WILD PRIMATE GUT MICROBIOTA PROTECT AGAINST OBESITY

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Background

- The gastrointestinal tract hosts trillions of bacteria, together forming the gut microbiome, that play major roles in metabolism, immune system development, and pathogen resistance
- There is increasing evidence that low dietary fiber in Westernized societies is associated with dramatic loss of natural human gut microbiome diversity, the role of this loss in obesity and inflammation is not well understood
- Non-human primates (NHPs) can be used as model systems for studying the effects of diet and lifestyle disruption on the human gut microbiome
- Captive primates are typically exposed to low-fiber diets and tend to have human-associated microbiota in place of their native microbiota
- Interactions between gut microbiota, obesity and dietary fiber can be explored by using captive and wild primate gut microbiota as donors, and germ-free mice on either high- or low-fiber diets as a model system

Introduction

- Modern and Westernized societies are associated with rising levels of obesity as well as loss of natural human gut microbiome diversity
- Human populations consuming low-fiber diets have microbiomes more similar to those of modern Western society humans
- Wild primates have a more diverse gut microbiome and diet rich in fiber
- Humans on high-fiber diets and wild primates have similar microbiomes
- Captivity humanizes the primate microbiome decreasing bacterial diversity
- ***Central question: does the interaction between the modern human gut microbiome of Western societies and low fiber diets result in obesity and inflammation?***

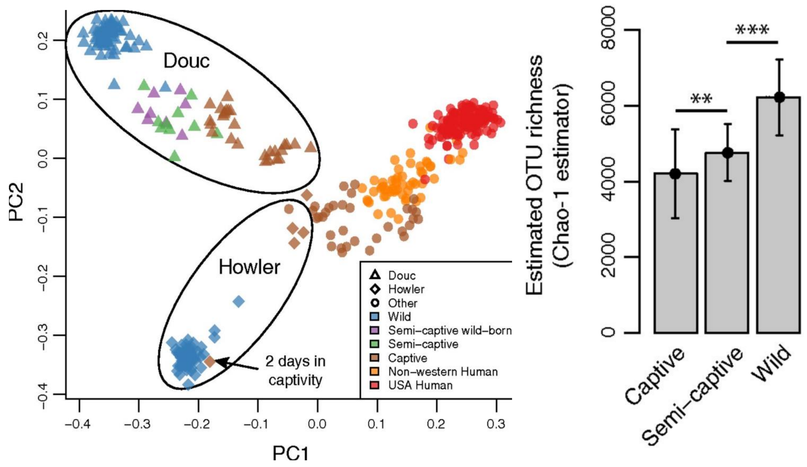
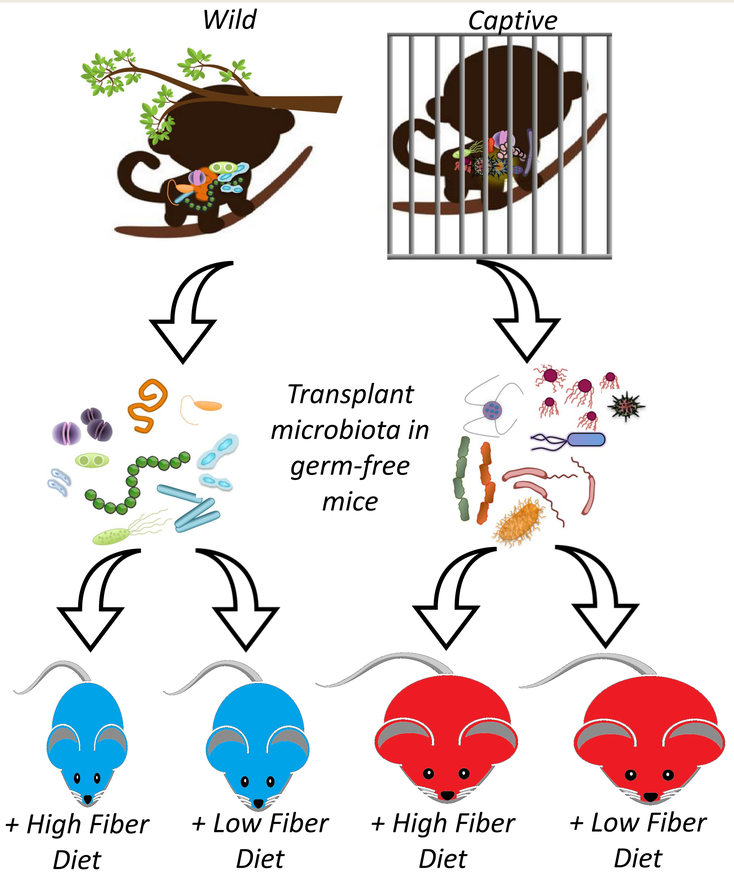


Figure 1. Similarity of microbiomes between primates and humans. Captive primate microbiomes are the closest to the Western human microbiome.

