Литература к подразделу II:

Комплексный взгляд на Метагеномы и Метаболомы кишечных заболеваний

Wanping Aw, Shinji Fukuda.
An Integrated Outlook on the Metagenome and Metabolome of Intestinal Diseases
Diseases **2015**, *3*(4), 341-359

1. Qin, J.; Li, R.; Raes, J.; Arumugam, M.; Burgdorf, K.S.; Manichanh, C.; Nielsen, T.; Pons, N.; Levenez, F.; Yamada, T.; *et al.* A human gut microbial gene catalogue established by metagenomic sequencing. *Nature* 2010, *464*, 59–65. [Google Scholar] [CrossRef] [PubMed][Green Version]
2. Bianconi, E.; Piovesan, A.; Facchin, F.; Beraudi, A.; Casadei, R.; Frabetti, F.; Vitale, L.; Pelleri, M.C.; Tassani, S.; Piva, F.; *et al.* An estimation of the number of cells in the human body. *Ann. Hum. Biol.* 2013, *40*, 463–471. [Google Scholar] [CrossRef] [PubMed]
3. Fukuda, S.; Ohno, H. Gut microbiome and metabolic diseases. *Semin. Immunopathol.* 2014, *36*, 103–114. [Google Scholar] [CrossRef] [PubMed]
4. Xu, J.; Mahowald, M.; Ley, R.; Lozupone, C.; Hamady, M.; Martens, E.; Henrissat, B.; Coutinho, P.; Minx, P.; Latreille, P.; *et al.* Evolution of symbiotic bacteria in the distal human intestine. *PLoS Biol.* 2007, *5*, 1574–1586. [Google Scholar] [CrossRef] [PubMed]
5. Turnbaugh, P.J.; Ley, R.E.; Mahowald, M.A.; Magrini, V.; Mardis, E.R.; Gordon, J.I. An obesity-associated gut microbiome with increased capacity for energy harvest. *Nature* 2006, *444*, 1027–1031. [Google Scholar] [CrossRef] [PubMed]
6. Ridaura, V.K.; Faith, J.J.; Rey, F.E.; Cheng, J.; Duncan, A.E.; Kau, A.L.; Griffin, N.W.; Lombard, V.; Henrissat, B.; Bain, J.R.; *et al.* Gut microbiota from twins discordant for obesity modulate metabolism in mice. *Science* 2013, *341*, 1241214. [Google Scholar] [CrossRef] [PubMed]
7. Turnbaugh, P.J.; Hamady, M.; Yatsunenko, T.; Cantarel, B.L.; Duncan, A.; Ley, R.E.; Sogin, M.L.; Jones, W.J.; Roe, B.A.; Affourtit, J.P.; *et al.* A core gut microbiome in obese and lean twins. *Nature* 2009, *457*, 480–484. [Google Scholar] [CrossRef] [PubMed]
8. Wen, L.; Ley, R.E.; Volchkov, P.Y.; Stranges, P.B.; Avanesyan, L.; Stonebraker, A.C.; Hu, C.; Wong, F.S.; Szot, G.L.; Bluestone, J.A.; *et al.* Innate immunity and intestinal microbiota in the development of type 1 diabetes. *Nature* 2008, *455*, 1109–1113. [Google Scholar] [CrossRef] [PubMed]
9. Wang, F.; Zhang, P.; Jiang, H.; Cheng, S. Gut bacterial translocation contributes to microinflammation in experimental uremia. *Dig. Dis. Sci.* 2012, *57*, 2856–2862. [Google Scholar] [CrossRef] [PubMed]
10. Molodecky, N.A.; Soon, I.S.; Rabi, D.M.; Ghali, W.A.; Ferris, M.; Chernoff, G.; Benchimol, E.I.; Panaccione, R.; Ghosh, S.; Barkema, H.W.; *et al.* Increasing incidence and prevalence of the inflammatory bowel diseases with time, based on systematic review. *Gastroenterology* 2012, *142*, 46–54. [Google Scholar] [CrossRef] [PubMed]
11. Scanlan, P.D.; Shanahan, F.; Clune, Y.; Collins, J.K.; O’Sullivan, G.C.; O'Riordan, M.; Holmes, E.; Wang, Y.; Marchesi, J.R. Culture-independent analysis of the gut microbiota in colorectal cancer and polyposis. *Environ. Microbiol.* 2008, *10*, 789–798. [Google Scholar] [CrossRef] [PubMed]
