



## ➤ Transcriptome analysis reveals a different immune response depending on a *SOCS2* gene point mutation

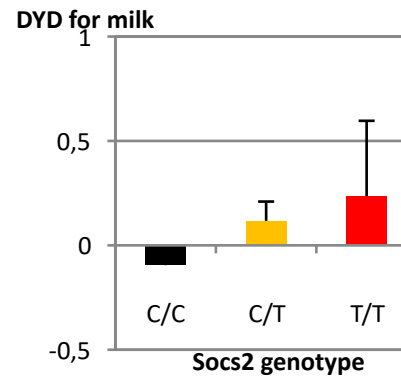
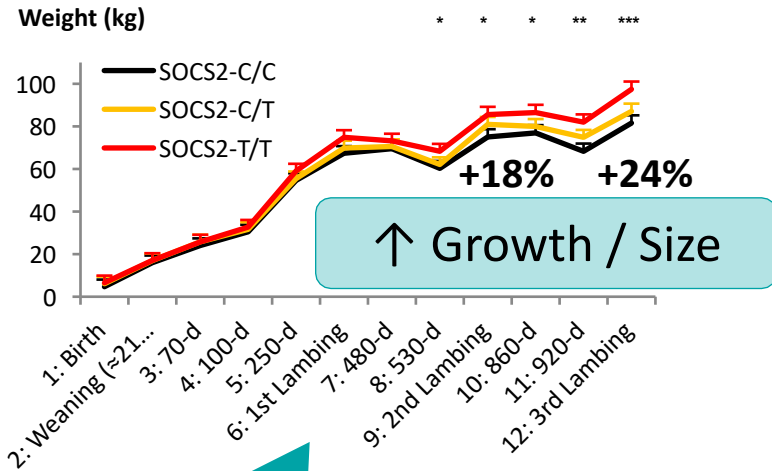
C. Oget-Ebrad, C. Cabau, S. Walachowski, N. Cebron, J. Sarry, C. Allain,  
R. Rupp, G. Foucras, G. Tosser-Klopp

29<sup>th</sup> August 2023 - Session 37

*Omics and integrative analyses towards understanding inter-organ cross-talk and whole body physiology of livestock*

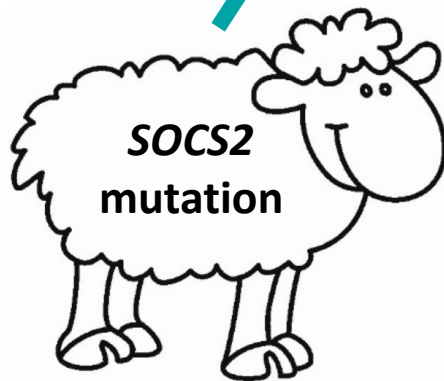
# The SOCS2 mutation shows pleiotropic effects

- Rupp *et al.* (2015) identified a **point mutation controlling mammary inflammation** in dairy sheep using a **GWAS** for the milk **SCC** (Somatic Cell Count)



C = wild allele  
T = mutated allele

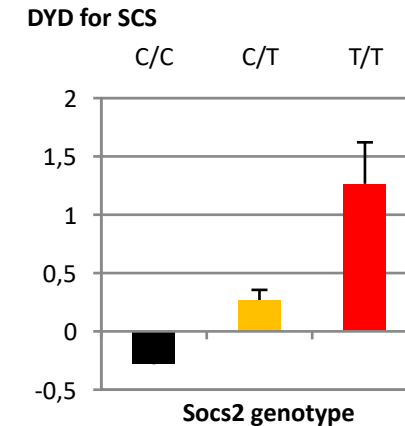
R96C : Arg → Cys  
= modified protein function



↑ Milk production

+4%

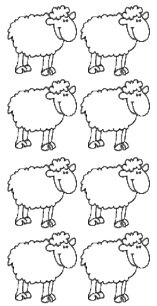
↑ Inflammation



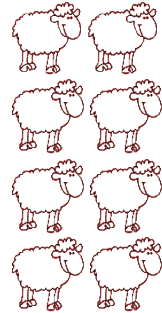
# Compare C/C and T/T ewes during an experimental infection

