Jak mikrobiom wpływa na organizm człowieka?

Żywienie bez granic
1 czerwca 2019 r.

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- genom
- proteom
- transkryptomom
- methylom
- lipidom
- mitointeraktom
- konektom
Gut Microbiota from Twins Discordant for Obesity Modulate Metabolism in Mice


Introduction: Establishing whether specific structural and functional configurations of a human gut microbiota are causally related to a given physiologic or disease phenotype is challenging. Twins discordant for obesity provide an opportunity to examine interrelations between obesity and its associated metabolic disorders, diet, and the gut microbiota. Transplanting the intact uncultured or cultured human fecal microbiota from each member of a discordant twin pair into separate groups of recipient germ-free mice permits the donors’ communities to be replicated, differences between their properties to be identified, the impact of these differences on body composition and metabolic phenotypes to be discerned, and the effects of diet-by-microbiota interactions to be analyzed. In addition, cohousing coprophagic mice harboring transplanted microbiota from discordant pairs provides an opportunity to determine which bacterial taxa invade the gut communities of cage mates, how invasion correlates with host phenotypes, and how invasion and microbial niche are affected by human diets.

Methods: Separate groups of germ-free mice were colonized with uncultured fecal microbiota from each member of four twin pairs discordant for obesity, or with culture collections from an obese (Ob) or lean (Ln) co-twin. Animals were fed a mouse chow low in fat and rich in plant polysaccharides (LF-HPP) or one of two diets reflecting the upper or lower (Hi or Lo) tertiles of consumption of saturated fats (SF) and fruits and vegetables (FV) based on the U.S. National Health and Nutrition Examination Survey (NHANES). Ln or Ob mice were cohoused 5 days after colonization. Body composition changes were determined by quantitative magnetic resonance. Microbiota or microbiome structure, gene expression, and metabolite signatures were characterized using high-throughput sequencing, and mass spectrometry. Host gene expression and metabolism were also characterized.

Results and Discussion: Establishment of the intact uncultured and culturable bacterial component of Ob co-twins’ microbiota in gnotobiotic mice. Cohousing Ob and Ln mice transforms the adiposity phenotype of cage mates harboring the obese co-twin’s culture collection to a leanlike state.

Fig. 1. Reliable replication of human donor microbiota in gnotobiotic mice.

Fig. 2. Cohousing Ob and Ln mice transforms the adiposity phenotype of cage mates harboring the obese co-twin’s culture collection to a leanlike state.

Fig. 3. Effect of cohousing on metabolic profiles in mice consuming the LF-HPP diet.

Fig. 4. Effects of NHANES-based LoSF-HiFV and HiSF-LoFV diets on bacterial invasion, body mass, and metabolic phenotypes.

Fig. 5. Invasion analysis of species-level taxa in Ob and Ln mice fed the NHANES-based LoSF-HiFV diet.

Fig. 6. Acylcarnitine profile in the skeletal muscle of mice colonized with the Ob or Ln culture collections from dizygotic twin pair 1 and fed the LoSF-HiFV diet.

SUPPLEMENTARY MATERIALS

References and Notes

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Figs. S1 to S17

Supplementary Text

Materials and Methods

FIGURES IN THE FULL ARTICLE

http://dx.doi.org/10.1126/science.1241214

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DOI: 10.1126/science.1241214
Danio pręgowany z otyłością

Diet Induced Obesity

Zdrowa

DIO

Zdrowa

DIO

Probiotic treatment reduces appetite and glucose level in the zebrafish model

Silvia Falcinelli\textsuperscript{1}, Ana Rodiles\textsuperscript{2}, Suraj Unniappan\textsuperscript{3}, Simona Picchietti\textsuperscript{4}, Giorgia Gioacchini\textsuperscript{1}, Daniel Lee Merrifield\textsuperscript{2} & Oliana Carnevali\textsuperscript{1}

The gut microbiota regulates metabolic pathways that modulate the physiological state of hunger or satiety. Nutrients in the gut stimulate the release of several appetite modulators acting at central and peripheral levels to mediate appetite and glucose metabolism. After an eight-day exposure of zebrafish larvae to probiotic \textit{Lactobacillus rhamnosus}, high-throughput sequence analysis evidenced the ability of the probiotic to modulate the microbial composition of the gastrointestinal tract. These changes were associated with a down-regulation and up-regulation of larval orexigenic and anorexigenic genes, respectively, an up-regulation of genes related to glucose level reduction and concomitantly reduced appetite and body glucose level. BODIPY-FL-pentanoic-acid staining revealed higher short chain fatty acids levels in the intestine of treated larvae. These results underline the capability of the probiotic to modulate the gut microbiota community and provides insight into how the probiotic interacts to regulate a novel gene network involved in glucose metabolism and appetite control, suggesting a
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Jarrow Formulas, Women's Fem Dophilus, 60 Veggie Caps

14,99 zł – eMAG
Loggi60 Lactobacillus Rhamnosus Gg 6ml 20 Kapsulek Pharmabet

22,56 zł – co najmniej w 10 sklepach
Swanson L.Reuteri Plus Probiotic (L.Rhamnosus L.Acidophilus ...
Figure 1. Gastrointestinal bacterial community analysis of 8 dpf zebrafish larvae. (A) Alpha rarefaction plot of observed species. Relative abundance of reads at the phylum (B) and genera (C) level (taxa accounting for >0.5% are represented). (D) Venn diagram showing the distribution of OTUs (those with >0.01% relative abundance are represented) revealing a shared community consisting of 43 OTUs. Cluster using Bray-Curtis metrics (E) and 2D Principal coordinate analysis (PCoA) plot of weighted UniFrac distances (F). *P < 0.05.

