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Christine Leroux, Christian Beauvallet, Laurence Bernard, Claudia Bevilacqua, Frédéric Bouvier, Cédric Cabau, Christelle Cebo, Eric Chanat, Isabelle Dugail, Thierry Fassier, et al.

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# **MilkChEST, an integrative approach of the secretion pathways in the mammary epithelial cell: molecular dissection of milk fat adaptability**

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During lactation, mammary epithelial cells (MEC) secrete huge quantities of components, the biosynthesis of which are known in general outline. There are some evidences that a close mechanistic relationship exist between the biosynthesis and secretion pathways of the major milk components: casein micelles and milk fat globules (MFG). However, our knowledge of the molecular events occurring during assembly, intracellular transport and secretion of the micelles and MFG remains scarce. Lately there is also a realization that MEC release in milk microparticules, including exosomes, which contain mRNA and microRNA. To go further into the molecular dissection of the biosynthetic and secretion pathways of the major milk components, processes that determine their structure, as well as their biological and technological properties, a large collaborative project involving several French teams has been launched (funded by the French National Agency for Research and Apis-Gené, France).

Our strategy is based on the relevance of the goat model, with a “naturally occurring Knock Out (KO)” at the CSN1S1 locus and on the use of global approaches (including NGS, proteomics and lipidomics analyses) to decipher the multiple effects of this natural KO on milk secretion and quality.

Our main research goals will be: i) to achieve a better definition of the genome fraction which is expressed in goat MEC during lactation, ii) to obtain a better understanding of the role played by  $\kappa$ s1-casein in the export of caseins from the endoplasmic reticulum to the Golgi apparatus, iii) to identify factors that determine the fatty acid profile of milk fat, iiiii) to go further into the molecular dissection of the mechanisms driving lipid droplets formation and their interaction with the apical plasma membrane during the course of MFG secretion.

The project includes a comparative study of lipid droplet formation in and microparticules release by MEC versus adipocytes, the later cells producing large lipid droplets but lacking the machinery to secrete them. On the other hand, we will focus on the consequences of the absence of the  $\kappa$ s1-casein on the protein and fat secretory pathways, as well as on the fine composition of milk. The ultimate goal is to identify genes playing key roles in the production of milk fat by MEC on which selection and breeding program might be engaged to modulate the fat composition of milk.