12. Kirjavainen, P.; Arvola, T.; Salminen, S.; Isolauri, E. Aberrant composition of gut microbiota of allergic infants: A target of bifidobacterial therapy at weaning? *Gut* 2002, *51*, 51–55. [Google Scholar] [CrossRef] [PubMed]

13. Berer, K.; Mues, M.; Koutrolos, M.; Rasbi, Z.A.; Boziki, M.; Johner, C.; Wekerle, H.; Krishnamoorthy, G. Commensal microbiota and myelin autoantigen cooperate to trigger autoimmune demyelination. *Nature* 2011, *479*, 538–541. [Google Scholar] [CrossRef] [PubMed]
14. Tang, W.H.; Wang, Z.; Levison, B.S.; Koeth, R.A.; Britt, E.B.; Fu, X.; Wu, Y.; Hazen, S.L. Intestinal microbial metabolism of phosphatidylcholine and cardiovascular risk. *N. Engl. J. Med.* 2013, *368*, 1575–1584. [Google Scholar] [CrossRef] [PubMed]
15. Koeth, R.A.; Wang, Z.; Levison, B.S.; Buffa, J.A.; Org, E.; Sheehy, B.T.; Britt, E.B.; Fu, X.; Wu, Y.; Li, L.; *et al.* Intestinal microbiota metabolism of l-carnitine, a nutrient in red meat, promotes atherosclerosis. *Nat. Med.* 2013, *19*, 576–585. [Google Scholar] [CrossRef] [PubMed]
16. Finegold, S.M. Therapy and epidemiology of autism—Clostridial spores as key elements. *Med. Hypotheses* 2008, *70*, 508–511. [Google Scholar] [CrossRef] [PubMed]
17. Ellis, D.I.; Dunn, W.B.; Griffin, J.L.; Allwood, J.W.; Goodacre, R. Metabolic fingerprinting as a diagnostic tool. *Pharmacogenomics* 2007, *8*, 1243–1266. [Google Scholar] [CrossRef] [PubMed]
18. Tringe, S.; Hugenholtz, P. A renaissance for the pionnering 16s rrna gene. *Curr. Opin. Microbiol.* 2008, *11*, 442–446. [Google Scholar] [CrossRef] [PubMed]
19. Nicholson, J.K.; Holmes, E.; Kinross, J.; Burcelin, R.; Gibson, G.; Jia, W.; Pettersson, S. Host-gut microbiota metabolic interactions. *Science* 2012, *336*, 1262–1267. [Google Scholar] [CrossRef] [PubMed]
20. Dettmer, K.; Aronov, P.A.; Hammock, B.D. Mass spectrometry based metabolomics. *Mass. Spectrom. Rev.* 2007, *26*, 51–78. [Google Scholar] [CrossRef] [PubMed]
21. Martin, F.P.; Wang, Y.; Sprenger, N.; Yap, I.K.; Lundstedt, T.; Lek, P.; Rezzi, S.; Ramadan, Z.; van Bladeren, P.; Fay, L.B.; *et al.* Probiotic modulation of symbiotic gut microbial-host metabolic interactions in a humanized microbiome mouse model. *Mol. Syst. Biol.* 2008, *4*, 157. [Google Scholar] [CrossRef] [PubMed]
22. Wikoff, W.R.; Anfora, A.T.; Liu, J.; Schultz, P.G.; Lesley, S.A.; Peters, E.C.; Siuzdak, G. Metabolomics analysis reveals large effects of gut microflora on mammalian blood metabolites. *Proc. Natl. Acad. Sci. USA* 2009, *106*, 3698–3703. [Google Scholar] [CrossRef] [PubMed]
23. Aw, W.; Fukuda, S. Toward the comprehensive understanding of the gut ecosystem via metabolomics-based integrated omics approach. *Semin. Immunopathol.* 2015, *37*, 5–16. [Google Scholar] [CrossRef] [PubMed]
24. Vogelstein, B.; Papadopoulos, N.; Velculescu, V.E.; Zhou, S.; Diaz, L.A.J.; Kinzler, K.W. Cancer genome landscapes. *Science* 2013, *339*, 1546–1558. [Google Scholar] [CrossRef] [PubMed]
25. Sears, C.L.; Garrett, W.S. Microbes, microbiota, and colon cancer. *Cell Host Microbe* 2014, *15*, 317–328. [Google Scholar] [CrossRef] [PubMed]
26. Jemal, A.; Bray, F.; Center, M.M.; Ferlay, J.; Ward, E.; Forman, D. Global cancer statistics. *CA Cancer J. Clin.* 2011, *61*, 69–90. [Google Scholar] [CrossRef] [PubMed]