Fermentation of carbohydrates by the gut microbiota results in the production of short chain fatty acids (SCFAs). We evidenced an expansion of intestine epithelium structure (indicated by different letters and asterisk) in larvae treated with probiotics compared to control larvae. TEM micrographs showed the presence of lipid droplets located in the basal enterocytes, suggesting an accumulation of SCFAs. In vivo imaging revealed that probiotic treatment reduced whole organism glucose levels in zebrafish larvae. Moreover, probiotic treatment modulates the expression of genes involved in appetite control and decreases insulin and leptin release, as well as promoting an increase in the expression of leptin receptor (leptin and mc4r). Artemia salina nauplii feeding rates were significantly reduced by probiotic treatment. Transmission Electron Microscopy (TEM) shows the ultrastructure of the intestinal epithelium in control and probiotic-treated larvae, indicating undamaged epithelial barrier and absence of cell debris in the treated intestines.
Fermentation of carbohydrates by the gut microbiota results in the production of short-chain fatty acids (SCFAs), principally propionic, acetic and butyric acids which stimulate the growth of colonic epithelial cells and confers protection to the host against infection by pathogens.

In vivo experiments support a role for SCFAs in regulating appetite and glucose metabolism. In this study, probiotic administration decreased appetite and reduced whole larval glucose levels. This effect was mediated by the transcriptional regulation of genes involved in appetite control and glucose metabolism.

**Figure 2:**
- **Probiotic treatment** significantly decreases the whole organism glucose levels in zebrafish larvae.

**Figure 3:**
- Probiotic treatment modulates the expression of genes involved in appetite control and decreases leptin levels, indicating a potential role in appetite regulation.

**Figure E and F:**
- Electron micrographs show organized microvilli on the apical surface in the enterocyte of control zebrafish larvae. Probiotic treatment results in the absence of cell debris and undamaged epithelial barrier.

In conclusion, the probiotic treatment modulates the gut microbiota, leading to changes in SCFAs content and transcriptional regulation of appetite-related genes.

**References:**
Human microbiome
1,000,000+ genes

Human genome
23,000 genes
The impact of perinatal probiotic intervention on the development of overweight and obesity: follow-up study from birth to 10 years

R Luoto\textsuperscript{1,2}, M Kalliomäki\textsuperscript{1,2}, K Laitinen\textsuperscript{3,4} and E Isolauri\textsuperscript{1,2}

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Background: The achievements in combating the increasing trend of overweight and obesity have thus far been inadequate. The recently discovered instrumental role of the gut microbiota in host metabolism may offer a novel target in the prevention and management of obesity.

Objective: To evaluate the impact of perinatal probiotic intervention on childhood growth patterns and the development of overweight during a 10-year follow-up.

Patients and methods: Altogether 159 women were randomized and double-blinded to receive probiotics ($1 \times 10^{10}$ colony-forming units of \textit{Lactobacillus rhamnosus} GG, ATCC 53103) or placebo 4 weeks before expected delivery; the intervention extending for 6 months postnatally. Anthropometric measurements of the children were taken at the ages of 3, 6, 12 and 24 months and at 4, 7 and 10 years in 113 (72\%) children.

Results: The excessive weight gain was detected to be two-parted; the initial phase of excessive weight gain initiating during fetal period and continuing until 24–48 months of age and a second phase of excessive weight gain starting after the age of 24–48 months. The perinatal probiotic intervention appeared to moderate the initial phase of excessive weight gain, especially among children who later became overweight, but not the second phase of excessive weight gain, the impact being most pronounced at the age of 4 years ($P = 0.063$, analysis of variance for repeated measures). The effect of intervention was also shown as a tendency to reduce the birth-weight-adjusted mean body mass index at the age of 4 years ($P = 0.080$, analysis of covariance).

Conclusions: Early gut microbiota modulation with probiotics may modify the growth pattern of the child by restraining excessive weight gain during the first years of life. This novel observation calls for further epidemiological and clinical trials, with precise data on early growth patterns and on confounding factors influencing weight development.

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Keywords: growth; overweight; probiotics

Introduction

Obesity with its comorbidities can currently be considered as a major threat to the health and well-being of human-kind. In particular, the increasing incidence of obesity in children is a source of concern, in that it is likely to persist to adulthood. Epidemiological data point to high birth weight on the one hand or faster postnatal growth on the other as the initial requisite for later obesity. Nonetheless, the most critical and sensitive period of childhood growth and the underlying denominators for obesity remain elusive.

