

Gabler Laboratory Research Program

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My Background

- La Trobe University
 - B. Agricultural Science
 - Ph.D.
- Purdue and Iowa State University
 - Postdoctoral research associate
- Iowa State University Fall 2008
 - Animal Science faculty
 - 30% Research
 - 70% Research

Swine Research Areas

- Feed efficiency
- Maternal nutrition and fetal programming
- Gastrointestinal tract
 - Health
 - Nutrient transport
 - Endotoxin transport
 - Mycotoxin transport
- Skeletal muscle protein synthesis and degradation

Swine Residual Feed Intake (RFI)

- RFI: The difference between actual feed intake and that predicted on the basis of requirements for production and maintenance of body weight

 (Feed consumed over and above expected requirements for production and maintenance)
- Yorkshire Pigs
 - Control (random breed)
 - Select (low RFI, high efficiency selection breed)

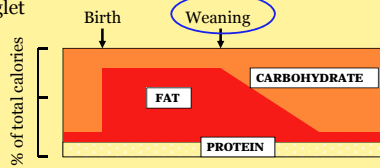
AFRI-USDA 2009 Growth and Nutrient Utilization Grant

- Aim #1: Evaluate dietary nutrient retention, energy balance, protein and lean accretion rates in finisher pigs selected for low RFI
- Aim #2: Determine the extent to which appetite regulatory peptides contribute to altered feeding behavior, reduce feed intake and enhances feed efficiency in low RFI pigs
- Aim #3: Identify key metabolite, sarcoplasmic and mitochondrial proteins that correlate with improved skeletal muscle metabolism and accretion in finisher pigs selected for low RFI

Long chain n-3 Fatty Acids, Fetal Programming and Swine

Suckling and Weaning Pig Challenges

- The newborn experiences life-threatening situations which are exacerbated by its physical weakness and low energy reserves
- Maternal diet influences the fatty acid profile of milk and the piglet



Hypothesis

Increasing the n-3 fatty acid content of piglet tissues via the maternal diet will improve intestinal morphology and glucose uptake at the weaning transition

Gabler et al. (2007) *Journal of Nutrition* 137(11): 2351-8

Gabler et al. (2009) *Journal of Nutritional Biochemistry* 20(1): 17-25

Sow Milk Fatty Acid Profile

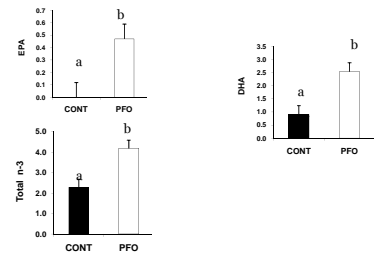


	CONT	PFO
(g/100g total fatty acid)		
α-LA	0.61	0.57
EPA	0.00	0.07
DPA	0.00 ^a	0.27 ^b
DHA	0.00 ^a	0.24 ^b
Total n3	0.61 ^a	1.16 ^b

PFO = Protected Fish Oil rich in DHA and EPA

Different letters within rows represent significant differences between treatments (P < 0.05)
Means ± SEM, n = 4 milk samples from different sows/treatment

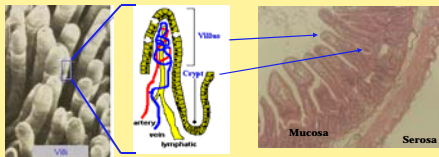
n-3 Fatty Acid Concentrations in Piglet Small Intestinal Tissue



Different letters a,b represent significant differences between treatments (P < 0.05)
Means ± SEM, n = 4 piglets/treatment

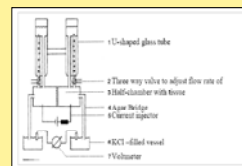
Jejunum Morphology was not Altered by n-3 Fatty Acids

