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Christian Beauvallet, Claudia Bevilacqua, Eric Chanat, Patrice Martin

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# LCM combined with MALDI-TOF Mass Spectrometry to demonstrate that $\alpha_{s1}$ -casein is required for efficient export of the other caseins from the Endoplasmic Reticulum to the Golgi apparatus

<sup>1</sup>Beauvallet C., <sup>1</sup>Bevilacqua C., <sup>2</sup>Chanat E. & <sup>1</sup>Martin P.



<sup>1</sup>INRA, UMR1313 Génétique animale et Biologie intégrative, Team « Lait, Génome & Santé » and Plateforme @BRIDGE-ICE, F-78350 Jouy en Josas, France

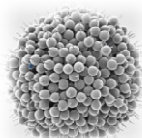


<sup>2</sup>INRA, UMR 1348 Physiologie Environnement et Génétique pour l'Animal et les Systèmes d'Elevage, 35590 Saint-Gilles, France

## Background

Caseins, the main milk proteins, aggregate in the secretory pathway of **mammary epithelial cells (MEC)** into large supramolecular structures, the so-called **casein micelles**.

The role of individual casein in this process and the detail structure of the casein micelle remain poorly understood. In the goat species, a **deficit in  $\alpha_{s1}$ -casein is responsible for the accumulation of caseins in distended RER cisternae** and for a perturbation of the secretion process of proteins and lipids that are synthesized as triglycerides at the ER level. In contrast, no accumulation was recorded in MEC lacking  $\beta$ -casein expression.

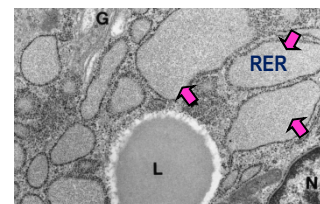
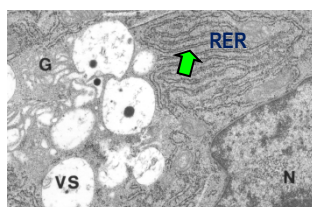


Casein micelles



**Defective:**  
Homozygous O/O at the *CSN1S1* locus

**Wild type: Homozygous A/A at the *CSN1S1* locus**

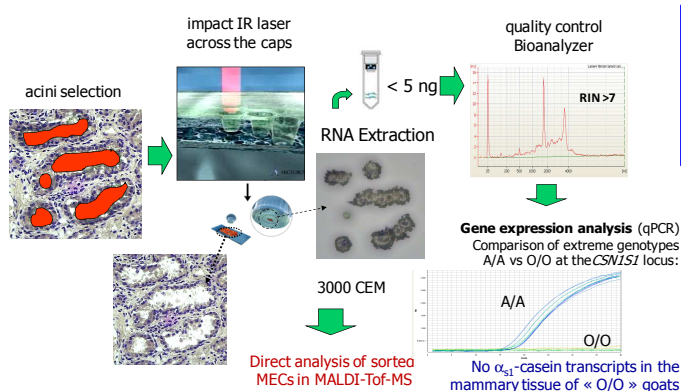


**Swelling of the Rough Endoplasmic Reticulum**

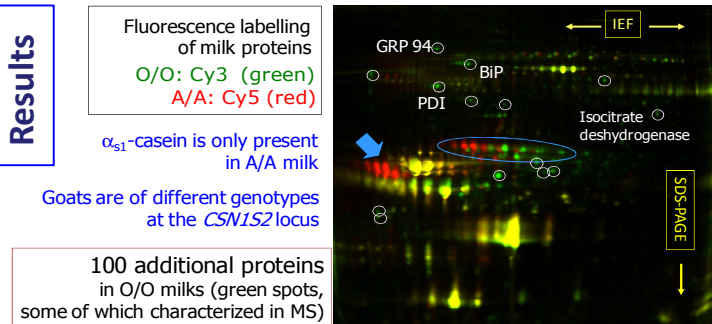
What are the mechanisms involved in MEC dysfunction?

## Materials & Methods

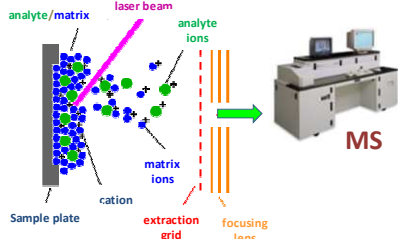
**Laser Capture Microdissection coupled with MALDI-ToF MS**



**Differential proteomic analysis O/O vs. A/A milks using 2D-DIGE**

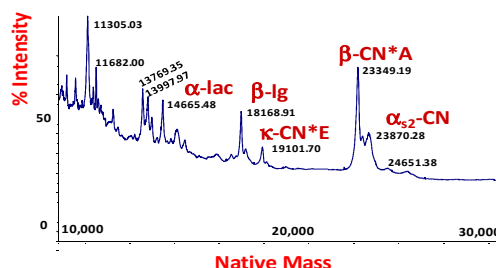


ER-Resident proteins (GRP94, BiP, PDI): signing a singular secretory mechanism



**Proteomic imaging:** microdissected cells from « extreme genotypes » at the *CSN1S1* locus were compared.

Caseins are detected only in O/O cells and are immature (not phosphorylated) meaning that they have **not yet reached the Golgi**



## Conclusions

Materials accumulating in the ER of MEC from goats homozygous O/O at the *CSN1S1* locus are immature milk proteins (without post-translational modifications). Our data strongly suggest that  $\alpha_{s1}$ -casein interacts with the other caseins in the rough endoplasmic reticulum to form a complex that is required for their efficient export to the Golgi apparatus where they will be phosphorylated to interact with  $Ca^{2+}$  ions.



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