Genetic Testing for Scrapie Resistance and Susceptibility

By: Mubrouka Elharram

With the recent developments in genomics, breeding for herd improvement will involve more than just selection based on desirable productivity traits. DNA testing will allow farmers to select for disease resistant animals, which will benefit overall long-term farm profitability. Here, I describe the process of testing for scrapie disease resistance and susceptibility based on recent research in Ontario goats, starting from animal sampling to performing DNA tests and the use of the results on-farm. The animal genotype is the key in determining whether a goat is disease resistant or susceptible. Thanks to this new DNA testing, we can now look towards managing the risk of scrapie disease in Ontario goat herds.

What is DNA and the Prion (PrP) Protein Gene?

DNA, or deoxyribonucleic acid is the genetic material that is in the cells of all living organisms. It contains the blueprint for all the molecules necessary for the development and function of an organism.

The strands of DNA are made up of four different letters or building blocks known as nucleotides. A DNA sequence or gene is determined by the arrangement of these four letters. A sequence of three nucleotides codes for an amino acid and a single amino acid change in a protein can change its function. In the case of scrapie susceptibility and resistance these types of changes have occurred in the prion protein (PrP) gene. The susceptible protein changes its shape and this triggers more proteins to change shape which then leads to disease. DNA testing detects these single nucleotide differences allowing us to assess scrapie susceptibility and resistance based on new research that has been conducted in Canada (Srithayakumar et al, 2016). http://bmcvetres.biomedcentral.com/articles/10.1186/s12917-016-0684-x)

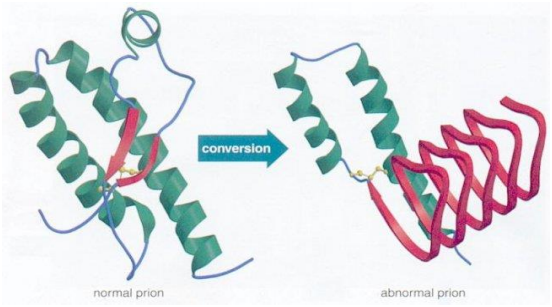

Figure 1: Cartoon of the conversion of a normal sheep prion protein shape to an abnormal state (scrapie disease) in the susceptible protein (Fidelis, K., 2004).

How is a DNA test performed?

A DNA test is performed by a laboratory technician using samples provided by the goat producer. For the PrP genotype test, nasal swabs are used for sampling and these have been shown to yield sufficient amounts of high quality DNA.

Figure 2: Nasal swab sampling by Ontario goat producer.

DNA Extraction and Quantification

DNA extraction is the process of isolating and purifying DNA from cells and removing proteins and other contaminants.

It is important to know exactly how much DNA we have isolated; therefore, quantification is an important step before

other procedures can be carried out. DNA can be quantified by staining it with fluorescent dyes. The DNA quantification test is sensitive to very small amounts, as low as 1ng (10^{-9} g) of DNA.

DNA Sequencing

Goats have a genome with 3x109 base pairs and 22,000 genes. DNA amplification techniques and sequencing of specific segments allows us to look at one of the 22,000 genes.

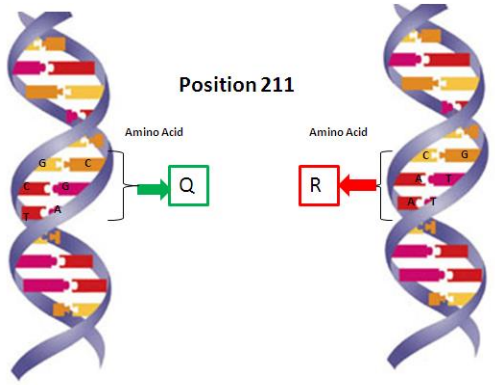

Figure 3: Example of how a difference in a DNA sequence translates to amino acids Glutamine (Q) and Arginine (R).

