Making Molecular Connections between Nutrition and Immunology in the Post-Genomic Era

An Immunological Spin on Nutritional Biology

Nutrition and Immunity

- Advances in molecular biology have resulted in an understanding of molecular pathways that control the immune system.
- The overall health of the animal affects the functionality of the immune system.
- Diet can directly affect the immune system. Specifically, nutrients can be part of signaling pathways that cause specific genes to be expressed.

Metabolism and Disease

- Negative Energy
- Ketosis
- Fatty Liver
- Hypocalcemia
- Ketosis
- Retained Placenta
- Lactose
- Rumen Acidosis
- Insufficient Fiber
- Decreased DMI

An Immunologist’s Bias

Immunology and Health

- Decreased Neutrophil Function Correlates with Increased Mastitis
- Immunosuppression around the time of calving (3 weeks prior to 3 week after).
- Manifestation includes impaired neutrophil and lymphocyte functions.

Vitamin D and Immunity

  - Vitamin D: A Candidate for the Environmental Effect in Multiple Sclerosis - Observations from Norway
  - The effect of ultrasound B-induced vitamin D levels on post-operative infection by Mycobacterium tuberculosis
  - Vitamin D status in gastrointestinal and liver disease
  - Vitamin D levels and disease status in T-cell patients with systemic lupus erythematosus

(Devilbeex et al 1995)
Serum Levels of Vitamin D

Three Thresholds of 25-Vitamin D

• Levels above 220 nM are accompanied by hypercalcemia.
• Levels below 15-20 nM can lead to rickets and evident osteomalacia.
• What level is necessary for full immune function?

What is Normal?

• Serum 25-VitD was determined for 10 mid-lactation Holstein cows.
• Cows were on a diet supplemented with 40-50,000 IU/day of Vitamin D.
• Current NRC recommendation for Vitamin D is 21,000 IU/day (mid-lac Holstein)
• Average serum vitamin D level in this herd is 134 nM.

Immunological and Vitamin D Signaling Pathway

The Interaction Between the Two Pathways

Molecular Immunology

Role of Vitamin D in Immunity
Stimulation of bovine macrophages with a TLR-4 ligand (LPS) or a TLR-2 ligand (Pam3CSK4), results in increased expression of Cyp27B1.

Stimulation of bovine macrophages with a TLR-4 ligand (LPS) or a TLR-2 ligand (Pam3CSK4), results in increased expression of VDR.

Stimulation of bovine macrophages with a TLR-4 ligand (LPS) or a TLR-2 ligand (Pam3CSK4), results in increased expression of Cyp24A1.

Role of Vitamin D in Mastitis

Gene Expression in Control and Infected Quarters

Effects of Vitamin D in the Cow

- Genomics
  - Sequencing of the bovine genome
- Microarrays
  - What genes are turned “on”? (mRNA)
- Proteomic
  - What proteins are being made?
Summary

• Vitamin D affects the bovine immune response.
• It is unknown what level of Vitamin D is necessary for full immune system function.
• The Vitamin D molecular pathway is activated in the infected quarter of a mastitic cow.
• What genes/proteins are regulated by Vitamin D? What is their impact on immune function?

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