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ENGLISH TRANSLATION OF THE MEDICAL ARTICLES

References

Modified microbiome in MS patients

"Although we have only just started the study, the data suggest that patients with MS have reduced levels of good gut bacteria that have health benefits for the whole body and can be obtained by eating healthy foods such as soybeans and flaxseed." says Mangalam, who is also a senior author of the Mayo Clinic study in Rochester, Minnesota.

Original publication:

Multiple sclerosis patients have a distinct gut microbiota compared to healthy controls Ashutosh Mangan et. al; Scientific Reports, doi: 10.1038 / srep28484, 2016
Helicobacter pylori Infection and Risk for Eosinophilic Esophagitis
Helicobacter pylori infection was associated with a reduced risk of developing EoE. The prevalence of H.pylori infection has decreased considerably in industrialised nations over the past three decades. This has been attributed to improved hygiene with less antigenic exposure, and a corresponding increase in many atopic diseases, such as asthma and dermatitis. Altogether, this suggests that H pylori exposure may in fact affect immune system development. EoE is an antigen-mediated allergic disease of the esophagus or "asthma of the esophagus".

1. by Arnim U, Wex T, Link A, et al. Helicobacter pylori infection is associated with a reduced risk of developing eosinophilic oesophagitis. Aliment Pharmacol Ther. 2016; 43: 825-833.

Gut Microbiota Profiling of Pediatric NAFLD and Obese Patients Unveiled by an Integrated Meta-omics Based Approach

Del Chierico F, Nobili V, Vernocchi P, et al; Hepatology. 2016 Mar 29. [Epub ahead of print]
The term "gut-liver axis" is used to describe the close relationship that is established between the gut and liver, beginning in the very early stages of fetal life. The quantitative and qualitative ariations in the bacteria that compose the gut microbiota may actively contribute to the pathogenesis of several liver diseases, including nonalcoholic fatty liver disease (NAFLD), alcoholic steatohepatitis, and cirrhosis.

Obesity is a major risk factor for NAFLD in children, and there is evidence that the gut microbiota can directly influence body weight in several ways:

•Affecting the proportion of calories obtained from the intestinal contents;
• Contributing to increased intestinal permeability through loss of epithelial barrier integrity; Increasing bacterial translocation into the systemic circulation and allowing more hepatic access for ethanol and bacterial endotoxins such as lipopolysaccharide, which triggers nuclear factor-KB mediated proinflammatory cytokine production; and
• Promoting development of insulin resistance in the host.

The investigators found that the most abundant operational taxonomic units at a phylum level in all patients were Firmicutes, followed by Bacteroidetes, Proteobacteria, Actinobacteria, Verrucomicrobia, and Tenericutes.
In children with NAFLD, compared with controls, Actinobacteria were significantly increased, and Bacteroidetes were reduced. Bacteroidaceae and Bacteroides were reduced in patients with NAFLD and NASH and increased in obese patients compared with controls. Overall, children with NAFLD had increased levels of Blautia, Bradyrhizobium, Anaerococcus, Peptoniphilus, Propionibacterium acnes, Dorea, and Ruminococcus and reduced proportions of Oscillospira and Rikenellaceae compared with control children. In the group with NASH, lower levels of Oscillospira were associated with higher abundance of Dorea and Ruminococcus and higher levels of 2-butanone, 4-methyl-2-pentanone compared with control children. Remarkably, Oscillospira was significantly less abundant in patients with NAFLD and NASH and in those who were obese compared with the control children.

The gut microbiome holds many secrets. Its composition affects digestion and the immune system. The more diverse the composition, the better. Now it became clear that wine and coffee apparently promote microbial diversity.
Good news for coffee and wine lovers:
According to a new study, both drinks increase the diversity of the microbiome in the gut. A diverse composition of the microbiome is considered an indication of health. Fruits, vegetables, yoghurt and buttermilk also have a positive effect on the microbial composition of the intestinal flora. A Dutch study involving 1,100 people identified a total of 126 factors that have an impact on the composition of the microbiome. Most of these factors are related to nutrition, but medication, diseases and tobacco consumption also play a role. For example, drinks and snacks with a high sugar content reduce the diversity of microorganisms in the intestine. Also interesting: The microbiome of women is more diverse than that of men and that of older people is more diverse than that of younger ones. Contrary to expectations, caesarean sections have no influence on the amount of microorganisms in the intestine of adults.

