

# Recent Studies and Publications on Gut Microbiome

## STUDIES

### 1. Metaproteomics Characterizes Human Gut Microbiome Function In Colorectal Cancer

Study results suggest that gut microbiome can vary in taxonomic abundance and function during the pathogenesis of Colorectal Cancer (CRC). This study shows that *metaproteomics will provide functional information on intestinal microflora that is of great value for pathogenesis research, and can help guide clinical diagnosis in the future*. Also, clinicians may use the 20 most discriminating proteins to diagnose CRC. Further, *fecal microbial transplantation to reduce the production of ROS and iron in gut can be a promising method for the prevention of CRC*.

Source: Liang Qiao, Department Of Chemistry, Shanghai Stomatological Hospital, Fudan University, China. *Metaproteomics Characterizes Human Gut Microbiome Function In Colorectal Cancer*. *npj Biofilms Microbiomes* 6, 14 (2020). <https://doi.org/10.1038/s41522-020-0123-4>

### 2. Association Of Flavonifractor Plautii, A Flavonoid-Degrading Bacterium, With The Gut Microbiome Of Colorectal Cancer Patients In India

Researchers from India have discovered that a diet high in flavonoids may contribute to the low prevalence of colorectal cancer (CRC) in the Indian population. The plausible role of *F. plautii* appears to be linked with the degradation of beneficial anticarcinogenic flavonoids, which is also found to be significantly correlated with the enzymes and modules involved in flavonoid degradation within Indian CRC samples. Scientists have also identified 20 potential microbial taxonomic markers and 33 potential microbial gene markers that discriminate the Indian CRC from healthy microbiomes with high accuracy based on machine learning approaches.

Source: Dr. Vineet Sharma, Indian Institute of Science Education And Research (IISER). *Association Of Flavonifractor Plautii, A Flavonoid-Degrading Bacterium, With The Gut Microbiome Of Colorectal Cancer Patients In India*. *mSystems* 4: e00438-19. <https://doi.org/10.1128/mSystems.00438-19>

### 3. 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 tumorigenesis. Researchers have identified two anti-tumourigenic strains of the microbiota—*Faecalibaculum rodentium* and its human homologue, *Holdemanella bififormis* that are strongly under-represented during tumorigenesis. Reconstitution of *ApcMin/+* or azoxymethane- and dextran sulfate sodium-treated mice with an isolate of *F. rodentium* (*F. PB1*) or its metabolic products reduce tumour growth. Both *F. PB1* and *H. bififormis* produced short-chain fatty acids 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). <https://doi.org/10.1038/s41564-019-0649-5>

### 4. Amending Microbiota By Targeting Intestinal Inflammation With TNF Blockade Attenuates Development Of Colorectal Cancer

In this study researchers used chemically induced (*DSS/Apc<sup>min/+</sup>*) and spontaneous (*Apc<sup>min/+</sup>;/I10<sup>-/-</sup>*) mouse CRC models colonized by colibactin-producing *Escherichia coli* to established the role of microbiota in mediating the antitumorigenic effect of anti-tumor necrosis factor (TNF) therapy. It was found that TNF blockade attenuated colitis and CRC development. Microbiota community structure and gene activities significantly changed with disease development, which is prevented by TNF blockade. Several microbiota functional pathways underwent similar changes in patients following anti-TNF therapy. Under cohousing condition, TNF blockade failed to prevent colitis, cancer development and disease-associated microbiota structural changes. Finally, microbiota transplantation showed reduced carcinogenic activity of microbiota from anti-TNF-treated mice. Further, study data demonstrated the plasticity of microbiota, which could be reverted to noncarcinogenic status by targeting inflammation.

Source: Christian Jobin, Department Of Medicine And Department Of Infectious Diseases And Immunology, University Of Florida, Gainesville, FL, USA. *Amending Microbiota By Targeting Intestinal Inflammation With TNF Blockade Attenuates Development Of Colorectal Cancer*. *Nat Cancer* 1, 723-734 (2020). <https://doi.org/10.1038/s43018-020-0078-7>

## 5. Taxonomic Diversity Of Sputum Microbiome In Lung Cancer Patients And Its Relationship With Chromosomal Aberrations In Blood Lymphocytes

This is a pilot-sized study to compare the taxonomic composition of sputum microbiome in 17 newly-diagnosed lung cancer (LC) patients and 17 controls. It also compares the representation of individual bacterial genera and species in sputum with the frequency of chromosomal aberrations in the blood lymphocytes of LC patients and in controls.

Both groups were male; average age  $56.1 \pm 11.5$  in patients and  $55.7 \pm 4.1$  in controls. Differences in the species composition of bacterial communities in LC patients and controls were significant. Increased prevalence in LC patients was detected for the genera *Haemophilus* and *Bergeyella*; whereas a decrease was observed for the genera *Atopobium*, *Stomatobaculum*, *Treponema* and *Porphyromonas*. Donors with high frequencies of chromosomal aberrations had a significant reduction in the microbiome of representatives of the genus *Atopobium* in the microbiome and a simultaneous increase in representatives of the species *Alloprevotella* compared to donors with a low level of chromosomal aberrations in lymphocytes. Thus, a comparison of the bacterial composition in the sputum of donors with cytogenetic damages in their lymphocytes, warrants further investigations on the potential role of microorganisms in the process of mutagenesis in somatic cells of the host body.

Source: L. V. Matskova, Kemerovo State University, Kemerovo; Institute Of Living Systems Immanuel Kant Baltic Federal University, Kaliningrad, Russian Federation And Department Of Microbiology, Tumor Biology And Cell Biology (MTC), Stockholm, Sweden. Taxonomic Diversity Of Sputum Microbiome In Lung Cancer Patients And Its Relationship With Chromosomal Aberrations In Blood Lymphocytes. *Sci Rep* 10, 9681 (2020). <https://doi.org/10.1038/s41598-020-66654-x>

## 6. Zeb2 Drives Invasive And Microbiota-Dependent Colon Carcinoma

Colorectal cancer (CRC) is highly prevalent in Western society, and increasing evidence indicates strong contributions of environmental factors and the intestinal microbiota to CRC initiation, progression and even metastasis. Researchers have identified a synergistic inflammatory tumor-promoting mechanism through which the resident intestinal microbiota boosts invasive CRC development in an epithelial-to-mesenchymal transition-prone tissue environment. Intestinal epithelial cell (IEC)-specific transgenic expression of the epithelial-to-mesenchymal transition regulator Zeb2 in mice (Zeb2IEC-Tg/+) leads to increased intestinal permeability, myeloid cell-driven inflammation and spontaneous invasive CRC development. Zeb2IEC-Tg/+ mice develop a dysplastic colonic epithelium, which progresses to severely inflamed neoplastic lesions while the small intestinal epithelium remains normal. Zeb2IEC-Tg/+ mice are characterized by intestinal dysbiosis, and microbiota depletion with broad-spectrum antibiotics or germ-free rederivation completely prevents cancer development. Zeb2IEC-Tg/+ mice represent the first mouse model of spontaneous microbiota-dependent invasive CRC and will promote better understand host-microbiome interactions driving CRC development in humans.

