

## Fine mapping of birthcoat type in the Romane breed sheep

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### Abstract

Birthcoat type is an important component of lamb survival for sheep raised under harsh environment. At birth two types of coat were observed: a long hairy coat or a short woolly one. It was shown that hairy coat lambs are more adapted to survive around lambing time due to a better coat protection with less heat losses at coat surface and show better growth performances up to the age of 10 days than woolly coat lambs. Birthcoat type was estimated to be a highly heritable trait and it was reported that its determinism seems to be under the control a few major genes. A QTL detection design was initiated in a Romane breed population to search for loci influencing adaptive traits including birthcoat type through a whole genome scan with the OvineSNP50 beadchip on 824 lambs issued from 8 sire families. A highly significant ( $p < 0.1\%$  Genome Wide (GW)) and a putative QTL affecting birthcoat type were found on chromosomes 25 and 13 respectively. Fine mapping with additional markers, comparative mapping and sequencing of the QTL segment on OAR25 revealed the presence of a 2kb DNA deletion segment. All animals from the experimental design were genotyped for the presence or absence (ins/del) of this segment on OAR25. Homozygous del/del animals were all bearing a hairy coat at birth but not all the homozygous ins/ins animals were bearing a woolly coat. When including the ins/del genotype on OAR25 as a fixed effect within the linkage analysis model, a highly significant ( $p < 0.1\%$  GW) QTL was found on OAR13 with a significant interaction ( $p < 0.001$ ) between QTL on OAR13 and the ins/del genotype fixed effect of OAR25. It was suggested that both QTL on OAR13 and OAR25 are involved as major genes in the determinism of birthcoat type.

# Fine Mapping of a QTL Affecting Lamb Birthcoat Type in the Romane Breed Sheep



*M. Cano, D. Allain, D. Foulquié, C. Moreno, P. Mulsant, D. François, J. Demars, G. Tosser-Klopp*



EAAP – Nantes – 29/08/2013



1/12



## Variability of lamb birthcoat type

- **Hairy long coat  $\approx$  23.1 mm** (Noire du Velay, Romanov...)



- **Short woolly coat  $\approx$  8.3 mm** (Merinos, Texel, Berrichon du Cher...)



*J. Demars - Fine Mapping of a QTL Affecting Lamb Birthcoat Type in the Romane Breed Sheep*

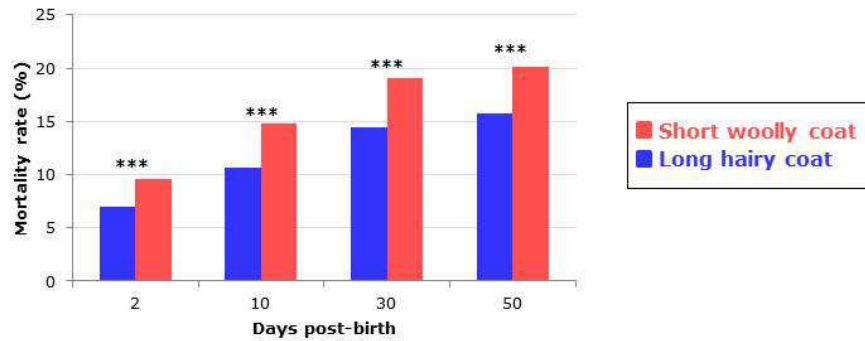
2/12



## Importance of lamb birthcoat type

### ➤ Important survival component (Allain et al, submitted)

- Less total mortality rate in long hairy bearing coats lambs



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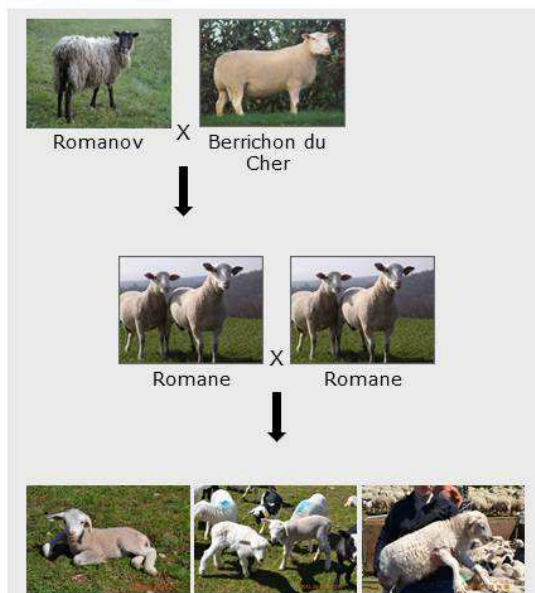