	CONT	PFO	SEM	P-value
Villus height (µm)	499.8	496.2	56.92	0.32
Crypt depth (µm)	131.8	139.3	7.03	0.41
Villus:Crypt ratio	3.8	3.6	0.40	0.53

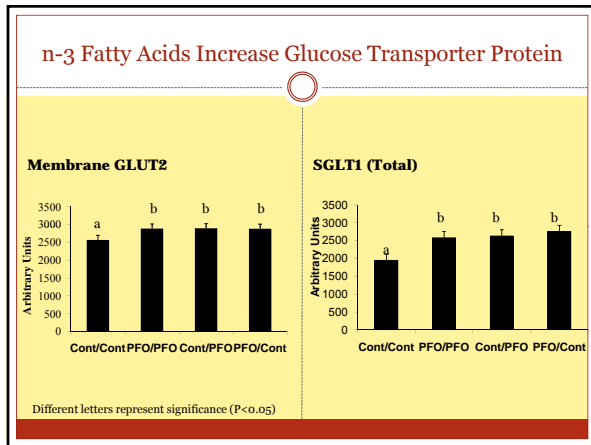
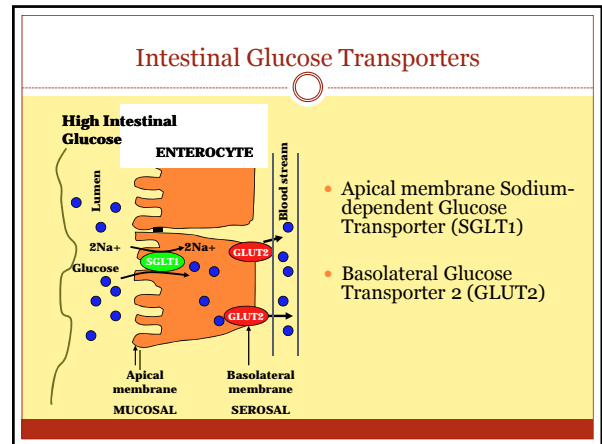
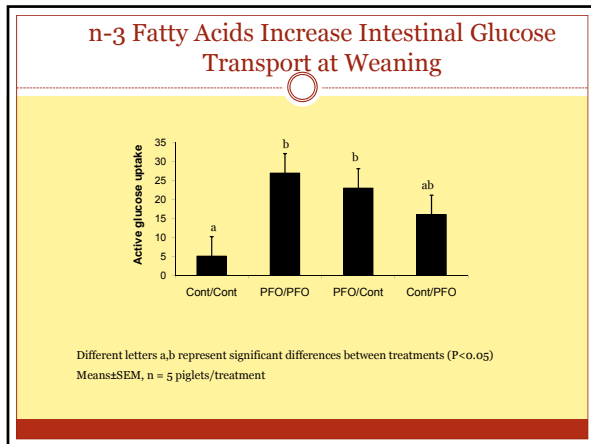


Intestinal Glucose Transport

- Ussing Chambers used to measure active glucose transport
 - Change in current across the intestine
 - High change in current = Increased Active Glucose Transport
 - Mucosa buffer solution → serosa buffer solution

