# **Recent Studies and Publications on Gut Microbiome**

## **STUDIES**

## 1. Minor Changes In The Composition And Function Of The Gut Microbiota During A 12-Week Whole Grain Wheat Or Refined Wheat Intervention Correlate With Liver Fat In Overweight And Obese Adults

In middle-aged overweight and obese adults, a 12-week whole grain wheat intervention increased Ruminococcaceae bacteria and increased predicted fermentation pathways when compared with a refined wheat diet intervention.

Whole grain wheat (WGW) products are advocated as a healthy choice when compared with refined wheat (RW). One proposed mechanism for these health benefits is via the microbiota, because WGW contains multiple fibers. WGW consumption has been proposed to ameliorate nonalcoholic fatty liver disease, in which microbiota might play a role.

Source: Lydia A Afman, Nutrition, Metabolism & Genomics Group, Division Of Human Nutrition And Health, Wageningen University, Wageningen, The Netherlands. Minor Changes In The Composition And Function Of The Gut Microbiota During A 12-Week Whole Grain Wheat Or Refined Wheat Intervention Correlate With Liver Fat In Overweight And Obese Adults. The Journal Of Nutrition, Volume 151, Issue 3, March (2021), Pages 491–502. <u>https://doi.org/10.1093/jn/nxaa312</u>

#### 2. Microbiome Connections With Host Metabolism And Habitual Diet From 1,098 Deeply Phenotyped Individuals

Researchers have found that many significant associations between microbes and specific nutrients, foods, food groups and general dietary indices, which were driven especially by the presence and diversity of healthy and plant-based foods. Microbial biomarkers of obesity were reproducible with circulating blood metabolites that are indicators of cardiovascular disease risk. While some microbes, such as *Prevotella copri* and *Blastocystis spp*., were indicators of favorable postprandial glucose metabolism, overall microbiome composition was predictive for a large panel of cardiometabolic blood markers including fasting and postprandial glycemic, lipemic and inflammatory indices.

Further, the panel of intestinal species associated with healthy dietary habits overlapped with those associated with favorable cardiometabolic and postprandial markers, indicating that the large-scale resource can potentially stratify the gut microbiome into generalizable health levels in individuals without clinical manifestation of disease.

Source: Sarah E. Berry, Department Of Nutritional Sciences, King's College London, London, UK. Microbiome Connections With Host Metabolism And Habitual Diet From 1,098 Deeply Phenotyped Individuals. Nat Med 27, 321–332 (2021). https://doi.org/10.1038/s41591-020-01183-8

#### 3. A Genome-Wide MicroRNA Screen Identifies The MicroRNA-183/96/182 Cluster As A Modulator Of Circadian Rhythms

Scientists have found that all three members of this miRNA cluster can modulate circadian rhythms. Particularly, miR-96 which directly targeted a core circadian clock gene, PER2. The knockout of the miR-183/96/182 cluster in mice showed tissue-specific effects on circadian parameters and altered circadian rhythms at the behavioral level. This study identified a large number of miRNAs, including the miR-183/96/182 cluster, as circadian modulators. Furthermore, this study provides a resource for further understanding the role of miRNAs in the circadian network and highlights the importance of miRNAs as a genome-wide layer of circadian clock regulation.

Source: Steve A. Kaya, Keck School Of Medicine, University Of Southern California, Los Angeles. A Genome-Wide MicroRNA Screen Identifies The MicroRNA-183/96/182 Cluster As A Modulator Of Circadian Rhythms. PNAS January 5, (2021) 118 (1) e2020454118. <u>https://doi.org/10.1073/pnas.2020454118</u>

#### 4. Improved Metagenome Binning And Assembly Using Deep Variational Autoencoders

In this study researchers have developed variational autoencoders for metagenomic binning (VAMB), a program that uses deep variational autoencoders to encode sequence co-abundance and k-mer distribution information before clustering.

