USDA Ongoing Research on The Impacts of Nutrition on Animal Health

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Current Research at USDA

- Quantify the impact of swine dietary regimens on nutrient metabolism and immune function of the G.I. tract and the whole animal.
- Multidisciplinary/collaborative approach.
  - Integration of physiological, molecular, and whole animal studies.

Oxidative Stress

- Defined as imbalance between oxidants and AOX defense mechanisms.
- Altered inflammatory responses.
  - Promotes inflammation
  - Marker of inflammation
- Increased cellular and tissue damage.
  - "Rancid" fats increase enterocyte turnover in swine and poultry (Dibner et al., 1996).
- Disease states in livestock
  - Mulberry heart disease, white muscle disease
  - Immune dysregulation in transition dairy cows (Sordillo et al., 2009)
  - Sow longevity, companion animals
- Relationship with feed efficiency.
  - Inverse relationship between markers of oxidative stress & g:f in poultry (Bottje and Carstens 2009)
- Impact of feeding byproducts?
  - DDGS
  - Fats – AV blends. Rancidity?
  - High amounts of PUFA in swine diets
  - Relationships with dietary fiber?

Biology of 4-HNE

- Highly reactive molecule – binds proteins and nucleic acids.
  - Detoxified by glutathione.
- Associated with pathological states in humans.
  - Alzheimer's, diabetes, respiratory (COPD).
- Alters expression of inflammatory genes.
- Can invoke arthritis.
  - Laminits associated with ↑ 4-HNE (Yin et al., 2009)
  - Sow lameness?
- Impacts of oxidized fats on intestinal barrier function?

Lipid aldehydes – 4-HNE

- 4-Hydroxynonenal – 4-HNE
  - Produced by heating of oils, mainly 18:2. Can be absorbed from diet.
  - Produced endogenously via peroxidation of PUFA both a marker and mediator of oxidative stress.
  - Impacted by dietary fat type.

In Vitro Studies with 4-HNE

- Porcine 3D4/31 alveolar macrophages (MØ).
- Treated cells with various levels of 4-HNE.
  - 0, 10, or 20 μM 4-HNE for 1 h.
  - MØ were stimulated with poly I:C RNA – a TLR3 agonist used to mimic viral inflammation.
- Supernatant and cells harvested for cytokine secretion and mRNAs.
  - Cellular glutathione levels determined.
Inflammation-related mRNAs

Means with different letters differ P < 0.05.

**In Vitro Studies with 4-HNE**

- 4-HNE augments expression of inflammatory mediators.
  - In short term incubations 4-HNE depleted cells of glutathione.
  - Demonstrates that oxidative stress can impact porcine response to viral challenges via 4-HNE.
- Ongoing studies to look at mechanisms and time course.
  - Glutathione regulation.
  - n-acetylcysteine and other compounds/nutrients ability to reverse 4-HNE induced hyperstimulation.

**Future Directions**

- National Pork Board Grant – “Evaluation of lipid source and oxidation level on digestible and metabolizable energy concentration, and the impact of lipid oxidation on intestinal barrier function.”

**Objectives:**

1. Determine DE and ME content of 4 dietary fat sources ranging from 2 saturated animal fats: beef tallow, poultry fat; and 2 unsaturated oil sources: canola, corn oil.
2. Determine the impact of lipid oxidation on DE, ME and N retention.
   - Each fat source will be heated at 190°C for 6h.
   - Measure 4-HNE and other polar and non-polar aldehydes.
   - Other “quality” indicators: fatty acid profiles, PV, anisidine, etc.

3. Determine the impact of dietary fat source and lipid oxidation on indicators of oxidative stress, inflammation and intestinal barrier function.
   - Serum and urinary TBARS, 4-HNE, and other aldehydes.
   - Urinary lactulose and mannitol will be determined as an indicator of intestinal permeability.
   - Serum endotoxin, acute phase proteins, and fecal IgA.

**Questions?**