

Ссылки к разделу: Болезни, лекарства и дисбактериоз: понимание микробных сигнатур при метаболических заболеваниях и медицинских вмешательствах

## References

1. Trevathan, S.M.; Sherman, C.D.; Huggett, M.J.; Campbell, A.H.; Laverock, B.; Hurtado-McCormick, V.; Seymour, J.R.; Firl, A.; Messer, L.F.; Ainsworth, T.D.; et al. A horizon scan of priorities for coastal marine microbiome research. *Nat. Ecol. Evol.* **2019**, *3*, 1509–1520.
2. Cho, I.; Yamanishi, S.; Cox, L.M.; Methe, B.A.; Zavadil, J.; Li, K.; Gao, Z.; Mahana, D.; Raju, K.; Teitler, I.; et al. Antibiotics in early life alter the murine colonic microbiome and adiposity. *Nature* **2012**, *488*, 621.
3. Byrd, A.L.; Belkaid, Y.; Segre, J.A. The human skin microbiome. *Nat. Rev. Microbiol.* **2018**, *16*, 143.
4. Paissé, S.; Valle, C.; Servant, F.; Courtney, M.; Burcelin, R.; Amar, J.; Lelouvier, B. Comprehensive description of blood microbiome from healthy donors assessed by 16S targeted metagenomic sequencing. *Transfusion* **2016**, *56*, 1138–1147.
5. Wade, W.G. The oral microbiome in health and disease. *Pharmacol. Res.* **2013**, *69*, 137–143.
6. Dominguez-Bello, M.G.; Costello, E.K.; Contreras, M.; Magris, M.; Hidalgo, G.; Fierer, N.; Knight, R. Delivery mode shapes the acquisition and structure of the initial microbiota across multiple body habitats in newborns. *Proc. Natl. Acad. Sci. USA* **2010**, *107*, 11971–11975.
7. Arumugam, M.; Raes, J.; Pelletier, E.; Le Paslier, D.; Yamada, T.; Mende, D.R.; Fernandes, G.R.; Tap, J.; Bruls, T.; Batto, J.M.; et al. Enterotypes of the human gut microbiome. *Nature* **2011**, *473*, 174.
8. Karlsson, F.H.; Tremaroli, V.; Nielsen, J.; Bäckhed, F. Assessing the Human Gut Microbiota in Metabolic Diseases. *Diabetes* **2013**, *62*, 3341–3349.
9. Consortium, I.H.G.S. Finishing the euchromatic sequence of the human genome. *Nature* **2004**, *431*, 931.
10. Alfa, M.J.; Strang, D.; Tappia, P.S.; Graham, M.; Van Domselaar, G.; Forbes, J.D.; Laminman, V.; Olson, N.; DeGagne, P.; Bray, D.; et al. A randomized trial to determine the impact of a digestion resistant starch composition on the gut microbiome in older and mid-age adults. *Clin. Nutr.* **2018**, *37*, 797–807.
11. Gaulke, C.A.; Sharpton, T.J. The influence of ethnicity and geography on human gut microbiome composition. *Nat. Med.* **2018**, *24*, 1495–1496.
12. Singh, R.K.; Chang, H.-W.; Yan, D.; Lee, K.M.; Ucmak, D.; Wong, K.; Abrouk, M.; Farahnik, B.; Nakamura, M.; Zhu, T.H.; et al. Influence of diet on the gut microbiome and implications for human health. *J. Transl. Med.* **2017**, *15*, 73.
13. Pasini, E.; Corsetti, G.; Assanelli, D.; Testa, C.; Romano, C.; Dioguardi, F.S.; Aquilani, R. Effects of chronic exercise on gut microbiota and intestinal barrier in human with type 2 diabetes. *Minerva Med.* **2019**, *110*, 3–11.
14. Smith, P.M.; Howitt, M.R.; Panikov, N.; Michaud, M.; Gallini, C.A.; Bohlooly, M.; Glickman, J.N.; Garrett, W.S. The Microbial Metabolites, Short-Chain Fatty Acids, Regulate Colonic Treg Cell Homeostasis. *Science* **2013**, *341*, 569–573.

15. Khosravi, A.; Mazmanian, S.K. Disruption of the gut microbiome as a risk factor for microbial infections. *Curr. Opin. Microbiol.* **2013**, *16*, 221–227.
16. Shreiner, A.B.; Kao, J.Y.; Young, V.B. The gut microbiome in health and in disease. *Curr. Opin. Gastroenterol.* **2015**, *31*, 69–75.
17. Lewis, J.D.; Chen, E.Z.; Baldassano, R.N.; Otley, A.R.; Griffiths, A.M.; Lee, D.; Bittinger, K.; Bailey, A.; Friedman, E.S.; Hoffmann, C.; et al. Inflammation, Antibiotics, and Diet as Environmental Stressors of the Gut Microbiome in Pediatric Crohn's Disease. *Cell Host Microbe* **2015**, *18*, 489–500.
18. Zhao, L.; Lou, H.; Peng, Y.; Chen, S.; Zhang, Y.; Li, X. Comprehensive relationships between gut microbiome and faecal metabolome in individuals with type 2 diabetes and its complications. *Endocrine* **2019**, *66*, 526–537.