Read more about the test results here.
Original publications:
Population-based metagenomics analysis reveals markers for gut microbiome composition and diversity Alexandra Zhernakova et al .; Science, doi: 10.1126 / science. aad3369; 2016 population-level analysis of gut microbiome variation Gwen Falony et al .; Science, doi: 10.1126 / science.aad3503, 2016

If you have any questions, please contact Dr. Sepp Fegerl at sepp@praxisfegerl.at

Study: DNA repair capacity improved by Mayr therapy

In a study by the Albstadt-Sigmaringen University of Applied Sciences in cooperation with the Center for TCM and Naturopathic Medicine in Sigmaringen, the DNA repair capacity was measured before and after 6 weeks of Mayr outpatient therapy. It was shown that in patients who had previously had a reduced DNA repair capacity, there was a significant increase in DNA repair capacity after just one week of Mayr intensive diet, which continued even after the therapy had been completed. The remaining patients with higher DNA repair capacity remained at a comparable level during and after therapy. The study was carried out by Katja Matt et al. as part of her doctorate published by the Faculty of Life Sciences at Albstadt-Sigmaringen University in February 2016 in the Journal Mechanisms of Aging and Development. (Matt et al. (2016) Influence of calorie reduction on DNA repair capacity of human peripheral blood mononuclear cells. Mech Aging Dev. Mar; 154: 24
9) In the human organism, DNA damages in every cell several thousand times a day, that are fixed by various DNA repair systems. The extent of the organism's ability to repair this damage through the cell's own repair mechanisms plays a significant role in the development of numerous diseases and in the course of the aging process and is the subject of intensive scientific research.
The modified Host Cell Reactivation Assay (HCRA) is an established method for measuring a special DNA repair mechanism, the nucleotide excision repair. The Faculty of Life Sciences at the Albstadt-Sigmaringen University under the direction of Prof. Jörg Bergemann has optimized this test for use on human mononuclear leukocytes in peripheral blood (PBMC) to investigate changes in DNA repair ex vivo. This makes it possible to examine changes in DNA repair capacity not only in cell cultures, but in blood samples from living organisms. When performing the HCRA, two different reporter plasmids, i.e. small circular DNA molecules, are introduced (transfected) into the mononuclear leukocytes of the blood sample, one of which codes for a green fluorescent protein and the other for a red fluorescent protein. One of the two plasmids is damaged by UVC radiation before being introduced into the cell; the other plasmid is not damaged and serves as a control. If the cell is able to repair the UV-specific DNA damage, it can synthesize both fluorescent proteins, if not, only the undamaged control plasmid is produced. The quantitative measurement of the result is performed using flow cytometry-based single cell analysis. The amount of fluorescent protein synthesized by the previously damaged plasmid is directly proportional to the DNA repair capacity of the cell. Prior to the practical study, a reproducibility study of this method was carried out with blood samples from two subjects from the university with a total of three series of measurements over the course of 10 months. Two practical studies were carried out, one in spring 2014 with 8 patients, the second in spring 2015 with 18