## Importance of lamb birthcoat type

- **Important survival component** *(Allain et al, submitted)*
  - Less total mortality rate in long hairy bearing coats lambs
  - More heat losses in woolly bearing coat lambs
  - Long hairy coat lambs are more resistant to weather changes
- **Heritability of lamb birthcoat type** *(Allain et al, submitted)*
  - Binary trait, heritability = 0.85
  - Continous trait, heritability = 0.56
- **Sheep breeding permanent outdoor**
  - Economical and agronomical trait = Importance to use in selection
  - French Romane breed, high productive potential breed



## Description of the study design



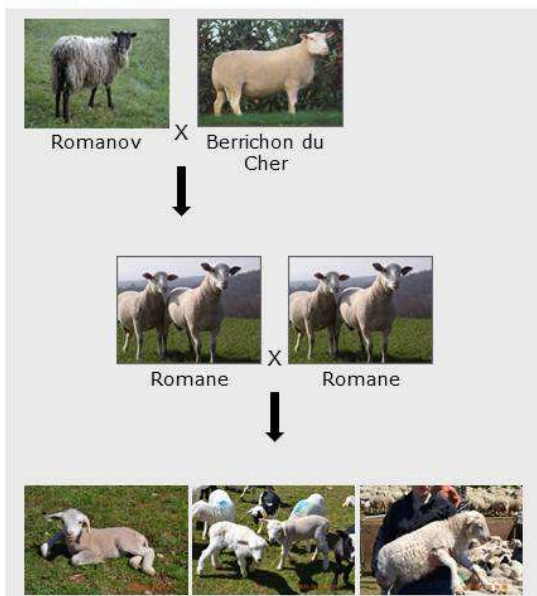
- **Half-sib design**
  - 8 sires Romane \* dams Romane
  - $\approx$  100 genotyped lambs / sire







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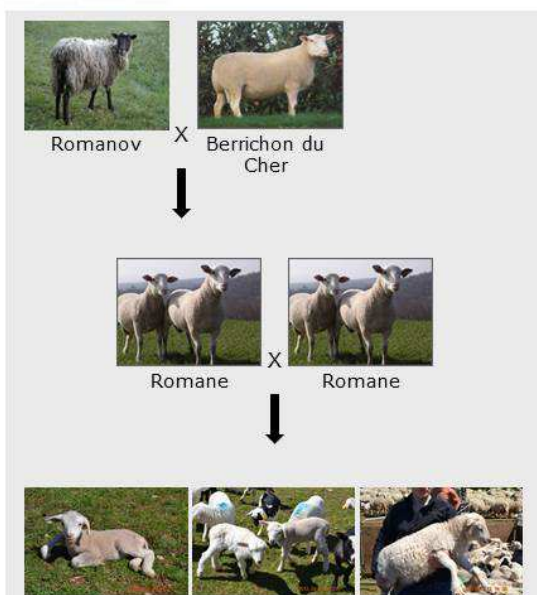
### ➤ Materials