Genotyping

Genotyping involves the process of determining genetic variations in an animal. Scrapie susceptibility and resistance in sheep is affected by changes in amino acids at three positions in the prion protein. In Ontario goats, position 211 has been shown to be important in determining resistance and susceptibility. Codon 211 can specify the amino acid Glutamine (**Q**) or Arginine (**R**). Since goats will inherit two copies of the prion protein gene from its parents, there are two (forms) alleles in each animal. Therefore, goats will have a genotype of either **QQ**, **QR**, or **RR** at position 211 of the PrP gene. A recently published study, looking at one breed of Ontario goats, shows an association with having the genotype **QQ** and goats being resistant to scrapie disease, while **RR** appeared to be highly susceptible. A genotype of **QR** would indicate that a goat has a low risk of being affected by scrapie disease.
(http://bmcvetres.biomedcentral.com/articles/10.1186/s12917-016-0684-x).

How do I use DNA test results?

The results of this test will assist producers in making informed decisions with breeding strategies as well as purchasing and selling animals. It is desirable to select for the resistant **QQ** genotype, while also maintaining high production traits as well as genetic diversity within a herd. The more **Q** and fewer **R** forms may reduce the risk of a scrapie outbreak. The use of **QQ** bucks or **QQ** semen can accelerate the increase in **Q** and reduction of **R** in the herd. As is seen in *Figure 4a)* **RR** bred with a **QR** goat will result in half the offspring being **RR** and highly susceptible and half being **QR** weakly susceptible. When breeding occurs between two weakly susceptible goats **QR** X **QR**, there will still be a 25 per cent chance of having a highly susceptible or resistant kid, and a 50 per cent chance of a weakly susceptible offspring (*Figure 4b*). When breeding occurs between **QQ** X **QR**, then half the offspring will be resistant and half weakly susceptible (*Figure 4c*). The most ideal situation will be when breeding occurs between two **QQ** goats in which all of their offspring will be **QQ** (*Figure 4d*). Once all of the herd is **QQ** no further testing will be needed.

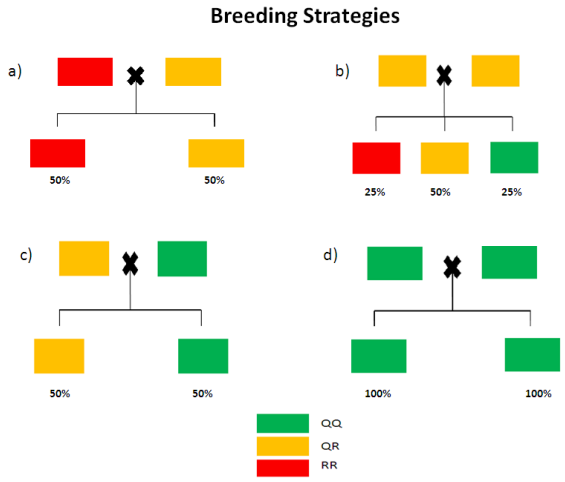

Figure 4: Example s of breeding strategies between goats with susceptible (RR), weakly susceptible (QR) and resistant (QQ) genotypes.

In time it may be possible to reduce scrapie susceptibility in herds and move the Ontario goat population towards more resistant genotypes. Scrapie genotyping is a tool that can be used in an overall plan to manage the risk of scrapie on a particular premises. Further work with the Canadian Food Inspection Agency and further research in Canadian goats will be required before we will eliminate the need to de-populate complete herds when a positive case of scrapie is found on farm. However, this project is the first step in that process and these potentially resistant genotypes may also facilitate the export of Ontario goat genetics to international markets.

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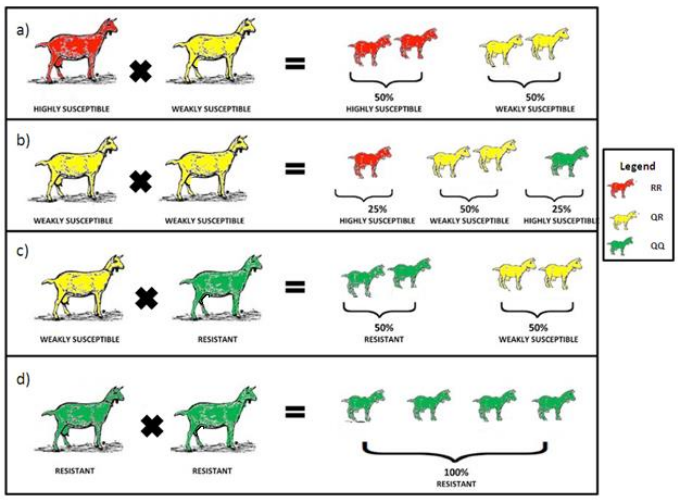

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