- **Objective:** Determine **differences in infection response mechanisms** between the two *SOCS2* genotypes

8 C/C



8 T/T



**envt** école nationale vétérinaire Toulouse

2018



Monitoring during 152h post-inoculation

## Experimental challenge

with *Staphylococcus aureus* (strain SA9A)



### CLINICAL DATA & AUTOPSY

Temperature, clinical scores

### MILK PHENOTYPES

Milk production, SCC, bacteriology, characterization of cells



### BLOOD PHENOTYPES

Inflammatory proteins, cytokines, characterization of cells

### BLOOD TRANSCRIPTOME - RNA-SEQ DATA

14 ewes x 7 check times ~ 95 samples  
20,017 normalized genes

INRAE

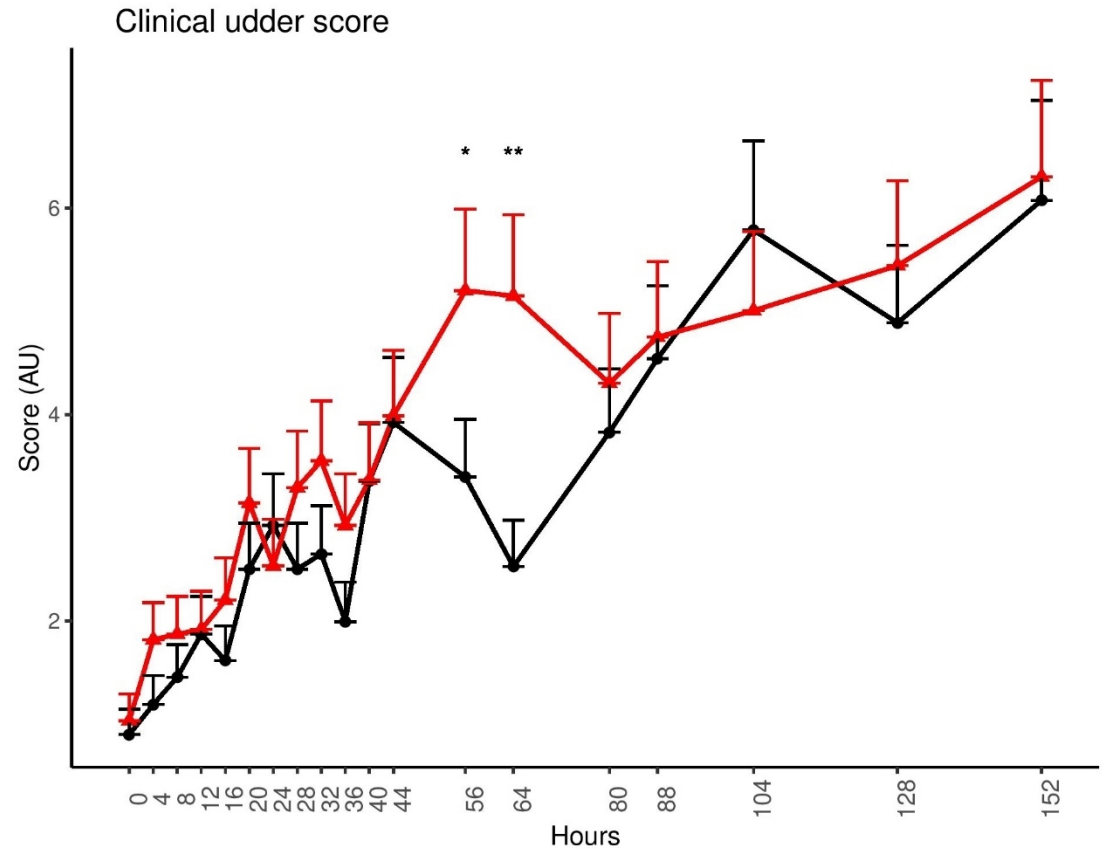
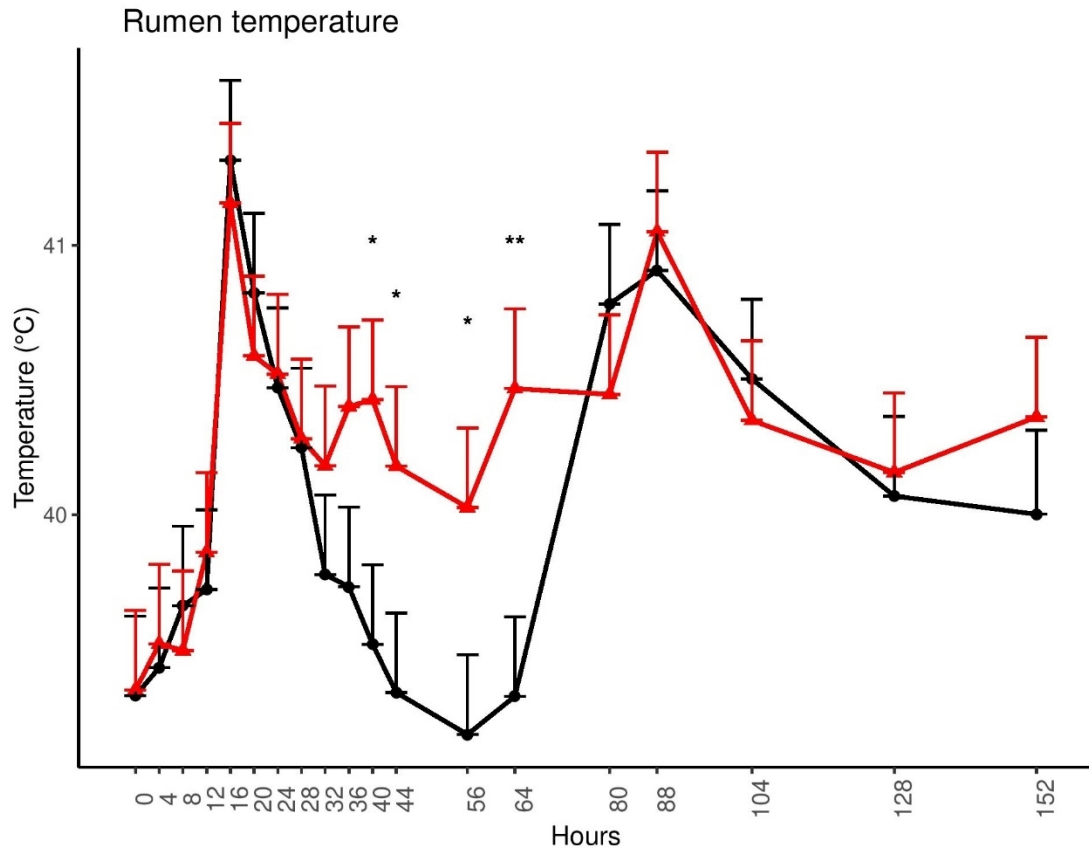
Transcriptome analysis reveals a different immune response depending on a *SOCS2* gene point mutation

