Nutrition and the Gut Microbiome – What is the impact in IBD?

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Financial Disclosure

Consultant for Abbvie, Janssen, Shire, Takeda

Grant support: CIHR, Alberta Innovates
Learning Objectives

Understand how gut microbiome affects health

Learn how diets affect microbiome composition and function

Understand the pathogenesis of IBD and role of diets
The Intestinal Microbiome – an “organ” of its own

Human gut contains more than 1000 species with 99% belonging to about 40 species 10-fold the number of human cells, and predicted to encode 100-fold more unique genes than our own genome.
Beneficial role of microflora

- Harvest of energy from food not digested by the host
- Production of vitamin K
- Production of short chain fatty acids
- Trophic effects on the intestinal epithelium
- Maturation of the host’s innate and adaptive immune responses
Dominant fecal microbiota remains stable at intra-individual level but is unique for each individual – data from β-fructans (oligofructose enriched-inulin) interventional study in active UC.

**DGGE**

**16S rDNA sequencing**

**In silico T-RFLP**
How to analyze the gut microbiome and use them in clinical medicine?

Who is there – species/strains – 16s rRNA gene sequencing

What is their function? Metagenomics

What are they doing? Metabolomics
Host-microbe interactions in the GI tract maintain health

Role in Disease
- Complex immune disorders
  - IBD
  - Allergic disorders
  - RA
  - T1 diabetes
- Metabolism
  - T2 diabetes
  - Obesity
- Cancer
- Development
- Infectious diseases
- Neurological/motor disorders
There is evidence for an involvement of intestinal dysbiosis in chronic diseases, with inflammation as one of the mechanistic links.
Intestinal microbiota dysbiosis and chronic inflammation

Abnormal gut barrier, pro-inflammatory immune response

- **Obesity**
  - Bacteroidetes ↓
  - Firmicutes ↑
- **Nonalcoholic Fatty Liver**
- **Type 2 Diabetes**
  - Faecalibacterium prausnitzii ↓
  - Akkermansia municiphila ↓
- **Inflammatory Bowel Disease**
  - Butyrate-producing ↓
  - Enterobacteriaceae ↑

Intestinal microbiota dysbiosis and chronic inflammation
Crohn’s disease and ulcerative colitis have unique geographic features.
IBD has been increasing over the past half century
Model of the Etiopathogenesis of IBD

Genetics
- Nod2
- TLR, TNF
- Autophagy
- IL23R

Environment
- Microbes
- Diet
- Smoking

Immune imbalance
Defective Host defense

IBD
Diets in the US have changed dramatically over the past century

http://longbottomline.com/tag/forks-over-knives/
Dietary Changes in Western Society

Increase
- Animal protein
- Fat
- Refined Carbohydrates

Decrease
- Whole grains
- Fruits and vegetables
Impact of diet in shaping gut (fecal) microbiota – a study of modern versus rural diet

Enterotypes of the human gut microbiome

Enterotypes are strongly associated with long term diets:
- *Bacteroides* enterotype – protein and animal fat
- *Prevotella* enterotype – fermentable carbohydrates

Animal-based diet showed greater impact on the gut microbiota than the plant-based diet.

Western Diet decreased microbial diversity

Mouse species and Treatment group

- IL10 control chow
- IL10 western diet
- WT control chow
- WT western diet

Shannon-Wiener index

Day 0 vs Day 35

* indicates significant difference
Can diet affect the function of the gut microbiome?

C57Bl/6 mice fed different diets; Cecal samples harvested 21 days later

16S rRNA gene sequences were determined by Sanger-based clone library sequencing
Bilophila wadsworthia is a sulfite-reducing microbe that is uncommon in gut microbiota

- Discovered in 1988
- Often recovered from a variety of infections (pathobiont)
- Bilophila = “bile-loving”
- Sulfite-reducing bacteria (SRB- dsrA)
- Production of H2S

B. wadsworthia colonizes only when mice are on MF diet
Could differences in dietary fat-induced bile acid conjugation promote B. wadsworthia growth?
B. wadsworthia induces TH1-mediated colitis (Bw monoassociation of GF mice)
Dietary strategies to modulate the gut microbiota and redress disease associated dysbioses.

**Therapeutic:**
- Fecal transplantation
- Antimicrobials (Bacteriophages)
- Probiotics

**Nutritional:**
- Probiotics
- Prebiotics
- Fibers, resistant starches, and whole grain

**Dysbiosis**
- Microbiota diversity reduced
- Elevated *Enterobacteriaceae*/opportunistic pathogens
- Skewed SCFA profile
- Disruption of mucosal barrier
- Host inflammatory response initiated

- Bifidobacteria
- Functional targets
- SCFAs and Butyrate producers
- Community diversity
Dose-dependent clinical response in active UC by adjunct prebiotic inulin-enriched oligofructans

- 15g/day (10/23 patients):
  - Remission: 50%
  - Response: 10%
  - No response: 0%
  - Worsened: 0%

- 7.5g/day (13/23 patients):
  - Remission: 39%
  - Response: 0%
  - No response: 38%
  - Worsened: 23%
Correlations between colitis and mucosa-associated bacterial taxa
Exhalation and Flatulence

Gases: CO₂, H₂, CH₄

Fermented by Intestinal Bacteria

Inulin & Oligofructose

Excretion

Acetic Acid
Propionic Acid
Butyric Acid
Lactic Acid

Bacterial Biomass

Criterium 2: Prebiotics are fermented by the (endogenous) intestinal microbiota.
Intestinal butyrate metabolism is improved in UC patients responding to beta-fructans.
High sucrose diet plus FOS worsens colitis and arthritis

Valcheva et al, poster CDDW 2015
Diet rich in refined sugars changes the function of colonic bacteria.

Diet rich in refined sugars, but deficient in complex fiber and polyphenol sources promotes protein fermentation versus carbohydrate (fiber) fermentation in cecum and colon of a rat colitis model (Koleva, et al PlosOne 2014)
The “Omics” Cascade

What can happen
GENOME

What appears to be happening
TRANSCRIPTOME

What makes it happen
PROTEOME

What has happened and is happening
METABOLOME

PHENOTYPE
Urine metabolomics differ in UC versus non-IBD controls

PLS-DA, P<0.001

Hassanzadeh Keshteli CDDW 2015
Dietary and bacterial-derived metabolites in serum and urine of UC patients predict future relapse
Take Home Points

- Diets as well the prevalence of certain “western GI disorders” have drastically changed in the last 50 years
- Diets affect the composition and function of the human microbiome
- Dietary therapy may be the solution to prevent and possibly cure these disorders