1 **Effects of dietary fatty acids on nutrient digestion, energy partitioning, and milk fat synthesis.** A. L. Lock* and J. de Souza, Michigan State University, East Lansing, MI.

Our understanding of fatty acid (FA) digestion and metabolism in dairy cows has advanced significantly in the last few decades. We now recognize that FA, both of dietary and rumen origin, can have different and specific effects on feed intake, rumen metabolism, small intestine digestibility, milk component synthesis in the mammary gland, and energy partitioning between the mammary gland and other tissues. We will present research focusing on specific FA and how dairy cows respond differently to combinations of FA. Recent research has highlighted differences in intestinal digestibility among palmitic acid (C16:0), stearic acid (C18:0), and oleic (cis-9 C18:1) acids, which impacts the amount and profile of absorbed FA available for metabolic purposes. C16:0, C18:0, and cis-9 C18:1 usually comprise the majority of FA present in milk fat and adipose tissue of dairy cows. In addition, these FA comprise the major FA in a wide range of commercially available fat supplements.

While these FA have different functions in metabolism, they may also interact with each other by competitive or complementary mechanisms under different physiological conditions. In the mammary gland, milk FA are derived from 2 sources: <16 carbon FA from de novo synthesis in the mammary gland and >16 carbon FA originating from extraction from plasma. 16-carbon FA originate from either de novo or preformed sources. Milk lipid synthesis in the mammary gland is dependent upon the simultaneous supply of short/medium-chain FA and long-chain FA. C16:0 has a higher preference as a substrate to start triglyceride synthesis than C18:0 or cis-9 C18:1. Also, if the amount of preformed FA surpasses the capacity of the mammary gland, these might be redirected to other tissues (e.g., adipose tissue) altering energy partitioning. In the future, the opportunity and challenge will be to continue to improve our understanding of how and which FA affect nutrient digestion, energy partitioning, and milk synthesis in lactating dairy cows and effectively apply this knowledge in the feeding and management of today’s high-producing dairy cows.

**Key Words:** energy partitioning, fatty acids, milk fat synthesis

2 **Amino acid uptake by the mammary glands: Where does the control lie?** J. P. Cant*, J. J. M. Kim†, S. R. L. Cieslar†, and J. Doelman2, 1University of Guelph, Guelph, ON, Canada, 2Nutreco Nederland BV, Boxmeer, the Netherlands.

Milk protein yield responses to changes in the profile of essential amino acids absorbed by the gastrointestinal tract or circulating in blood plasma do not follow the classic limiting amino acid response, in part because of an ability of the mammary glands to modify their blood flow rate and net clearance of amino acids out of plasma. The hypothesis that mammary blood flow is locally regulated to maintain ATP balance accounts for observed changes in flow due to postprandial glucose, insulin and EAA infusions. An additional hypothesis that net mammary uptakes of metabolites from blood are affected by perturbations in their respective arterial concentrations and the rate of mammary blood flow also appears to hold for the energy metabolites glucose, acetate, BHBA and FA. However, net EAA uptakes by the mammary glands are poorly predicted by models considering arterial concentrations and blood flow rates only. Evidence points to intramammary protein synthesis and secretion as the determinant of net EAA uptake. The intracellular signaling network anchored by the mechanistic target of rapamycin complex 1 (mTORC1) stands as an excellent candidate to explain nutritional effects on milk protein synthesis because it integrates information on physiological and nutritional state to affect protein synthesis and cell metabolism, growth, proliferation and differentiation in many cell types. In mammary cells in vivo and in vitro, the mTORC1, integrated stress response, and insulin signaling networks that contribute to regulation of initiation of mRNA translation are responsive to acute changes in nutrient supply and EAA profile. However, after several days of postprandial infusions of balanced and imbalanced EAA profiles, these signaling networks do not appear to continue to account for changes in milk protein yields. Gene expression evidence suggests that regulation of components of the unfolded protein response that control biogenesis of the endoplasmic reticulum and differentiation of a secretory phenotype may contribute to effects of nutrition on milk protein yield. Connections between early signaling events and their long-term consequences are proposed.

**Key Words:** mammary blood flow, milk protein synthesis, translational regulation

3 **Influences of heat stress on the bovine mammary gland.** S. Tao*, R. M. Orellana, X. Weng, T. N. Marins, and J. K. Bernard, University of Georgia, Tifton, GA.

