Role of stomatin in milk lipid droplet biosynthesis

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Research : The specific nature of our research is that it concerns mammary gland development and lactation functions in animals, our aim objective is to improve milk quality and production in dairy ruminants. The mammary gland is a complex organ, composed of different cell types including the mammary epithelial cells (MEC) which synthesize and secrete milk. During mammary development, which continues throughout the life of female individuals, the MEC goes through different stages of differentiation. During pregnancy, the MEC will switch from a low differentiation stage associated with high proliferation potency to a highly differentiated stage associated with milk production and secretion. This highly differentiated stage is maintained throughout lactation. At the end of lactation, the mammary tissue involutes and the few MEC which then form the tissue are in a low differentiation state. They can evolve again through a new cycle of pregnancy and lactation. Each of these steps is finely tuned by a large number of endocrine and paracrine factors which act in concert within epithelial-stroma cell interactions.

Context, stakes, scientific issues, purpose
Lipid droplets can be synthesized by many cell types, but mammary epithelial cells (MEC) are only cells which secrete lipids. Milk lipid synthesis initiate at specialized regions of the endoplasmic reticulum, leading to the release of cytoplasmic lipid droplets coated with a phospholipid monolayer. Lipid droplets reach the apical pole of the cell, where they are progressively enveloped by the plasma membrane and released as fat globules into milk by MEC. Despite a consensus on broad outlines of lipid secretory pathways in MEC, the identity of molecular partners engaged in these pathways is a controversial issue and several models for lipid synthesis have already been reported (Jeong et al., 2013).

Stomatin is a 31 kDa lipid droplet-associated protein (Umlauf et al., 2004). The expression of stomatin is linked to the milk fat content and the milk fat globule size and composition in several species, including the goat (Cebo et al., 2012) and the bovine species (Lu et al., 2015). To date, the role of stomatin in lipid droplet dynamics is unclear. On the other hand, we have recently found that stomatin contains four phosphorylation sites that may play a role in stomatin function (Henry et al., 2015).

We propose to go further in the comprehension of stomatin involvement in lipid secretory pathways in MEC. A stomatin-GFP fusion protein will be overexpressed in lipid droplet producing cells. Conserved phosphosites will be mutated and effects on lipid droplet biology will be assessed by cellular imaging, molecular biology, and biochemical techniques. We aim to understand the complex interplay between stomatin expression and lipid droplet size and composition in lipid-producing cells.
Work to be done
Stomatin-GFP vector cloning and transfection experiments into mammalian cells.
Site-directed mutagenesis on stomatin phosphosites and effects on lipid biosynthesis (lipid droplet imaging, analysis of lipid droplet size and composition, lipid droplet proteomics, gene expression studies).

References


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