

Faecal microbiota transplantation from children to mice mediates the transfer of cognitive, cardiac, intestinal and metabolic phenotype

Maria Angela Guzzardi¹, Federica La Rosa¹, Francesco Faita¹, Lamia Ait-Ali¹, Daniele Panetta¹,
Claudia Kusmic¹, Mercedes Pardo-Tendero^{1,2}, Federico Granziera^{1,3}, Monica Barone⁴, Silvia
Turroni⁴, Daniel Monleon², Patrizia Brigidi⁴, Patricia Iozzo¹

¹ Institute of Clinical Physiology (IFC-CNR)

² University of Valencia (Spain)

³ University School S. Anna (Italy)

⁴ University of Bologna (Italy)

Background:

The involvement of the gut microbiota in the pathophysiology of metabolic syndrome and type 2 diabetes is supported by studies of faecal microbiota transplantation (FMT). In the JPI-HDHLINTIMIC GUTMOM project, we asked whether the phenotype of children donors predicts the organ-specific phenotype of mice recipients in the long-term.

Methods and Results:

We performed FMT from five-years old children into young, sex-matched mice. Recipients were monitored (food intake, body weight, Y-maze test) until adult age, when they underwent echocardiography, PET-CT imaging, ex vivo tissue histology, and fecal microbiota and metabolite characterization. So far, we have examined brain, heart, caecum and adipose tissue. Between donors and recipients, we observed significant correlations ($p < 0.05$) in cognitive and cardiac parameters; children's BMI or waist circumference were related to recipient food intake, body weight, glucose levels, brown- and white-fat lipid accumulation, fat radiodensity, white-fat glucose uptake and inflammation, caecum crypt and goblet cell morphology.

Conclusions and Significance:

The results support a potent cause-effect role of the microbiota affecting the phenotype of recipients in a donor-consistent and durable manner. FMT in mice seems to be a valid translational model.

Keywords:

faecal microbiota transplantation, phenotype transfer, cognitive function, cardio-metabolic phenotype, PET-CT-US imaging



References:

1. Guzzardi MA, La Rosa F, Iozzo P. Trust the gut: Outcomes of gut microbiota transplant in metabolic and cognitive disorders. 2023, *Neurosci Biobehav Rev* 27;149:105143
2. Guzzardi MA, Ait Ali L, D'Aurizio R, Rizzo F, Saggese P, Sanguinetti E, Weisz A, Pellegrini M, Iozzo P. Fetal cardiac growth is associated with in utero gut colonization, 2019, *Nutr Metab Cardiovasc Dis*;29(2):170-176
3. Guzzardi MA, Ederveen THA, Rizzo F, Weisz A, Collado MC, Muratori F, Gross G, Alkema W, Iozzo P. Maternal pre-pregnancy overweight and neonatal gut bacterial colonization are associated with cognitive development and gut microbiota composition in pre-school-age offspring. 2022, *Brain Behav Immun*. 100:311-320
4. Sanguinetti E, Guzzardi MA, Tripodi M, Panetta D, Selma-Royo M, Zega A, Telleschi M, Collado MC, Iozzo P. Microbiota signatures relating to reduced memory and exploratory behaviour in the offspring of overweight mothers in a murine model. 2019, *Sci Rep*. 30;9(1):12609
5. Sanguinetti E, Collado MC, Marrachelli VG, Monleon D, Selma-Royo M, Pardo-Tendero MM, Burchielli S, Iozzo P. Microbiome-metabolome signatures in mice genetically prone to develop dementia, fed a normal or fatty diet, 2018, *Sci Rep*, 20;(8):4907

Thematic Area:

- Frontiers in Microbiome Research
- Microbiome: from Research to Clinics

Infrastructures:

N.A.