27. Belcheva, A.; Irrazabal, T.; Robertson, S.J.; Streutker, C.; Maughan, H.; Rubino, S.; Moriyama, E.H.; Copeland, J.K.; Kumar, S.; Green, B.; *et al.* Gut microbial metabolism drives transformation of msh2-deficient colon epithelial cells. *Cell* 2014, *158*, 288–299. [Google Scholar] [CrossRef] [PubMed]
28. Jess, T.; Gamborg, M.; Matzen, P.; Munkholm, P.; Sorensen, T.I. Increased risk of intestinal cancer in crohn's disease: A meta-analysis of population-based cohort studies. *Am. J. Gastroenterol.* 2005, *100*, 2724–2729. [Google Scholar] [CrossRef] [PubMed]
29. Danese, S.; Malesci, A.; Vetrano, S. Colitis-associated cancer: The dark side of inflammatory bowel disease. *Gut* 2011, *60*, 1609–1610. [Google Scholar] [CrossRef] [PubMed]
30. Arthur, J.C.; Perez-Chanona, E.; Muhlbauer, M.; Tomkovich, S.; Uronis, J.M.; Fan, T.J.; Campbell, B.J.; Abujamel, T.; Dogan, B.; Rogers, A.B.; *et al.* Intestinal inflammation targets cancer-inducing activity of the microbiota. *Science* 2012, *338*, 120–123. [Google Scholar] [CrossRef] [PubMed]

31. Schwabe, R.F.; Jobin, C. The microbiome and cancer. *Nat. Rev. Cancer* 2013, *13*, 800–812. [Google Scholar] [CrossRef] [PubMed]
32. Baena, R.; Salinas, P. Diet and colorectal cancer. *Maturitas* 2015, *80*, 258–264. [Google Scholar] [CrossRef] [PubMed]
33. Baumgart, D.C.; Sandborn, W.J. Inflammatory bowel disease: Clinical aspects and established and evolving therapies. *Lancet* 2007, *369*, 1641–1657. [Google Scholar] [CrossRef]
34. Loftus, E.V. Clinical epidemiology of inflammatory bowel disease: Incidence, prevalence, and environmental influences. *Gastroenterology* 2004, *126*, 1504–1517. [Google Scholar] [CrossRef] [PubMed]
35. M'Koma, A.E. Inflammatory bowel disease: An expanding global health problem. *Clin. Med. Insights Gastroenterol.* 2013, *6*, 33–47. [Google Scholar] [CrossRef] [PubMed]
36. Barrett, J.C.; Hansoul, S.; Nicolae, D.L.; Cho, J.H.; Duerr, R.H.; Rioux, J.D.; Brant, S.R.; Silverberg, M.S.; Taylor, K.D.; Barmada, M.M.; *et al.* Genome-wide association defines more than 30 distinct susceptibility loci for crohn's disease. *Nat. Genet.* 2008, *40*, 955–962. [Google Scholar] [CrossRef] [PubMed]
37. Frank, D.N.; St Amand, A.L.; Feldman, R.A.; Boedeker, E.C.; Harpaz, N.; Pace, N.R. Molecular-phylogenetic characterization of microbial community imbalances in human inflammatory bowel diseases. *Proc. Natl. Acad. Sci. USA* 2007, *104*, 13780–13785. [Google Scholar] [CrossRef] [PubMed]
38. Sokol, H.; Pigneur, B.; Watterlot, L.; Lakhdari, O.; Bermudez-Humaran, L.G.; Gratadoux, J.J.; Blugeon, S.; Bridonneau, C.; Furet, J.P.; Corthier, G.; *et al.* Faecalibacterium prausnitzii is an anti-inflammatory commensal bacterium identified by gut microbiota analysis of crohn disease patients. *Proc. Natl. Acad. Sci. USA* 2008, *105*, 16731–16736. [Google Scholar] [CrossRef] [PubMed]
39. Norman, J.M.; Handley, S.A.; Baldridge, M.T.; Droit, L.; Liu, C.Y.; Keller, B.C.; Kambal, A.; Monaco, C.L.; Zhao, G.; Fleshner, P.; *et al.* Disease-specific alterations in the enteric virome in inflammatory bowel disease. *Cell* 2015, *160*, 447–460. [Google Scholar] [CrossRef] [PubMed]