Source: Geert van Loo, VIB Center For Inflammation Research; Department Of Biomedical Molecular Biology; Ghent Gut Inflammation Group, Ghent University And Cancer Research Institute Ghent, Ghent, Belgium. Zeb2 Drives Invasive And Microbiota-Dependent Colon Carcinoma. *Nat Cancer* 1, 620-634 (2020). <https://doi.org/10.1038/s43018-020-0070-2>

## 7. Seasonal Changes Of Circulating 25-Hydroxyvitamin D Correlate With The Lower Gut Microbiome Composition In Inflammatory Bowel Disease Patients

In the present study scientists investigated the possible link between the seasonal serum vit D levels to the microbial composition of the lower gut of Inflammatory Bowel disease (IBD) patients using 16S rRNA sequencing. They have found that there is a decrease in serum vit D level during winter/spring season in a cohort of 35 ulcerative colitis (UC) patients and 39 Crohn's disease (CD) patients. Low gut microbiota composition of patients with IBD correlated with the serum level of 25(OH)D that directly coupled to seasonal variability of the sunshine in the central European countries. It related to increased abundance of *Actinobacteria* and *Proteobacteria* in UC and *Actinobacteria*, *Fusobacteria*, *Firmicutes* and *Bacteroidetes* in CD. In summer/autumn period there is a reduction in abundance of bacterial genera typical for inflammation like *Eggerthella lenta*, *Fusobacterium spp.*, *Bacteroides spp.*, *Collinsella aerofaciens*, *Helicobacter spp.*, *Rhodococcus spp.*, *Faecalibacterium prausnitzii*; and increased abundance of *Pediococcus spp.* and *Clostridium spp.* and of *Escherichia/Shigella spp.*

Source: Katarina Soltys, Department Of Microbiology And Virology; Comenius University Science Park And Department Of Molecular Biology, Comenius University In Bratislava, Slovakia. Seasonal Changes Of Circulating 25-Hydroxyvitamin D Correlate With The Lower Gut Microbiome Composition In Inflammatory Bowel Disease Patients. *Sci Rep* 10, 6024 (2020). <https://doi.org/10.1038/s41598-020-62811-4>

## **8. 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>

## **9. Cholesterol Metabolism By Uncultured Human Gut Bacteria Influences Host Cholesterol Level**

In this study researchers have focused on the conversion of cholesterol to the poorly absorbed sterol coprostanol by the gut microbiota to develop a framework for the identification of functional enzymes and microbes.

By integrating paired metagenomics and metabolomics data from existing cohorts with biochemical knowledge and experimentation scientists have predicted and validated a group of microbial cholesterol dehydrogenases that contribute to coprostanol formation. These enzymes are encoded by ismA genes in a clade of uncultured microorganisms, which are prevalent in geographically diverse human cohorts. Individuals harboring coprostanol-forming microbes have significantly lower fecal cholesterol levels and lower serum total cholesterol with effects comparable to those attributed to variations in lipid homeostasis genes. Thus, cholesterol metabolism by these microbes may play important roles in reducing intestinal and serum cholesterol concentrations, directly impacting human health.

**Source:** Ramnik J. Xavier, Broad Institute Of MIT And Harvard; Centre For Microbiome Informatics And Therapeutics, Massachusetts Institute Of Technology, Cambridge And Centre For Computational And Integrative Biology And Department Of Molecular Biology, Massachusetts General Hospital And Harvard Medical School, Boston, USA. *Cholesterol Metabolism By Uncultured Human Gut Bacteria Influences Host Cholesterol Level*. *Cell Host & Microbe*, 2020; <https://doi.org/10.1016/j.chom.2020.05.013>

## **10. Exposure To Air Pollutants And The Gut Microbiota: A Potential Link Between Exposure, Obesity, And Type 2 Diabetes**

The current review summarizes recent findings regarding the impact of inhaled and ingested air pollutants on the gut microbiota. Animal and human studies provide evidence that air pollutants, such as particulate matter, nitrogen oxides, and ozone, have the potential to alter the gut microbiota. Further, studies suggest that such exposure-induced alterations to the gut microbiota may contribute to increased risk for obesity and type 2 diabetes through inflammatory pathways. Future work is needed to fully understand the complex interactions between air pollution, the gut microbiome, and human health. Additionally, advanced sequencing methods for gut microbiome research present unique opportunities to study the underlying pathways that link increased air pollution exposure with obesity and type 2 diabetes risk.

**Source:** Tanya L. Alderete, Department Of Integrative Physiology, University Of Colorado Boulder, USA. *Exposure To Air Pollutants And The Gut Microbiota: A Potential Link Between Exposure, Obesity, And Type 2 Diabetes*. *Gut Microbes*, Volume 11, 2020, Issue 5, Page no.1188-1202. <https://doi.org/10.1080/19490976.2020.1749754>

## 11. Serum Metabolites Reflecting Gut Microbiome Alpha Diversity Predict Type 2 Diabetes

Type 2 diabetes (T2D) is associated with reduced gut microbiome diversity, although the cause is unclear. Metabolites generated by gut microbes also appear to be causative factors in T2D. Scientists have investigated whether serum metabolites are predictive of gut microbiome diversity in 1018 females from TwinsUK with concurrent metabolomic profiling and microbiome composition.

Study results show that Microbial Metabolites Diversity (MMD) scores of six circulating metabolites has 18% of the variance in microbiome alpha diversity. Moreover, the MMD score was associated with significantly lower odds of prevalent and incident type 2 diabetes (T2D). The MMD score mediated 28% of the total effect of gut microbiome on T2D after adjusting for confounders. Metabolites predicting higher microbiome diversity included **3-phenylpropionate (hydrocinnamate), indolepropionate, cinnamoylglycine and 5-alpha-pregnan-3beta,20 alpha-diol monosulfate(2)** of which **indolepropionate** and **phenylpropionate** have already been linked to lower incidence of T2D. Metabolites correlating with lower microbial diversity included **glutarate** and **imidazole propionate**, of which the latter has been implicated in insulin resistance.

Study results suggest that the effect of gut microbiome diversity on T2D is largely mediated by microbial metabolites, which might be modifiable by diet.

Source: Anna M Valdes, Department Of Twin Research and Genetic Epidemiology, Kings College London, School Of Medicine And Nottingham Biomedical Research Centre, Nottingham, UK. Serum Metabolites Reflecting Gut Microbiome Alpha Diversity Predict Type 2 Diabetes. *Gut Microbes*, Volume 11, Issue 6, 2019, Page no. 1633-1642.

<https://doi.org/10.1080/19490976.2020.1778261>

## 12. 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>

## 13. Directed Remodeling Of The Mouse Gut Microbiome Inhibits The Development Of Atherosclerosis

In this study researchers devised an in vitro screening protocol of the mouse gut microbiome to discover molecules that can selectively modify bacterial growth. This approach is used to identify cyclic D,L- $\alpha$ -peptides that remodelled the Western diet (WD) gut microbiome toward the low-fat-diet microbiome state.

Study result shows that daily oral administration of the peptides in WD-fed LDLr<sup>-/-</sup> mice reduced plasma total cholesterol levels and atherosclerotic plaques. Depletion of the microbiome with antibiotics abrogated these effects. Peptide treatment reprogrammed the microbiome transcriptome, suppressed the production of pro-inflammatory cytokines (including interleukin-6, tumor necrosis factor- $\alpha$  and interleukin-1 $\beta$ ), rebalanced levels of short-chain fatty acids and bile acids, improved gut barrier integrity and increased intestinal T regulatory cells. Directed chemical manipulation provides an additional tool for deciphering the chemical biology of the gut microbiome and might advance microbiome-targeted therapeutics.

Source: M. Reza Ghadiri, Department of Chemistry, Scripps Research and The Skaggs Institute of Chemical Biology, Scripps Research, La Jolla, CA, USA. Directed Remodeling Of The Mouse Gut Microbiome Inhibits The Development Of Atherosclerosis. *Nat Biotechnol* (2020). <https://doi.org/10.1038/s41587-020-0549-5>

## **14. High Fat Diet Induces Microbiota-Dependent Silencing Of Enteroendocrine Cells**

While using the zebra fish to examine cells that normally tell the brain and the rest of the body what is going on inside the gut after a meal, a team of Duke researchers discovered that a high-fat meal completely shuts down that communication between the intestine and the rest of the body for a few hours. The cells they were looking at are the entero-endocrine cells, which occur sparsely throughout the lining of the gut, but play a key role in signalling the body about the all-important alimentary canal. In addition to releasing hormones, the cells also have a recently-discovered direct connection to the nervous system and the brain. These cells produce at least 15 different hormones to send signals to the rest of the body about gut movement, feelings of fullness, digestion, nutrient absorption, insulin sensitivity and energy storage.