This study shows that a variational auto encoder is able to integrate these two distinct data types without any previous knowledge of the datasets. VAMB outperforms existing state-of-the-art binners, reconstructing 29–98% and 45% more near-complete (NC) genomes on simulated and real data, respectively. Furthermore, VAMB is able to separate closely related strains up to 99.5% average nucleotide identity (ANI), and reconstructed 255 and 91 NC Bacteroides vulgatus and Bacteroides dorei sample-specific genomes as two distinct clusters from a dataset of 1,000 human gut microbiome samples. They have also use 2,606 NC bins from this dataset to show that species of the human gut microbiome have different geographical distribution patterns.

Source: Simon Rasmussen, Novo Nordisk Foundation Center For Protein Research, Faculty Of Health And Medical Sciences, University Of Copenhagen, Copenhagen, Denmark. Improved Metagenome Binning And Assembly Using Deep Variational Autoencoders. Nat Biotechnol 39, 555–560 (2021). https://doi.org/10.1038/s41587-020-00777-4

#### 5. Early-Life Effects Of Juvenile Western Diet And Exercise On Adult Gut Microbiome Composition In Mice

This study examined the effects of early-life diet and exercise manipulations on the adult microbiome by sequencing the hypervariable internal transcribed spacer region of the bacterial gut community in mice.

Study result shows that juvenile western diet reduced bacterial richness and diversity after 8-weeks. Scientists have also found interactive effects of genetic line type, juvenile diet and/or juvenile exercise on microbiome composition and diversity. Microbial community structure clustered significantly in relation to both line type and diet. Western diet also reduced the relative abundance of Muribaculum intestinale. These results constitute one of the first reports of juvenile diet having long-lasting effects on the adult microbiome after a substantial washout period. Moreover, they have also found interactive effects of diet with early-life exercise exposure, and a dependence of these effects on genetic background.

Source: Theodore Garland, Department Of Evolution, Ecology, And Organismal Biology, University Of California, Riverside, Riverside, USA. Early-Life Effects Of Juvenile Western Diet And Exercise On Adult Gut Microbiome Composition In Mice. J Exp Biol (2021) 224 (4): Jeb239699. <u>Https://Doi.Org/10.1242/Jeb.239699</u>

## 6. Porphyromonas Gingivalis Impairs Glucose Uptake In Skeletal Muscle Associated With Altering Gut Microbiota

Scientists have found that anti-*Porphyromonas gingivalis* (*Pg*) antibody titers positively correlated with intramuscular adipose tissue content (IMAC), fasting blood glucose, and HOMA-IR in metabolic syndrome patients.

They have also found that in C57BL/6J mice fed a high-fat diet, recipients of oral Pg (HFPg) had impaired glucose tolerance, insulin resistance, and higher IMAC compared to recipients of saline (HFco). The soleus muscle in HFPg mice exhibited fat infiltration and lower glucose uptake with higher *Tnfa* expression and lower insulin signaling than in HFco mice. Gene set enrichment analysis shows that TNF $\alpha$  signaling via NF $\kappa$ B gene set is enriched in the soleus muscle of HFPg mice. Moreover, TNF- $\alpha$  also decreased glucose uptake in C2C12 myoblast cells in vitro. Based on 16S rRNA sequencing, *Pg* administration altered the gut microbiome, particularly by decreasing the abundance of genus *Turicibacter*.

Hence, the finding of the study suggests that infection with Pg is a risk factor for metabolic syndrome and skeletal muscle metabolic dysfunction via gut microbiome alteration.

Source: Sayaka Katagiri, Department Of Periodontology, Graduate School Of Medical And Dental Sciences, Tokyo Medical And Dental University (TMDU), Tokyo, Japan. Porphyromonas Gingivalis Impairs Glucose Uptake In Skeletal Muscle Associated With Altering Gut Microbiota. The FASEB Journal. (2021); 35:e21171. https://doi.org/10.1096/fj.202001158R

## 7. Avocado Consumption Alters Gastrointestinal Bacteria Abundance and Microbial Metabolite Concentrations among Adults with Overweight or Obesity: A Randomized Controlled Trial

This study concluded that daily consumption of avocado results in lower fecal bile acid concentrations, greater fecal fatty acid and short chain fatty acids (SCFAs), and greater relative abundances of bacteria capable of fiber fermentation. Further, it also provides evidence that this nutrient-dense food affects digestive physiology, as well as the composition and metabolic functions of the intestinal microbiota.