Heat stress (HS) reduces cows’ milk production, resulting in a significant economic loss for the dairy industry. During lactation, HS lowers milk yield by 25–40% with half of the decrease in milk synthesis due to factors unrelated to feed intake. In vitro studies indicate that primary bovine mammary epithelial cells display greater rates of programmed cell death when exposed to high ambient temperature, which may lead to a decrease in total number of milk synthetic cells in the mammary gland (MG) and partially explain the lower milk production of lactating cows under HS. The function of mammary cells is also altered by HS. In response to HS, mammary cells display higher gene expression of heat shock proteins, indicating a need for cytoprotection from protein aggregation and degradation. Further, HS results in increased gene expression but similar protein expression of mammary epithelial junction proteins, and doesn’t substantially influence the integrity of mammary epithelium, indicating an effort to maintain cell-to-cell junction by synthesizing more proteins to compensate for protein loss by HS. Bovine mammary epithelial cells also have reduced gene expression of proteins involved in milk synthesis suggesting that HS directly reduces milk synthetic capacity of MG. During the dry period, HS negatively affects MG development by reducing mammary cell proliferation before parturition, resulting in a dramatic decrease in milk production in the subsequent lactation. In addition to mammary growth, MG of the HS cow has reduced protein expression of autophagy proteins in the early dry period, suggesting HS influences mammary involution. Emerging evidence also indicates that heifers born to late gestation HS cows have lower milk production during their first lactation, implying that the maternal environment may alter MG development of the offspring. It is not clear if this is due to a directly epigenetic modification of prenatal MG development by maternal HS. More research is needed to elucidate the impact of HS on MG development and function.

**Key Words:** heat stress, mammary gland, lactation
The disparate impacts of inflammatory signaling pathways on lactogenesis, galactopoiesis, and cessation of lactation. B. J. Bradford*, C. M. Ylioja1, and K. M. Daniels2, 1Kansas State University, Manhattan, KS, 2Virginia Polytechnic Institute and State University, Blacksburg, VA.

Inflammation is a well-characterized process used by the immune system as a component of the response to infection or tissue damage. The repertoire of signals used in immune inflammation, however, is neither limited to immune cells nor confined to adverse health events. Inflammatory signals affect mammogenesis, lactogenesis, lactation, and involution, often in dramatic ways. The role of inflammatory mediators in lactogenesis should not be surprising, given that lactogenic factors such as prolactin and growth hormone utilize cytokine receptors with second messengers that overlap with inflammatory cytokine signaling pathways. Some eye-opening studies have demonstrated that tissue-specific gene knockout mice lacking certain inflammatory mediators completely lack a functional mammary gland. Inflammatory signals are also critical mediators of mastitis-induced decreases in milk synthesis. Evidence for this role ranges from the molecular to the whole-animal level, implicating pattern recognition receptors which trigger inflammatory transcription factors that act as transcriptional repressors for milk synthesis genes. A poorly understood mechanism that contributes to this phenomenon is the transient but dramatic change in methylation of milk component gene promoters, which may or may not revert completely to the pre-mastitis condition after resolution of the inflammation. More recent findings demonstrated that inflammatory mediators such as interleukin-6 are essential for normal mammary involution at the end of lactation. Changes in lipid metabolism in dairy cows around parturition due to negative energy balance can profoundly change the composition and concentration of oxylipids in the mammary gland that may be responsible for dysfunctional inflammatory responses during this time. This presentation will provide a brief overview of the role that oxylipids play in contributing to the onset and resolution of inflammation. Factors associated with periparturient cows that can contribute to dysfunctional regulation of inflammation as a function of altered oxylipid biosynthesis and metabolism also will be described. Understanding the role oxylipids may play in mediating the onset and resolution of mastitis is key to developing novel prevention and control programs for the dairy industry.

Key Words: lactation, development, mastitis

Oxylipids and the regulation of bovine inflammatory responses. L. Sordillo*, Michigan State University, East Lansing, MI.

Inflammation is a critical aspect of the innate immune system that can determine the outcome of several economically important diseases of dairy cattle including mastitis. The purpose of the inflammatory response is to eliminate the source of tissue injury and then return tissues to normal function. Aggressive inflammatory responses, however, can cause damage to host tissues and contribute significantly to the pathophysiology of mastitis. A precarious balance between pro-inflammatory and pro-resolving mechanisms is needed to ensure optimal pathogen clearance and the prompt return to immune homeostasis. Therefore, inflammatory responses must be tightly regulated to avoid bystander damage to the milk synthesizing tissues of the mammary gland. Oxylipids are potent lipid mediators that can regulate all aspects of the inflammatory response. The biosynthetic profiles of oxylipids are dependent on both the availability of diverse polyunsaturated fatty acids substrates and their subsequent metabolism through various oxidizing pathways. Changes in lipid metabolism in dairy cows around parturition due to negative energy balance can profoundly change the composition and concentration of oxylipids in the mammary gland that may be responsible for dysfunctional inflammatory responses during this time. This presentation will provide a brief overview of the role that oxylipids play in contributing to the onset and resolution of inflammation. Factors associated with periparturient cows that can contribute to dysfunctional regulation of inflammation as a function of altered oxylipid biosynthesis and metabolism also will be described. Understanding the role oxylipids may play in mediating the onset and resolution of mastitis is key to developing novel prevention and control programs for the dairy industry.

Key Words: lipid mediator, inflammation, mastitis