Since entero-endocrine cells are key players in digestion, the feeling of being full and subsequent feeding behaviour, this silencing may be a mechanism that somehow causes people eating a high-fat diet to eat even more. It might cause a change in insulin signalling, which could in turn contribute to the development of insulin resistance and Type 2 diabetes.

The team tried the high-fat diet on a line of germ-free zebra fish raised in the absence of any microbes, and found they didn't experience the same silencing effect. So they began looking for gut microbes that might be involved in the process. After screening through all the kinds of bacteria found in the gut, they saw that the silencing appeared to be the work of a single type of gut bacteria, called *Acinetobacter*. These bugs are normally less than 0.1 percent of the total gut microbiome, but they increased 100-fold after a high-fat meal and were the only bacteria able to induce the silencing effect.

**Source:** John Rawls, Department Of Molecular Genetics And Microbiology, The Duke School Of Medicine, Duke University. High Fat Diet Induces Microbiota-Dependent Silencing Of Enteroendocrine Cells. *eLife* 2019;8: e48479. DOI: 10.7554/eLife.48479

## **15. Long-Term Dietary Intervention Reveals Resilience Of The Gut Microbiota Despite Changes In Diet And Weight**

In this study investigators determined whether baseline microbiota composition or diversity is associated with weight-loss success and also tracked the longitudinal associations of changes to lower-carbohydrate or lower-fat diets and concomitant weight loss with the composition and diversity of the gut microbiota.

Study shows that baseline microbiota composition is not predictive of weight loss, each diet results in substantial changes in the microbiota. Three months after the start of the intervention; the study revealed that some of these changes are diet specific (14 taxonomic changes specific to the healthy low-carbohydrate diet, 12 taxonomic changes specific to the healthy low-fat diet) and others tracked with weight loss (7 taxonomic changes in both diets). After these initial shifts, the microbiota returned near its original baseline state for the remainder of the intervention i.e. 12 months, despite participants maintaining their diet and weight loss for the entire study.

These results suggest a resilience to perturbation of the microbiota's starting profile. When considering the established contribution of obesity-associated microbiotas to weight gain in animal models, microbiota resilience may need to be overcome for long-term alterations to human physiology.

**Source:** Christopher D Gardner, Stanford Prevention Research Center, Department Of Medicine, Stanford School Of Medicine, Stanford, US. Long-Term Dietary Intervention Reveals Resilience Of The Gut Microbiota Despite Changes In Diet And Weight. *The American Journal of Clinical Nutrition*, Volume 111, Issue 6, June 2020, Pages 1127-1136, <https://doi.org/10.1093/ajcn/nqaa046>

## **16. Modest Sodium Reduction Increases Circulating Short-Chain Fatty Acids In Untreated Hypertensives**

New study suggests that reducing salt intake can benefit the gut microbiome and blood pressure in women with untreated hypertension. In the randomized, placebo-controlled study, the researchers examined the blood of 145 adults aged 30–75 with untreated high blood pressure. Circulating short-chain fatty acids (SCFAs) which is the primary metabolite produced by gut microbiota was measured. It was found that just six weeks of a daily sodium intake close to the 2,300 mg resulted in increased levels of all eight of the short-chain fatty acids (SCFAs). The increased SCFA levels were consistently associated with lower blood pressure and enhanced blood vessel flexibility.

**Source:** Haidong Zhu, Georgia Prevention Institute, Department Of Medicine, Medical College Of Georgia, Augusta University, Augusta. Modest Sodium Reduction Increases Circulating Short-Chain Fatty Acids In Untreated Hypertensives. *Hypertension*. 2020; 76:73-79, <https://doi.org/10.1161/HYPERTENSIONAHA.120.1480>

## 17. Effects Of A High Fat Diet On Gut Microbiome Dysbiosis In A Mouse Model Of Gulf War Illness

The present study was undertaken to determine if gut microbiome dysbiosis is evident in a mouse model of Gulf War Illness (GWI) and to determine if a high fat diet (HF) would alter GWI outcomes. Researchers have found that the taxonomic structure of the gut microbiome is significantly altered in the GWI model and after HF exposure. Their combined effects were significantly different from either treatment alone. Most treatment-induced changes occurred at the level of phylum in Firmicutes and Bacteroidetes. If mice fed HF were returned to a normal diet, the gut microbiome recovered towards normal levels in both controls and GWI agent-treated mice. These results support that dysbiosis in the gut microbiome plays a role in GWI and that life-style risk factors such as an unhealthy diet can accentuate the effects of GWI by impacting the gut microbiome. The reversibility of the effect of HF on the gut microbiome suggests new avenues for treating GWI through dietary intervention.

Source: Donald M. Kuhn, Research and Development Service, John D. Dingell VA Medical Center and Department of Psychiatry and Behavioral Neurosciences, Wayne State University School of Medicine, Detroit, Michigan, USA. *Effects Of A High Fat Diet On Gut Microbiome Dysbiosis In A Mouse Model Of Gulf War Illness*. *Sci Rep* 10, 9529 (2020). <https://doi.org/10.1038/s41598-020-66833-w>

## 18. Gut Microbes And Metabolites As Modulators Of Blood-Brain Barrier Integrity And Brain Health

Gut microbiome research is rapidly expanding, with recent advances in high-throughput 'omics technologies' providing a better understanding of the composition and functionality of such a complex ecosystem. Further investigation of bacterial metabolites and their effects on hormone production, immune signaling, and neural function will enable a fuller understanding of brain responses to age- and disease-associated alterations in the microbiota. Despite current limited knowledge of specific mechanisms, dietary and microbial modulations show as potential strategies to tackle some neurodegenerative and neurological diseases. A deeper understanding of gut microbial ecology, metabolism, and signaling networks within the host may lead to a new generation of microbiome-targeted strategies, both for disease treatment and prevention.

Source: Simon R Carding, Gut Microbes And Health Research Programme, Quadram Institute Bioscience, Norwich Medical School, University Of East Anglia, UK. *Gut Microbes And Metabolites As Modulators Of Blood-Brain Barrier Integrity And Brain Health*. *Gut Microbes*. 2020; 11(2): 135-157. <https://doi.org/10.1080/19490976.2019.1638722>

## 19. Microbiota Modulate Sympathetic Neurons Via A Gut-Brain Circuit

In the present study researchers characterized the influence of the microbiota on enteric-associated neurons by combining gnotobiotic mouse models with transcriptomics, circuit-tracing methods and functional manipulations.