patients. The patients had a wide variety of symptoms such as overweight, increased blood pressure, increased liver and lipid levels, hyperuricaemia, polyarthritis, fibromyalgia, rosacea and chronic fatigue. Individual patients carried out Mayr therapy in the sense of preventive health care. Before performing therapy according to F.X. In addition to general internal diagnosis and Mayr diagnostics, Mayr always carries out bioenergetic diagnostics in our practice using applied kinesiology to clarify food intolerances and, with the corresponding symptoms, to clarify an intestinal candidiasis. This resulted in the prescription of an individually adapted intensive diet, which consisted of a morning meal with z. B. Spelled buns and sheep yogurt with omega-3 oils and a lunch meal consisted of potatoes and root vegetables with a protein supplement and omega-3 oil or also entirely from a potato-vegetable-protein-omega-3 diet if an intestinal candidiasis was present (5th Patients in spring 2015; nonePatients in spring 2014). For this purpose, an individually tested substitution with minerals and vitamins, basic therapy and, if necessary, antifungal therapy were carried out.
To build up the 6-week outpatient Mayr therapy: after the week of relief (preliminary cure), there follows a three-week intensive diet with initially three, later two medical treatment appointments per week with manual abdominal treatment. This is followed by a two-week post-treatment phase with slow cost building. Three blood samples were taken per patient: the first before the start of the relief week, the second on the 8th day of intensive diet, and the third after completion of the three-week intensive diet. According to the existing DNA repair capacity, the participants in both studies were divided into two groups: one half with the lower values and the other half with the higher values. In the four patients of the 2014 study with reduced DNA repair capacity, there was already a significant increase on the 8th day of intensive diet therapy and thus a normalization of the DNA repair capacity, which was also detectable at the end of the therapy. The remaining patients with the higher DNA repair capacity remained at a comparable level until the end of the study. These encouraging results led to the study being repeated in spring 2015 with a larger patient population. This study confirmed the results of the previous year: in patients with previously reduced DNA repair capacity, there was already a significant increase in repair capacity on the 8th day of therapy. In the remaining patients, the values remained essentially unchanged over the course of the therapy. There were no differences between female and male patients. The results of the two practical studies are a good indication of the effectiveness of holistic intestinal rehabilitation according to Dr. F.X. Mayr and may be an important building block for a better understanding of this therapy, although it is still largely open which effects, individually or in combination, are responsible for the proven effect of normalizing a previously reduced DNA repair capacity. If the study by Matt et al. the calorie restriction was cited as a causal factor for the normalization of DNA repair capacity, since animal experiments have already shown that calorie restriction increases base excision repair in the cell nucleus, protective against age-related diseases such as e.g. B. Atherosclerosis works and slows down aging in certain model organisms, so it remains reserved for further studies to clarify these relationships in more detail.

1) Matt et al. (2016) Influence of calorie reduction on DNA repair capacity of human peripheral blood mononuclear cells. Mech Aging Dev. Mar; 154: 24-9

This study was published in the Elsevier Journal.
Original article “Influence of calorie reduction on DNA repair capacity of human peripheral blood mononuclear cells” Katja Matt (Department of Life Scieneces, Albstadt-Sigmaringen University of Applied Sciences, Sigmaringen, Germany), Katharina Burger, Daniel Gebhard, Jörg Bergemann
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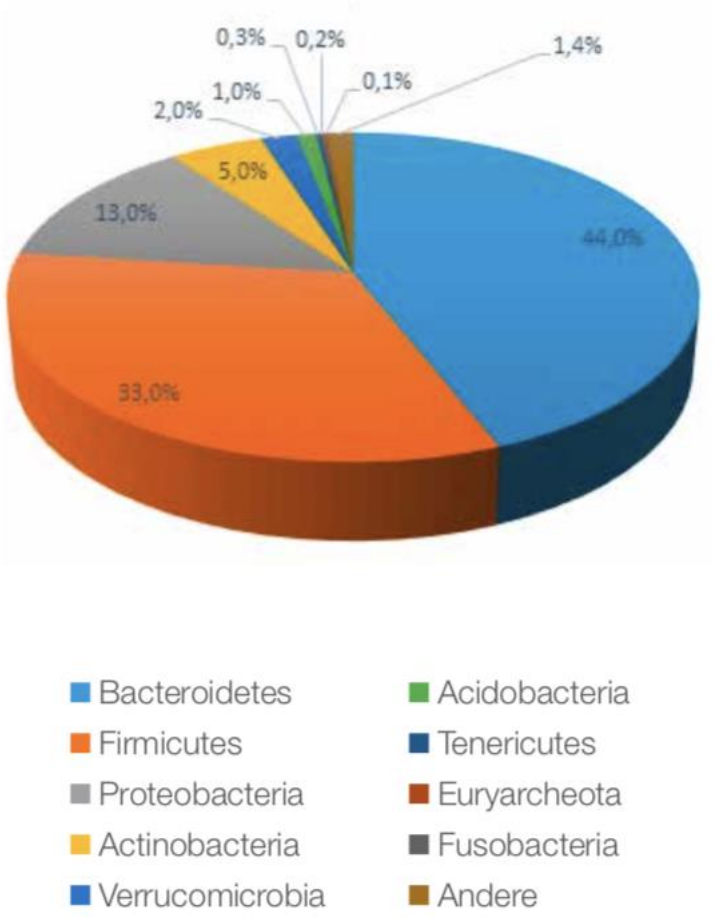
The intestinal microbiome: New molecular genetic analysis using next-generation sequencing

