Wine & Cheese

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2025 ADSA Annual Meeting Wine & Cheese Presentation Summary: Balancing the Equation: Nutrition and Immunity in Dairy Herds

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Core Theme

In his presentation Dr. Rostoll-Cangiano explored the intricate relationship between metabolism, immune function and nutrition in dairy cows, particularly during the transition period when cows experience many physiological changes. Here are the key takeaways:

Key Concepts

Transition Period Challenges

- 30–50% of dairy cows experience at least one disease postpartum. During this time, nutrient demands spike, but feed intake lags, creating a nutrient deficit. This results in increased nutrient partitioning towards milk production, making cows susceptible to metabolic stress, immune dysregulation and disease.
- Postpartum cows often exhibit a paradoxical immune phenotype after calving - heightened inflammation but impaired pathogen clearance.

Homeorrhesis vs. Allostasis

- Homeorrhesis is a concept that encompasses the programmed shifts in nutrient partitioning in response the new physiological state, i.e. lactation.
- However, in addition to internal physiological demands to meet lactation requirements, external stressors (environmental, social, nutritional) also increase nutrient demands, a concept called allostasis. These external stressors can overwhelm adaptive capacity, leading to allostatic overload.

Mitochondrial Allostatic Load

- Mitochondria generate ATP to fuel cells (oxidative phosphorylation; OxPhos), produce reactive oxygen species as signaling molecules, and direct innate immune signaling via mitochondrial DNA release.
- Sustained metabolic stress, such as the transition period, impairs mitochondrial function, which can contribute to immune dysfunction.

Immune Cell Function and Metabolism

T Helper CD4+ Lymphocytes: A Model to Study Transition Period Immunometabolism

- These cells play a key role in orchestrating systemic immunity and inappropriate activation of T cells contributes to a wide array of diseases.
- The metabolic function of the CD4+ cells is tightly linked with cell proliferation capacity and cytokine production.
- When activated, CD4+ cells switch from using OxPhos, to a combination of OxPhos and glycolysis to produce energy.

CD4+ Metabolic Activity, Proliferation and Cytokines

- Bioenergetic profiling of CD4+ cells from transition cows showed that both OxPhos and glycolysis were increased after calving, indicating that they were metabolically more active compared to the dry period. This also reflects a potentially higher metabolic load on the immune system postpartum, which may not be beneficial as the cow is already under extreme physiological stress.
- Cell proliferation assays indicated that immune cell proliferation was upregulated postpartum compared to the dry period.
- Production of pro-inflammatory cytokines (interleukin-6, interferon gamma and interleukin-1 beta) also increased postpartum.
- The timing of these changes in bioenergetics, proliferation and cytokines suggests that increased mitochondrial allosteric load may be shaping T cell responses during the transition period.

Paradoxical Immune Phenotypes After Calving: Systemic and Intestinal

- The abundance of cells of the adaptive immune system changes throughout the transition period, with T cells reaching their abundance in blood around 7 d postpartum.
- There is growing interest on the importance of intestinal health in dairy cows. Interestingly, the increase in T cells postpartum is associated with an increase in gut permeability and immune cells in the colon at 7 d postpartum. Increased gut permeability may be a factor in altered immune responses during the transition period.
- Systemic inflammation is also increased during the transition period as evidenced by elevated serum amyloid A and haptoglobin.

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mTOR: The Link Between Nutrition and Immune Cells

Nutrient-Sensing Pathways: mTOR Signaling

- Mechanistic target of rapamycin (mTOR) is a key nutrient-sensing kinase regulating protein synthesis and immune cell activation and function. Activation of mTOR promotes anabolic and proliferative functions of immune cells in response to energy and amino acids.
- Downregulation of mTOR is a connection between postpartum nutrient deficits and immune dysfunction- without mTOR activation, immune cells can be skewed towards catabolic and pro-inflammatory states.

Nutritional Interventions

- Nutrition plays a large role in promoting health of dairy cattle and is intrinsically linked with immunometabolism via signaling pathways such as mTOR.
- Supplementation with amino acids (e.g., methionine) may reduce the metabolic load during the transition period and thereby restore immune function,
- Supplementation of methionine via rumen-protected sources can improve neutrophil function and reduce pro-inflammatory cytokine production during the transition period, which may be driven in part by increased mTOR activation in immune cells.
- Enhancing methionine in the diets of calves may also increase adaptive immune cell proliferation and function.

Conclusion

- Physiological adaptations, along with external stressors increases the allosteric load of immune cells during the transition period, contributing to immune dysregulation.
- Nutritional strategies, such as amino acid supplementation, may help to overcome this dysfunction by promoting immune cell function via stimulation of mTOR.