

References

1. Funkhouser LJ, Bordenstein SR (2013) Mom knows best: the universality of maternal microbial transmission. *PLoS Biol* 11: e1001631
2. Jimenez E, Fernandez L, Marin ML et al. (2005) Isolation of commensal bacteria from umbilical cord blood of healthy neonates born by cesarean section. *Curr Microbiol* 51: 270–274
3. Aagaard K, Ma J, Antony KM et al. (2014) The placenta harbors a unique microbiome. *Sci Transl Med* 6: 237ra265
4. Jimenez E, Marin ML, Martin R et al. (2008) Is meconium from healthy newborns actually sterile? *Res Microbiol* 159: 187–193
5. Rautava S, Kainonen E, Salminen S et al. (2012) Maternal probiotic supplementation during pregnancy and breast-feeding reduces the risk of eczema in the infant. *J Allergy Clin Immunol* 130: 1355–1360
6. Palmer C, Bik EM, Duglio DB et al. (2007) Development of the Human Infant Intestinal Microbiota. *PLoS Biol* 5: e177
7. Favier CF, Vaughan EE, De Vos WM et al. (2002) Molecular monitoring of succession of bacterial communities in human neonates. *Appl Environ Microbiol* 68: 219–226
8. La Rosa PS, Warner BB, Zhou Y et al. (2014) Patterned progression of bacterial populations in the premature infant gut. *Proc Natl Acad Sci U S A* 111: 12522–12527
9. Qin J, Li R, Raes J et al. (2010) A human gut microbial gene catalogue established by metagenomic sequencing. *Nature* 464: 59–65
10. Turnbaugh PJ, Hamady M, Yatsunenko T et al. (2009) A core gut microbiome in obese and lean twins. *Nature* 457: 480–484
11. Heseker (2014) Ein Mix gesunder Fasern: Systematik und Eigenschaften der Ballaststoffe. *Aktuel Ernahrungsmed* 39, Supplement 1: S2–S4
12. Gill SR, Pop M, Debey RT et al. (2006) Metagenomic analysis of the human distal gut microbiome. *Science* 312: 1355–1359
13. Gibson GR, Cummings JH, Macfarlane GT et al. (1990) Alternative pathways for hydrogen disposal during fermentation in the human colon. *Gut* 31: 679–683
14. Sommer F, Adam N, Johansson ME et al. (2014) Altered mucus glycosylation in core 1 O-glycan-deficient mice affects microbiota composition and intestinal architecture. *PLoS One* 9: e85254
15. Juge N (2012) Microbial adhesins to gastrointestinal mucus. *Trends Microbiol* 20: 30–39
16. Derrien M, Collado MC, Ben-Amor K et al. (2008) The Mucin degrader Akkermansia muciniphila is an abundant resident of the human intestinal tract. *Appl Environ Microbiol* 74: 1646–1648
17. Collado MC, Derrien M, Isolauri E et al. (2007) Intestinal integrity and Akkermansia muciniphila, a mucin-degrading member of the intestinal microbiota present in infants, adults, and the elderly. *Appl Environ Microbiol* 73: 7767–7770
18. Everard A, Belzer C, Geurts L et al. (2013) Cross-talk between Akkermansia muciniphila and intestinal epithelium controls diet-induced obesity. *Proc Natl Acad Sci U S A* 110: 9066–9071
19. Berry D, Stecher B, Schintlmeister A et al. (2013) Host-compound foraging by intestinal microbiota revealed by single-cell stable isotope probing. *Proc Natl Acad Sci U S A* 110: 4720–4725
20. Macfarlane GT, Gibson GR, Cummings JH (1992) Comparison of fermentation reactions in different regions of the human colon. *J Appl Bacteriol* 72: 57–64
21. Smith EA, Macfarlane GT (1997) Dissimilatory amino Acid metabolism in human colonic bacteria. *Anaerobe* 3: 327–337
22. Macpherson AJ, Harris NL (2004) Interactions between commensal intestinal bacteria and the immune system. *Nat Rev Immunol* 4: 478–485
23. Hansson GC, Johansson ME (2010) The inner of the two Muc2 mucin-dependent mucus layers in colon is devoid of bacteria. *Gut Microbes* 1: 51–54
24. Hooper LV, Stappenbeck TS, Hong CV et al. (2003) Angiogenins: a new class of microbicidal proteins involved in innate immunity. *Nat Immunol* 4: 269–273
25. Ayabe T, Satchell DP, Wilson CL et al. (2000) Secretion of microbicidal alpha-defensins by intestinal Paneth cells in response to bacteria. *Nat Immunol* 1: 113–118
