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How Mammary Glucose Metabolism is Altered by Energy and Protein Supply

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In INRA (2018) feeding system, the first parameter estimated in response to net energy (E) and metabolizable protein (P) supply is milk protein yield (MPY). Milk yield response is then calculated from the MPY response using a linear function. This suggests an important link between milk protein secretion and milk volume. However, MPY and lactose yield did not respond totally in parallel to E and P supplies (Lemosquet et al. 2010. EAAP pub #127: 177; Daniel et al., 2016. *Animal*: 1). Indeed, milk volume greatly depends on mammary lactose synthesis, the most important osmotic nutrient synthesized within the mammary epithelial cells. The main precursor of lactose is glucose taken up by the mammary gland. Mammary glucose uptake can also contribute to furnish energy through oxidation. This energy is necessary for milk synthesis. Both mammary protein turnover and milk protein synthesis required ATP as energy. In this presentation, partition of mammary glucose uptake between lactose synthesis and other utilizations (mainly oxidation) will be discussed using results from experiments reporting mammary glucose uptake in response to variations in E and P supplies.

Increasing P supply or modifying E supply (via propionate or glucose digestive infusions) both increased whole-body glucose rate of appearance (WBRA, i.e. glucose entry rate from gluconeogenesis, intestinal absorption and glycogenolysis). However, in mid-lactation cows, an increased WBRA did not always increase mammary glucose uptake, lactose and milk yields (Lemosquet et al., 2009. *JDS*: 3244; *JDS*: 6068). Mammary glucose uptake and lactose yield both significantly increased in 2 experiments among 3 increasing E or intestinal glucose supplies. It was also the case in 3 experiments among 5 increasing P or AA supply. Interestingly, lactose yield increased once without any increase in mammary glucose uptake in response to P supply (Lemosquet et al., 2009. *JDS*: 6068). In Haque et al. (2015. *JDS*: 3951), mammary glucose uptake tended to increase in response to an « ideal » EAA profile while lactose yield did not change. Overall, in the 6 experiments considered an increased glucose uptake led to decrease the lactose: glucose uptake ratio, suggesting an increase in glucose utilization in other pathways than lactose synthesis. Using a biochemical model (Abdou Arbi et al. 2015. *BMC Systems Biology*: 8), we confirmed the large mammary gland flexibility to oxidize glucose to produce energy or to use glucose toward lactose synthesis. Analyses on mRNA in milk mammary epithelial cells suggested that glucose utilization pathways seemed not strongly regulated at transcription level when E and P supplies varied except if an important decrease of both supplies is induced at the beginning of lactation (Boutinaud et al., 2015. *Frontiers in Genetics*: 00323).

Overall, these data suggest that in mid-lactation cows, increasing milk protein synthesis and mammary glucose oxidation in response to increased E and P supplies could be a priority over increasing in lactose yield.

Sophie Lemosquet was graduated and awarded PhD from National School of Agronomy from Rennes (Agrocampus Ouest; Rennes, France). She worked on lactating ruminants in INRA UMR PEGASE, Saint-Gilles, France. Between 1998 to 2009, she analyzed the effect of nutrients on glucose metabolism developing quantitative methods to assess fluxes combining stable isotope and mammary net balance techniques. Until 2003, she worked on amino acid metabolism in interaction with energy supply. Until 2009, she began to work on the AA requirements during the EU FP7 project KBB-2007-1 "RedNEx". She is now in charge of Amino Acids Digestible in Intestine (AADI) system (supplies and requirements) in the new INRA (2018) feeding system.