19. Jie, Z.; Xia, H.; Zhong, S.-L.; Feng, Q.; Li, S.; Liang, S.; Zhong, H.; Liu, Z.; Gao, Y.; Zhao, H.; et al. The gut microbiome in atherosclerotic cardiovascular disease. *Nat. Commun.* **2017**, *8*, 845.
20. Liu, R.; Hong, J.; Xu, X.; Feng, Q.; Zhang, D.; Gu, Y.; Shi, J.; Zhao, S.; Liu, W.; Wang, X.; et al. Gut microbiome and serum metabolome alterations in obesity and after weight-loss intervention. *Nat. Med.* **2017**, *23*, 859.
21. Shao, L.; Ling, Z.; Chen, D.; Liu, Y.; Yang, F.; Li, L. Disorganized Gut Microbiome Contributed to Liver Cirrhosis Progression: A Meta-Omics-Based Study. *Front. Microbiol.* **2018**, *9*, 3166.
22. Falony, G.; Joossens, M.; Vieira-Silva, S.; Wang, J.; Darzi, Y.; Faust, K.; Kurilshikov, A.; Bonder, M.J.; Valles-Colomer, M.; Vandeputte, D.; et al. Population-level analysis of gut microbiome variation. *Science* **2016**, *352*, 560–564.
23. Peterfreund, G.L.; Vandivier, L.E.; Sinha, R.; Marozsan, A.J.; Olson, W.C.; Zhu, J.; Bushman, F.D. Succession in the Gut Microbiome following Antibiotic and Antibody Therapies for *Clostridium difficile*. *PLoS ONE* **2012**, *7*, e46966.
24. Imhann, F.; Bonder, M.J.; Vila, A.V.; Fu, J.; Mujagic, Z.; Vork, L.; Tigchelaar, E.F.; Jankipersadsing, S.A.; Cenit, M.C.; Harmsen, H.J.M.; et al. Proton pump inhibitors affect the gut microbiome. *Gut* **2015**, *65*, 740–748.
25. Forslund, K.; Hildebrand, F.; Nielsen, T.G.; Falony, G.; Le Chatelier, E.; Sunagawa, S.; Prifti, E.; Vieira-Silva, S.; Gudmundsdottir, V.; Pedersen, H.K.; et al. Disentangling type 2 diabetes and metformin treatment signatures in the human gut microbiota. *Nature* **2015**, *528*, 262–266.
26. Tremaroli, V.; Karlsson, F.H.; Werling, M.; Ståhlman, M.; Kovatcheva-Datchary, P.; Olbers, T.; Fändriks, L.; Le Roux, C.W.; Nielsen, J.; Bäckhed, F. Roux-en-Y Gastric Bypass and Vertical Banded Gastroplasty Induce Long-Term Changes on the Human Gut Microbiome Contributing to Fat Mass Regulation. *Cell Metab.* **2015**, *22*, 228–238.
27. Gentile, C.L.; Weir, T.L. The gut microbiota at the intersection of diet and human health. *Science* **2018**, *362*, 776–780.
28. Noble, D.; Mathur, R.; Dent, T.; Meads, C.; Greenhalgh, T. Risk models and scores for type 2 diabetes: Systematic review. *BMJ* **2011**, *343*, d7163.
29. Roglic, G. WHO Global report on diabetes: A summary. *Int. J. Noncommunicable Dis.* **2016**, *1*, 3.
30. Balakumar, P.; Maung, K.; Jagadeesh, G. Prevalence and prevention of cardiovascular disease and diabetes mellitus. *Pharmacol. Res.* **2016**, *113*, 600–609.
31. Stanislowski, M.A.; Dabelea, D.; Lange, L.A.; Wagner, B.D.; Lozupone, C. Gut microbiota phenotypes of obesity. *NPJ Biofilms Microbiomes* **2019**, *5*, 1–9.
32. Einarson, T.R.; Acs, A.; Ludwig, C.; Panton, U.H. Prevalence of cardiovascular disease in type 2 diabetes: A systematic literature review of scientific evidence from across the world in 2007–2017. *Cardiovasc. Diabetol.* **2018**, *17*, 83.
33. Schmieder, R.E.; Jumar, A.; Fronk, E.M.; Alexandre, A.F.; Bramlage, P. Quality of life and emotional impact of a fixed-dose combination of antihypertensive drugs in patients with uncontrolled hypertension. *J. Clin. Hypertens.* **2017**, *19*, 126–134.
34. Do, A.N.L.; Dagogo-Jack, S. Comorbidities of Diabetes and Hypertension: Mechanisms and Approach to Target Organ Protection. *J. Clin. Hypertens.* **2011**, *13*, 244–251.
35. Sugeran, H.J.; Wolfe, L.G.; Sica, D.A.; Clore, J.N. Diabetes and Hypertension in Severe Obesity and Effects of Gastric Bypass-Induced Weight Loss. *Ann. Surg.* **2003**, *237*, 751–758.
36. Pevsner-Fischer, M.; Blacher, E.; Tatirovsky, E.; Ben-Dov, I.Z.; Elinav, E. The gut microbiome and hypertension. *Curr. Opin. Nephrol. Hypertens.* **2017**, *26*, 1–8.

37. Pasolli, E.; Truong, D.T.; Malik, F.; Waldron, L.; Segata, N. Machine Learning Meta-analysis of Large Metagenomic Datasets: Tools and Biological Insights. *PLoS Comput. Boil.* **2016**, *12*, e1004977.