29<sup>th</sup> August 2023 / [C. Oget-Ebrad](#), C. Cabau, S. Walachowski, N. Cebron, J. Sarry, C. Allain, R. Rupp, G. Foucras, G. Tosser-Klopp



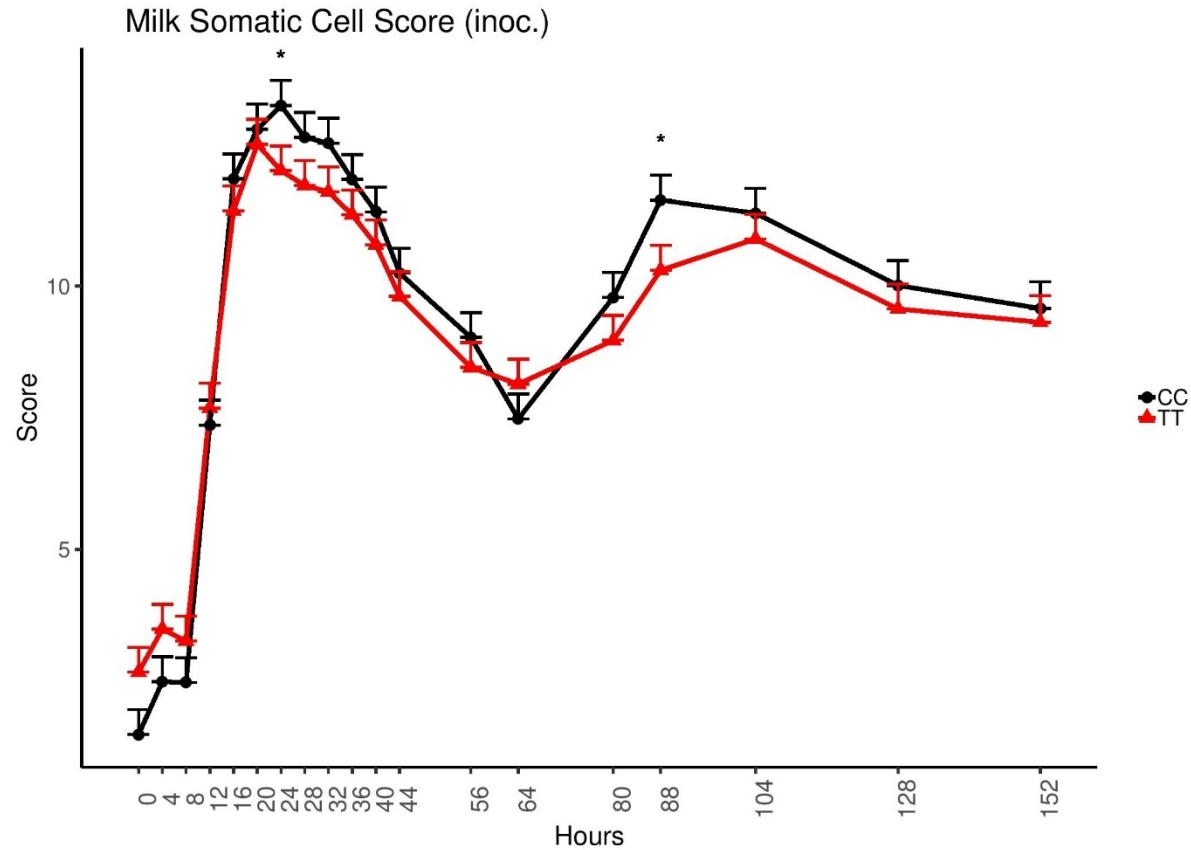
# Increased clinical reaction in T/T

- **More severe fever** in T/T around T56 (56 post-inoculation hours), with **deteriorated clinical condition**

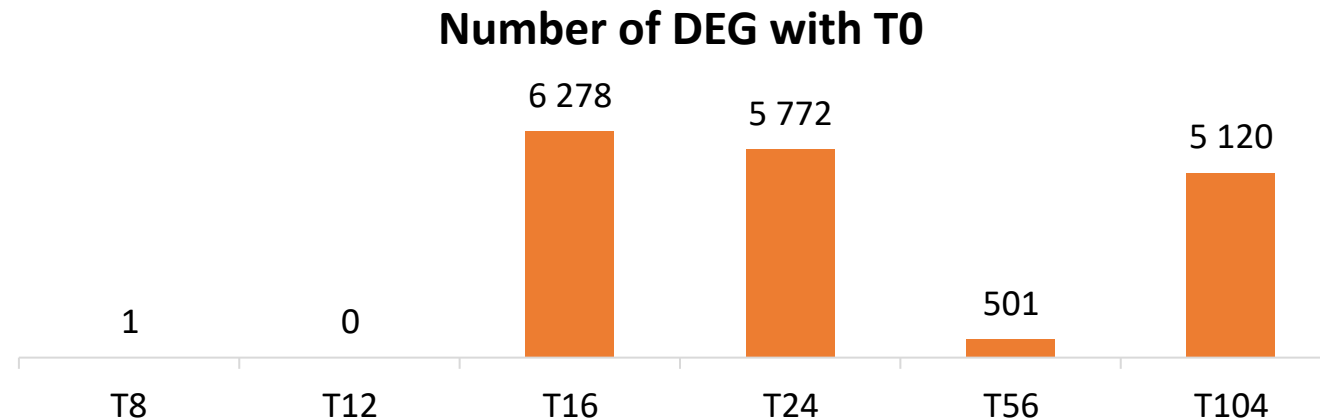


# Less effective immune response in T/T

- **Fewer immune cells** recruited in T/T milk to fight infection during the two waves



