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**Using genotypes to reduce susceptibility to Ovine Progressive Pneumonia (OPP)**

In the U.S., the disease Ovine Progressive Pneumonia (OPP) causes extensive welfare and financial losses due to decreased ewe productivity of about 20% and eventual culling or death of breeding stock. Surveys of U.S. sheep have shown that 36% of sheep operations have infected animals and 24% of all animals tested were seropositive. Once infected, sheep remain infected for life, and there is no effective treatment or vaccine.

Sheep producers can eradicate OPP from a flock in two ways. First, is by serological testing and removing all infected sheep with the obvious reduction in genetic diversity and reduced opportunity for making gains for other economically important traits. Second, is creation of a second separate negative flock by testing and isolating all young ewe lambs after weaning until serological testing at 9 months of age. As time goes on the second flock ultimately replaces the infected flock, but with less impact on loss of genetic diversity or gains on other traits. While effective, these management procedures are time consuming, expensive, and do little to improve sheep flocks in terms of genetic resistance to OPP. Thus, OPP-free flocks may continue to remain genetically predisposed to the virus causing OPP infection, with risk of re-infection if exposed to infected sheep.

Genetic variation within the ovine gene known as *TMEM154* is associated with reduced susceptibility, although not complete resistance, to OPP infection. The testing for this relative susceptibility requires consideration of the entire protein rather than evaluating a single genetic marker. Those markers are more formally known as nucleotide polymorphisms (SNP). Variation at multiple SNP define the form of the *TMEM154* gene expressed in each animal. The four most common versions of the *TMEM154* protein, called haplotypes, in U.S. sheep were designated “1” through “4” and represent 97% of the animals tested. The occurrence of one or two copies of either haplotype “2” or “3” is associated with increased susceptibility to OPP virus infection. Conversely, animals with combinations of haplotypes “1” and/or “4” have decreased susceptibility. In fact, such animals are nearly 10 times less likely to become infected with OPP than those carrying either haplotype “2” or “3”. The haplotype “4” version while favorably impacting susceptibility to OPP results in a deletion of the *TMEM154* protein. When homozygous, it results in animals with a complete knock-out and loss of function of the *TMEM154* protein.

The genetic markers used to identify *TMEM154* haplotypes are drawn from the genotyping platform used in Sheep GEMS. That entire platform has 50,000 SNP. The reliability of these *TMEM154* haplotypes is being assessed in two ways. First, they were compared with known *TMEM154* genotypes on a set of animals. They matched perfectly to previously recorded genotypes. Second, the SNP we use to determine an animal’s genetic status for OPP susceptibility appear multiple times on the genotyping platform. When determining an animal’s *TMEM154* haplotype, the consistency of those repeated SNP is checked. This second strategy resulted in 92.7% of the animals having genetic status determined and reported for *TMEM154* for 15,586 sheep evaluated in the four breeds contributing to Sheep GEMS.

Genotypic status at *TMEM154* differs substantially among Katahdin, Polypay, Rambouillet, and Suffolk breeds. Nearly 60% of Katahdin and Suffolk sheep contained at least one of the highly susceptible alleles relative to OPP. On the other hand, in Polypay, only 8%, and in Rambouillet, 15%, were highly susceptible. It may be tempting to use the *TMEM154* genotype as a primary selection criterion. However, we recommend a more balanced approach, where this information is incorporated into an existing breeding program. This allows breeders to continue to make genetic progress on their current priorities, while still reducing OPP genetic susceptibility in their flock. One approach is favoring sires with the more favorable haplotypes of “1” and/or “4”. Another is to avoid mating a ram and ewe that both carry an unfavorable “2” or “3” haplotype. If all other factors are equal, breeders should favor selection of haplotype “1” over haplotype “4”, until more is known about the true function of *TMEM154*.

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