38. Inoue, R.; Ohue-Kitano, R.; Tsukahara, T.; Tanaka, M.; Masuda, S.; Inoue, T.; Yamakage, H.; Kusakabe, T.; Hasegawa, K.; Shimatsu, A.; et al. Prediction of functional profiles of gut microbiota from 16S rRNA metagenomic data provides a more robust evaluation of gut dysbiosis occurring in Japanese type 2 diabetic patients. *J. Clin. Biochem. Nutr.* **2017**, *61*, 217–221.
39. Zhong, H.; Ren, H.; Lu, Y.; Fang, C.; Hou, G.; Yang, Z.; Chen, B.; Yang, F.; Zhao, Y.; Shi, Z.; et al. Distinct gut metagenomics and metaproteomics signatures in prediabetics and treatment-naïve type 2 diabetics. *EBioMedicine* **2019**, *47*, 373–383.
40. Talley, N.J.; Spiller, R. Irritable bowel syndrome: A little understood organic bowel disease? *Lancet* **2002**, *360*, 555–564.
41. Vila, A.V.; Imhann, F.; Collij, V.; Jankipersadsing, S.A.; Gurry, T.; Mujagic, Z.; Kurilshikov, A.; Bonder, M.J.; Jiang, X.; Tigchelaar, E.F.; et al. Gut microbiota composition and functional changes in inflammatory bowel disease and irritable bowel syndrome. *Sci. Transl. Med.* **2018**, *10*, eaap8914.
42. Jones, C.M.A.; Connors, J.; Dunn, K.A.; Bielawski, J.P.; Comeau, A.M.; Langille, M.G.I.; Van Limbergen, J. Bacterial Taxa and Functions Are Predictive of Sustained Remission Following Exclusive Enteral Nutrition in Pediatric Crohn’s Disease. *Inflamm. Bowel Dis.* **2020**, *26*, 1026–1037.
43. Duranti, S.; Gaiani, F.; Mancabelli, L.; Milani, C.; Grandi, A.; Bolchi, A.; Santoni, A.; Lugli, G.A.; Ferrario, C.; Mangifesta, M.; et al. Elucidating the gut microbiome of ulcerative colitis: Bifidobacteria as novel microbial biomarkers. *FEMS Microbiol. Ecol.* **2016**, *92*, fiw191.
44. Knoll, R.L.; Forslund, K.; Kultima, J.R.; Meyer, C.U.; Kullmer, U.; Sunagawa, S.; Bork, P.; Gehring, S. Gut microbiota differs between children with Inflammatory Bowel Disease and healthy siblings in taxonomic and functional composition: A metagenomic analysis. *Am. J. Physiol. Liver Physiol.* **2017**, *312*, G327–G339.
45. Glass, L.M.; Hunt, C.M.; Fuchs, M.; Su, G.L. Comorbidities and Nonalcoholic Fatty Liver Disease: The Chicken, the Egg, or Both? *Fed. Pract.* **2019**, *36*, 64.
46. Wang, B.; Jiang, X.; Cao, M.; Ge, J.; Bao, Q.; Tang, L.; Chen, Y.; Li, L. Altered Fecal Microbiota Correlates with Liver Biochemistry in Nonobese Patients with Non-alcoholic Fatty Liver Disease. *Sci. Rep.* **2016**, *6*, 32002.
47. Dong, T.S.; Katzka, W.; Lagishetty, V.; Luu, K.; Hauer, M.; Piseigna, J.; Jacobs, J.P. A Microbial Signature Identifies Advanced Fibrosis in Patients with Chronic Liver Disease Mainly Due to NAFLD. *Sci. Rep.* **2020**, *10*, 1–10.
48. Chen, Y.; Ji, F.; Guo, J.; Shi, D.; Fang, D.; Li, L. Dysbiosis of small intestinal microbiota in liver cirrhosis and its association with etiology. *Sci. Rep.* **2016**, *6*, 34055.
49. Ashrafian, H.; Harling, L.; Darzi, A.; Athanasiou, T. Neurodegenerative disease and obesity: What is the role of weight loss and bariatric interventions? *Metab. Brain Dis.* **2013**, *28*, 341–353.
50. Nussbaum, R.L.; Ellis, C.E. Alzheimer’s disease and Parkinson’s disease. *N. Engl. J. Med.* **2003**, *348*, 1356–1364.
51. Hill-Burns, E.M.; Debelius, J.W.; Morton, J.T.; Wissemann, W.T.; Lewis, M.R.; Wallen, Z.D.; Peddada, S.D.; Factor, S.A.; Molho, E.; Zabetian, C.P.; et al. Parkinson’s disease and Parkinson’s disease medications have distinct signatures of the gut microbiome. *Mov. Disord.* **2017**, *32*, 739–749.
52. Petrov, V.A.; Saltykova, I.V.; Zhukova, I.A.; Alifirova, V.M.; Zhukova, N.G.; Dorofeeva, Y.B.; Tyakht, A.V.; Kovarsky, B.A.; Alekseev, D.G.; Kostryukova, E.S.; et al. Analysis of Gut Microbiota in Patients with Parkinson’s Disease. *Bull. Exp. Boil. Med.* **2017**, *162*, 734–737.