The intestinal microbiome, the entirety of all microorganisms that colonize the intestine, is of essential importance for humans. Dysbiosis of the intestinal microbiome is - as numerous studies show - associated with various diseases: metabolic syndrome, diabetes, inflammatory bowel diseases such as Crohn's disease and ulcerative colitis, irritable bowel syndrome, colon cancer, calcium oxalate urinary stones, cardiovascular diseases, rheumatoid arthritis and neurological disorders. Since June 2016, GANZIMMUN Diagnostics AG has been offering the next generation sequencing method used in research in stool diagnostics. This method revolutionized diagnostics because it enables the detection of almost all known bacteria. Using next-generation sequencing, the effects of individual, highly complex microbiota on colonization resistance, digestive processes, absorption of nutrients and vitamins as well as on immunity can be assessed more precisely. This molecular biological test procedure also detects anaerobic bacteria at the highest technical level that cannot be cultured.
Definition "intestinal microbiome"
A microbiome is the entirety of all microorganisms that colonize a biotope. The intestinal microbiome includes bacteria, fungi, viruses and parasites. The microbiome analysis specifically examines the bacteria. The human body consists of approximately 10 trillion (1013) cells. The microorganisms living on the skin, on the mucous membranes and in the intestine in symbiosis reach a number that is 10 times higher than that of human cells (1014). The number of genes in the microbiome contains around 30 times the human genome (Shreiner A. et al. 2015). It is therefore not surprising that due to the enormous metabolic performance of the bacterial mass of the intestine, which weighs up to 1.5 kg, it has the role of an independent organ.

Bacterial diversity

The diversity of the microbiome, otherwise known as diversity, guarantees the stability of the bacterial symbiosis. The higher it is, d. H. the more different species of bacteria there are, the more the ecosystem is more stable. The Yanomami Indians' study has shown how much current civilization influences the microbiome through dieting and antibiotic treatment. The microbiome of this strain, which was only discovered a few years ago in the South American jungle, is characterized by the greatest diversity that has ever been determined. On average, this is about twice as large as that of the United States (Clemente J. et al. 2015). In addition, the inter-individual variability of the microbiome is so great that to date no two identical microbiomes have been found in the thousands of samples examined. If the diversity is disturbed by malnutrition, this is shown by the occurrence of diseases that are associated with the intestinal flora. A reduced diversity, especially among infants and the elderly, makes them susceptible to infections with toxin-forming clostridia (Schumacher B. 2014). Clostridium spp. To a certain extent it is part of the physiological intestinal flora of humans and does not cause any complaints. When antibiotics are used, individual species such as Clostridium difficile can overgrow. Some of these bacteria are able to produce a toxin that leads to severe diarrhoea. In addition, Clostridium difficile can spread very quickly through endospores and is a feared bacterium in hospitals where many seriously ill patients are treated with antibiotics. Diarrhoea associated with severe Clostridium difficile, which is understood as a model disease of a disturbed microbiome, is currently becoming different Therapy options tested. One of these is the transplantation of a healthy donor microbiome, which is already practiced in some countries in order to restore a diversity of the intestinal flora (Alang N. Kelly C. 2015).