Source: Hannah D Holscher, Division Of Nutritional Sciences; Department Of Food Science And Human Nutrition; Department Of Kinesiology And Community Health; National Center For Supercomputing Applications And Institute Of Genomic Biology, University Of Illinois, Urbana-Champaign, IL, USA. Avocado Consumption Alters Gastrointestinal Bacteria Abundance And Microbial Metabolite Concentrations Among Adults With Overweight Or Obesity: A Randomized Controlled Trial. He Journal Of Nutrition, Volume 151, Issue 4, April, (2021), Pages 753–762. <u>https://doi.org/10.1093/jn/nxaa219</u>

#### 8. Endogenous Murine Microbiota Member Faecalibaculum Rodentium And Its Human Homologue Protect From Intestinal Tumour Growth

This study demonstrates that changes in the microbiota and mucus composition are concomitant with tumourigenesis. Researchers have identified two anti-tumourigenic strains of the microbiota— Faecalibaculum rodentium and its human homologue, Holdemanella biformis that are strongly underrepresented during tumourigenesis. Reconstitution of ApcMin/+ or azoxymethane- and dextran sulfate sodium-treated mice with an isolate of F. rodentium (F. PB1) or its metabolic products reduced tumour growth. Both F. PB1 and H. biformis produced short-chain fatty acids that contributed to control protein acetylation and tumour cell proliferation by inhibiting calcineurin and NFATc3 activation in mouse and human settings.

Source: Maria Rescigno, Humanitas Clinical And Research Center, IRCCS And Department Of Biomedical Sciences, Humanitas University, Milan, Italy. Endogenous Murine Microbiota Member Faecalibaculum Rodentium And Its Human Homologue Protect From Intestinal Tumour Growth. Nat Microbiol 5, 511–524 (2020). <u>Https://Doi.Org/10.1038/S41564-019-0649-5</u>

## 9. Intestinal Permeability, Microbial Translocation, Changes In Duodenal And Fecal Microbiota, And Their Associations With Alcoholic Liver Disease Progression In Humans

This study shows that only a subset of alcohol use disorders (AUD) patients had increased 51Cr-EDTA and fecal albumin together with disrupted tight junctions and vasculature expression of plasmalemma Vesicle-Associated Protein-1. The so-defined increased intestinal permeability is not related to changes of the duodenal microbiota or alterations of the intestinal epithelium but associated with compositional changes of the fecal microbiota. Leaky gut alone did not explain increased microbial translocation in AUD patients. By contrast, duodenal dysbiosis with a dominance shift toward specific potential pathogenic bacteria genera (Streptococcus, Shuttleworthia, Rothia), increased IP and elevated markers of microbial translocation characterized AUD patients with progressive ALD (steato-hepatitis, steato-fibrosis).

Source: Sophie Leclercq, Institute Of Neuroscience And Louvain Drug Research Institute, Uclouvain, Universite Catholique De Louvain, Brussels, Belgium. Intestinal Permeability, Microbial Translocation, Changes In Duodenal And Fecal Microbiota, And Their Associations With Alcoholic Liver Disease Progression In Humans. Gut Microbes, (2020), 12:1. Doi: 10.1080/19490976.2020.1782157

#### 10. Neonatal Diet Alters Fecal Microbiota And Metabolome Profiles At Different Ages In Infants Fed Breast Milk Or Formula

Breastfeeding, dairy-based formula and soy-based formula differentially impact the infant fecal microbiome and metabolome in the first year of life. The study showed that at 3, 6, and 9 mo of age BF infants had the lowest α-diversity, SF infants had the highest diversity, and MF was intermediate. Bifidobacterium was 2.6- to 5- fold lower in SF relative to BF infants through 1y of life.

An unidentified genus from Ruminococcaceae higher in the SF (2%) than in the MF (0.4%) and BF (0.08%) infants at 3 mo of age was observed. In BF infants higher levels of butyric acid, d-sphingosine, kynurenic acid, indole-3-lactic acid, indole3-acetic acid, and betaine were observed than in MF and SF infants. At 3 moRuminococcaceae was positively correlated to azelaic, gentisic, isocitric, sebacic, and syringic acids. At 6 moOscillospira was negatively correlated with 3- hydroxybutyric-acid, hydroxy-hydrocinnamic acid, and betaine whereas Bifidobacterium was negatively associated with 5- hydroxytryptamine. At 12 mo of age, Lachnospiraceae was negatively associated with hydroxyphenyllactic acid.