# Differentially Expressed Genes (DEG) showing the immune response



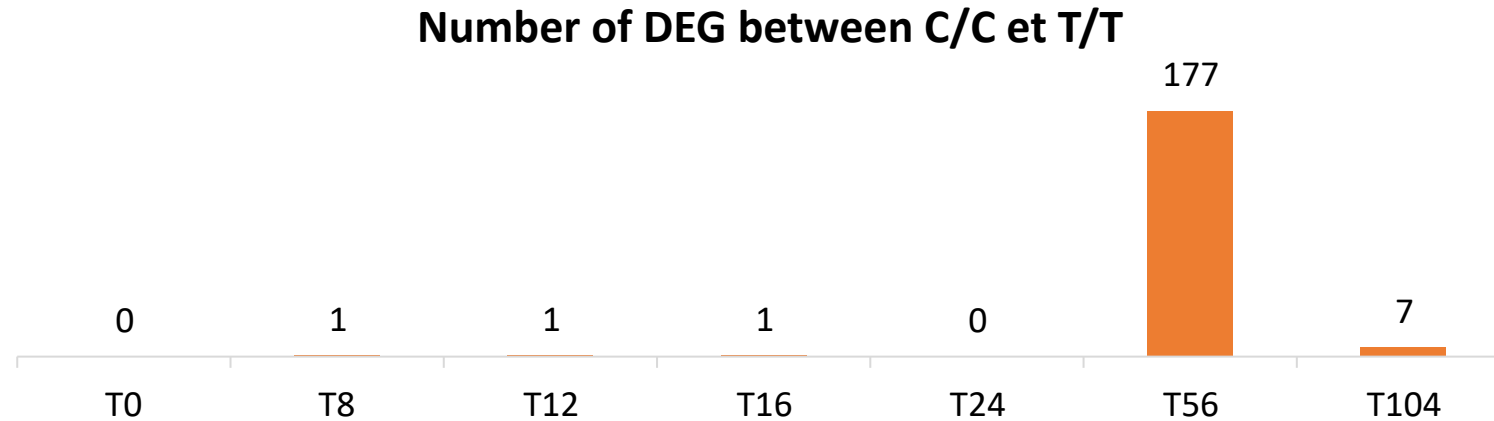
- Genes differentially expressed (independently of the genotype) in **response to infection from T16** as revealed by **edgeR** analysis

- **Functional analysis:**



- Activation of the **immune response**:
  - Lymphocytes (between T0 and T16)
  - Monocytes, macrophages and NK cells (between T0 and T24)
- **From T56**, the activated pathways are those of **cell cycle regulation/apoptosis** (immune response in place)