Fig. 1: Example of the distribution of the bacterial strains in the intestinal flora



Enterotypes

Thanks to new technologies, gene sequencing of the intestinal microbiome can be statistically evaluated. A large part of the bacterial genes are found in every human gut and form a so-called nuclear microbiome. Depending on the dominant bacterial genus, this can be divided into three enterotypes (Siezen R., Kleerebezem M. 2011).

• Type 1 is characterized by an excess of germs of the genus Bacteroides, which the butyric acid produces in fermentative processes. This type is associated with a high proportion of animal proteins and fats in the diet and is most common in the western population.
• Type 2 is dominated by the genus Prevotella, which plays a major role in the degradation of glycoproteins on the intestinal mucosa. This type is found in population groups that have a high proportion of carbohydrates and simple sugar in their diet.
• Type 3 is characterized by a relatively high proportion of Ruminococcus. This type of bacteria binds the mucins and can break down the sugar residues it contains. In addition, Type 3 shows a relatively high proportion of methane-producing bacteria.

The bacterial flora that characterizes the enterotype has long-term stability. According to studies, no significant changes in the enterotypes were found in subjects after a diet change lasting several days. This classification therefore hardly allows statements about the short-term eating habits of the patients. The enterotypes do not correlate with the BMI or the age of the patients. However, this individual microbiome constellation could have diagnostic and even prognostic meanings for a number

of diseases such as colorectal cancer, metabolic syndrome, diabetes and cardiovascular diseases (Manimozhiyan A. et al. 2011).

Interferences for the development of a "healthy microbiome"

Unfavourable eating habits, which have a negative impact on the development of the microbiome, can manifest themselves in infancy - e.g. B. through the use of formula food in the first months of life. In adolescence and adulthood, stress, industrially produced foods and ingredients such as sweeteners, alcohol or environmental toxins in the food disrupt the development of the microbiome. In addition, (unnecessary) antibiotic therapy, which does not differentiate between pathogenic and physiological germs, is a main reason for the development of dysbiosis. During and afterwards, antibiotic administration with a probiotic or symbiotic therapy of dysbiosis should be prevented or that Restoration of a "healthy" microbiome.

Microbiome-associated disease risks

Disorders of the microbiome (dysbiosis), reduced diversity or incorrect colonization can be considered risk factors for numerous diseases. These include impaired peristalsis (diarrhoea or constipation), irritable bowel syndrome, metabolic diseases such as diabetes mellitus, obesity or lipid metabolism disorders, autoimmune diseases such as allergies or psoriasis, chronic inflammatory bowel diseases (ulcerative colitis or Crohn's disease), malignant or even neurologically psychiatric disorders (Frank D. et al. 2011). The basis for these observed processes can be of different types. Interactions between receptors of the epithelial and immune cells of the intestinal mucosa and the products of bacterial metabolism such as short-chain fatty acids or lipopolysaccharides are possible. GANZIMMUN Diagnostics AG has compiled a risk profile for dysbiosis-related diseases based on literature information on the risky germs. This profile takes risks for the following diseases into account:

- obesity
- Type 2 diabetes mellitus
- inflammatory bowel diseases
- Irritable bowel syndrome
- colorectal cancer
- Rheumatoid arthritis
- cardiovascular diseases
- Calcium oxalate urinary stones
- neuropsychiatric disorders

Laboratory diagnostics

The metagenomic stool analysis offered by GANZIMMUN Diagnostics AG for the detection of dysbiosis and the associated risks for dysbiosis-related diseases includes the molecular genetic analysis of the entire bacterial intestinal microbiome. In contrast to conventional stool diagnostics, with which only a limited area of the existing intestinal germs can be identified with the new method, up to 400 bacterial species can be detected. The microbiome data and their expertise will be updated and expanded at regular intervals in the future, so that new findings will be reflected in the findings.

For the list of literature and further information, please contact:

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