Escola Superior de Tecnologia da Saúde
Politécnico de Coimbra

# The Human Microbiome and Obesity: Moving beyond Associations

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## Introduction

The gut microbiome refers to all the microbes that inhabit our intestines, whose functions are interconnected with the physiology and pathophysiology of the host.The purpose of this presentation is to expose the current state of knowledge and provide specific recommendations and actionable solutions to advance microbiological research in the areas of obesity and metabolic diseases

## Host physiology, gut microbiome and obesity: how are they linked?

1. Fat levels are controlled through the physiological regulation of food intake and energy expenditure (EE). So, obesity would be easily treated by reducing food intake and consequently reducing energy consumption (EI) and increasing energy expenditure (EE).
However:
- EI and EE are interconnected;
- EI and EE are regulated by the central and endocrine nervous system through the release of hormones such as leptin, ghrelin and other intestinal peptide hormones and appetite-regulating neuropeptides.

2. One of the strategies used to combat obesity are bariatric surgical methods, but they do not cause a change in the physiological response to caloric restriction. Metabolic changes observed after the procedure are caused by the alter of the gut microbiota composition throughout the entire intestinal lumen.

3. When host-microbiota interaction is disturbed by exposure to antibiotics, changes in diet, genetic manipulation of the circadian genetic network, or chronic jet lag induction, metabolic homeostasis is also disturbed.

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|---|---|
| Diet | The transfer of fecal microbiota in rats without germs, using microbiota from obese donors, leads to an increase in fat mass, and the reverse is also true. |
| Circadian rhythms | The intestinal microbiota can also respond to host circadian rhythms in a diet-dependent manner, which has been proven through studies in rats. |
| Antibiotics | Studies indicate an association between the use of prenatal and perinatal antibiotics and an increased risk of childhood obesity. |

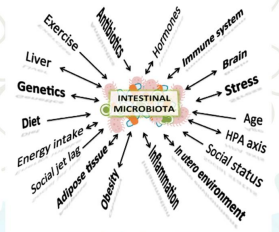


Figure 1 - Environmental Factors that Influence Gut Microbiome

4. Recent observations in therapies with target microbiomes to prevent and treat disease:
- Prebiotic resistant starches (fiber)
- Probiotics
- Fecal Microbiota Transfer (FMT)

## Microbiome and Obesity Research

| Challenges | How to overcome these challenges? |
|---|---|
| Gnotobiotic Studies | To involve cross-cutting interdisciplinary teams and dialogue and interaction between researchers pursuing microbiological and obesity research |
| Lack of communication between researchers | Improved experimental models and systems:<br>• Germ free animal models with human microbiota through FMT<br>• Mini-bioreactors that mimic the human GI tract<br>• Ex vivo organoid models |
| Difficulties inherent to research in human subjects | The development of innovative technologies and sophisticated bioinformatics tools<br>• Biomarkers and crowd-sourcing applications to assess dietary intake and exposure<br>• New culture techniques and better simulation of host environment<br>• Technologies that allow bio-sampling of the microbiota along the entire length of the intestine<br>• Wearable equipment and other new biosensors that are emerging<br>• Application of stable dietary components isotopically labeled, such as fibers or vitamins labeled with $^{13}C$<br>• Ex vivo or in vivo organoid models<br>• Synthetic biology exploring new synthetic bacteria |

## Future Directions

Targeted approaches can range from simple dietary manipulation adapted to an individual's microbiota, to designer probiotics and FMT, which can be individualized with high precision, although few human studies have shown the effectiveness of these approaches, due to the interference of several factors.

In addition, the development of innovative technologies and sophisticated bioinformatics tools that integrate data from both the host and the microbiome will facilitate a better understanding of the causal role.
Finally, it is important to involve public-private partnerships to facilitate and support research projects and to inform and involve the community, increasing voluntary participation in clinical studies.

**References** Maruvada, P. et al. *The Human Microbiome and Obesity: Moving Beyond Associations*. Cell Host & Microbe 22, November 8, 2017: 589-599. Elsevier Inc.

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