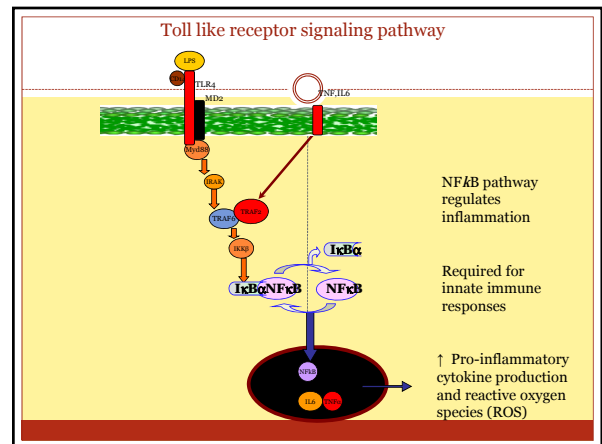


<http://online.sagepub.com>
<http://www.oxford.com>

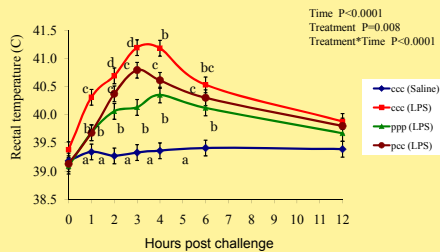


- ### Where to From Here?
- What is happening to amino acid transporter?
 - Link between AMPK and ATPase?
 - AMPK or ATPase knockdown studies in pig enterocytes
 - Do “fall off” pigs have different nutrient transport capacities than rigorous littermates?

- ### Innate Immunity and n-3 Fatty Acids
- Toll like receptor (Tlr) antagonized by n-3 fatty acids (Gabler et al., 2008)
 - n-3 fatty acids are able to block LPS transmembrane signaling (Chu et al., 1999)
 - Anti-inflammatory properties



n-3 Fatty Acids Attenuate the Febrile Response to LPS



Pigs (30.5 ± 3.2 kg) were challenged with 10 µg/kg BW of lipopolysaccharide (LPS) or saline by intramuscular injection. n = 10 pigs per treatment.

Questions We Are Asking?

- Role of Tlr4, CD14?
- Mycotoxin?
- Diarrhea, E. coli F18 and K88 in weaned pigs?
- Endotoxin and its impact on nutrient transport?
- Can n-3 fatty acids attenuate endotoxin transfer across the intestinal mucosa?

Intestinal Endotoxin and Mycotoxin Transport

- The transepithelial transport of fluorescein isothiocyanate labeled LPS (FITC-LPS) or Aflatoxin B1 and B2
- Mounted jejunum samples from pigs are mounted into Ussing chambers
- The mounted intestines will be incubated with FITC-LPS or mycotoxin on the mucosal side
- Aliquots of medium from the mucosal and serosal sides will be taken at 15 min intervals for up to 120 min and the luorescence of the aliquots determined in a plate reader
- The apparent permeation coefficient (Papp) will be calculated using the following equation:
 - $Papp = dQ / (dt \times A \times C_0)$
 - Where dQ/dt is the transport rate and corresponds to the slope of the regression line, C_0 is the initial concentration in the donor chamber, and A is the surface area of the tissue

The effects of fatty acids and fiber on pig intestinal endotoxin and mycotoxin transport

EMILY KUNTZ

INDEPENDENT RESEARCH PROJECT (ANS 490)

DEPARTMENT OF ANIMAL SCIENCES
IOWA STATE UNIVERSITY

Background

- The digestive tract is a major entry point for pathogens
- The intestines form a major physical barrier to pathogens from entering circulation and then activating the acquired and innate immune systems
 - Bacteria (endotoxin)
 - Fungal mycotoxin
 - Other toxic compounds
- Immune challenges (acute or chronic) directly impact the growth and reproductive performance of swine

Endotoxin

- Endotoxin can be derived from gram negative bacteria such as E. coli and Salmonella
- Endotoxin activates receptor mediated inflammatory processes
- Endotoxin is absorbed by the intestine
 - Paracellular transport through the tight junctions
 - Transcellular pathway via passive diffusion through the enterocyte (absorptive cells)
- This absorption of the gut-derived bacteria endotoxin plays an important role in the development of intestinal dysfunction, inflammation, peripheral tissue catabolism and metabolic disease

Mycotoxin

- The mycotoxin is commonly found in cereals and can cause:
 - Vomiting
 - Anorexia
 - Necrosis
 - Diarrhoea
 - Malabsorption of nutrients
 - Mortality
 - Porcine pulmonary edema
 - Slow growth rates
 - Decreased protein synthesis
 - Reduced reproductive performance
 - Compromised immunity in pigs

