

Scrapie Canada
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Sheep Genetics and Scrapie Resistance

Genetic makeup has been determined to be a significant factor in a sheep's resistance or susceptibility to classical scrapie. Research has shown that there is a link between sheep prion proteins, susceptibility levels and disease progression.

A sheep's genes (which cumulatively are its genetic makeup) are made up of stretches of folded proteins, formed by specific groupings of amino acids. If a protein folds incorrectly (misfolding), it becomes a prion protein with infectious properties. When a scrapie prion protein enters an animal's body, it can cause normal prion proteins to misfold triggering a chain reaction producing a large amount of abnormal prions that accumulate in the animal's brain and neural tissue. The accumulation of these abnormal prion proteins cause tissue damage and cell death that leads to the neuro-degenerative disease that is scrapie. An animal's resistance to protein misfolding is tied to the amino acids determined by the codons 136, 154, and 171 (section of genetic code) in the animal.

In North American, the most studied codons associated with scrapie are 136, 154 and 171, with particular emphasis placed on codons 136 and 171. Varying amino acid combinations at these codons give rise to 5 commonly seen codon alleles: ARR, AHQ, ARH, VRQ, and ARQ (at codons 136, 154 and 171 respectively). The susceptibility of sheep to scrapie in North America has been shown to differ widely between genotypes as follows:

Genotype (codon 136 codon 171)	Genotype (Allele 1/ Allele 2)	Susceptibility to Classical Scrapie
AA RR	ARR/ARR	negligible
AA QR	ARQ/ARR	very low
AV QR	VRQ/ARR	intermediate
AA QQ AV QQ VV QQ	ARQ/ARQ ARQ/VRQ VRQ/VRQ	high

The genotypes of 249 sheep confirmed as scrapie positive cases in Canada between 1998-2008 were determined where 91.6% were ARQ/ARQ, 5.2% were VRQ/ARQ, 1.2% were VRQ/VRQ, 1.2% were VRQ/ARR, 0.4% ARQ/AHQ and 0.4% VRQ/AHQ. This study also looked at genotypes of infected sheep compared with their healthy flock mates. The ARR/ARR and ARR/ARQ genotypes were the only numerically significant genotypes of Canadian sheep for which no scrapie cases were reported. Findings from this study support the idea that a breeding strategy that produces a high frequency of ARR animals will produce a large number of animals resistant to the strain of classical scrapie currently circulating in Canada (Harrington et al, 2010).

Such programs would be useful in improving resistance to classical scrapie in Canada, HOWEVER they raise important issues including possible unintended (negative) impacts on performance traits, inbreeding, and lack of genetic diversity in commercial populations. As well, selection for genotypes resistant to the current strain of classical scrapie found in Canada may result in greater susceptibility to another scrapie strain such as atypical scrapie.

It is important to remember that genetic resistance to scrapie does not guarantee that an animal will never develop scrapie, just as genetic susceptibility to scrapie does not mean that an animal will develop scrapie. But the genetic selection of scrapie resistant animals **at the farm level** is a useful tool in a box full of scrapie risk control measures. Scrapie disease surveillance (deadstock testing) and the limited acquisition of females from those low or negligible risk flocks or herds remain the gold standard for controlling the risk of developing scrapie.

Genetic information can easily be determined by genotype testing sheep. A list of Canadian labs conducting scrapie genotype testing can be found at: www.scrapiecanada.ca/genotyping_labs.html. For more information please contact Scrapie Canada at 1-866-534-1302 or by e-mail at admin@Scrapiecanada.ca.