- Phenotype = Lamb birthcoat type
- Genotype = Ovine SNP50 BeadChip

	Phenotype	Genotype
<b>Sire</b>		X
<b>Dam</b>	X	?
<b>Lamb</b>	X	X



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### ➤ Methods

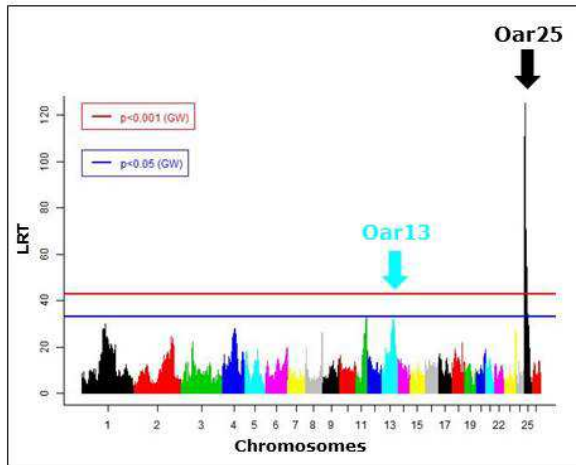
- Genome wide analyses
- Haplotype phasing and clustering
- IBD segment identification



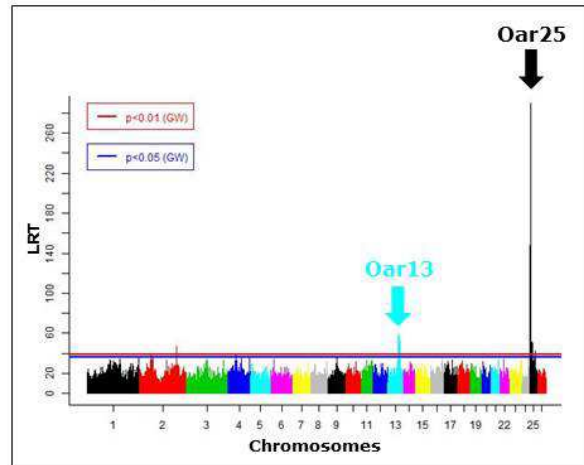


## Genome Wide Association Studies

Linkage analysis



Linkage Disequilibrium analysis



## About the QTL located on Oar25 (QTL<sub>Oar25</sub>)

- **Genetic determinism of the lamb birthcoat type**
  - 2/3 lambs with long hairy coat vs. 1/3 lambs with short woolly coat
  - Long hairy coat : Romanov dominant allele = allele **Q**
  - Short woolly coat : Berrichon du Cher recessive allele = allele **q**
  
- **3/8 sires are heterozygous **Qq** for the QTL<sub>Oar25</sub>**
  
- **QTL<sub>Oar25</sub> located within a 1.6 Mb interval**
  
- **Selective sweep overlapping the QTL<sub>Oar25</sub> region** (Kijas et al, Plos Biol)
  - Merinos and Lacaune animals harbor a short woolly coat
  - Size of the selective sweep is 270 Kb





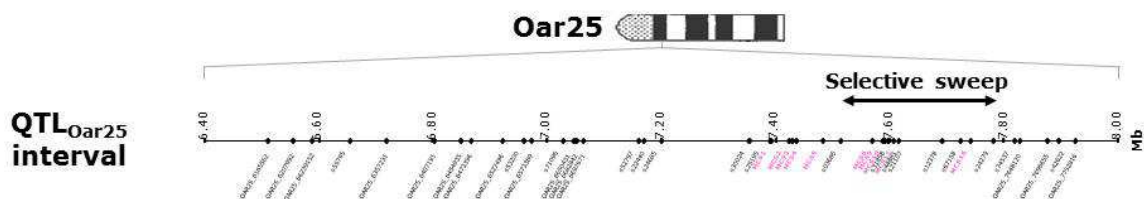
## Haplotypic origin characterization

- **Identification of haplotypes in pure breeds**
  - Genotyping of 11 additional microsatellites
  - Berrichon de Cher (**q**) vs. Romanov (**Q**) haplotypes
- **Genotyping of the 8 sires from the QTL protocol**