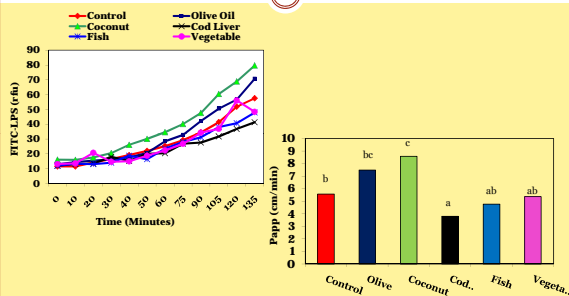
Mycotoxin

- Aflatoxin B1 & B2
- Deoxynivalenol (Vomitoxin)
- Zearalanone
- Tricothecene

Diet, Endotoxin and Mycotoxin Transport

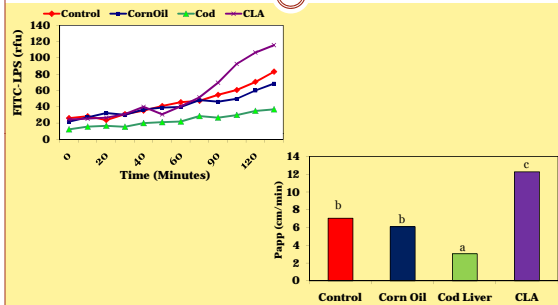
- Do different dietary compound effect the rate of transport of endotoxin and mycotoxin?
 - Dietary fatty acids
 - Saturated fatty acids (coconut oil)
 - Unsaturated fatty acids (corn oil, olive oil, veg. oil, fish oil)
 - Dietary fiber
 - Starch
 - Cellulose
 - Citrus pectin

FITC-LPS Transport and Fatty Acids (1)



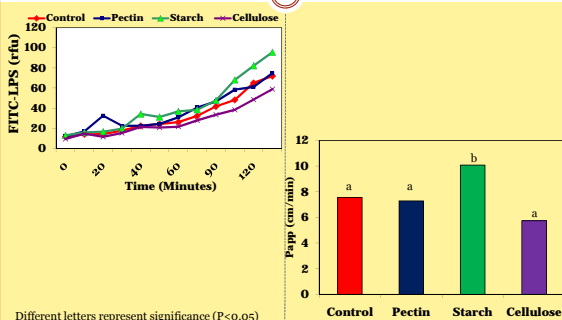
Different letters represent significance (P<0.05)

FITC-LPS Transport and Fatty Acids (2)



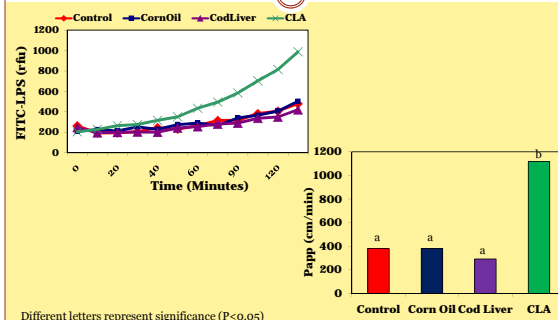
Different letters represent significance (P<0.05)

FITC-LPS Transport and Fiber



Different letters represent significance (P<0.05)

Mycotoxin



Different letters represent significance (P<0.05)

Summary

- Saturated fats increases endotoxin transport rates
- n-3 fatty acids (fish oils) decrease endotoxin transport
- Conjugated linoleic acid augments both intestinal endotoxin and mycotoxin transport
- Potato starch aids in the transport of endotoxin across the intestine, while cellulose decreases this transport
- Dietary fat differentially alters aflatoxin transport

Conclusion

- Dietary compounds could be utilized to decrease the amounts of endotoxin and mycotoxin transport across the intestine
- Better understanding of how different dietary compounds influence endotoxin and mycotoxin could lead to better diet formulations and improved growth and reproductive performance in swine
- Further research needs to confirm this hypothesis