Does Consumption of Xanthohumol Alter the Microbiota Composition of the Gut?

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What is Xanthohumol?

A polyphenol found in beer hops

Observed characteristics

- Antioxidant
- Anti-inflammatory
- Antimicrobial
- Cancer chemopreventive agent
- Immune system modulator
Effects of Xanthohumol

The Stevens lab has shown that:

Of mice fed a high fat diet, those that were fed a high fat diet + xanthohumol gained 15-20% less weight than those without
Effects of Xanthohumol

Maier, Stevens and Gombart have evidence that:

• Xanthohumol binds to the Farnesoid X receptor (FXR)

• FXR appears to bind to the Vitamin D response element in the promoter of the cathelicidin antimicrobial peptide (CAMP) gene

• FXR regulates CAMP gene expression
Antimicrobial peptides (AMPs) are expressed in tissues exposed to environmental microbes

• Skin, oral mucosa, tongue and colon

• Salivary & sweat glands

• Various white blood cell populations
CAMP is important for innate immunity

Found in
- Epithelial cells
- Macrophages
- Neutrophils

Protects against
- G+ and G- bacteria
- Enveloped viruses

CAMP knockout mice showed an increase in:
- Skin and urinary tract infections
- Eye infections
- The severity of inflammation in gut epithelia
CAMP protein structure

Proteinase 3
Kallikreins 5 & 7

Cathelin-derived precursor stored in neutrophil specific granules

Amphipathic $\alpha$-helix
AMPs disrupt integrity of bacterial membrane

Oren et al., Biochem J. 1999; 341: 501–513
AMPs are important for gut health.
Hypothesis

Consumption of Xanthohumol induces CAMP gene expression in the gut which alters the bacterial composition.

The question I addressed this quarter

When compared to mice eating only a high-fat diet, do mice fed a high fat diet and xanthohumol show changes in their gut microbiota?
Experiment Setup

• 12 control mice - fed a high fat diet
• 12 test mice – fed a high fat diet + xanthohumol
  • Xanthohumol dosage was 30mg/kg
• Euthanized at 14 weeks
  • Tissue and feces samples were collected
16s rRNA Sequencing

- gDNA isolation use MO BIO Kit
- Quantification of gDNA
- Gel electrophoresis
16s rRNA Sequencing

- PCR of the 16s rRNA gene
  - Amplification of the V3 and V4 hypervariable regions
- Illumina Miseq
- Analysis of sequencing
Predictions

• Consumption of Xanthohumol will alter the bacterial composition of the gut

• The bacterial composition may favor a lean phenotype
  For example:
  Fewer *Firmicutes*
  More *Bacteroidetes*

Future plans

• Metagenomics

• Metabolomics
Thank You

Dr. Gombart

Miles Thompson