26. Cash HL, Whitham CV, Behrendt CL et al. (2006) Symbiotic bacteria direct expression of an intestinal bactericidal lectin. *Science* 313: 1126–1130
27. Atarashi K, Tanoue T, Oshima K et al. (2013) Treg induction by a rationally selected mixture of Clostridia strains from the human microbiota. *Nature* 500: 232–236
28. Mutius E (2007) Allergies, infections and the hygiene hypothesis – the epidemiological evidence. *Immunobiology* 212: 433–439
29. Olszak T, An D, Zeissig S et al. (2012) Microbial exposure during early life has persistent effects on natural killer T cell function. *Science* 336: 489–493
30. Takeuchi O, Akira S (2010) Pattern recognition receptors and inflammation. *Cell* 140: 805–820
31. Macpherson AJ, Uhr T (2004) Induction of protective IgA by intestinal dendritic cells carrying commensal bacteria. *Science* 303: 1662–1665
32. van der Waaij LA, Limburg PC, Mesander G et al. (1996) In vivo IgA coating of anaerobic bacteria in human faeces. *Gut* 38: 348–354
33. Brandtzaeg P (2013) Secretory IgA: Designed for Anti-Microbial Defense. *Front Immunol* 4: 222
34. Molodecky NA, Soon IS, Rabi DM et al. (2012) Increasing incidence and prevalence of the inflammatory bowel diseases with time, based on systematic review. *Gastroenterology* 142: 46–54 e42; quiz e30
35. Hold GL, Smith M, Grange C et al. (2014) Role of the gut microbiota in inflammatory bowel disease pathogenesis: what have we learnt in the past 10 years? *World J Gastroenterol* 20: 1192–1210
36. Manichanh C, Rigottier-Gois L, Bonnaffon E et al. (2006) Reduced diversity of faecal microbiota in Crohn's disease revealed by a metagenomic approach. *Gut* 55: 205–211
37. Frank DN, St Amand AL, Feldman RA et al. (2007) Molecular-phylogenetic characterization of microbial community imbalances in human inflammatory bowel diseases. *Proc Natl Acad Sci U S A* 104: 13780–13785
38. Wohlgemuth S, Haller D, Blaut M et al. (2009) Reduced microbial diversity and high numbers of one single *Escherichia coli* strain in the intestine of colitic mice. *Environ Microbiol* 11: 1562–1571
39. Sokol H, Seksik P, Furet JP et al. (2009) Low counts of *Faecalibacterium prausnitzii* in colitis microbiota. *Inflamm Bowel Dis* 15: 1183–1189
40. Joossens M, Huys G, Cnockaert M et al. (2011) Dysbiosis of the faecal microbiota in patients with Crohn's disease and their unaffected relatives. *Gut* 60: 631–637
41. Sokol H, Pigneux B, Watterlot L et al. (2008) *Faecalibacterium prausnitzii* is an anti-inflammatory commensal bacterium

- identified by gut microbiota analysis of Crohn disease patients. *Proc Natl Acad Sci U S A* 105: 16731–16736
42. Quevrain E, Maubert MA, Michon C et al. (2015) Identification of an anti-inflammatory protein from *Faecalibacterium prausnitzii*, a commensal bacterium deficient in Crohn's disease. *Gut*: doi: 10.1136/gutjnl-2014-307649. [Epub ahead of print]
43. Singh N, Gurav A, Sivaprakasam S et al. (2014) Activation of Gpr109a, receptor for niacin and the commensal metabolite butyrate, suppresses colonic inflammation and carcinogenesis. *Immunity* 40: 128–139
44. Darfeuille-Michaud A, Neut C, Barnich N et al. (1998) Presence of adherent *Escherichia coli* strains in ileal mucosa of patients with Crohn's disease. *Gastroenterology* 115: 1405–1413
45. Schumann S, Alpert C, Engst W et al. (2013) Mild gut inflammation modulates the proteome of intestinal *Escherichia coli*. *Environ Microbiol* 16: 2966–2979
46. Schumann S, Alpert C, Engst W et al. (2012) Dextran sodium sulfate-induced inflammation alters the expression of proteins by intestinal *Escherichia coli* strains in a gnotobiotic mouse model. *Appl Environ Microbiol* 78: 1513–1522
47. Darfeuille-Michaud A, Boudeau J, Bulois P et al. (2004) High prevalence of adherent-invasive *Escherichia coli* associated with ileal mucosa in Crohn's disease. *Gastroenterology* 127: 412–421