Infant diet has a large impact on the fecal microbiome and metabolome in the first year of life.

Source: Laxmi Yeruva, Arkansas Children's Nutrition Center, University Of Arkansas For Medical Sciences, Little Rock; Department Of Pediatrics, University Of Arkansas For Medical Sciences, Little Rock And Arkansas Children's Research Institute, Little Rock, AR, USA. Neonatal Diet Alters Fecal Microbiota And Metabolome Profiles At Different Ages In Infants Fed Breast Milk Or Formula. The American Journal Of Clinical Nutrition, Volume 111, Issue 6, June (2020), Pages 1190–1202. <u>https://doi.org/10.1093/ajcn/nqaa076</u>

## 11. Therapeutic Methods Of Gut Microbiota Modification In Colorectal Cancer Management – Fecal Microbiota Transplantation, Prebiotics, Probiotics, And Synbiotics

In this review the link between gut microbiota and the development of colorectal cancer has been investigated. An imbalance in the gut microbiota promotes the progress of colorectal carcinogenesis via multiple mechanisms, including inflammation, activation of carcinogens, and tumorigenic pathways as well as damaging host DNA. Several therapeutic methods are available with which to alter the composition and the activity of gut microbiota, such as administration of prebiotics, probiotics, and synbiotics; these can confer various benefits for colorectal cancer patients.

Now a days, fecal microbiota transplantation is the most modern way of modulating the gut microbiota. Even though data regarding fecal microbiota transplantation in colorectal cancer patients are still rather limited, it has been approved as a clinical method of treatment recurrent Clostridium difficile infection, which may also occur in these patients. The major benefits of fecal microbiota transplantation include modulation of immunotherapy efficacy, amelioration of bile acid metabolism, and restoration of intestinal microbial diversity.

Source: Karolina Kazmierczak- Siedlecka, Department Of Surgical Oncology, Medical University Of Gdsank, Poland. Therapeutic Methods Of Gut Microbiota Modification In Colorectal Cancer Management – Fecal Microbiota Transplantation, Prebiotics, Probiotics, And Synbiotics. Gut Microbes, 11:6, 1518-1530, (2020). DOI: 10.1080/19490976.2020.1764309

#### 12. Growth Effects Of N-Acylethanolamines On Gut Bacteria Reflect Altered Bacterial Abundances In Inflammatory Bowel Disease

In this study scientists have analysed the influences of metabolites that are differentially abundant in inflammatory bowel disease (IBD) on the growth and physiology of gut bacteria that are also differentially abundant in IBD.

Researchers have found that N-acylethanolamines (NAEs), a class of endogenously produced signalling lipids elevated in the stool of IBD patients and a T-cell transfer model of colitis, stimulated growth of species over-represented in IBD and inhibited that of species depleted in IBD in vitro. Using metagenomic sequencing, researchers recapitulated the effects of NAEs in complex microbial communities ex vivo, with Proteobacteria blooming and Bacteroidetes declining in the presence of NAEs. Metatranscriptomic analysis of the same communities identified components of the respiratory chain as important for the metabolism of NAEs, and this was verified using a mutant deficient for respiratory complex I.

Source: Hera Vlamakis, Broad Institute Of Mit And Harvard, Cambridge, MA, USA. Growth Effects Of N-Acylethanolamines On Gut Bacteria Reflect Altered Bacterial Abundances In Inflammatory Bowel Disease. Nat Microbiol 5, 486–497 (2020). https://doi.org/10.1038/s41564-019-0655-7

#### 13. Microbiome And Health Implications For Ethnic Minorities After Enforced Lifestyle Changes

Lifestyle affects the microbiome early in life, when the microbiome is assembled and the immune system is undergoing maturation. Moreover, the influence of lifestyle has been separated from genetic and geographic factors by studies of genetically similar populations and ethnically distinct groups living in the same geographic location.

