

A reverse genetic screen method to investigate lamb mortality in French Dairy Sheep

Lamb mortality poses significant challenges to agriculture, affecting animal health, welfare, and economic outcomes; early lamb losses are a key concern for sheep breeders. High mortality rates in the first month of life are attributable to a variety of environmental and other factors, and recessive deleterious genomic variants are known to segregate in livestock populations potentially causing lethality when homozygous.

The Small Ruminants Genomics team at INRAE, France is devoted to identifying genes and their polymorphisms underlying traits in sheep and goats and the understanding of the molecular mechanisms of their phenotypes. The team have developed a workflow for screening, identifying and validating for genetic variants associated with lamb mortality, applied in Manech Tete Rousse (MTR) and Lacaune dairy sheep breeds.

The group use a reverse genetic screen strategy to specifically identify recessive lethal variants. Initially, high-density SNP chips and WGS enable fine mapping of genomic regions and the identification of trait causal variants. The segregation of the variants is then studied in multiple sheep breeds and the lethal effect validated with controlled mating trials between heterozygous carriers. Specific variant genotyping assays are then performed using PACE PCR genotyping.

Work in recently published studies has identified causal recessive variants in three key genes linked to homozygous deficient haplotypes and associated with rearing loss in the studied breeds. By this approach, variants have also been identified in genes known to impact sheep morphological traits such as horns and coat colour.



References:

- Ben Braiek *et al.* "A single base pair duplication in SLC33A1 gene causes fetal losses and neonatal lethality in Manech Tete Rousse dairy sheep." *bioRxiv* (2023).
- Ben Braiek *et al.* "Homozygous haplotype deficiency in Manech Tête Rousse dairy sheep revealed a nonsense variant in MMUT gene affecting newborn lamb viability." *bioRxiv* (2023).
- Ben Braiek *et al.* "A Nonsense Variant in CCDC65 Gene Causes Respiratory Failure Associated with Increased Lamb Mortality in French Lacaune Dairy Sheep." *Genes* 13.1(2022).