A recent hypothesis envisages the gut microbiota as instrumental in the control of bodyweight and energy metabolism, affecting the two main causes of obesity: energy acquisition and storage. Moreover, the composition of the gut microbiota contributes to the insulin resistance and the inflammatory state characterizing obesity. High prepregnancy body mass index (BMI) and excessive weight gain during pregnancy are associated with aberrancies in the gut microbiota composition of the mother, this acting as the inoculum for the development of the infant gut microbiota, and thus carrying a potential to interfere with the child's growth.

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Lactobacillus rhamnosus
Raz dziennie, przez 28 dni przed porodem

<table>
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<th>Probability Estimate</th>
<th>Standard Error</th>
<th>OR (95% CI)</th>
<th>P-Value</th>
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<td>Overweight - placebo (N=12)</td>
<td>1.30 (0.56–3.18)</td>
<td>0.564</td>
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</tr>
<tr>
<td>Overweight - probiotic (N=13)</td>
<td>0.86 (0.33–2.26)</td>
<td>0.759</td>
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</table>

Randomization at the third trimester of pregnancy to placebo or probiotics group; n = 159

**Placebo group**
- n = 82

**Probiotics group**
- n = 77

**Start of follow-up**

**Lost of follow-up n = 23**

**Continued follow-up for 10 y n = 59**

**Lost of follow-up n = 23**

**Continued the follow-up for 10 y n = 54**

**Figure 1**

**BMI and the frequency of overweight and obesity at 2, 4, 7 and 10 years of age in the probiotic group and in the placebo group**

**Table 1**

<table>
<thead>
<tr>
<th>Age (months)</th>
<th>BMI (kg m⁻²)</th>
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<tbody>
<tr>
<td>0</td>
<td>12</td>
</tr>
<tr>
<td>36</td>
<td>12</td>
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<td>84</td>
<td>12</td>
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<tr>
<td>120</td>
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Luoto et al. (2010) *Int. J. Obesity*
The Integrative Human Microbiome Project

The Integrative HMP (iHMP) Research Network Consortium*

The NIH Human Microbiome Project (HMP) has been carried out over ten years and two phases to provide resources, methods, and discoveries that link interactions between humans and their microbiomes to health–related outcomes. The recently completed second phase, the Integrative Human Microbiome Project, comprised studies of dynamic changes in the microbiome and host under three conditions: pregnancy and preterm birth; inflammatory bowel diseases; and stressors that affect individuals with prediabetes. The associated research begins to elucidate mechanisms of host–microbiome interactions under these conditions, provides unique data resources (at the HMP Data Coordination Center), and represents a paradigm for future multi–omic studies of the human microbiome.

Although the ‘omics era has accelerated all aspects of biological research, its effects have been particularly apparent in studies of microbial communities and the human microbiome. In the 18 years since the publication of the first human genome, studies of the microbiome have grown from culture-based surveys of the oral cavity and gut to molecular profiles of microbial biochemistry in all ecological niches of the human body. Epidemiology and model systems have been used to identify associations between changes in the microbiome and conditions ranging from autism to cancer, and microbial and immunological mechanisms have been identified that affect, for example, the efficacy of drugs used to treat cardiac conditions or survival during infection. Protocols to support reproducible body-wide microbiome sampling and the generation of nucleotide sequences of microorganisms and communities from a large number of isolates, individuals, and populations of one or more species have been established for the HMP (HMP1). The iHMP thus yielded a wealth of information about the relationship between host and microbiome mechanics, as well as the interplay between host responses and microbial inter–relationships. A collection of more than 100,000 strains and 1000 microbial communities is available in the HMP database, together with a rich multi–omic data resource to be mined by future work.
microbiomes of pregnant women to gauge their effects on risk of PTB and lead to premature rupture of the membranes (proteases or toxins) that compromise the integrity of fetal membranes and/or by the release of microbial products (for example, collagenases, maternal immune balance, leading to spontaneous preterm labour, abortion of the fetus into the uterus is thought to precipitate PTB by disrupting the fetal membranes, and intra-amniotic infection)

The vaginal microbiome, pregnancy and preterm birth

Contributors to PTB include breakdown in maternal–fetal tolerance, a delicate balance of pro- and anti-inflammatory effectors has not decreased

The Multi-Omic Microbiome Study: Pregnancy Initiative

The ten-year NIH Human Microbiome Project (HMP) program, HMP1 focused on the characterization of microbial skin) in a baseline study of healthy adult subjects, and included a set of demonstration projects that focused on specific diseases or disorders. The HMP2 expanded the repertoire of biological properties analysed for both community. The HMP1 focused on the characterization of microbial sequencing, multi-omic data sets, computational and statistical tools, and analytical and clinical protocols as resources for the broader research network.

Healthy cohort study

Demonstration projects

Preterm birth

Inflammatory bowel diseases

Pre-diabetes