The lifestyle of Irish Travellers, an ethnically distinct subpopulation, changed with legislation in 2002 that effectively ended nomadism and altered their living conditions. Comparative metagenomics of gut microbiomes shows that Irish Travellers retain a microbiota similar to that of non-industrialized societies. Their microbiota is associated with non-dietary factors and is proportionately linked with risk of microbiome-related metabolic disease. The findings of the study suggest that there are microbiome-related public health implications when ethnic minorities are pressurized to change lifestyles.

Source: Fergus Shanahan, Apc Microbiome Ireland And Department Of Medicine, University College Cork, Cork, Ireland. Microbiome And Health Implications For Ethnic Minorities After Enforced Lifestyle Changes. Nat Med 26, 1089–1095 (2020). https://doi.org/10.1038/s41591-020-0963-8

#### 14. Microbiota-Derived Metabolite Promotes HDAC3 Activity In The Gut

The coevolution of mammalian hosts and their beneficial commensal microbes has led to development of a symbiotic host-microbiota relationship. This present study reveals a highly selective pathway through which microbiota-derived inositol phosphate regulates histone deacetylase 3 (HDAC3) activity in the intestine.

Despite abundant HDAC inhibitors in the intestine such as butyrate, researchers unexpectedly found that HDAC3 activity was sharply increased in intestinal epithelial cells (IECs) of microbiota-replete mice compared to germ-free mice. This discordance was reconciled by finding that commensal bacteria, including E. coli, stimulated HDAC activity through metabolism of phytate and inositol trisphosphate production.

Intestinal exposure to inositol trisphosphate and phytate ingestion both promoted recoveries following intestinal damage. Remarkably, inositol trisphosphate also induced growth of patient-derived intestinal organoids, stimulated HDAC3-dependent proliferation, and countered butyrate inhibition of colonic growth. Collectively, these data reveal 9 that inositol trisphosphate as a microbiota-derived metabolite that activates a mammalian histone deacetylase to promote epithelial repair. *Thus, HDAC3 represents a converging epigenetic sensor of distinct metabolites that calibrates host responses to diverse microbial signals.* 

Source: Theresa Alenghat, Division Of Immunobiology And Center For Inflammation And Tolerance, Cincinnati Children's Hospital Medical Center And Department Of Pediatrics, University Of Cincinnati College Of Medicine, Cincinnati, OH, USA. Microbiota-Derived Metabolite Promotes Hdac3 Activity In The Gut. Nature 586, 108–112 (2020). https://doi.org/10.1038/s41586-020-2604-2

#### **15. Gut Bacteria Support Antiviral Immunity**

A healthy gut microbiome is linked to protection from a variety of ills and to a properly functioning immune system. A new study extends its role to supporting antiviral immunity, providing protection from infection and dissemination with Chikungunya virus (CHIKV) an emerging, mosquito transmitted alphavirus.

The study shows that perturbation of the microbiome dampens antiviral type I interferon (IFN) responses, which could be restored by a single Clostridium symbiont and it's associated secondary bile acid. The researchers found that depletion of plasmacytoid dendritic cells (pDCs) (which are a known source of type I IFNs) reduces the effect of microbiome disruption on CHIKV viraemia. Gene expression analysis showed an altered antiviral, but not basal, immune response in pDCs. Thus, the microbiome provides antiviral protection through a bile acid–pDC–IFN signalling axis.

Source: Lucy Bird, Gut Bacteria Support Antiviral Immunity. Nat Rev Immunol 20, 520–521 (2020). https://doi.org/10.1038/s41577-020-00412-y

#### 16. The Gut Microbiome: An Unexpected Player In Cancer Immunity

Numerous independent studies link gut microbiota composition and disease and imply a causal role of select commensal microbes in disease etiology. In the gut, commensal microbiota or pathobionts secrete metabolites that underlie pathological conditions, often impacting proximal tissues and gaining access to the bloodstream.

This study focuses on extrinsic and intrinsic factors affecting composition of gut microbiota and their impact on the immune system, as key drivers of anti-tumor immunity.