Scientists found that the gut microbiome modulates gut-extrinsic sympathetic neurons: microbiota depletion leads to increased expression of the neuronal transcription factor cFos, and colonization of germ-free mice with bacteria that produce short-chain fatty acids suppresses cFos expression in the gut sympathetic ganglia. Chemogenetic manipulations, translational profiling and anterograde tracing identify a subset of distal intestine-projecting vagal neurons that are positioned to have an afferent role in microbiota-mediated modulation of gut sympathetic neurons. Retrograde polysynaptic neuronal tracing from the intestinal wall identifies brainstem sensory nuclei that are activated during microbial depletion, as well as efferent sympathetic premotor glutamatergic neurons that regulate gastrointestinal transit. ***These results reveal microbiota-dependent control of gut-extrinsic sympathetic activation through a gut-brain circuit.***

Source: Paul A. Muller, Kallyope Inc. and Laboratory of Mucosal Immunology, The Rockefeller University, New York, NY, USA. *Microbiota Modulate Sympathetic Neurons Via A Gut-Brain Circuit*. *Nature* 583, 441-446 (2020). <https://doi.org/10.1038/s41586-020-2474-7>

## 20. Permissive Microbiome Characterizes Human Subjects With A Neurovascular Disease Cavernous Angioma

In a nationwide study in US, researchers have found that the presence of abnormal bundles of brittle blood vessels in the brain or spinal cord, called cavernous angiomas (CA), are linked to the composition of a person's gut bacteria. Scientists have found that on average the CA patients had more gram-negative bacteria whereas the controls had more gram-positive bacteria, and that the relative abundance of three gut bacterial species distinguished CA patients from controls regardless of a person's sex, geographic location, or genetic predisposition to the disease. Moreover, gut bacteria from the CA patients appeared to produce more lipopolysaccharide molecules which have been shown to drive CA formation in mice.

These results provided the first demonstration in humans of a "permissive microbiome" associated with the formation of neurovascular lesions in the brain. Further analysis shows that some gut bacteria compositions could identify aggressive versus non-aggressive forms of the disease as well as those with recent symptomatic hemorrhages.

Source: Issam A. Awad, Section Of Neurosurgery, Department Of Surgery, The University Of Chicago, USA. *Permissive Microbiome Characterizes Human Subjects With A Neurovascular Disease Cavernous Angioma*. *Nat Commun* 11, 2659 (2020). <https://doi.org/10.1038/s41467-020-16436-w>

## 21. Bacterial Colonization Reprograms The Neonatal Gut Metabolome

In this study researchers evaluated the gut microbiome, proteome and metabolome in 88 African-American new-borns using faecal samples collected in the first few days of life.

Detailed analysis of the three most common species, *Escherichia coli*, *Enterococcus faecalis* and *Bacteroides vulgatus*, did not suggest a genomic signature for neonatal gut colonization. The appearance of bacteria was associated with reduced abundance of approximately 50 human proteins, decreased levels of free amino acids and an increase in products of bacterial fermentation, including acetate and succinate.

Further, using flux balance modelling and in vitro experiments provided evidence that fermentation of amino acids provides mechanism for the initial growth of *E. coli*, the most common early colonizer, under anaerobic conditions. These results provide a deep characterization of the first microbes in the human gut and show how the biochemical environment is altered by their appearance.

Source: Gary D. Wu, Division Of Gastroenterology, Perelman School Of Medicine, University Of Pennsylvania, USA. Bacterial Colonization Reprograms The Neonatal Gut Metabolome. *Nat Microbiol* 5, 838-847 (2020).

<https://doi.org/10.1038/s41564-020-0694-0>

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

In this study scientists have investigated fecal microbiota and metabolites at different ages in infants who were breastfed (BF), received dairy-based milk formula (MF), or received soy-based formula (SF).

Study showed that at 3, 6, and 9 months of age BF infants had the lowest  $\alpha$ -diversity, SF infants had the highest diversity, and MF had intermediate. *Bifidobacterium* was 2.6- to 5-fold lower in SF relative to BF infants through 1 year of life. An unidentified genus from *Ruminococcaceae* was higher in the SF (2%) than in the MF (0.4%) and BF (0.08%) infants at 3 months of age. In BF infants' higher levels of *butyric acid*, *D-sphingosine*, *kynurenic acid*, *indole-3-lactic acid*, *indole-3-acetic acid*, and *betaine* were observed than in MF and SF infants. At 3 months *Ruminococcaceae* was positively correlated to *azelaic*, *gentisic*, *isocitric*, *sebacic*, and *syringic acids*. At 6 months *Oscillospira* was negatively correlated with *3-hydroxybutyric-acid*, *hydroxy-hydrocinnamic acid*, and *betaine* whereas *Bifidobacterium* was negatively associated with *5-hydroxytryptamine*. At 12 months of age, *Lachnospiraceae* was negatively associated with *hydroxyphenyllactic acid*. Thus, this study concluded that 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; Department Of Pediatrics, University Of Arkansas For Medical Sciences 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, <https://doi.org/10.1093/ajcn/nqaa076>

## 23. Enterococci From Breast-Fed Infants Exert Higher Antibacterial Effects Than Those From Adults: A Comparative Study

This study assesses and compares the antibacterial effects of enterococci from breast-fed infants and those from adults. Fecal isolates of *enterococci* were isolated from infants and healthy adults and were identified to the species level by phenotypic and genotypic methods.

Total of eighty-nine recovered enterococcal isolates, *Enterococcus faecium* and *E. faecalis* were the most common species (98%) which show inhibitory effects against one indicator strain. Comparison between isolates from two studied groups shows that isolates from neonates introduced significantly higher growth inhibitory effects against six indicator strains and these effects were frequently attributable to *E. faecium* isolates. In addition, the highest growth inhibitory effect was observed against *Listeria monocytogenes*. Antimicrobial effects of enterococci in human microbiota change during time. The beneficial role of these organisms within the neonatal period suggests the potential of enterococci from breast-fed infants for probiotic application.

Source: Shahla Mansouri, Medical Mycology And Bacteriology Research Center, Kerman University Of Medical Sciences, Kerman, Iran. Enterococci From Breast-Fed Infants Exert Higher Antibacterial Effects Than Those From Adults: A Comparative Study. *Human Microbiome Journal*, 10 July 2020, 100072. <https://doi.org/10.1016/j.humic.2020.100072>

## 24. Bile Acids Drive The Newborn's Gut Microbiota Maturation

The present study analyses the influence of the developing hepatic function and liver metabolism on the early intestinal microbiota. Scientists have observed major age-dependent microbial and metabolic changes and identified bile acids as potent drivers of the early intestinal microbiota maturation. Consistently, oral administration of tauro-cholic acid or  $\beta$ -tauro-murocholic acid to new born mice accelerated postnatal microbiota maturation.

Source: M. W. Hornef, Institute Of Medical Microbiology, RWTH University Hospital Aachen, RWTH University, Aachen, Germany. Bile Acids Drive The Newborn's Gut Microbiota Maturation. *Nat Commun* 11, 3692 (2020).

<https://doi.org/10.1038/s41467-020-17183-8>

## **25. A Longitudinal Study Of The Development Of The Saliva Microbiome In Infants 2 Days To 5 Years Compared To The Microbiome In Adolescents**

In this study the oral microbiota was longitudinally characterized in children from 2 days (n = 206) to 5 years of age and in young adults (n = 175) by sequencing of the v3-v4 region of the 16S rRNA gene from saliva extracted DNA.

Study result shows that alpha diversity increased by age, with 2-day- and 3-month-old infants in one sub-group, and 18-month- and 3-year-old children in another. Firmicutes decreased up to 3 years of age, whereas Proteobacteria, Actinobacteria, Bacteroidetes and Fusobacteria abundances increased. *Abiotrophia*, *Actinomyces*, *Capnocytophaga*, *Corynebacterium*, *Fusobacterium*, *Kingella*, *Leptotrichia*, *Neisseria* and *Porphyromonas* appeared from 18-months of age. This is paralleled by expansions in the core microbiome that continued up to adulthood. The age-related microbiota transformation is paralleled by functional alterations, e.g., changed metabolic pathways that reflected e.g., breastfeeding and increasing proportions of anaerobic species. Oral microbiotas differed by feeding mode and weakly by mode of delivery, but not gender, pacifier use or cleaning method or probiotic intake.