Figure 2. Microbiome diversity in captive, semi-captive and wild primates. Captive primate microbiomes are least diverse and wild primates are the most diverse.

Experimental Design

- Stool samples from wild monkeys (Doucs) in Vietnam, and captive monkeys housed in the Philadelphia zoo were used to create two master donor pools for the transplant
- 32 Germ-free mice were exposed to either a high-fiber or a low fiber diet
- After a week of acclimation, mice received the microbiota via gavage
- At day 50 on diets, mice were sacrificed. Blood, stool and tissue samples were collected



Results

- Wild microbiota mice exposed to the high fiber diet were the most lean group at the time of sacrifice
- Captive microbiota mice exposed to low fiber diet were the most obese, with the most significant increase in body mass
- Biopsies showed a greater increase of adipose tissue in captive microbiota mice, indicating that weight gain was due to fat production, and not growth
- Wild microbiota mice exposed to low fiber diet had intermediate change in body mass
- Cytokine and chemokine levels in blood showed that captive microbiota mice have greater signs of inflammation with the exception of TGF1 β which was higher in wild microbiota mice

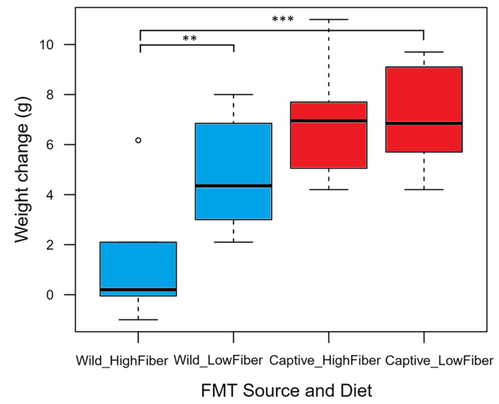


Figure 3. Weight gain in mice from the beginning of the study to sacrifice. In blue are mice that received the wild donor microbiota, in red are the mice that received the captive donor microbiota. Captive donor mice on either diet showed significantly greater weight gain than mice receiving the wild donor microbiota. Mice on the high fiber diet that received the wild donor pool remained lean. ** = 0.0061 Pvalue, *** = <0.0001 Pvalue (each group *n* = 8).

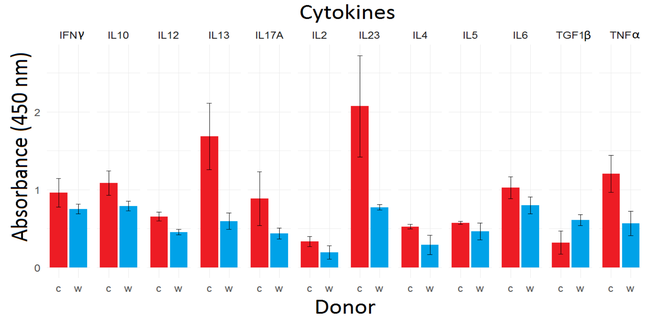


Figure 4. ELISA cytokines array absorbance values in blood samples from mice that received wild and captive donor microbiota. Captive microbiota mice on high fiber diet showed greater levels of cytokines than wild microbiota mice on high fiber diet. Error bars represent standard error (*n* = 3).

Conclusions & Future Directions

Captive primate microbiomes may
- Cause obesity under high-fiber and low-fiber diets
- Promote systemic inflammation including circulating TNF-α, IL-23

Wild primate microbiomes may
- Reduce obesity on low-fiber diet
- Cause no weight gain on high-fiber diet
- Suggest a possible clinical role for manipulation of the microbiota in the treatment of obesity

Future work: ongoing microbiome sequencing of longitudinal stool samples and biopsy gene expression to study host interactions with captive or wild microbiota

References

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Acknowledgements

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