Source: Zeev A Ronai, Sanford Burnham Prebys Medical Discovery Institute, La Jolla, United States. The Gut Microbiome: An Unexpected Player In Cancer Immunity. Current Opinion In Neurobiology Volume 62, June (2020), Pages 48-52. <u>https://doi.org/10.1016/j.conb.2019.09.016</u>

## 17. Faecal Microbiota Transplantation In The Treatment Of Clostridioides Difficile Infection

Faecal microbiota transplantation (FMT) represents a unique procedure targeted at restoring the natural diversity of the gastrointestinal microbiome and prevent recurrence of a key nosocomial disease, namely, Clostridioides difficile infection (CDI). The present study assessed the success rate and clinical efficacy of FMT at a clinic that introduced this procedure in Czechia in 2010 and still leads in the number of transplantations performed to date.

Patients enrolled in the study received primary targeted antibiotic therapy, and after the CDI episode treatment, FMT was administered as a secondary prophylaxis. In this study 172 patients were treated using faecal microbiota transplantation. The overall success rate was 76%. Subgroup analysis identified higher age, higher Charlson Comorbidity Index reflecting the presence and severity of long-term comorbidities and higher Eastern Cooperative Oncology Group (ECOG) performance scores as risk factors for treatment failure. In the period monitored, two serious adverse events were observed: Both were rectal-wall perforations occurring during the application of enemas of stool suspension.

Source: Roman Stebel, Department Of Infectious Diseases, University Hospital Brno And Faculty Of Medicine, Masaryk University, Czech Republic. Faecal Microbiota Transplantation In The Treatment Of Clostridioides Difficile Infection. Human Microbiome Journal Volume 16, June (2020), 100070. https://doi.org/10.1016/j.humic.2020.100070

#### **18.** The Small Intestine Shields The Liver From Fructose-Induced Steatosis

This study shows that intestinal fructose catabolism mitigates fructose-induced hepatic lipogenesis. In mice, intestine-specific enzyme ketohexokinase (KHK-C) deletion increases dietary fructose transit to the liver and gut microbiota and sensitizes mice to fructose's hyperlipidaemic effects and hepatic steatosis. In contrast, intestine-specific KHK-C overexpression promotes intestinal fructose clearance and decreases fructose-induced lipogenesis. Hence, intestinal fructose clearance capacity controls the rate at which fructose can be safely ingested. Further, it also shows that the same amount of fructose is more strongly lipogenic when drunk than eaten, or when administered as a single gavage, as opposed to multiple doses spread over 45 min. Collectively, these data demonstrate that fructose induces lipogenesis when its dietary intake rate exceeds the intestinal clearance capacity.

Source: Zoltan Arany, Perelman School Of Medicine, University Of Pennsylvania, Philadelphia, USA. The Small Intestine Shields The Liver From Fructose-Induced Steatosis. Nat Metab 2, 586–593 (2020). https://doi.org/10.1038/s42255-020-0222-9

#### **19.** The Gut Microbiota Is Associated With Immune Cell Dynamics In Humans

The gut microbiota influences development and homeostasis of the mammalian immune system, and is associated with human inflammatory and immune diseases as well as responses to immune- therapy. Researchers have studied hundreds of hospitalized and closely monitored patients with cancer receiving haematopoietic cell transplantation as they recover from chemotherapy and stem-cell engraftment. This study analysis establishes and guantifies the link between the gut microbiota and the human immune system, with implications for microbiota-driven modulation of immunity.

Source: Jonas Schluter, Institute For Computational Medicine, NYU Langone Health And Computational And Systems Biology Program, Sloan Kettering Institute, Memorial Sloan Kettering Cancer Center, New York, NY, USA. The Gut Microbiota Is Associated With Immune Cell Dynamics In Humans. Nature 588, 303–307 (2020). https://doi.org/10.1038/s41586-020-2971-8

#### 20. Maternal Fecal Microbiota Transplantation In Caesarean-Born Infants Rapidly Restores Normal Gut Microbial Development: A Proof-Of Concept Study

In this study researchers have evaluated whether disturbed intestinal microbiota development could be restored in Caesarean section (CS)-born infants by postnatal, orally delivered fecal microbiota transplantation (FMT). Out of 17 mothers, 7 were selected after careful screening. The infants received a diluted fecal sample from their own mothers, taken 3 weeks prior to delivery. All seven infants had an uneventful clinical course during the 3-month follow-up and showed no adverse effects. The team of scientists has found that the temporal development of the fecal microbiota composition of FMT treated CS-born infants no longer resembled to that of untreated CS-born infants but showed significant similarity to that of vaginally born infants. This proof-of-concept study demonstrates that the intestinal microbiota of CS-born infants can be restored postnatal by maternal FMT.

