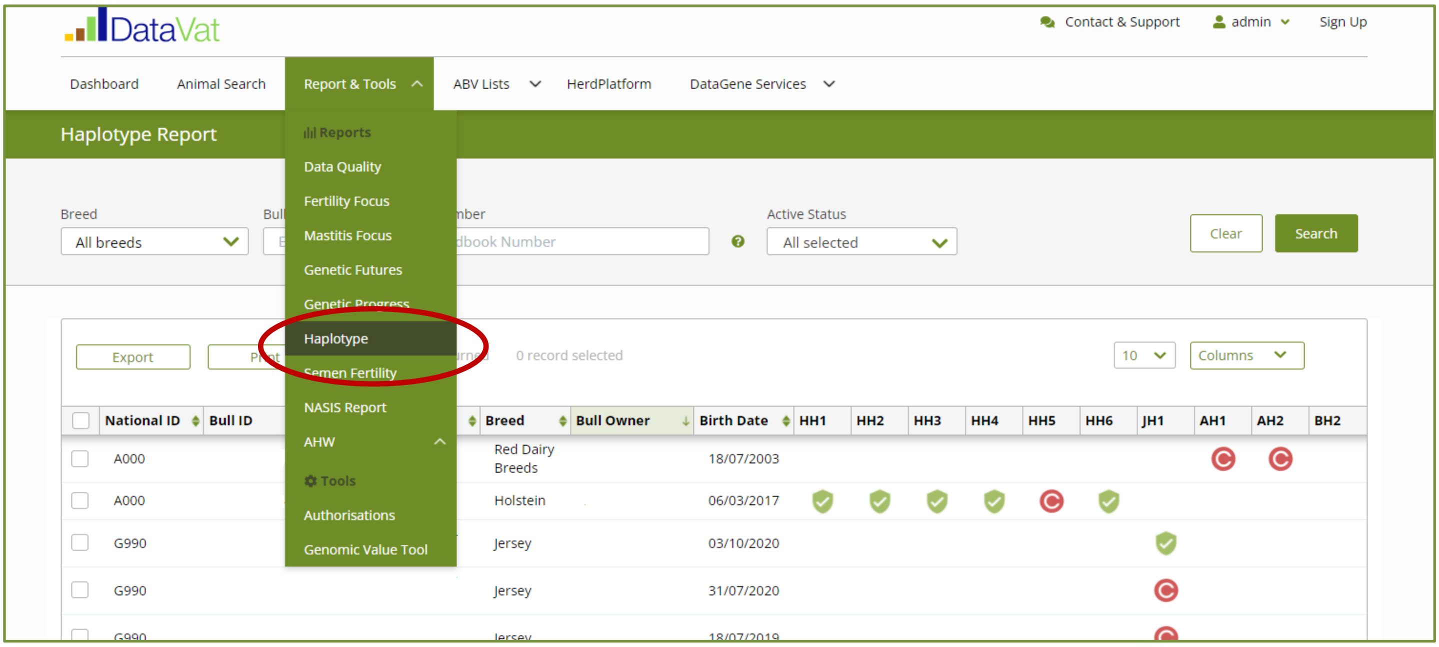
$$\frac{1.0 \times 0.5}{4} = 0.13\%$$

Example high frequency

$$\frac{6.5 \times 0.5}{4} = 0.8\%$$

Haplotypes On DataVat

Haplotype status of animals can be looked up on DataVat.com.au. There is a search function under "Reports and Tools" that allows you to find haplotype results for tested bulls.



Implications for your breeding program

Daughter Fertility ABVs and semen fertility values remain the most useful tools when selecting bulls to improve fertility. The Daughter Fertility ABV captures the effect of all genes affecting fertility, not just the ones tracked by the haplotypes.

Attempting to eradicate every animal with an undesirable gene defect is not recommended because these animals may carry desirable genes for other traits. Also, it is not practical because it is likely that more undesirable gene defects will be found in further investigations.

The use of inbreeding reports is a useful risk management strategy. Mating programs can be uses reduce the risk of haplotype carrier to carrier matings. This may be particularly useful for cows used in embryo transfer programs.

Acknowledgement

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References

1. Cole, J.B et al 2018. Haplotype tests for recessive disorders that affect fertility and other traits

2. Hayes, B. 2011. Report on frequency and effect of Jersey Haplotype 1 (JH1) in Australian Jerseys

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Inheritance basics

Simple inheritance traits

Simple inheritance traits are traits largely controlled by one major gene. These are 'yes' or 'no' characteristics that are either present or absent in an animal. In some cases, simple inheritance traits may involve more than one gene however the pattern of inheritance remains fairly simple. Testing for these genes allows breeders to effectively select for or against the trait/disease.

Dominant vs recessive?

Most simple inheritance traits can be divided into either 'dominant' or 'recessive'. We'll use coat colour as an example. The dominant gene is black (B) and the recessive gene is red (b).

Animals carry two copies of every gene – one is inherited from the dam and the other from the sire. The different variants of a gene are known as alleles (in this example, the alleles are for black or red coat colour).

The combination of alleles determines how a trait is expressed. Where the allele controlling a trait is dominant the animal only requires one copy for that trait to be expressed. Conversely a recessive trait requires both alleles (one from each parent) to be expressed.

Figure 1: Example mating between heterozygous coat colour

		Sire Heterozygous black	
		B	**b**
Dam Heterozygous black	**B**	**BB**	**Bb**
	b	**Bb**	**bb**

Allele combinations are be described as either :

- Heterozygous: one allele is dominant and one recessive(Bb). In the case of coat colour, this will be expressed as a black coat because black is the dominant gene)
- Homozygous: both alleles are the same eg BB, bb), In the case of coat colour, a homozygous dominant animal (BB) will have a black coat while a homozygous recessive animal (bb) will be expressed as a red coat.

Simple maths can be used to predict the proportion of offspring with a particular trait. In the following example both parents are heterozygous black (Bb) ie they are black cattle who carry both the black and red alleles.

When these two animals are mated there are three possible outcomes:

- Homozygous black calf (BB) – 25% of progeny,
- Heterozygous black calf (Bb): 50% progeny
- Homozygous red calf (bb): 25% progeny

Multi-gene traits

Multiple gene traits are controlled by a larger number of genes. This group includes many economically important traits such as daughter fertility and kilograms of protein. In these cases, Australian Breeding Values (ABVs) are used to identify superior/inferior animals as it much more difficult to clearly identify animals with the favourable variants of each gene.

Haplotype inheritance

While overall daughter fertility is a multi-gene trait, recessive haplotypes affecting fertility are controlled by specific genes, so the principles of simple inheritance can be applied.

About DataGene

DataGene is an independent and industry-owned organisation responsible for driving genetic gain and herd improvement in the Australian dairy industry. DataGene performs pre-competitive herd improvement functions such as genetic evaluation, herd testing and herd improvement software development and data systems. DataGene is a Dairy Australia and industry collaboration.

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