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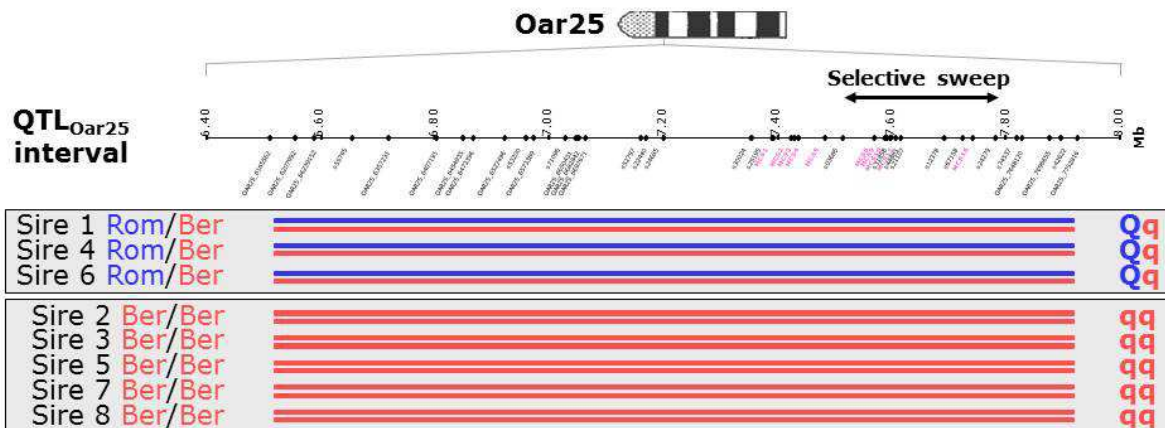






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## Fine mapping of the QTL<sub>Oar25</sub>

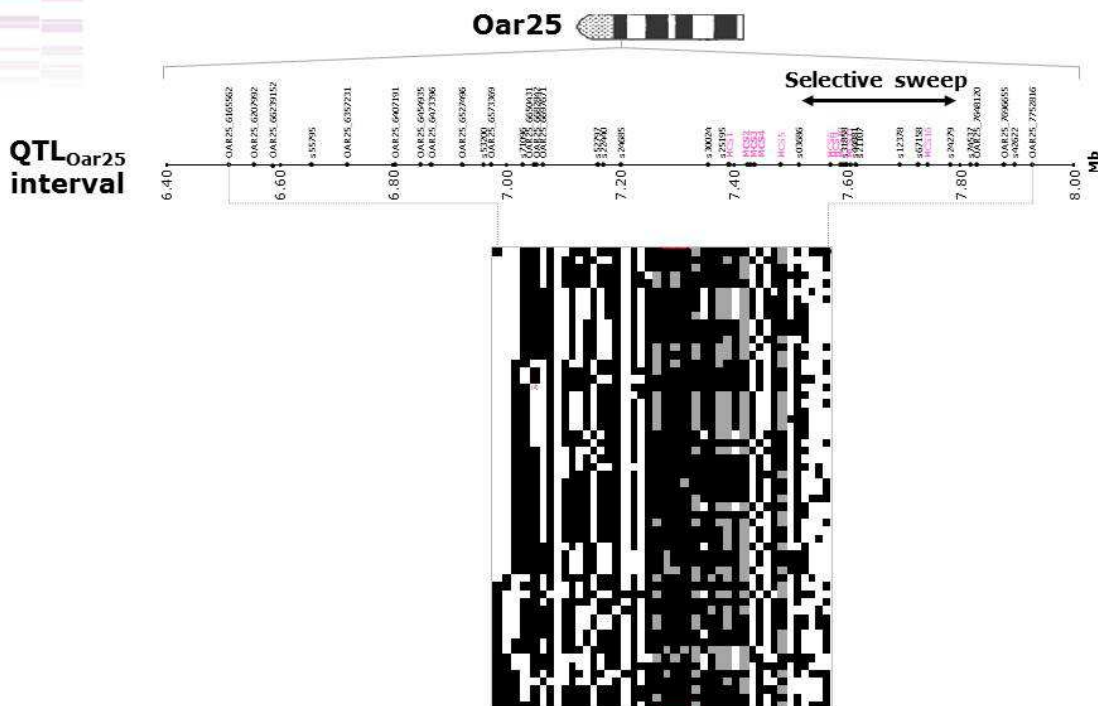
- **Identity By Descent (IBD) haplotype determination**
  - Identical segment shared by all **q** haplotypes
  - Reduction of the QTL<sub>Oar25</sub> interval
- **Fine mapping of the QTL<sub>Oar25</sub> using IBD strategy**
  - Region of 1.6Mb, 32 SNP and 11 MCS
  - Haplotype phasing for all the lambs of the protocol
  - Selection of individuals with a short woolly coat **qq**
  - Identification of 58 different **q** haplotypes
  - Clusterization of the whole dataset