40. Marcobal, A.; Kashyap, P.C.; Nelson, T.A.; Aronov, P.A.; Donia, M.S.; Spormann, A.; Fischbach, M.A.; Sonnenburg, J.L. A metabolomic view of how the human gut microbiota impacts the host metabolome using humanized and gnotobiotic mice. *ISME J.* 2013, *7*, 1933–1943. [Google Scholar] [CrossRef] [PubMed]
41. Louis, P.; Hold, G.L.; Flint, H.J. The gut microbiota, bacterial metabolites and colorectal cancer. *Nat. Rev. Microbiol.* 2014, *12*, 661–672. [Google Scholar] [CrossRef] [PubMed]
42. Flint, H.J.; Scott, K.P.; Duncan, S.H.; Louis, P.; Forano, E. Microbial degradation of complex carbohydrates in the gut. *Gut Microbes* 2012, *3*, 289–306. [Google Scholar] [CrossRef] [PubMed]
43. Sieber, J.R.; McInerney, M.J.; Gunsalus, R.P. Genomic insights into syntrophy: The paradigm for anaerobic metabolic cooperation. *Ann. Rev. Microbiol.* 2012, *66*, 429–452. [Google Scholar] [CrossRef] [PubMed]
44. Baughn, A.D.; Malamy, M.H. The strict anaerobe bacteroides fragilis grows in and benefits from nanomolar concentrations of oxygen. *Nature* 2004, *427*, 441–444. [Google Scholar] [CrossRef] [PubMed]
45. Khan, M.T.; Duncan, S.H.; Stams, A.J.; van Dijl, J.M.; Flint, H.J.; Harmsen, H.J. The gut anaerobe faecalibacterium prausnitzii uses an extracellular electron shuttle to grow at oxic-anoxic interphases. *ISME J.* 2012, *6*, 1578–1585. [Google Scholar] [CrossRef] [PubMed]
46. Nava, G.M.; Carbonero, F.; Croix, J.A.; Greenberg, E.; Gaskins, H.R. Abundance and diversity of mucosa-associated hydrogenotrophic microbes in the healthy human colon. *ISME J.* 2012, *6*, 57–70. [Google Scholar] [CrossRef] [PubMed]
47. Carbonero, F.; Benefiel, A.C.; Gaskins, H.R. Contributions of the microbial hydrogen economy to colonic homeostasis. *Nat. Rev. Gastroenterol. Hepatol.* 2012, *9*, 504–518. [Google Scholar] [CrossRef] [PubMed]

48. Sleeth, M.L.; Thompson, E.L.; Ford, H.E.; Zac-Varghese, S.E.; Frost, G. Free fatty acid receptor 2 and nutrient sensing: A proposed role for fibre, fermentable carbohydrates and short-chain fatty acids in appetite regulation. *Nutr. Res. Rev.* 2010, *23*, 135–145. [Google Scholar] [CrossRef] [PubMed]
49. Fung, K.Y.; Cosgrove, L.; Lockett, T.; Head, R.; Topping, D.L. A review of the potential mechanisms for the lowering of colorectal oncogenesis by butyrate. *Br. J. Nutr.* 2012, *108*, 820–831. [Google Scholar] [CrossRef] [PubMed]
50. Wilson, A.J.; Chueh, A.C.; Togel, L.; Corner, G.A.; Ahmed, N.; Goel, S.; Byun, D.S.; Nasser, S.; Houston, M.A.; Jhawer, M.; *et al.* Apoptotic sensitivity of colon cancer cells to histone deacetylase inhibitors is mediated by an sp1/sp3-activated transcriptional program involving immediate-early gene induction. *Cancer Res.* 2010, *70*, 609–620. [Google Scholar] [CrossRef] [PubMed]
51. Hamer, H.M.; Jonkers, D.; Venema, K.; Vanhoutvin, S.; Troost, F.J.; Brummer, R.J. Review article: The role of butyrate on colonic function. *Aliment. Pharmacol. Ther.* 2008, *27*, 104–119. [Google Scholar] [CrossRef] [PubMed]
52. Chang, P.V.; Hao, L.; Offermanns, S.; Medzhitov, R. The microbial metabolite butyrate regulates intestinal macrophage function via histone deacetylase inhibition. *Proc. Natl. Acad. Sci. USA* 2014, *111*, 2247–2252. [Google Scholar] [CrossRef] [PubMed]