# DEG showing the effect of the SOCS2 genotype



➤ Only time with DEGs: **T56 (edgeR)**

➤ **Functional analysis:**

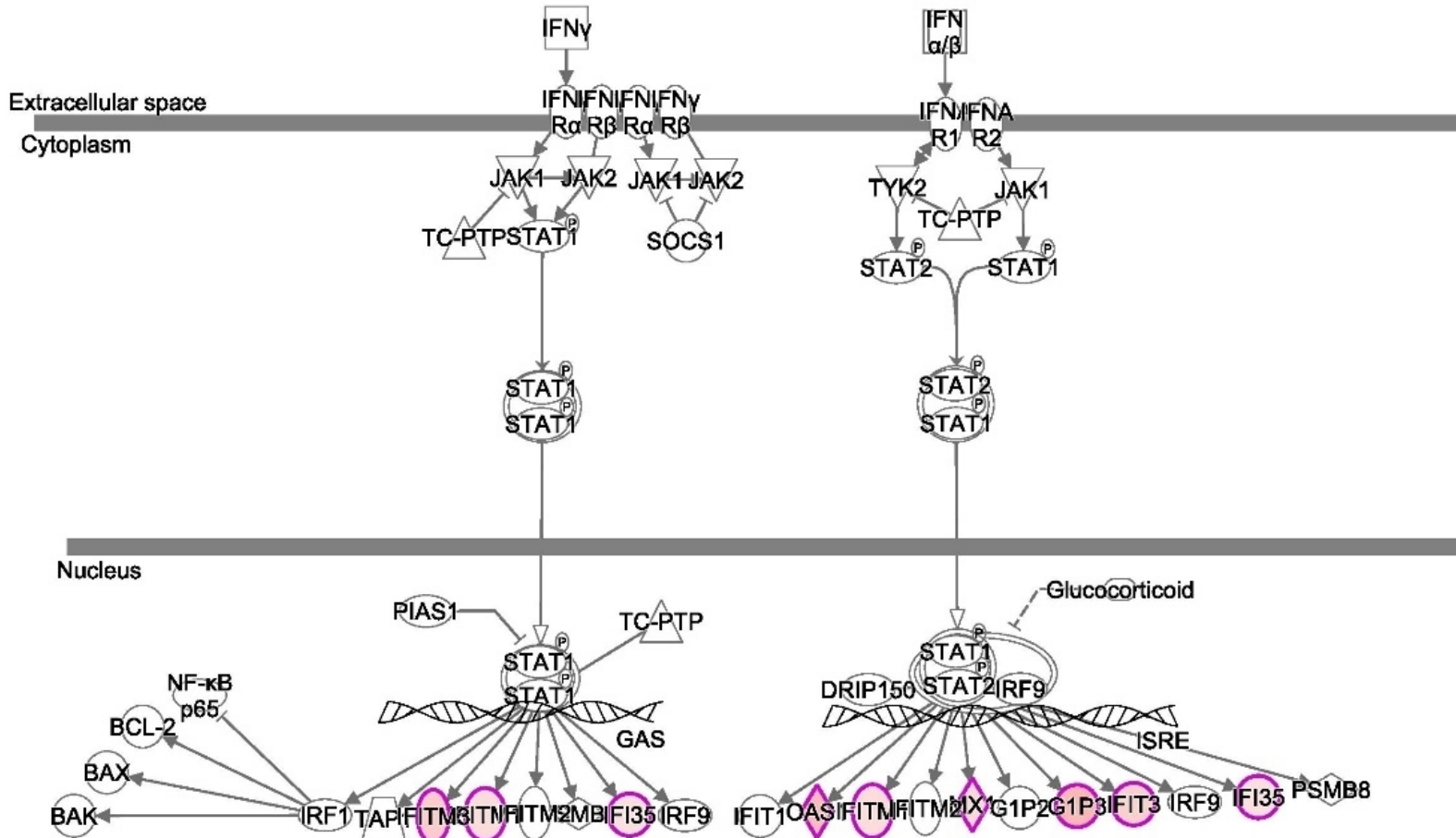
- Overactivation of interferon and **STAT-3** pathways in T/T vs. C/C



# Role of SOCS-2 in the immune response: hypotheses



➤ Interferon signaling pathway overactivated in T/T at T56



## ➤ Hypothesis:

- Indirect regulation of **SOCS-1**, a protein inhibitor of the interferon pathway
- Regulation of **interferon receptors**
- Inhibition of receptors for **STAT-3**-inducing signaling molecules





# Discussion - Take home message

- **Clear differences** (increased clinical response in mutants) despite the design limitations:
  - Limited number of animals
  - Potential influence of pre-existing infection in a half-udder?
  - Mastitis under polygenic control (use of ½ sisters)
- Significant **overactivation of STAT-3 and interferon pathways** in T/T vs. C/C
- T/T have an **increased inflammatory response**:
  - Increased production of pro-inflammatory factors
  - Poorer control of inflammatory response
  - Or both





74<sup>TH</sup> ANNUAL MEETING OF THE  
EUROPEAN FEDERATION OF  
ANIMAL SCIENCE

LYON – FRANCE  
AUGUST 26<sup>th</sup> – SEPTEMBER 1<sup>st</sup>  
2023

➤ **Thank you  
for your attention**

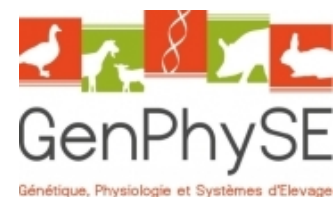


Source : R. Rupp



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