For the OPP Concerned Sheep Breeders Society Newsletter at the Board's request:

Genetic association of *Ovar-DRB1* with ovine progressive pneumonia virus (OPPV): A next phase in genotyping sheep?

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Ovine progressive pneumonia virus (OPPV) is a lentivirus, which is horizontally transmitted predominantly through direct contact of infected adult animals with naive animals and affects the lungs, mammary gland, joints, and in rare cases, the brain of infected sheep. One in five are infected with OPPV within the United States, and this increases to one in two sheep in open rangeland sheep. It is estimated that OPPV costs 2.7 million dollars annually to the U.S. Sheep Industry, and the presence of OPPV in ewes has been recently shown in Canada to significantly lower weaning weights and increase lamb mortality. The vast majority (70-80%) of OPPV infected sheep do not manifest outward clinical signs in the forms of respiratory distress, mastitis, arthritis, wasting, and ataxia. The disease is typically insidious and inconspicuous whereby producers often times do not know they have the infection in their flock unless they test serum from the whole flock for the presence of anti-OPPV antibodies.

OPPV diagnosis is confirmed by detecting anti-OPPV antibodies in the serum of sheep 1 year of age and older using a competitive enzyme linked immunosorbent assay (cELISA) or agar gel immunodiffusion assay (AGID). In addition, diagnosis can now be confirmed by quantifying OPP provirus levels in the peripheral blood leukocytes of sheep using a new, validated OPPV real-time quantitative PCR (qPCR) assay. These diagnostic tests are highly sensitive and specific, but because of the insidious nature of OPPV, in order to keep an OPPV free flock, annual diagnostic testing for at least 3 years and testing of new flock members prior to placing them into the flock is strongly recommended. Because of this, diagnostic testing can be quite expensive. In a flock of 500, cELISA tests can approach $2-2.5K per year and OPPV qPCR can approach 10-times the cost of cELISA per year. Some other test is needed to help lower OPPV seroprevalence while keeping the cost low for producers.

The obvious and best example of a test that helps to lower disease incidence is genotyping at codon 171 in the prion gene (*PRNP*) for scrapie. Removing animals with homozygous *PRNP* genotypes encoding for Q at codon 171 (QQ171) has greatly aided the sheep industry in reducing scrapie incidence. Although initial costs for genotyping are high whereby a flock of 500 would cost ~

$5.5K, this price substantially lowers after the first year when rams and new ewes are only tested.

Previous research papers showed that the Rambouillet breed had the lowest ovine progressive pneumonia virus (OPPV) seroprevalence as compared to other breeds including Columbia, Polypay, and Finnsheep cross breeds. In addition, monozygotic twins shared similar lung pathology at post-mortem after each twin was infected with a different strain of OPPV, but between the monozygotic twin sets, there were significant pathological differences in the lung. These early studies strongly suggested that there was a host genetic factor that could be affecting OPPV infection status.

Our laboratory at USDA-ARS Pullman, WA is currently evaluating several sheep genes for links to higher or lower OPP provirus levels. One host gene, Ovis aries (*Ovar)-DRB1*, is of particular interest since it has been described as a putative cellular receptor for OPPV and is currently being evaluated for associations to ovine progressive pneumonia (OPP) provirus levels in 383 Idaho sheep of the Rambouillet, Columbia, and Polypay breeds. In this first study, there are several *Ovar-DRB1* genotypes (Y31, T32, N37, T51, Q60 or N74) that associate with lower OPP provirus levels. Five of six of these OPP provirus level-lowering *Ovar-DRB1* genotypes are also predominantly found in the Rambouillet breed. In contrast, there are three *Ovar-DRB1* genotypes encoding for H32, A38, or I67 that associate with higher OPP provirus levels, and these genotypes are found in all three breeds. Overall, these association results suggest that specific genotypes in *Ovar-DRB1* contribute as OPP provirus level controllers especially in the Rambouillet breed. However, prior to implementing breeding strategies, production trait analyses needs to be performed to ensure there are no links between a specific *Ovar-DRB1* genotype and undesirable production traits. Our collaborators, Dr. Michelle Mousel and Dr. Gregory Lewis, at the U.S. Sheep Experiment Station (USSES) in Dubois, Idaho are currently evaluating production traits in relationship to the *Ovar-DRB1* findings.

In summary, if you are running Rambouillet sheep, you may already have lower OPP provirus levels in your flock. We are working on a high-throughput, low cost genetic test to determine the presence of these OPP provirus load-lowering genotypes. If you have flocks with some Rambouillet sheep, *Ovar-DRB1* may be a future genetic tool for lowering OPP provirus load in your flock. Our study has only examined the Rambouillet, Columbia and Polypay breeds; therefore, extending these results into other breeds should not be done. Further investigations in more breeds in flocks with >50% OPPV seroprevalence will establish whether these and/or other DRB1 genotypes significantly associate with OPP provirus levels.