53. Vogt, N.M.; Kerby, R.L.; Dill-McFarland, K.A.; Harding, S.J.; Merluzzi, A.P.; Johnson, S.C.; Carlsson, C.M.; Asthana, S.; Zetterberg, H.; Blennow, K.; et al. Gut microbiome alterations in Alzheimer’s disease. *Sci. Rep.* **2017**, *7*, 13537.
54. Haran, J.P.; Bhattarai, S.K.; Foley, S.E.; Dutta, P.; Ward, D.V.; Bucci, V.; McCormick, B.A.; Gilbert, J.; Faith, J. Alzheimer’s Disease Microbiome Is Associated with Dysregulation of the Anti-Inflammatory P-Glycoprotein Pathway. *MBio* **2019**, *10*, e00632-19.
55. Geirnaert, A.; Calatayud, M.; Grootaert, C.; Laukens, D.; Devriese, S.; Smagghe, G.; De Vos, M.; Boon, N.; Van De Wiele, T. Butyrate-producing bacteria supplemented in vitro to Crohn’s disease patient microbiota increased butyrate production and enhanced intestinal epithelial barrier integrity. *Sci. Rep.* **2017**, *7*, 11450.

56. Wu, G.D.; Chen, J.; Hoffmann, C.; Bittinger, K.; Chen, Y.-Y.; Keilbaugh, S.A.; Bewtra, M.; Knights, D.; Walters, W.A.; Knight, R.; et al. Linking Long-Term Dietary Patterns with Gut Microbial Enterotypes. *Science* **2011**, *334*, 105–108.
57. Scher, J.U.; Nayak, R.R.; Ubeda, C.; Turnbaugh, P.J.; Abramson, S.B. Pharmacomicrobiomics in inflammatory arthritis: Gut microbiome as modulator of therapeutic response. *Nat. Rev. Rheumatol.* **2020**, *16*, 282–292.
58. Javdan, B.; Lopez, J.G.; Chankhamjon, P.; Lee, Y.-C.J.; Hull, R.; Wu, Q.; Wang, X.; Chatterjee, S.; Donia, M.S. Personalized Mapping of Drug Metabolism by the Human Gut Microbiome. *Cell* **2020**, *181*, 1661–1679.e22.
59. Dimidi, E.; Cox, S.R.; Rossi, M.; Whelan, K. Fermented Foods: Definitions and Characteristics, Impact on the Gut Microbiota and Effects on Gastrointestinal Health and Disease. *Nutrients* **2019**, *11*, 1806.
60. Li, L.; Abou-Samra, E.; Ning, Z.; Zhang, X.; Mayne, J.; Wang, J.; Cheng, K.; Walker, K.; Stintzi, A.; Figeys, D. An in vitro model maintaining taxon-specific functional activities of the gut microbiome. *Nat. Commun.* **2019**, *10*, 1–11.
61. Schellenberg, E.S.; Dryden, D.M.; VanderMeer, B.; Ha, C.; Korownyk, C. Lifestyle Interventions for Patients With and at Risk for Type 2 Diabetes. *Ann. Intern. Med.* **2013**, *159*, 543–551.
62. Cotillard, A.; Kennedy, S.; Kong, L.C.; Prifti, E.; Pons, N.; Le Chatelier, E.; Almeida, M.; Quinquis, B.; Levenez, F.; Galleron, N.; et al. Dietary intervention impact on gut microbial gene richness. *Nature* **2013**, *500*, 585–588.
63. Rodriguez-Castaño, G.P.; Caro-Quintero, A.; Reyes, A.; Lizcano, F. Advances in Gut Microbiome Research, Opening New Strategies to Cope with a Western Lifestyle. *Front. Genet.* **2017**, *7*, 224.
64. Louis, S.; Tappu, R.M.; Damms-Machado, A.; Huson, D.H.; Bischoff, S.C. Characterization of the gut microbial community of obese patients following a weight-loss intervention using whole metagenome shotgun sequencing. *PLoS ONE* **2016**, *11*, e0149564.
65. Shoelson, S.E.; Lee, J.; Goldfine, A.B. Inflammation and insulin resistance. *J. Clin. Investig.* **2006**, *116*, 1793–1801.
66. Liu, Z.; Liu, H.-Y.; Zhou, H.; Zhan, Q.; Lai, W.; Zeng, Q.; Ren, H.; Xu, D. Moderate-Intensity Exercise Affects Gut Microbiome Composition and Influences Cardiac Function in Myocardial Infarction Mice. *Front. Microbiol.* **2017**, *8*, 1687.
67. Klepser, T.B.; Kelly, M.W. Metformin hydrochloride: An antihyperglycemic agent. *Am. J. Heal. Pharm.* **1997**, *54*, 893–903.
68. Madiraju, A.K.; Erion, D.M.; Rahimi, Y.; Zhang, X.-M.; Braddock, D.T.; Albright, R.A.; Prigaro, B.J.; Wood, J.L.; Bhanot, S.; Macdonald, M.J.; et al. Metformin suppresses gluconeogenesis by inhibiting mitochondrial glycerophosphate dehydrogenase. *Nature* **2014**, *510*, 542–546.