48. Gradel KO, Nielsen HL, Schonheyder HC et al. (2009) Increased short- and long-term risk of inflammatory bowel disease after salmonella or campylobacter gastroenteritis. *Gastroenterology* 137: 495–501
49. Gevers D, Kugathasan S, Denson LA et al. (2014) The treatment-naïve microbiome in new-onset Crohn's disease. *Cell Host Microbe* 15: 382–392
50. Asakura H, Suzuki K, Kitahora T et al. (2008) Is there a link between food and intestinal microbes and the occurrence of Crohn's disease and ulcerative colitis? *J Gastroenterol Hepatol* 23: 1794–1801
51. Kuhn R, Lohler J, Rennick D et al. (1993) Interleukin-10-deficient mice develop chronic enterocolitis. *Cell* 75: 263–274
52. Devkota S, Wang Y, Musch MW et al. (2012) Dietary-fat-induced taurocholic acid promotes pathobiont expansion and colitis in *Il10*-/- mice. *Nature* 487: 104–108
53. Ley RE, Backhed F, Turnbaugh P et al. (2005) Obesity alters gut microbial ecology. *Proc Natl Acad Sci U S A* 102: 11070–11075
54. Ley RE, Turnbaugh PJ, Klein S et al. (2006) Human gut microbes associated with obesity. *Nature* 444: 1022–1023
55. David LA, Maurice CF, Carmody RN et al. (2014) Diet rapidly and reproducibly alters the human gut microbiome. *Nature* 505: 559–563
56. Islam KB, Fukuya S, Hagio M et al. (2011) Bile acid is a host factor that regulates the composition of the cecal microbiota in rats. *Gastroenterology* 141: 1773–1781
57. Turnbaugh PJ, Ley RE, Mahowald MA et al. (2006) An obesity-associated gut microbiome with increased capacity for energy harvest. *Nature* 444: 1027–1031
58. Turnbaugh PJ, Backhed F, Fulton L et al. (2008) Diet-induced obesity is linked to marked but reversible alterations in the mouse distal gut microbiome. *Cell Host Microbe* 3: 213–223
59. Turnbaugh PJ, Ridaura VK, Faith JJ et al. (2009) The effect of diet on the human gut microbiome: a metagenomic analysis in humanized gnotobiotic mice. *Sci Transl Med* 1: 6ra14
60. Backhed F, Ding H, Wang T et al. (2004) The gut microbiota as an environmental factor that regulates fat storage. *Proc Natl Acad Sci U S A* 101: 15718–15723
61. Ridaura VK, Faith JJ, Rey FE et al. (2013) Gut microbiota from twins discordant for obesity modulate metabolism in mice. *Science* 341: 1241214
62. DiBaise JK, Zhang H, Crowell MD et al. (2008) Gut microbiota and its possible relationship with obesity. *Mayo Clin Proc* 83: 460–469
63. Cani PD, Amar J, Iglesias MA et al. (2007) Metabolic endotoxemia initiates obesity and insulin resistance. *Diabetes* 56: 1761–1772
64. Slavin JL (2005) Dietary fiber and body weight. *Nutrition* 21: 411–418
65. Schwietz A, Taras D, Schafer K et al. (2010) Microbiota and SCFA in lean and overweight healthy subjects. *Obesity (Silver Spring)* 18: 190–195
66. Teixeira TF, Grzeskowiak L, Franceschini SC et al. (2013) Higher level of faecal SCFA in women correlates with metabolic syndrome risk factors. *Br J Nutr* 109: 914–919
67. Duncan SH, Belenguer A, Holtrop G et al. (2007) Reduced dietary intake of carbohydrates by obese subjects results in decreased concentrations of butyrate and butyrate-producing bacteria in feces. *Appl Environ Microbiol* 73: 1073–1078
68. Brown AJ, Goldsworthy SM, Barnes AA et al. (2003) The Orphan G protein-coupled receptors GPR41 and GPR43 are activated by propionate and other short chain carboxylic acids. *J Biol Chem* 278: 11312–11319
69. Tazoe H, Otomo Y, Kaji I et al. (2008) Roles of short-chain fatty acids receptors, GPR41 and GPR43 on colonic functions. *J Physiol Pharmacol* 59 Suppl 2: 251–262
70. Tolhurst G, Heffron H, Lam YS et al. (2012) Short-chain fatty acids stimulate glucagon-like peptide-1 secretion via the G-protein-coupled receptor FFAR2. *Diabetes* 61: 364–371