The study shows that in the saliva microbiota is diverse 2 days after birth and under transformation up to 5 years of age and beyond, with fluctuations possibly reflecting age-related environmental influences.

Source: Pernilla Lif Holgerson, Department Of Odontology, Section Of Pediatric Dentistry, Umeå University, Sweden. A Longitudinal Study Of The Development Of The Saliva Microbiome In Infants 2 Days To 5 Years Compared To The Microbiome In Adolescents. *Sci Rep* 10, 9629 (2020). <https://doi.org/10.1038/s41598-020-66658-7>

## **26. Human Behavior, Not Race Or Geography, Is The Strongest Predictor Of Microbial Succession In The Gut Bacteriome Of Infants**

Colonization of the gastrointestinal tract with microorganisms during infancy represents a critical control point for shaping life-long immune-mediated disease susceptibility. Abnormal colonization or an imbalance of microbes, termed dysbiosis, is implicated in several diseases. This review provides a comprehensive account of what is currently known about the infant microbiome from a global context. In general, this review shows that the influence of cultural variations in feeding practices, delivery modes and hygiene are the biggest contributors to microbial variability. Despite geography or race, all humans have similar microbial succession during infancy.

Source: Deanna L. Gibson, Department Of Biology And Department Of Medicine, University Of British Columbia, Kelowna, Canada. Human Behavior, Not Race Or Geography, Is The Strongest Predictor Of Microbial Succession In The Gut Bacteriome. *Gut Microbes*, Volume 11, 2020, Issue 5, Page no. 1143-1171. <https://doi.org/10.1080/19490976.2020.1736973>

## **27. Antidepressant Treatment With Fluoxetine During Pregnancy And Lactation Modulates The Gut Microbiome And Metabolome In A Rat Model Relevant To Depression**

Recent evidence suggests that selective serotonin reuptake inhibitor (SSRIs) is capable of altering the gut microbiota. However, the interaction between maternal depression and SSRI use on bacterial community composition and the availability of microbiota-derived metabolites during pregnancy and lactation is not clear.

Scientists have found that pregnancy and lactation segregate in terms of fecal microbiome diversity and composition, accompanied by changes in metabolite availability. This study also shows that fluoxetine treatment alters important features of this transition from pregnancy to lactation most clearly in previously stressed dams, with lower fecal amino acid concentrations. Amino acid concentrations, in turn, correlated negatively with the relative abundance of bacterial taxa such as *Prevotella* and *Bacteroides*.

The present study demonstrates an important relationship between antidepressant use during the perinatal period and maternal fecal metabolite availability in a rat model relevant to depression, possibly through parallel changes in the gut microbiome. Since microbial metabolites contribute to homeostasis and development, insults to the maternal microbiome by SSRIs might have health consequences for mother and offspring.

Source: Jocelien DA Olivier, Department Of Neurobiology, Groningen Institute Of evolutionary Life Sciences, University Of Groningen, The Netherlands. Antidepressant Treatment With Fluoxetine During Pregnancy And Lactation Modulates The Gut Microbiome And Metabolome In A Rat Model Relevant To Depression. *Gut Microbes*, Volume 11, 2020, Issue 4, Page no. 735-753. <https://doi.org/10.1080/19490976.2019.1705728>

## 28. Ecological Succession In The Vaginal Microbiota During Pregnancy And Birth

The mother's vaginal microbiota represents the first microbes to which a child is exposed when delivered vaginally. However, little is known about the composition and development of the vaginal microbiota during pregnancy and birth.

In this study researchers have analysed the vaginal microbiota of 57 women in pregnancy week 24, 36 and at birth after rupture of membranes but before delivery, and further compared the composition with that of the gut and airways of the 1-week-old child. The vaginal community structure had dramatic changes in bacterial diversity and taxonomic distribution, yet carried an individual-specific signature. The relative abundance of most bacterial taxa increased stepwise from week 24 of pregnancy until birth, with a gradual decline of *Lactobacillus*. Mother-to-child vertical transfer, as suggested by sharing, is modest, with the strongest transfer being for *Clostridiales* followed by *Lactobacillales* and *Enterobacteriales*.

In conclusion, late gestation is associated with an increase in maternal vaginal microbiota diversity, and vaginal bacteria at birth only modestly predict the composition of the neonatal microbiota.

Source: J. Stokholm, OPSAC, Copenhagen Prospective Studies on Asthma in Childhood, Herlev and Gentofte Hospital, University of Copenhagen, Copenhagen, Denmark. Ecological Succession In The Vaginal Microbiota During Pregnancy And Birth. ISME J (2020). <https://doi.org/10.1038/s41396-020-0686-3>

## 29. Control Of Ecological Outcomes Through Deliberate Parameter Changes In A Model Of The Gut Microbiome

Researchers proposed a technique based on data from mouse model experiments which uses Lotka-Volterra (gLV) equations for driving a mathematical gut microbiome model toward a target microbiome composition by manipulating certain parameters of the model called SPARC (SSR-guided parameter change), this approach reduces the complexity of the system without sacrificing it and it also offers a systematic understanding of how environmental factors and species-species interactions can be manipulated to control ecological outcomes.

Source: Zipeng Wang, Department Of Physics, University Of California, Santa Barbara, USA. Control Of Ecological Outcomes Through Deliberate Parameter Changes In A Model Of The Gut Microbiome. Physical Review E, 2020; 101 (5). DOI: 10.1103/PhysRevE.101.052402

## 30. Macroecological Dynamics Of Gut Microbiota

In the present study, scientists have used multiple high-resolution time series data obtained from humans and mice to demonstrate that, despite their inherent complexity, gut microbiota dynamics can be characterized by several robust scaling relationships. The power-law relationships describe short- and long-term changes in gut microbiota abundances, species residence and return times, and the correlation between the mean and the temporal variance of species abundances. Researchers have found that the observed scaling laws are altered in mice receiving different diets and are affected by context-specific perturbations in humans. Overall, study results suggest that a quantitative macroecological framework will be important for characterizing and understanding the complex dynamics of diverse microbial communities.

Source: Dennis Vitkup, Department Of Systems Biology And Department Of Biomedical Informatics, Columbia University, New York, USA. Macroecological Dynamics Of Gut Microbiota. Nat Microbiol 5, 768-775 (2020). <https://doi.org/10.1038/s41564-020-0685-1>

## 31. The Impact Of Environmental Chemicals On The Gut Microbiome

The microbes that inhabit bodies are influenced by what one eats, drinks, breathe and absorb through skin, and most people are chronically exposed to natural and human-made environmental contaminants. Scientists have reviewed the research linking dozens of environmental chemicals to changes in the gut microbiome and associated health challenges. Study data together suggest that exposure to many of these environmental chemicals during various stages of life can alter the gut microbiome in ways that influence health. The pathologies associated with altered microbiomes after exposure to environmental chemicals include immune dysfunction, altered carbohydrate and lipid metabolism, and neurological and behavioral impairments. These effects highly depend on an individual's sex and age.

Source: Wenyan Mei, Department Of Comparative Biosciences, College Of Veterinary Medicine And Carl R. Woese Institute For Genomic Biology, University Of Illinois At Urbana-Champaign, USA. The Impact Of Environmental Chemicals On The Gut Microbiome. Toxicological Sciences, kfaa065, <https://doi.org/10.1093/toxsci/kfaa065>

### **32. Faecal Virome Transplantation Decreases Symptoms Of Type 2 Diabetes And Obesity In A Murine Model**

Development of obesity and type 2 diabetes (T2D) are associated with gut microbiota (GM) changes. The gut viral community was predominated by bacteriophages (phages), which are viruses that attack bacteria in a host-specific manner. The antagonistic behaviour of phages has the potential to alter the GM. As a proof-of-concept this study demonstrates the efficacy of faecal virome transplantation (FVT) from lean donors for shifting the phenotype of obese mice into closer resemblance of lean mice.

