Impact of basal diet on obesity phenotype of recipient mice following fecal transfer from obese or lean human donors

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OBESITY

34%

METABOLIC SYNDROME

Cluster of physiological and biochemical factors associated with the development of obesity and heart disease.

Central Obesity  
High Blood Pressure  
High Triglycerides  
High Fasting Plasma Glucose

GUT MICROBIOTA

• Our colon is home to about 100 trillion microorganisms

• 400-500 different species

• 2/3 of those bacteria are found in everyone while 1/3 is unique to the individual

Quigley, E. Gastroenterology & hepatology 9.9 (2013): 560-69
Dysbiosis is a condition that favors pathogenic (harmful) bacteria which may precede disease, including metabolic syndrome, inflammatory bowel syndrome and colorectal cancer.
FACTORS IMPACTING MICROBIOME

- Age
- Birth
- Genetics
- Antibiotics
- Diet
- Stress
OBJECTIVE

Determine the contribution of gut microbiota from lean or obese donors on the phenotype of mice fed one of three diets, control (AIN), Western (TWD) or high-fat (DIO).
STUDY

Human Donors  Fecal Samples  Mouse Recipient  Diets

ENDPOINTS

Body Weight

oGTT

Food Intake

MRI

Fecal Collection

Sacrifice
FOOD AND ENERGY INTAKE

Mixed model main effects  | p value
Diet                   | 0.0090
Body type              | 0.0490
Diet x body type       | 0.0080
Donor ID[body type]    | 0.7502

Mixed model main effects  | p value
Diet                   | <0.0001
Body type              | 0.0490
Diet x body type       | 0.0080
Donor ID[body type]    | 0.7502
**BODY WEIGHT GAIN**

### Week-by-Week Weight Gain

- **Body Weight (g)**
  - AIN, Ln
  - AIN, Ob
  - DIO, Ln
  - DIO, Ob
  - TWD, Ln
  - TWD, Ob

- **Mixed model main effects**
  - Diet: $<0.0001$
  - Body type: 0.5054
  - Diet x body type: 0.8989
  - Donor ID[body type]: 0.7077

### Final Body Weight (g)

- **Final body weight (g)**
  - AIN, Ln
  - AIN, Ob
  - DIO, Ln
  - DIO, Ob
  - TWD, Ln
  - TWD, Ob

- **Mixed model main effects**
  - Diet: $<0.0001$
  - Body type: 0.6164
  - Diet x body type: 0.8703
  - Donor ID[body type]: 0.7218

### Change in Body Weight (g)

- **Change in body weight (g)**
  - AIN, Ln
  - AIN, Ob
  - DIO, Ln
  - DIO, Ob
  - TWD, Ln
  - TWD, Ob

- **Mixed model main effects**
  - Diet: $<0.0001$
  - Body type: 0.6164
  - Diet x body type: 0.8703
  - Donor ID[body type]: 0.7218

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HCC and PCA for donor and mouse initial

Source
- Bacteroidales S24-7
- Lactobacillaceae
- Streptococcaceae
- Veillonellaceae
- Bifidobacteriaceae
- Enterobacteriaceae
- Alcaligenaceae
- Barnesiellaceae
- Verrucomicrobiaceae
- Turicibacteraceae
- Anaeroplasmataceae
- Planococcaceae
- Clostridiaceae
- Odoribacteraceae
- Paraprevotellaceae
- Coriobacteriaceae
- Porphyromonadaceae
- Erysipelotrichaceae
- Rikenellaceae
- Prevotellaceae
- Bacteroidaceae
- Lachnospiraceae
- Clostridiales unknown
- Ruminococcaceae

PC1 (49.5%)
PC2 (23.3%)

Mouse pre-AB
Lean donor
Obese donor
HCC and PCA for post FMT

- Fraction of total reads
- PC1 (52.2%)
- PC2 (28.4%)
- Diet
  - AIN
  - DIO
  - TWD

- Donor body type
  - Lean
  - Obese

- Body types
  - Lean human donor
  - Lean mouse recipients
  - Obese human donor
  - Obese mouse recipients

Bacterial families:
- Lachnospiraceae
- Streptococcaceae
- Porphyromonadaceae
- Barnesiellaceae
- Alcaligenaceae
- Turicibacteraceae
- Enterococcaceae
- Coriobacteriaceae
- Alphaproteobacteria RF32
- Enterobacteriaceae
- Bifidobacteriaceae
- Prevotellaceae
- Clostridiaceae
- Veillonellaceae
- Rikenellaceae
- Ruminococcaceae
- Erysipelotrichaceae
- Clostridiales unknown
- Bacteroidaceae
- Verrucomicrobiaceae
CONCLUSION

- Diet plays a larger role on the microbiota composition compared to donor microbiota, suggesting that dietary practices may be the most effective way to change the microbiome.
- Source of fecal transfer (lean vs. obese) did not impact body weight gain, body composition or glucose tolerance in recipient mice.
- As expected, mice fed high fat diet gained excess body weight and fat composition and had impaired glucose tolerance. Mice fed TWD were not statistically different from counterparts fed either AIN or DIO diets.
- The microbiome may be more of a correlative as opposed to a causative factor in the etiology of obesity.
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