69. Musi, N.; Hirshman, M.F.; Nygren, J.; Svanfeldt, M.; Bavenholm, P.; Rooyackers, O.; Zhou, G.; Williamson, J.M.; Ljunqvist, O.; Efendic, S.; et al. Metformin increases AMP-activated protein kinase activity in skeletal muscle of subjects with type 2 diabetes. *Diabetes* **2002**, *51*, 2074–2081.
70. Bryrup, T.; Thomsen, C.W.; Kern, T.; Allin, K.H.; Brandslund, I.; Jørgensen, N.R.; Vestergaard, H.; Hansen, T.; Hansen, T.H.; Pedersen, O.; et al. Metformin-induced changes of the gut microbiota in healthy young men: Results of a non-blinded, one-armed intervention study. *Diabetologia* **2019**, *62*, 1024–1035.
71. Ejtahed, H.-S.; Tito, R.Y.; Siadat, S.-D.; Hasani-Ranjbar, S.; Hoseini-Tavassol, Z.; Rymenans, L.; Verbeke, K.; Soroush, A.R.; Raes, J.; Larijani, B. Metformin induces weight loss associated with gut microbiota alteration in non-diabetic obese women: A randomized double-blind clinical trial. *Eur. J. Endocrinol.* **2019**, *180*, 165–176.
72. Wu, H.; Esteve, E.; Tremaroli, V.; Khan, M.T.; Caesar, R.; Mannerås-Holm, L.; Ståhlman, M.; Olsson, L.M.; Serino, M.; Planas-Fèlix, M.; et al. Metformin alters the gut microbiome of individuals with treatment-naive type 2 diabetes, contributing to the therapeutic effects of the drug. *Nat. Med.* **2017**, *23*, 850.
73. Insull, W., Jr. The Pathology of Atherosclerosis: Plaque Development and Plaque Responses to Medical Treatment. *Am. J. Med.* **2009**, *122*, S3–S14.
74. Maron, D.J.; Fazio, S.; Linton, M.F. Current perspectives on statins. *Circulation* **2000**, *101*, 207–213.
75. Young, S.G.; Fong, L.G. Lowering Plasma Cholesterol by Raising LDL Receptors—Revisited. *N. Engl. J. Med.* **2012**, *366*, 1154.
76. Lee, S.E.; Han, K.; Kang, Y.M.; Kim, S.-O.; Cho, Y.K.; Ko, K.S.; Park, J.-Y.; Lee, K.-U.; Koh, E.H.; on Behalf of the Taskforce Team of Diabetes Fact Sheet of the Korean Diabetes Association. Trends in the prevalence

- of metabolic syndrome and its components in South Korea: Findings from the Korean National Health Insurance Service Database (2009–2013). *PLoS ONE* **2018**, *13*, e0194490.
77. Vieira-Silva, S.; Falony, G.; Belda, E.; Nielsen, T.G.; Aron-Wisnewsky, J.; Chakaroun, R.; Forslund, S.K.; Assmann, K.; Valles-Colomer, M.; Nguyen, T.T.D.; et al. Statin therapy is associated with lower prevalence of gut microbiota dysbiosis. *Nature* **2020**, *581*, 310–315.
  78. Vila, A.V.; Collij, V.; Sanna, S.; Sinha, T.; Imhann, F.; Bourgonje, A.R.; Mujagic, Z.; Jonkers, D.M.A.E.; Masclee, A.A.M.; Fu, J.; et al. Impact of commonly used drugs on the composition and metabolic function of the gut microbiota. *Nat. Commun.* **2020**, *11*, 1–11.
  79. Liu, J.; LaHousse, L.; Nivard, M.G.; Bot, M.; Chen, L.; Van Klinken, J.B.; Thesing, C.S.; Beekman, M.; Akker, E.B.V.D.; Sliker, R.C.; et al. Integration of epidemiologic, pharmacologic, genetic and gut microbiome data in a drug–metabolite atlas. *Nat. Med.* **2020**, *26*, 110–117.
  80. Clooney, A.G.; Bernstein, C.N.; Leslie, W.D.; Vagianos, K.; Sargent, M.; Laserna-Mendieta, E.J.; Claesson, M.J.; Targownik, L.E. A comparison of the gut microbiome between long-term users and non-users of proton pump inhibitors. *Aliment. Pharmacol. Ther.* **2016**, *43*, 974–984.
  81. Aron-Wisnewsky, J.; Prifti, E.; Belda, E.; Ichou, F.; Kayser, B.D.; Dao, M.C.; Verger, E.; Hedjazi, L.; Bouillot, J.-L.; Chevallier, J.-M.; et al. Major microbiota dysbiosis in severe obesity: Fate after bariatric surgery. *Gut* **2018**, *68*, 70–82.
  82. Graessler, J.; Qin, Y.; Zhong, H.; Zhang, J.; Licinio, J.; Wong, M.L.; Xu, A.; Chavakis, T.; Bornstein, A.B.; Ehrhart-Bornstein, M.; et al. Metagenomic sequencing of the human gut microbiome before and after bariatric surgery in obese patients with type 2 diabetes: Correlation with inflammatory and metabolic parameters. *Pharm. J.* **2013**, *13*, 514–522.
  83. Pallejà, A.; Kashani, A.; Allin, K.H.; Nielsen, T.G.; Zhang, C.; Li, Y.; Brach, T.; Liang, S.; Feng, Q.; Jørgensen, N.B.; et al. Roux-en-Y gastric bypass surgery of morbidly obese patients induces swift and persistent changes of the individual gut microbiota. *Genome Med.* **2016**, *8*, 67.