The FVT consists of viromes with distinct profiles extracted from the caecal content of mice from different vendors that were fed a low-fat (LF) diet for 14 weeks. Male C57BL/6NTac mice were divided into five groups: LF (as diet control), high-fat (HF) diet, HF+ampicillin (Amp), HF+Amp+FVT and HF+FVT. At weeks 6 and 7 of the study, the HF+FVT and HF+Amp+FVT mice were treated with FVT by oral gavage. The Amp groups were treated with Amp 24 hours prior to first FVT treatment.

Six weeks after first FVT, the HF+FVT mice showed a significant decrease in weight gain compared with the HF group. Further, glucose tolerance was comparable between the LF and HF+FVT mice, while the other HF groups all had impaired glucose tolerance. These observations were supported by significant shifts in GM composition, blood plasma metabolome and expression levels of genes associated with obesity and T2D development.

Transfer of caecal viral communities from mice with a lean phenotype into mice with an obese phenotype led to reduced weight gain and normalised blood glucose parameters relative to lean mice. This effect was mediated via FVT-induced GM changes.

**Source:** Torben Sølbeck Rasmussen, Food Science, University of Copenhagen, Frederiksberg, Denmark. *Faecal Virome Transplantation Decreases Symptoms Of Type 2 Diabetes And Obesity In A Murine Model*. Gut Published Online First: 12 March 2020. DOI: 10.1136/gutjnl-2019-320005

### **33. Fecal Microbiota Transplantation For Antibiotic Resistant Bacteria Decolonization**

Patients colonized with antibiotic resistant bacteria are at risk of infections and spontaneous decolonization delays are highly variable between patients. The management of these patients is therefore time-consuming; requires patient isolation, and cohort policies. Fecal microbiota transplantation (FMT) has been used with the aim of shortening this gut colonization.

Researchers undertook a comprehensive literature review on FMT utilization for gut antibiotics resistant bacteria decolonization and analysed 23 studies with description of FMT utilization and analyse of gut decolonization. In total, the data involved 197 patients, 153 of whom underwent FMT.

Study results show that 66.7% (102/153) of the patients were decolonized after FMT. There was a lot of interpretation bias, such as variation in colonization definition and high disparities in FMT administration modalities. Overall, the use of FMT is a promising perspective for intestinal decolonization, but it requires greater standardization.

**Source:** Jean-Christophe Lagier, Aix Marseille Univ, IRD, APHM, MEPHI, IHU - Méditerranée Infection, France. *Fecal Microbiota Transplantation For Antibiotic Resistant Bacteria Decolonization*. Human Microbiome Journal, Volume 16, June 2020, 100071. <https://doi.org/10.1016/j.humic.2020.100071>

### **34. 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>

### **35. An Individualized Mosaic Of Maternal Microbial Strains Is Transmitted To The Infant Gut Microbial Community**

Researchers used microbiome "fingerprint" method to report that an individualized mosaic of microbial strains is transmitted to the infant gut microbiome from a mother giving birth through vaginal delivery. They detailed this transmission by analysing existing metagenomic databases of fecal samples from mother-infant pairs, as well as analysing mouse dam and pup transmission in a germ-free, or gnotobiotic, mouse model at 11 UAB, where the dams were inoculated with human fecal microbes.

The results demonstrated that multiple strains of maternal microbes, some that are not abundant in the maternal fecal community can be transmitted during birth to establish a diverse infant gut microbial community. This analysis provides new insights into the origin of microbial strains in the complex infant microbial community.

*Source: Hyunmin Koo, Department Of Genetics, University Of Alabama At Birmingham, Birmingham, USA. An Individualized Mosaic Of Maternal Microbial Strains Is Transmitted To The Infant Gut Microbial Community. R. Soc. open sci.7192200. <https://doi.org/10.1098/rsos.192200>*

### **36. High Oscillospira Abundance Indicates Constipation And Low BMI In The Guangdong Gut Microbiome Project**

Oscillospira is a common yet rarely cultivated gut bacterial genus. To study the ecology of Oscillospira and gain insights into Oscillospira-related host physiological conditions, scientists analysed data from the Guangdong Gut Microbiome Project, one of the largest gut microbiota data base currently.

Data of 6376 participants were analysed. This study shows the prevalence and relative abundance of Oscillospira as well as the profiles of associated microbial communities. Researchers found that Oscillospira is closely related to human health because its abundance is positively correlated with microbial diversity, high density lipoprotein, and sleep time, and is inversely correlated with diastolic blood pressure, systolic blood pressure, fasting blood glucose, triglyceride, uric acid and Bristol stool type. Moreover, random forest analysis with five-fold cross validation showed Oscillospira could be a predictor of low BMI and constipation in the subset. Overall, this study provides a basic understanding of Oscillospira-related microbiota profile and physiological parameters of the host. Study results indicate Oscillospira may play a role in aggravating constipation.

*Source: Zhi-cong Yang, Guangzhou Center For Disease Control And Prevention, Guangzhou, Guangdong, China. High Oscillospira Abundance Indicates Constipation And Low BMI In The Guangdong Gut Microbiome Project. Sci Rep 10, 9364 (2020). <https://doi.org/10.1038/s41598-020-66369-z>*

### **37. Diversity Within Species: Interpreting Strains In Microbiomes**

Studying within-species variation has traditionally been limited to culturable bacterial isolates and low-resolution microbial community fingerprinting. Metagenomic sequencing and technical advances have enabled culture-free, high-resolution strain and subspecies analyses at high throughput and in complex environments. This holds great scientific promise but has also led to an overwhelming number of methods and terms to describe infraspecific variation. This Review aims to clarify these advances by focusing on the diversity within bacterial and archaeal species in the context of microbiomics. This study cover foundational microevolutionary concepts relevant to population genetics and summarizes how within-species variation can be studied and stratified directly within microbial communities with a focus on metagenomics. Further, this study helps to describe how common applications of within-species variation can be achieved using metagenomic data. It also guides the selection of appropriate terms and analytical approaches to facilitate researchers in benefiting from the increasing availability of large, high-resolution microbiome genetic sequencing data.

*Source: Peer Bork, European Molecular Biology Laboratory, Structural and Computational Biology Unit; Max Delbrück Centre for Molecular Medicine; Molecular Medicine Partnership Unit, University of Heidelberg and European Molecular Biology Laboratory and Department of Bioinformatics, Biocenter, University of Würzburg, Germany. Diversity Within Species: Interpreting Strains In Microbiomes. Nat Rev Microbiol (2020). <https://doi.org/10.1038/s41579-020-0368-1>*

### **38. Biphasic Chemotaxis Of Escherichia Coli To The Microbiota Metabolite Indole**

In this study scientists studied the response of the beneficial gut bacteria, E. coli to indole. They found that there are two receptors in E. coli that sense indole. One senses indole as a repellent, and one senses indole as an attractant. Sustained exposure to high concentrations of indole desensitizes the receptor that interprets it as a repellent. This leads to indole being sensed only as an attractant. Bacteria that produce indole could group together and be attracted to niches where indole concentrations are high. Since the bacteria that produce indole in the gut typically are enmeshed in mucus layers among other bacteria, the indole concentration drops as one gets further away from the source of indole. Since pathogens tend to pass through the gut relatively far from the bacteria that produce indole, they are not likely to encounter high concentrations of indole for a sustained period. Therefore, they are not sensitized to indole, and any indole they encounter repels them. This study shows that it is important to have a diverse mix of beneficial bacteria in the gut.