71. Xiong Y, Miyamoto N, Shibata K et al. (2004) Short-chain fatty acids stimulate leptin production in adipocytes through the G protein-coupled receptor GPR41. *Proc Natl Acad Sci U S A* 101: 1045–1050
72. Turton MD, O'Shea D, Gunn I et al. (1996) A role for glucagon-like peptide-1 in the central regulation of feeding. *Nature* 379: 69–72
73. Batterham RL, Cowley MA, Small CJ et al. (2002) Gut hormone PYY(3-36) physiologically inhibits food intake. *Nature* 418: 650–654
74. Friedman JM, Halaas JL (1998) Leptin and the regulation of body weight in mammals. *Nature* 395: 763–770
75. Lin HC, Neevel C, Chen JH (2004) Slowing intestinal transit by PYY depends on serotonergic and opioid pathways. *Am J Physiol Gastrointest Liver Physiol* 286: G558–563
76. Samuel BS, Shaito A, Motoike T et al. (2008) Effects of the gut microbiota on host adiposity are modulated by the short-chain fatty-acid binding G protein-coupled receptor, Gpr41. *Proc Natl Acad Sci U S A* 105: 16767–16772
77. De Vadder F, Kovatcheva-Datchary P, Goncalves D et al. (2014) Microbiota-generated metabolites promote metabolic benefits via gut-brain neural circuits. *Cell* 156: 84–96
78. Wang A, Si H, Liu D et al. (2012) Butyrate activates the cAMP-protein kinase A-cAMP response element-binding protein signaling pathway in Caco-2 cells. *J Nutr* 142: 1–6
79. Chambers ES, Viardot A, Psichas A et al. (2014) Effects of targeted delivery of propi-

- onate to the human colon on appetite regulation, body weight maintenance and adiposity in overweight adults. *Gut*: doi: 10.1136/gutjnl-2014-307913. Epub 2014 Dec 10
80. Fleissner CK, Huebel N, Abd El-Bary MM et al. (2010) Absence of intestinal microbiota does not protect mice from diet-induced obesity. *Br J Nutr* 104: 919–929
 81. Blaut M, Klaus S (2012) Intestinal microbiota and obesity. *Handb Exp Pharmacol*: 251–273
 82. Creely SJ, McTernan PG, Kusminski CM et al. (2007) Lipopolysaccharide activates an innate immune system response in human adipose tissue in obesity and type 2 diabetes. *Am J Physiol Endocrinol Metab* 292: E740–747
 83. Medzhitov R (2001) Toll-like receptors and innate immunity. *Nat Rev Immunol* 1: 135–145
 84. Hotamisligil GS, Erbay E (2008) Nutrient sensing and inflammation in metabolic diseases. *Nat Rev Immunol* 8: 923–934
 85. Erridge C, Attina T, Spickett CM et al. (2007) A high-fat meal induces low-grade endotoxemia: evidence of a novel mechanism of postprandial inflammation. *Am J Clin Nutr* 86: 1286–1292
 86. Fei N, Zhao L (2013) An opportunistic pathogen isolated from the gut of an obese human causes obesity in germfree mice. *ISME J* 7: 880–884
 87. Wotring A, Pfeiffer N, Loh G et al. (2014) Clostridium ramosum promotes high-fat diet-induced obesity in gnotobiotic mouse models. *MBio* 5: e01530–01514
 88. Karlsson FH, Tremaroli V, Nookaew I et al. (2013) Gut metagenome in European women with normal, impaired and diabetic glucose control. *Nature* 498: 99–103
 89. Le Chatelier E, Nielsen T, Qin J et al. (2013) Richness of human gut microbiome correlates with metabolic markers. *Nature* 500: 541–546
 90. Irrazabal T, Belcheva A, Girardin SE et al. (2014) The multifaceted role of the intestinal microbiota in colon cancer. *Mol Cell* 54: 309–320
 91. Bingham SA, Hughes R, Cross AJ (2002) Effect of white versus red meat on endogenous N-nitrosation in the human colon and further evidence of a dose response. *J Nutr* 132: 3522S–3525S
 92. Kuhnle GG, Bingham SA (2007) Dietary meat, endogenous nitrosation and colorectal cancer. *Biochem Soc Trans* 35: 1355–1357
 93. Sobko T, Reinders Cl, Jansson E et al. (2005) Gastrointestinal bacteria generate nitric oxide from nitrate and nitrite. *Nitric Oxide* 13: 272–278
 94. Geypens B, Claus D, Evenepoel P et al. (1997) Influence of dietary protein supplements on the formation of bacterial metabolites in the colon. *Gut* 41: 70–76.