  84. Lee, C.J.; Florea, L.; Sears, C.L.; Maruthur, N.; Potter, J.J.; Schweitzer, M.; Magnuson, T.; Clark, J.M. Changes in Gut Microbiome after Bariatric Surgery Versus Medical Weight Loss in a Pilot Randomized Trial. *Obes. Surg.* **2019**, *29*, 3239–3245.
  85. Murphy, R.; Tsai, P.; Jüllig, M.; Liu, A.; Krebs, J.D.; Booth, M. Differential Changes in Gut Microbiota after Gastric Bypass and Sleeve Gastrectomy Bariatric Surgery Vary According to Diabetes Remission. *Obes. Surg.* **2016**, *27*, 917–925.
  86. Ülker, I.; Yildiran, H. The effects of bariatric surgery on gut microbiota in patients with obesity: A review of the literature. *Biosci. Microbiota Food Health* **2018**, *38*, 3–9.
  87. Al Assal, K.; Prifti, E.; Belda, E.; Sala, P.C.; Clemént, K.; Dao, M.-C.; Doré, J.; Levenez, F.; Taddei, C.R.; Fonseca, D.C.; et al. Gut Microbiota Profile of Obese Diabetic Women Submitted to Roux-en-Y Gastric Bypass and Its Association with Food Intake and Postoperative Diabetes Remission. *Nutrients* **2020**, *12*, 278.
  88. Soletsky, B.; Feig, D.I. Uric Acid Reduction Rectifies Prehypertension in Obese Adolescents. *Hypertension* **2012**, *60*, 1148–1156.
  89. Karlsson, F.H.; Fåk, F.; Nookaew, I.; Tremaroli, V.; Fagerberg, B.; Petranovic, D.; Bäckhed, F.; Nielsen, J. Symptomatic atherosclerosis is associated with an altered gut metagenome. *Nat. Commun.* **2012**, *3*, 1245.
  90. Kampoli, A.-M.; Tousoulis, D.; Antoniadis, C.; Siasos, G.; Stefanadis, C. Biomarkers of premature atherosclerosis. *Trends Mol. Med.* **2009**, *15*, 323–332.
  91. Bhole, V.; Choi, J.W.J.; Kim, S.W.; De Vera, M.; Choi, H. Serum Uric Acid Levels and the Risk of Type 2 Diabetes: A Prospective Study. *Am. J. Med.* **2010**, *123*, 957–961.
  92. Chakraborty, A.; Chowdhury, S.; Bhattacharyya, M. Effect of metformin on oxidative stress, nitrosative stress and inflammatory biomarkers in type 2 diabetes patients. *Diabetes Res. Clin. Pract.* **2011**, *93*, 56–62.
  93. Fernández-Bergés, D.; Consuegra-Sanchez, L.; Penafiel, J.; De León, A.C.; Vila, J.; Félix-Redondo, F.J.; Segura-Fragoso, A.; Lapetra, J.; Guembe, M.J.; Vega, T.; et al. Metabolic and Inflammatory Profiles of Biomarkers in Obesity, Metabolic Syndrome, and Diabetes in a Mediterranean Population. DARIOS Inflammatory Study. *Revista Española de Cardiología (Engl. Ed.)* **2014**, *67*, 624–631.
  94. Pouliot, M.-C.; Després, J.-P.; Nadeau, A.; Moorjani, S.; Prud'Homme, D.; Lupien, P.J.; Tremblay, A.; Bouchard, C. Visceral Obesity in Men: Associations with Glucose Tolerance, Plasma Insulin, and Lipoprotein Levels. *Diabetes* **1992**, *41*, 826–834.

95. Jennis, M.; Cavanaugh, C.R.; Leo, G.C.; Mabus, J.R.; Lenhard, J.; Hornby, P.J. Microbiota-derived tryptophan indoles increase after gastric bypass surgery and reduce intestinal permeability in vitro and in vivo. *Neurogastroenterol. Motil.* **2017**, *30*, e13178.
96. Cason, C.A.; Dolan, K.T.; Sharma, G.; Tao, M.; Kulkarni, R.; Helenowski, I.B.; Doane, B.M.; Avram, M.J.; McDermott, M.M.; Chang, E.B.; et al. Plasma microbiome-modulated indole- and phenyl-derived metabolites associate with advanced atherosclerosis and postoperative outcomes. *J. Vasc. Surg.* **2017**, *68*, 1552–1562.e7.
97. Monteleone, I.; Rizzo, A.; Sarra, M.; Sica, G.; Sileri, P.; Biancone, L.; Macdonald, T.T.; Pallone, F.; Monteleone, G. Aryl Hydrocarbon Receptor-Induced Signals Up-regulate IL-22 Production and Inhibit Inflammation in the Gastrointestinal Tract. *Gastroenterology* **2011**, *141*, 237–248.e1.
98. Kadow, S.; Jux, B.; Zahner, S.P.; Wingerath, B.; Chmill, S.; Clausen, B.E.; Hengstler, J.G.; Esser, C. Aryl Hydrocarbon Receptor Is Critical for Homeostasis of Invariant  $\gamma\delta$  T Cells in the Murine Epidermis. *J. Immunol.* **2011**, *187*, 3104–3110.