*Source: Arul Jayaraman, Artie McFerrin Department Of Chemical Engineering, Texas A&M University And Department Of Molecular Pathogenesis And Immunology, Texas A&M Health Science Center, Bryan. Biphasic Chemotaxis Of Escherichia Coli To The Microbiota Metabolite Indole. PNAS March 17, 2020 117 (11) 6114-6120. <https://doi.org/10.1073/pnas.1916974117>*

### **39. Automatic Extraction, Prioritization And Analysis Of Gut Microbial Metabolites From Biomedical Literature**

This study presents a novel integrated approach to automatically extract and analyse microbial metabolites from 28 million published biomedical records. Researchers systematically analysed the interactions between extracted microbial metabolites and human genes.

A total of 11,846 metabolites were extracted from 28 million MEDLINE articles. The combined text classification and signal prioritization significantly enriched true positives among top: manual curation of top 100 metabolites showed a true precision of 0.55, representing a significant 38.3-fold enrichment as compared to the precision of 0.014 for baseline extraction. More importantly, 29% extracted microbial metabolites were not been captured by existing databases. performed data-driven analysis of the interactions between the extracted microbial metabolite and human genetics. This study represents the first effort towards automatically extracting and prioritizing microbial metabolites from published biomedical literature, which can set a foundation for future tasks of microbial metabolite relationship extraction from literature and facilitate data-driven studies of how microbial metabolism contributes to human diseases.

*Source: Rong Xu, Center For Artificial Intelligence In Drug Discovery, School Of Medicine, Case Western Reserve University, Cleveland, USA. Automatic Extraction, Prioritization And Analysis Of Gut Microbial Metabolites From Biomedical Literature. Sci Rep 10, 9996 (2020). <https://doi.org/10.1038/s41598-020-67075-6>*

### **40. Randomized Trial Of Lactin-V To Prevent Recurrence Of Bacterial Vaginosis**

Bacterial vaginosis is one of the most frequent bacterial infections, affecting nearly 30 percent of women of reproductive age in the United States, and anywhere from 15 to 50 percent of women around the world. It is associated with the spread of HIV in Africa, where women make up the majority of those infected, as well as preterm birth and low-birth weight around the world.

The randomized, placebo-controlled, double-blind trial of LACTIN-V, a so-called "live biotherapeutic" showed a significant reduction in the recurrence of bacterial vaginosis (BV) and found no safety risks from the bacteria used in the LACTIN-V formulation of the species *Lactobacillus crispatus* CTV-05, a common bacterium found in healthy vaginal microbiomes. The LACTIN-V comes in a powder form and women can self-administer it with a vaginal applicator. In this study researchers have found that LACTIN-V powder contains a healthy bacteria which colonize the vagina and they produce lactic acid, which inhibits the growth of bacteria which is associated with BV and this will significantly reduce these recurrences of BV. Just 30 percent of women who were given LACTIN-V after initial antibiotic treatment had a recurrence within 12 weeks, compared to 45 percent of the women who received the antibiotic and a placebo.

*Source: Craig R. Cohen, University Of California, San Francisco, USA. Randomized Trial Of Lactin-V To Prevent Recurrence Of Bacterial Vaginosis. May 14, 2020, N Engl J Med 2020; 382:1906-1915. DOI: 10.1056/NEJMoa1915254*

### **41. The Microbiota Programs DNA Methylation To Control Intestinal Homeostasis And Inflammation**

Epigenetic mechanisms have recently been suggested to operate at the interface between the microbiota and the intestinal epithelium. In this study investigators performed whole-genome bisulfite sequencing on conventionally raised and germ-free mice, and discovered that exposure to commensal microbiota induced localized DNA methylation changes at regulatory elements, which are TET2/3-dependent. This culminated in the activation of a set of 'early sentinel' response genes to maintain intestinal homeostasis. Furthermore, exposure to the microbiota in dextran sodium sulfate-induced acute inflammation results in profound DNA methylation and chromatin accessibility changes at regulatory elements, leading to alterations in gene expression programs enriched in colitis- and colon-cancer-associated functions. Finally, by employing genetic intervention in the study it shows that microbiota-induced epigenetic programming is necessary for proper intestinal homeostasis in vivo.

*Source: Yehudit Bergman, Department Of Developmental Biology And Cancer Research, Institute For Medical Research Israel-Canada, Hebrew University Medical School, Jerusalem, Israel. The Microbiota Programs DNA Methylation To Control Intestinal Homeostasis And Inflammation. Nat Microbiol 5, 610-619 (2020). <https://doi.org/10.1038/s41564-019-0659-3>*

### **42. Statin Therapy Is Associated With Lower Prevalence Of Gut Microbiota Dysbiosis**

New study explored obesity-associated microbiota alterations in the quantitative faecal metagenomes of the cross-sectional MetaCardis Body Mass Index Spectrum cohort. Researchers found that statin therapy is a key covariate of microbiome diversification.

By focusing on a sub cohort of participants that were not medicated with statins, researchers found that the prevalence of Bact2 (*Bacteroides*2) correlates with body mass index, increasing from 3.90% in lean or overweight participants to 17.73% in obese participants. Systemic inflammation levels in Bact2-enterotyped individuals was higher than predicted on the basis of their obesity status, indicative of Bact2 as a dysbiotic microbiome constellation. Researchers concluded that obesity-associated microbiota dysbiosis is negatively associated with statin treatment, resulting in a lower Bact2 prevalence of 5.88% in statin-medicated obese participants.

*Source: Jeroen Raes, Laboratory Of Molecular Bacteriology, Department Of Microbiology And Immunology, Rega Institute And Centre For Microbiology, VIB, Leuven, Belgium. Statin Therapy Is Associated With Lower Prevalence Of Gut Microbiota Dysbiosis. Nature 581, 310-315 (2020). <https://doi.org/10.1038/s41586-020-2269-x>*

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

Animal data suggest a role of the gut-liver axis in progression of alcoholic liver disease (ALD), but human data are scarce especially for early disease stages.

Study result shows that only a subset of alcohol use disorders (AUD) patients had increased <sup>51</sup>Cr-EDTA and fecal albumin together with disrupted tight junctions and vasculature expression of plasmalemma Vesicle-Associated Protein-1. The so-defined increased intestinal permeability was 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, volume11, Issue6, 2020. DOI: 10.1080/19490976.2020.1782157*

### **44. Gut Microbiome Composition And Diversity Are Related To Human Personality Traits**

The gut microbiome has a measurable impact on the brain, influencing stress, anxiety, depressive symptoms and social behaviour. This microbiome–gut–brain axis may be mediated by various mechanisms including neural, immune and endocrine signalling. In this study the composition and diversity of the gut microbiome is investigated with respect to human personality.

Using regression models to control for possible confounding factors, the abundances of specific bacterial genera are shown to be significantly predicted by personality traits. Diversity analyses of the gut microbiome reveal that people with larger social networks tend to have a more diverse microbiome, suggesting that social interactions may shape the microbial community of the human gut. In contrast, anxiety and stress are linked to reduced diversity and an altered microbiome composition. Together, these results add a new dimension to the understanding of personality and reveal that the microbiome–gut–brain axis may also be relevant to behavioural variation in the general population as well as to cases of psychiatric disorders.

*Source: Katerina V.-A.Johnson, University of Oxford, Department of Experimental Psychology, New Radcliffe Building, Radcliffe Observatory Quarter, United Kingdom. 34. Gut Microbiome Composition And Diversity Are Related To Human Personality Traits. Human Microbiome Journal, Volume 15, March 2020, 100069. <https://doi.org/10.1016/j.humic.2019.100069>*

### **45. Children With Autism Spectrum Disorder: Pilot Studies Examining The Salivary Microbiome And Implications For Gut Metabolism And Social Behavior**

Autism Spectrum Disorder (ASD) is a collection of neurodevelopmental disorders defined by core deficits, including impaired communication, reciprocal social interaction, and stereotyped and repetitive patterns of behaviors. The salivary microbiota may serve as important indicators of oral and systemic health. In this pilot study researchers identified components of the salivary microbiome in children with ASD.