Source: Willem M. De Vos, Human Microbiome Research Program, Faculty Of Medicine, University Of Helsinki, Finland And Laboratory Of Microbiology, Wageningen University, The Netherlands. Maternal Fecal Microbiota Transplantation In Caesarean-Born Infants Rapidly Restores Normal Gut Microbial Development: A Proof-Of concept Study. Journal Cell, Volume 183, Issue 2, P324-334.E5, October 15 (2020). DOI: <a href="https://doi.org/10.1016/j.cell.2020.08.047">https://doi.org/10.1016/j.cell.2020.08.047</a>

#### 21. Gut Microbiota Depletion By Chronic Antibiotic Treatment Alters The Sleep/Wake Architecture And Sleep EEG Power Spectra In Mice

Researchers used a cocktail of antibiotics to deplete gut microbes in mice. They found that metabolites in the gut differed in these mice compared with controls. In particular, metabolic pathways involved in making important neurotransmitters like serotonin were affected. Additionally, these mice showed abnormal day-night distribution in sleep/wake patterns, particularly the amount of REM sleep, and frequent transitions between REM and non-REM sleep episodes.

Source: Masashi Yanagisawa, International Institute For Integrative Sleep Medicine (WPI-IIIS), University Of Tsukuba, 1-1-1 Tennodai; Life Science Center For Survival Dynamics, Tsukuba Advanced Research Alliance (TARA), University Of Tsukuba, 1-1-1 Tennodai; R&D Center For Frontiers Of Mirai In Policy And Technology (F-MIRAI), University Of Tsukuba, 1-1-1 Tennodai, Tsukuba, Ibaraki, 305-8575, Japan And Department Of Molecular Genetics, University Of Texas Southwestern Medical Center, Dallas, TX, 75390-8584, USA Yukino Ogawa, University Of Tsukuba. Gut Microbiota Depletion By Chronic Antibiotic Treatment Alters The Sleep/Wake Architecture And Sleep EEG Power Spectra In Mice. Sci Rep 10, 19554 (2020). https://doi.org/10.1038/s41598-020-76562-9

#### 22. Landscapes Of Bacterial And Metabolic Signatures And Their Interaction In Major Depressive Disorders

In this study researchers have identified 3 bacteriophages, 47 bacterial species, and 50 fecal metabolites along with notable differences in abundance between major depressive disorder (MDD) patients and healthy controls (HCs). Patients with MDD were mainly characterized by increased abundance of the genus Bacteroides and decreased abundance of the genera Blautia and Eubacterium. These multilevel omics alterations generated a characteristic MDD coexpression network. Disturbed microbial genes and fecal metabolites were consistently mapped to amino acid (γ-aminobutyrate, phenylalanine, and tryptophan) metabolism. Further, they have also identified a combinatorial marker panel that robustly discriminated MDD from HC individuals in both the discovery and validation sets.

This study provides a deep insight into understanding of the roles of disturbed gut ecosystem in MDD.

Source: Jian Yang, The National Clinical Research Center For Mental Disorders & Beijing Key Laboratory Of Mental Disorders, Beijing Anding Hospital, Capital Medical University, China And Advanced Innovation Center For Human Brain Protection, Capital Medical University, Beijing 100069, China.Et Al. Paediatrics Royal Children's Hospital, Melbourne, Australia. Landscapes Of Bacterial And Metabolic Signatures And Their Interaction In Major Depressive Disorders. Journal Of Science Advances, Vol. 6, No. 49, (2020). DOI: 10.1126/sciadv.aba8555

#### 23. A Lipid-Related Metabolomic Pattern Of Diet Quality

Adherence to a healthy diet has been associated with reduced risk of chronic diseases. Identifying nutritional biomarkers of diet quality may be complementary to traditional questionnaire-based methods and may provide insights concerning disease mechanisms and prevention.