99. Shah, S.H.; Bain, J.; Muehlbauer, M.J.; Stevens, R.D.; Crosslin, D.R.; Haynes, C.; Dungan, J.; Newby, L.K.; Hauser, E.R.; Ginsburg, G.S.; et al. Association of a Peripheral Blood Metabolic Profile with Coronary Artery Disease and Risk of Subsequent Cardiovascular Events. *Circ. Cardiovasc. Genet.* **2010**, *3*, 207–214.
100. Okeunle, A.P.; Li, Y.; Liu, L.; Du, S.; Wu, X.; Chen, Y.; Li, Y.; Qi, J.; Sun, C.-H.; Feng, R. Abnormal circulating amino acid profiles in multiple metabolic disorders. *Diabetes Res. Clin. Pract.* **2017**, *132*, 45–58.
101. Mangge, H.; Zelzer, S.; Prueller, F.; Schnedl, W.J.; Weghuber, D.; Enko, D.; Bergsten, P.; Haybaeck, J.; Meinitzer, A. Branched-chain amino acids are associated with cardiometabolic risk profiles found already in lean, overweight and obese young. *J. Nutr. Biochem.* **2016**, *32*, 123–127.
102. Lee, J.; Jung, S.; Kim, N.; Shin, M.-J.; Ryu, D.H.; Hwang, G.-S. Myocardial metabolic alterations in mice with diet-induced atherosclerosis: Linking sulfur amino acid and lipid metabolism. *Sci. Rep.* **2017**, *7*, 13597.
103. Zhao, L.; Zhang, F.; Ding, X.; Wu, G.; Lam, Y.Y.; Wang, X.; Fu, H.; Xue, X.; Lu, C.; Ma, J.; et al. Gut bacteria selectively promoted by dietary fibers alleviate type 2 diabetes. *Science* **2018**, *359*, 1151–1156.
104. Kim, K.-N.; Yao, Y.; Ju, S.-Y. Short Chain Fatty Acids and Fecal Microbiota Abundance in Humans with Obesity: A Systematic Review and Meta-Analysis. *Nutrients* **2019**, *11*, 2512.
105. Lefebvre, P.; Cariou, B.; Lien, F.; Kuipers, F.; Staels, B. Role of Bile Acids and Bile Acid Receptors in Metabolic Regulation. *Physiol. Rev.* **2009**, *89*, 147–191.
106. Miettinen, T.A.; Gylling, H. Cholesterol absorption efficiency and sterol metabolism in obesity. *Atherosclerosis* **2000**, *153*, 241–248.
107. Charach, G.; Rabinovich, A.; Argov, O.; Weintraub, M.; Rabinovich, P. The Role of Bile Acid Excretion in Atherosclerotic Coronary Artery Disease. *Int. J. Vasc. Med.* **2012**, *2012*, 949672.
108. Hofmann, A.F. Bile Acids: The Good, the Bad, and the Ugly. *Physiology* **1999**, *14*, 24–29.
109. Gregorio, F.; Ambrosi, F.; Filippini, P.; Manfrini, S.; Testa, I. Is metformin safe enough for ageing type 2 diabetic patients? *Diabetes Metab.* **1996**, *22*, 43–50.
110. Pihlajamäki, J.; Grönlund, S.; Simonen, M.; Käkälä, P.; Moilanen, L.; Pääkkönen, M.; Pirinen, E.; Kolehmainen, M.; Kärjä, V.; Kainulainen, S.; et al. Cholesterol absorption decreases after Roux-en-Y gastric bypass but not after gastric banding. *Metabolism* **2010**, *59*, 866–872.
111. Furet, J.-P.; Kong, L.-C.; Tap, J.; Poitou, C.; Basdevant, A.; Bouillot, J.-L.; Mariat, D.; Corthier, G.; Doré, J.; Henegar, C.; et al. Differential Adaptation of Human Gut Microbiota to Bariatric Surgery-Induced Weight Loss: Links with Metabolic and Low-Grade Inflammation Markers. *Diabetes* **2010**, *59*, 3049–3057.
112. Oberbach, A.; Neuhaus, J.; Inge, T.; Kirsch, K.; Schlichting, N.; Blüher, S.; Kullnick, Y.; Kugler, J.; Baumann, S.; Till, H. Bariatric surgery in severely obese adolescents improves major comorbidities including hyperuricemia. *Metabolism* **2014**, *63*, 242–249.
113. Alfaras, I.; Mitchell, S.J.; Mora, H.; Lugo, D.R.; Warren, A.; Navas-Enamorado, I.; Hoffmann, V.; Hine, C.; Mitchell, J.R.; Le Couteur, D.G.; et al. Health benefits of late-onset metformin treatment every other week in mice. *NPJ Aging Mech. Dis.* **2017**, *3*, 16.
114. Simonen, M.; Dali-Youcef, N.; Kaminska, D.; Venesmaa, S.; Kakela, P.; Pääkkönen, M.; Hallikainen, M.; Kolehmainen, M.; Uusitupa, M.; Moilanen, L.; et al. Conjugated bile acids associate with altered rates of glucose and lipid oxidation after Roux-en-Y gastric bypass. *Obes. Surg.* **2012**, *22*, 1473–1480.
