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Presenter abstracts

13. A recessive stop-gain mutation in *CCDC65* is associated with lamb mortality in French Lacaune dairy sheep

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In a previous work using 50k SNP data from Lacaune dairy sheep genotypes, we have identified 11 haplotypes with homozygous deficiency (LDHH) supposed to host recessive lethal mutations. Among them, LDHH6 located on OAR3 was the most frequent haplotype (12.1% of heterozygous carriers) and it was associated with an increase in the stillbirth rate.

In the present study, we have analyzed the whole-genome sequences of two Lacaune rams heterozygous carriers of LDHH6, and we have compared them to the sequences of 23 non-carriers Lacaune rams and 68 other animals from 14 different sheep breeds. After variant filtering, we have identified a SNP in the two LDHH6 carriers whose variant allele induced a premature stop-gain mutation in the Coiled-Coil Domain Containing 65 (*CCDC65*) gene. *CCDC65* is involved in the assembly of the nexin-dynein complex for the formation of microtubules in ciliated cells and mutations in *CCDC65* are associated with “*Ciliary dyskinesia, primary 27*” causing respiratory distress in human.

In order to identify the affected phenotype in sheep, we generated 17 at-risk matings between carrier rams and carrier ewes genotyped for the candidate mutation in *CCDC65*. A total of 16 lambs were born alive, and among them, five were identified as homozygous carriers and died between the age of one week and one month, all suffering from respiratory problems as tachypnea. At the autopsy, we particularly observed a broad hepatization of lungs involving infectious pneumonia.

Management of this causal mutation in the Lacaune dairy sheep selection scheme through reasoned mating of carrier rams and ewes could improve overall lamb viability by 2%.