## IBD haplotype identification

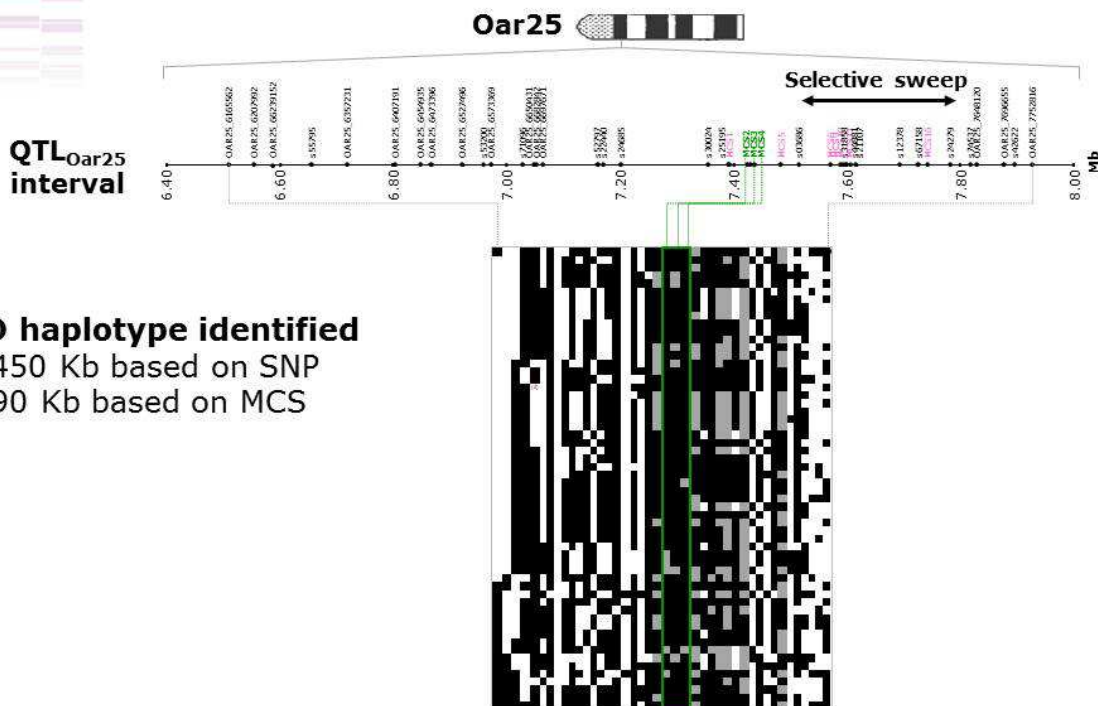


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9/12



## IBD haplotype identification



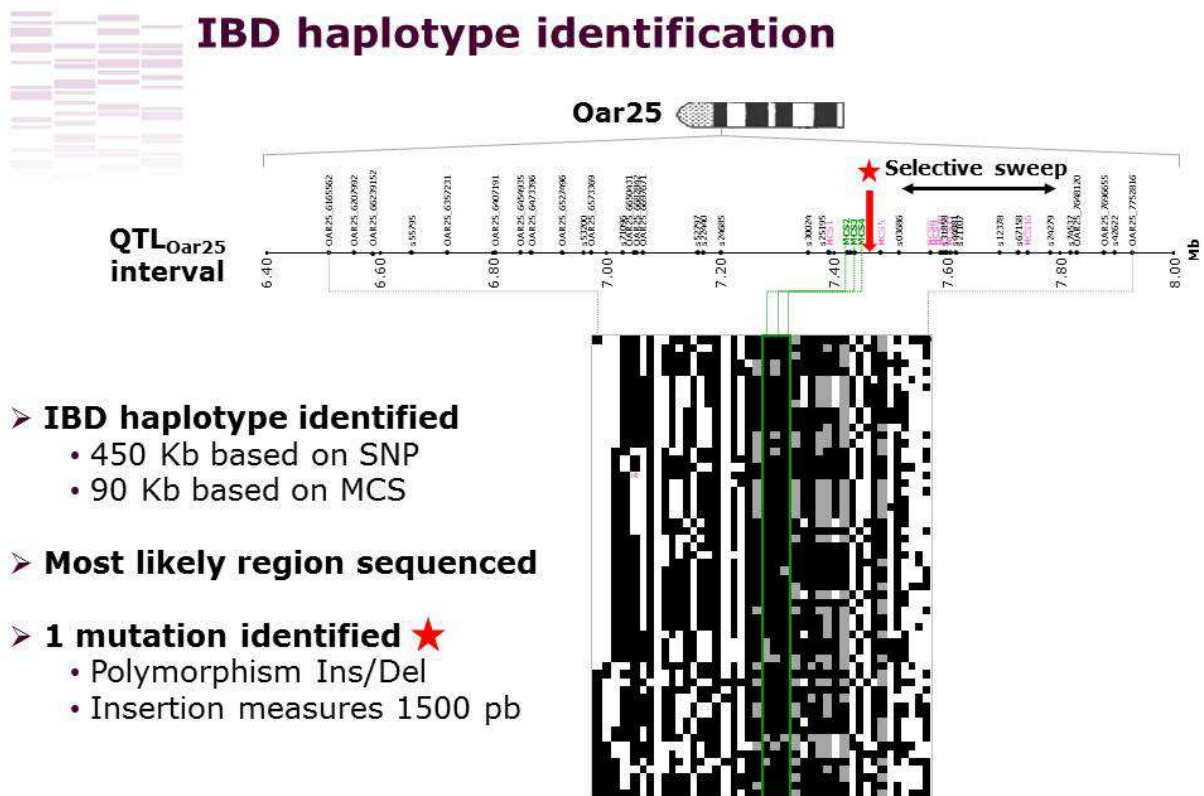
➤ **IBD haplotype identified**

- 450 Kb based on SNP
- 90 Kb based on MCS



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9/12



## Potential causal mutation identification - 1

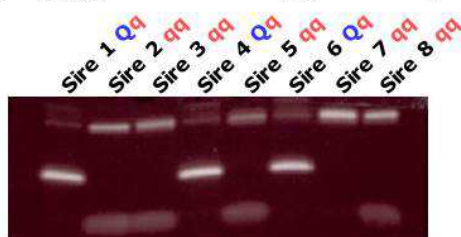
- **Segregation of the Ins/Del mutation in pure breeds**
  - All Berrichon du Cher animals are homozygous Ins/Ins (**qq**)
  - Romanov animals are homozygous Del/Del (**QQ**) or heterozygous





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- **Segregation of the Ins/Del mutation in pure breeds**
  - All Berrichon du Cher animals are homozygous Ins/Ins (**qq**)
  - Romanov animals are homozygous Del/Del (**QQ**) or heterozygous
- **Segregation of the Ins/Del mutation within the protocol**
  - 3 sires **Qq** to the QTL<sub>Oar25</sub> are heterozygous Ins/Del to the mutation