Study results show that *Rothia* species were statistically more prevalent in children with ASD in comparison to typically-developing children. Alternately, *Megasphaera*, *Moraxella*, *Neisseria*, and *Gemella* species were all found at significantly higher levels in typically-developing children than children with ASD, displaying 39.2-, 31.9-, 18.8- and 14.0-fold differences, respectively. In boys with ASD, *Moraxella* and *Neisseria* species were found at significantly-higher levels compared to typically-developing counterparts, exhibiting 42.36- and 28.62-fold differences, respectively.

*Source: Curtis A. Machida, Department of Pediatric Dentistry and Department of Integrative Biomedical and Diagnostic Sciences, Oregon Health & Science University School of Dentistry, United States. Children With Autism Spectrum Disorder: Pilot Studies Examining The Salivary Microbiome And Implications For Gut Metabolism And Social Behavior. Human Microbiome Journal Volume 15, March 2020, 100066. <https://doi.org/10.1016/j.humic.2019.100066>*

## 46. Impact Of PepT1 Deletion On Microbiota Composition And Colitis Requires Multiple Generations

In this study scientists have investigated that absence of di/tri-peptide transporter PepT1 altered microbiota composition resulting in resistance to colitis compelled scrutiny.

In this study researchers used PepT1<sup>-/-</sup> and wild type (WT) founder mice bred separately for multiple generations. Such mice were then bred to each other to generate F1 PepT1<sup>-/-</sup> and WT littermates, which were then bred within their genotype to generate F2, F3, and F4, offspring.

Scientists have found that founder PepT1<sup>-/-</sup> mice were, relative to their WT counterparts, resistant to dextran sulfate sodium (DSS) colitis. Such resistance is associated with alterations in gut microbiota, which, when transplanted to germfree mice, is sufficient to transfer resistance to colitis. Such differences were not observed when comparing F1 PepT1<sup>-/-</sup> to F1 WT littermates but rather, returned gradually over subsequent generations such that, relative to their F4 WT controls, F4 PepT1<sup>-/-</sup> displayed microbiota composition and colitis-resistant phenotype nearly identical to the founder PepT1<sup>-/-</sup> mice.

The findings of the study indicate a role for PepT1 in influencing microbiota composition and, consequently, proneness to colitis and cancer. Overall, the study indicates that littermate-controlled experiments can be insufficient for assessing microbiota-dependent phenotypes and prevent a full comprehension of genotype-driven phenomena. Rather, impact of a single genetic alteration on microbiota and host phenotype may take generations to manifest.

**Source:** Emilie Viennois, Institute For Biomedical Sciences, Center For Inflammation, Immunity And Infection, Digestive Disease Research Group, Georgia State University, Atlanta, GA, USA; Center Of Research On Inflammation And University Of Paris, Paris, France. Impact Of PepT1 Deletion On Microbiota Composition And Colitis Requires Multiple Generations. *npj Biofilms Microbiomes* 6, 27 (2020). <https://doi.org/10.1038/s41522-020-0137-y>

## 47. Dynamics Of The Lung Microbiome In Intensive Care Patients With Chronic Obstructive Pulmonary Disease And Community-Acquired Pneumonia

This study explores the longitudinal changes in microbial airway composition and its variations between chronic obstructive pulmonary disease (COPD) patients with different weaning outcomes.

Fifty-one endotracheal aspirate samples from 21 participants and 5 saline samples were collected as the patient and control group, respectively. Sequence analysis revealed significant increases and upward trends in the relative abundance of the *Acinetobacter genus* and *Acinetobacter baumannii* complex species in paired comparisons of sampling points and over time, respectively, in patients with failed weaning but not in those with successful weaning. Furthermore, significant changes in the composition of the bacterial community were observed in paired comparisons of sampling points in patients with failed weaning compared with those with successful weaning. The alpha diversity did not differ between the patients with different weaning outcomes.

The findings of the current study provide useful information that increases the awareness of researchers and clinicians with regards to the clinical application of longitudinal airway microbiome structure analysis in the management of critically ill patients with and without COPD.

**Source:** Chieh-Chen Huang, Department of Life Sciences, National Chung Hsing University, Taiwan. Dynamics Of The Lung Microbiome In Intensive Care Patients With Chronic Obstructive Pulmonary Disease And Community-Acquired Pneumonia. *Sci Rep* 10, 11046 (2020). <https://doi.org/10.1038/s41598-020-68100-4>

## 48. Large-Scale Metabolic Interaction Network Of The Mouse And Human Gut Microbiota

In this study scientists constructed a literature-curated, interspecies network of the mammalian gut microbiota for mouse and human hosts, called NJC19. This network is an extensive data resource, encompassing 838 microbial species (766 bacteria, 53 archaea, and 19 eukaryotes) and 6 host cell types, interacting through 8,224 small-molecule transport and macromolecule degradation events. Moreover, they compiled 912 negative associations between organisms and metabolic compounds that are not transportable or degradable by those organisms. This network may facilitate experimental and computational endeavors for the mechanistic investigations of host-associated microbial communities.

**Source:** Pan-Jun Kim, Department of Biology, Hong Kong Baptist University; Center for Quantitative Systems Biology, Hong Kong Baptist University; Institute of Computational and Theoretical Studies, Hong Kong Baptist University, Kowloon, Hong Kong and Abdus Salam International Centre for Theoretical Physics, Italy. Large-Scale Metabolic Interaction Network Of The Mouse And Human Gut Microbiota. *Sci Data* 7, 204 (2020). <https://doi.org/10.1038/s41597-020-0516-5>

## 49. Genome-Wide Associations Of Human Gut Microbiome Variation And Implications For Causal Inference Analyses

The present study shows an association between human host genotype and gut microbiome variation.

Using faecal 16S ribosomal RNA gene sequences and host genotype data from the Flemish Gut Flora Project and two German cohorts' scientists identified genetic associations involving multiple microbial traits. Two of these associations achieved a study-level threshold of  $P = 1.57 \times 10^{-10}$ ; an association between *Ruminococcus* and rs150018970 near RAPGEF1 on chromosome 9, and between *Coprococcus* and rs561177583 within LINC01787 on chromosome 1. Exploratory analyses were undertaken using 11 other genome-wide associations with strong evidence for association and a previously reported signal of association between rs4988235 (MCM6/LCT) and Bifidobacterium. Across these 14 single-nucleotide polymorphisms there was evidence of signal overlap with other genome-wide association studies, including those for age at menarche and cardiometabolic traits. Mendelian randomization analysis is able to estimate associations between microbial traits and disease (including *Bifidobacterium* and body composition); however, in the absence of clear microbiome-driven effects, caution is needed in interpretation. Overall, this work marks a growing catalogue of genetic associations that will provide insight into the contribution of host genotype to gut microbiome. Despite this, the uncertain origin of association signals will likely complicate future work looking to dissect function or use associations for causal inference analysis.

**Source:** Jeroen Raes, Department Of Microbiology And Immunology, Rega Instituut, KU Leuven-University Of Leuven And Center For Microbiology, VIB, Leuven, Belgium. *Genome-Wide Associations Of Human Gut Microbiome Variation And Implications For Causal Inference Analyses*. *Nat Microbiol* (2020). <https://doi.org/10.1038/s41564-020-0743-8>

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