 95. Kikugawa K, Kato T (1988) Formation of a mutagenic diazoquinone by interaction of phenol with nitrite. *Food Chem Toxicol* 26: 209–214
 96. Kassie F, Rabot S, Kundi M et al. (2001) Intestinal microflora plays a crucial role in the genotoxicity of the cooked food mutagen 2-amino-3-methylimidazo[4,5-f]quinoline. *Carcinogenesis* 22: 1721–1725
 97. Cuevas-Ramos G, Petit CR, Marcq I et al. (2010) Escherichia coli induces DNA damage in vivo and triggers genomic instability in mammalian cells. *Proc Natl Acad Sci U S A* 107: 11537–11542
 98. Arthur JC, Perez-Chanona E, Muhlbauer M et al. (2012) Intestinal inflammation targets cancer-inducing activity of the microbiota. *Science* 338: 120–123
 99. Eaden JA, Abrams KR, Mayberry JF (2001) The risk of colorectal cancer in ulcerative colitis: a meta-analysis. *Gut* 48: 526–535
 100. Rubinstein MR, Wang X, Liu W et al. (2013) Fusobacterium nucleatum promotes colorectal carcinogenesis by modulating E-cadherin/beta-catenin signaling via its FadA adhesin. *Cell Host Microbe* 14: 195–206
 101. Franco AA, Mundy LM, Trucksis M et al. (1997) Cloning and characterization of the *Bacteroides fragilis* metalloprotease toxin gene. *Infect Immun* 65: 1007–1013
 102. Wu S, Morin PJ, Maouyo D et al. (2003) *Bacteroides fragilis* enterotoxin induces c-Myc expression and cellular proliferation. *Gastroenterology* 124: 392–400
 103. Couturier-Maillard A, Secher T, Rehman A et al. (2013) NOD2-mediated dysbiosis predisposes mice to transmissible colitis and colorectal cancer. *J Clin Invest* 123: 700–711
 104. Hu B, Elinav E, Huber S et al. (2010) Inflammation-induced tumorigenesis in the colon is regulated by caspase-1 and NLRC4. *Proc Natl Acad Sci U S A* 107: 21635–21640
 105. Chen GY, Liu M, Wang F et al. (2011) A functional role for Nlrp6 in intestinal inflammation and tumorigenesis. *J Immunol* 186: 7187–7194
 106. Hu B, Elinav E, Huber S et al. (2013) Microbiota-induced activation of epithelial IL-6 signaling links inflammasome-driven inflammation with transmissible cancer. *Proc Natl Acad Sci U S A* 110: 9862–9867
 107. Schwabe RF, Jobin C (2013) The microbiome and cancer. *Nat Rev Cancer* 13: 800–812
 108. Kohane IS, McMurry A, Weber G et al. (2012) The co-morbidity burden of children and young adults with autism spectrum disorders. *PLoS One* 7: e33224
 109. de Magistris L, Familiari V, Pascotto A et al. (2010) Alterations of the intestinal barrier in patients with autism spectrum disorders and in their first-degree relatives. *J Pediatr Gastroenterol Nutr* 51: 418–424
 110. De Angelis M, Piccolo M, Vannini L et al. (2013) Fecal microbiota and metabolome of children with autism and pervasive developmental disorder not otherwise specified. *PLoS One* 8: e76993
 111. Hsiao EY, McBride SW, Hsien S et al. (2013) Microbiota modulate behavioral and physiological abnormalities associated with neurodevelopmental disorders. *Cell* 155: 1451–1463
 112. Stewart CS, Duncan SH, Cave DR (2004) Oxalobacter formigenes and its role in oxalate metabolism in the human gut. *FEMS Microbiol Lett* 230: 1–7
 113. Mittal RD, Kumar R (2004) Gut-inhabiting bacterium Oxalobacter formigenes: role in calcium oxalate urolithiasis. *J Endourol* 18: 418–424

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