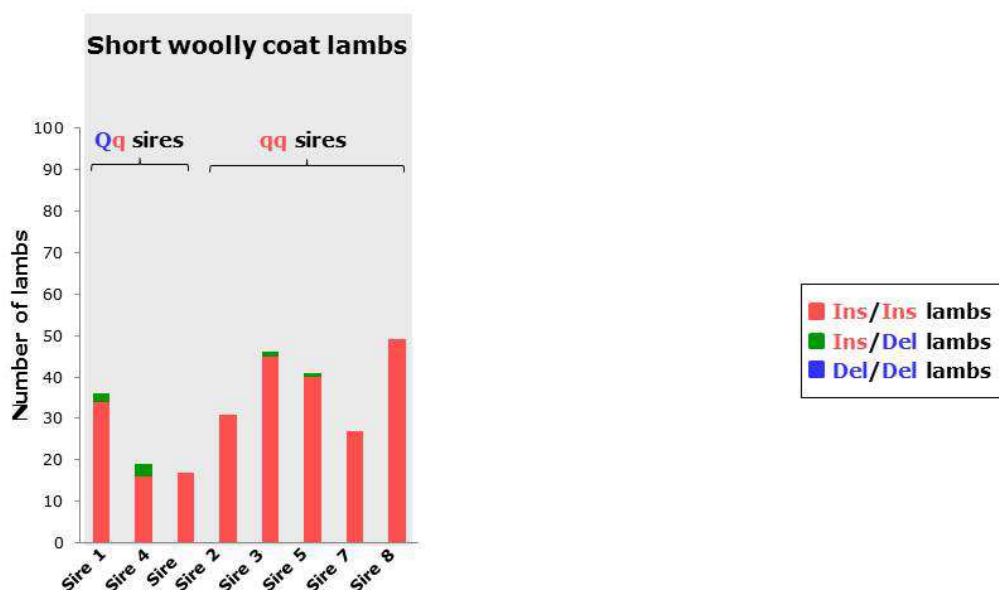


- Inconsistencies of segregation in long hairy coat lambs



## Potential causal mutation identification - 2

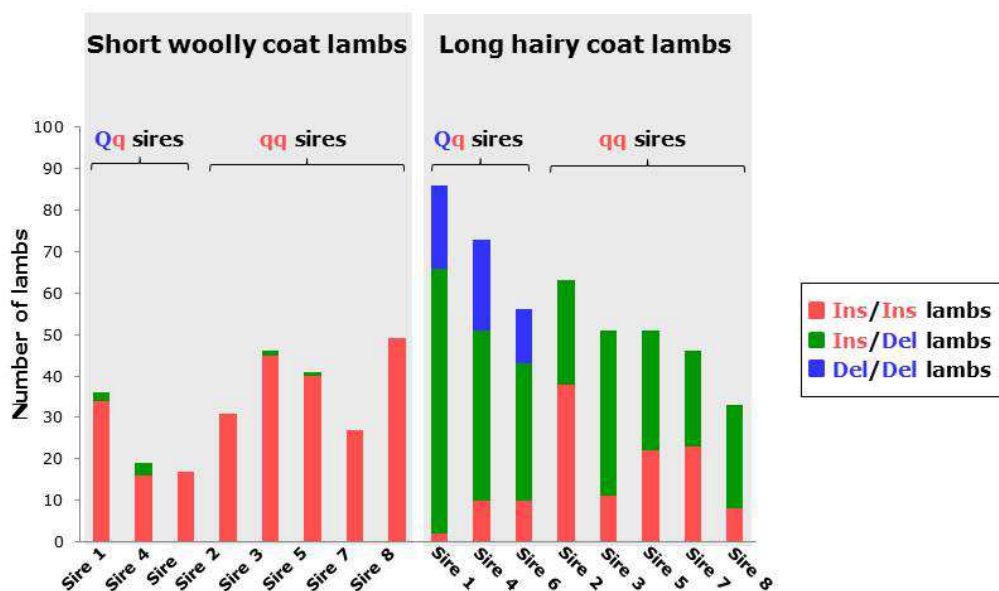
### Genotypic distribution of the Ins/Del mutation





## Potential causal mutation identification - 2

### Genotypic distribution of the Ins/Del mutation



## To conclude about the QTL<sub>Oar25</sub>

- **Identification of a IBD haplotype**
  - Fine mapping of the QTL<sub>Oar25</sub>
  - Novel interval of localization  $\approx$  between 90 kb and 450 kb
- **Identification of a potential causal mutation**
  - Ins/Del measuring 1500 bp
  - Mutation segregates with the short woolly coat phenotype
  - Existence of lambs with long hairy coat harboring the mutation
- **Interaction mechanisms between QTL<sub>Oar25</sub> and QTL<sub>Oar13</sub>**
  - Statistical analyses show an interaction between both QTL
  - Work ongoing...







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