115. McCreight, L.J.; Bailey, C.J.; Pearson, E.R. Metformin and the gastrointestinal tract. *Diabetologia* **2016**, *59*, 426–435.

116. Wijayatunga, N.N.; Sams, V.G.; Dawson, J.A.; Mancini, M.L.; Mancini, G.J.; Moustaid-Moussa, N. Roux-en-Y gastric bypass surgery alters serum metabolites and fatty acids in patients with morbid obesity. *Diabetes Metab. Res. Rev.* **2018**, *34*, e3045.
117. Preiss, D.; Rankin, N.; Welsh, P.; Holman, R.R.; Kangas, A.J.; Soininen, P.; Würtz, P.; Ala-Korpela, M.; Sattar, N. Effect of metformin therapy on circulating amino acids in a randomized trial: The CAMERA study. *Diabet. Med.* **2016**, *33*, 1569–1574.
118. Martinez, K.B.; Mackert, J.D.; McIntosh, M.K. Polyphenols and intestinal health. In *Nutrition and Functional Foods for Healthy Aging*; Elsevier: Amsterdam, The Netherlands, 2017; pp. 191–210.
119. Subramanian, I.; Verma, S.; Kumar, S.; Jere, A.; Anamika, K. Multi-omics Data Integration, Interpretation, and Its Application. *Bioinform. Boil. Insights* **2020**, *14*, 1177932219899051.
120. Karlsson, F.H.; Nookaew, I.; Petranovic, D.; Nielsen, J. Prospects for systems biology and modeling of the gut microbiome. *Trends Biotechnol.* **2011**, *29*, 251–258.
121. Mardinoglu, A.; Borén, J.; Smith, U.; Uhlén, M.; Nielsen, J. Systems biology in hepatology: Approaches and applications. *Nat. Rev. Gastroenterol. Hepatol.* **2018**, *15*, 365–377.
122. Green, S.; Şerban, M.; Scholl, R.; Jones, N.; Brigandt, I.; Bechtel, W. Network analyses in systems biology: New strategies for dealing with biological complexity. *Synthese* **2017**, *195*, 1751–1777.
123. Hill, C.B.; Czauderna, T.; Klapperstück, M.; Roessner, U.; Schreiber, F. Metabolomics, Standards, and Metabolic Modeling for Synthetic Biology in Plants. *Front. Bioeng. Biotechnol.* **2015**, *3*, 167.
124. O'Brien, E.J.; Monk, J.; Palsson, B.O. Using Genome-scale Models to Predict Biological Capabilities. *Cell* **2015**, *161*, 971–987.
125. Våremo, L.; Nookaew, I.; Nielsen, J. Novel insights into obesity and diabetes through genome-scale metabolic modeling. *Front. Physiol.* **2013**, *4*, 92.
126. Ghaffari, P.; Mardinoglu, A.; Asplund, A.; Shoaie, S.; Kampf, C.; Uhlen, M.; Nielsen, J. Identifying anti-growth factors for human cancer cell lines through genome-scale metabolic modeling. *Sci. Rep.* **2015**, *5*, 8183.
127. Magnúsdóttir, S.; Heinken, A.; Kutt, L.; Ravcheev, D.A.; Bauer, E.; Noronha, A.; Greenhalgh, K.; Jäger, C.; Baginska, J.; Wilmes, P.; et al. Generation of genome-scale metabolic reconstructions for 773 members of the human gut microbiota. *Nat. Biotechnol.* **2016**, *35*, 81.
128. Zomorodi, A.R.; Maranas, C.D. OptCom: A Multi-Level Optimization Framework for the Metabolic Modeling and Analysis of Microbial Communities. *PLoS Comput. Boil.* **2012**, *8*, e1002363.
129. Shoaie, S.; Karlsson, F.H.; Mardinoglu, A.; Nookaew, I.; Bordel, S.; Nielsen, J. Understanding the interactions between bacteria in the human gut through metabolic modeling. *Sci. Rep.* **2013**, *3*, 2532.
130. Shoaie, S.; Ghaffari, P.; Kovatcheva-Datchary, P.; Mardinoglu, A.; Sen, P.; Pujos-Guillot, E.; De Wouters, T.; Juste, C.; Rizkalla, S.; Chilloux, J.; et al. Quantifying Diet-Induced Metabolic Changes of the Human Gut Microbiome. *Cell Metab.* **2015**, *22*, 320–331.
131. Brunk, E.; Sahoo, S.; Zielinski, D.C.; Altunkaya, A.; Dräger, A.; Mih, N.; Gatto, F.; Nilsson, A.; Le, H.M.; Aurich, M.K.; et al. Recon3D enables a three-dimensional view of gene variation in human metabolism. *Nat. Biotechnol.* **2018**, *36*, 272.
132. Heinken, A.; Sahoo, S.; Fleming, R.M.T.; Thiele, I. Systems-level characterization of a host-microbe metabolic symbiosis in the mammalian gut. *Gut Microbes* **2013**, *4*, 28–40.
133. Baldini, F.; Heinken, A.; Heirendt, L.; Magnúsdóttir, S.; Fleming, R.M.T.; Thiele, I. The Microbiome Modeling Toolbox: From microbial interactions to personalized microbial communities. *Bioinformatics* **2018**, *35*, 2332–2334.