Researchers have identified metabolites associated with healthy and unhealthy eating behaviours. The observed associations were largely similar between men and women, suggesting that metabolomics can be a complementary approach to self-reported diet in studies of diet and chronic disease.

Source: A Heather Eliassen, Channing Division Of Network Medicine Harvard Medical School And Brigham And Women's Hospital And Department Of Epidemiology, Harvard T. H. Chan School Of Public Health, Boston, MA, USA. A Lipid-Related Metabolomic Pattern Of Diet Quality. The American Journal Of Clinical Nutrition, Volume 112, Issue 6, December (2020), Pages 1613–1630. <u>https://doi.org/10.1093/ajcn/nqaa242</u>

#### 24. Associations of Sodium and Potassium Consumption with the Gut Microbiota and Host Metabolites in a Population-Based Study in Chinese Adults

Sodium and potassium consumption is associated with gut microbiome taxa and metabolites implicated in cardiometabolic health, providing insights into the potential roles of gut microbiota and host metabolites in related diseases.

The findings suggest that sodium and potassium consumption is associated with taxa and metabolites that have been implicated in cardiometabolic health, providing insights into the potential roles of gut microbiota and host metabolites in the pathogenesis of sodium- and potassium-associated diseases. More studies are needed to confirm the results.

Source: Penny Gordon-Larsen, Department Of Nutrition, Gillings School Of Global Public Health And School Of Medicine, University Of North Carolina At Chapel Hill (UNC-Chapel Hill And Carolina Population Center, UNC-Chapel Hill, Chapel Hill, NC, USA. Associations Of Sodium And Potassium Consumption With The Gut Microbiota And Host Metabolites In A Population-Based Study In Chinese Adults. The American Journal Of Clinical Nutrition, Volume 112, Issue 6, December (2020), Pages 1599–1612. <u>https://doi.org/10.1093/ajcn/ngaa263</u>

#### 25. Should There Be A Recommended Daily Intake Of Microbes?

The collective findings from human microbiome research, randomized controlled trials on specific microbes (i.e., probiotics), and associative studies of fermented dairy consumption provide evidence for the beneficial effects of the regular consumption of safe live microbes.

To test the hypothesis that the inclusion of safe, live microbes in the diet supports and improves health, researchers propose assessment of the types and evidentiary quality of the data available on microbe intake, including the assembly and evaluation of evidence available from dietary databases.

Researchers recommend that such an analysis will help to identify gaps in the evidence needed to test this hypothesis, which can then be used to formulate and direct initiatives focused on prospective and randomized controlled trials on live microbe consumption. Outcomes will establish whether or not the evidence exists, or can be generated, to support the establishment of dietary recommendations for live microbes.

Source: Mary Ellen Sanders, International Scientific Association For Probiotics And Prebiotics, Centennial, CO, USA. Should There Be A Recommended Daily Intake Of Microbes? The Journal Of Nutrition, Volume 150, Issue 12, December (2020), Pages 3061–3067. https://doi.org/10.1093/jn/nxaa323

#### 26. Host Variables Confound Gut Microbiota Studies Of Human Disease

This study infers the greatest, generalized sources of heterogeneity in human gut microbiota profiles and also identifies human lifestyle and physiological characteristics. It also confounds microbiota analyses to produce spurious microbial associations with human diseases.

Scientists have identified that alcohol consumption frequency and bowel movement quality as unexpectedly strong sources of gut microbiota variance that differ in distribution between healthy participants and participants with a disease. This study demonstrate that for numerous prevalent, high-burden human diseases, matching cases and controls for confounding variables reduces observed differences in the microbiota and the incidence of spurious associations. On this basis researchers have presented a list of host variables and recommended that it should be captured in human microbiota studies for the purpose of matching comparison groups, which will increase robustness and reproducibility in resolving the members of the gut microbiota that are truly associated with human disease.

Source: Ivan Vujkovic-Cvijin, Metaorganism Immunity Section, Laboratory Of Immune Systems Biology, National Institute Of Allergy And Infectious Diseases, National Institutes Of Health, Bethesda, MD, USA. Host Variables Confound Gut Microbiota Studies Of Human Disease. Nature 587, 448–454 (2020). https://doi.org/10.1038/s41586-020-2881-9

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