The Human Gut Microbiota and Type 2 Diabetes

Matt Collison
• Introduction to the central concepts
• Proposed mechanisms of microbiota contributing to the disease
• Population level studies in humans
  • Chinese
  • European
• Potential therapeutic interventions involving the microbiota
What is the microbiome?

What is the microbiome?

**Human host**

- **Human Genome**
  - $10^{13}$ human cells
  - 30,000 unique genes (CNVs, SNPs)

**Microbiota**

- **GUT Microbiome**
  - $10^{14}$ prokaryotic cells
  - 4,500,000 genes (Taxonomic composition and LGT)

Type 2 Diabetes

Low glucose

Plasma glucose

Alpha cells

Beta cells

glucagon

insulin

Glycogenolysis
Gluconeogenesis
Ketones

Glycolysis
Glyogenesis
Lipogenesis

High glucose
Causes of Insulin Resistance

- Genetic predisposition
- Bad diet
- Increased adiposity
- Increased inflammation
- Insulin resistance
Causes of Insulin Resistance

Causes of Insulin Resistance

Causes of Insulin Resistance

Mechanisms of Insulin Resistance

Genetic predisposition → Bad diet → Increased adiposity → Increased inflammation → Insulin resistance


To what extent does microbiota dysbiosis contribute through each mechanism in humans?
Diabetes in Chinese population

- 345 (170 vs 174) Chinese metagenomes.
- Identified 60,000 differentially abundant genes.
- Degrees of dysbiosis:
  - Taxonomic
  - Decrease butyrate producers
  - Increase in opportunistic pathogens
  - Functional
  - Increase in sulphur reduction
  - Increase in oxidative stress resistance

Diabetes in Chinese population

Functional inference

Diabetes in European Women

• 145 metagenomes from European women
• Degree of dysbiosis:
  • Taxonomic
    • Decrease butyrate producers
    • Increase in opportunistic pathogens
  • Inconsistent contributors:
    • Akkermansia not discriminate in European T2DM
    • Lactobacillus not discriminate in Chinese T2DM

Can microbiome modulation have any therapeutic value in T2DM treatment?
Microbiome Modulation Approaches

- Probiotics – Everald et al, PNAS (2013)
- Prebiotics – Cani et al, Gut (2009)
- Antibiotics – Murphy et al, Gut (2013)
References