53. Smith, P.M.; Howitt, M.R.; Panikov, N.; Michaud, M.; Gallini, C.A.; Bohlooly, Y.M.; Glickman, J.N.; Garrett, W.S. The microbial metabolites, short-chain fatty acids, regulate colonic treg cell homeostasis. *Science* 2013, *341*, 569–573. [Google Scholar] [CrossRef] [PubMed]
54. Furusawa, Y.; Obata, Y.; Fukuda, S.; Endo, T.A.; Nakato, G.; Takahashi, D.; Nakanishi, Y.; Uetake, C.; Kato, K.; Kato, T.; *et al.* Commensal microbe-derived butyrate induces the differentiation of colonic regulatory t cells. *Nature* 2013, *504*, 446–450. [Google Scholar] [CrossRef] [PubMed]
55. Atarashi, K.; Tanoue, T.; Shima, T.; Imaoka, A.; Kuwahara, T.; Momose, Y.; Cheng, G.; Yamasaki, S.; Saito, T.; Ohba, Y.; *et al.* Induction of colonic regulatory t cells by indigenous clostridium species. *Science* 2011, *331*, 337–341. [Google Scholar] [CrossRef] [PubMed]
56. Geuking, M.B.; Cahenzli, J.; Lawson, M.A.; Ng, D.C.; Slack, E.; Hapfelmeier, S.; McCoy, K.D.; Macpherson, A.J. Intestinal bacterial colonization induces mutualistic regulatory t cell responses. *Immunity* 2011, *34*, 794–806. [Google Scholar] [CrossRef] [PubMed]
57. Round, J.L.; Mazmanian, S.K. Inducible foxp3+ regulatory t-cell development by a commensal bacterium of the intestinal microbiota. *Proc. Natl. Acad. Sci. USA* 2010, *107*, 12204–12209. [Google Scholar] [CrossRef] [PubMed]
58. O'Mahony, C.; Scully, P.; O'Mahony, D.; Murphy, S.; O'Brien, F.; Lyons, A.; Sherlock, G.; MacSharry, J.; Kiely, B.; Shanahan, F.; *et al.* Commensal-induced regulatory t cells mediate protection against pathogen-stimulated nf-kappab activation. *PLoS Pathog.* 2008, *4*, e1000112. [Google Scholar] [CrossRef] [PubMed]
59. Arpaia, N.; Campbell, C.; Fan, X.; Dikiy, S.; van der Veeken, J.; deRoos, P.; Liu, H.; Cross, J.R.; Pfeffer, K.; Coffer, P.J.; *et al.* Metabolites produced by commensal bacteria promote peripheral regulatory t-cell generation. *Nature* 2013, *504*, 451–455. [Google Scholar] [CrossRef] [PubMed]
60. Latham, T.; Mackay, L.; Sproul, D.; Karim, M.; Culley, J.; Harrison, D.J.; Hayward, L.; Langridge-Smith, P.; Gilbert, N.; Ramsahoye, B.H. Lactate, a product of glycolytic metabolism, inhibits histone deacetylase activity and promotes changes in gene expression. *Nucleic Acids Res.* 2012, *40*, 4794–4803. [Google Scholar] [CrossRef] [PubMed]
61. Brown, A.J.; Goldsworthy, S.M.; Barnes, A.A.; Eilert, M.M.; Tcheang, L.; Daniels, D.; Muir, A.I.; Wigglesworth, M.J.; Kinghorn, I.; Fraser, N.J.; *et al.* The orphan g protein-coupled receptors gpr41 and gpr43 are activated by propionate and other short chain carboxylic acids. *J. Biol. Chem.* 2003, *278*, 11312–11319. [Google Scholar] [CrossRef] [PubMed]
62. Singh, N.; Gurav, A.; Sivaprakasam, S.; Brady, E.; Padia, R.; Shi, H.; Thangaraju, M.; Prasad, P.D.; Manicassamy, S.; Munn, D.H.; *et al.* Activation of gpr109a, receptor for niacin and the

commensal metabolite butyrate, suppresses colonic inflammation and carcinogenesis. *Immunity* 2014, *40*, 128–139. [Google Scholar] [CrossRef] [PubMed]

63. Thangaraju, M.; Cresci, G.A.; Liu, K.; Ananth, S.; Gnanaprakasam, J.P.; Browning, D.D.; Mellinger, J.D.; Smith, S.B.; Digby, G.J.; Lambert, N.A.; *et al.* Gpr109a is a g-protein-coupled receptor for the bacterial fermentation product butyrate and functions as a tumor suppressor in colon. *Cancer Res.* 2009, *69*, 2826–2832. [Google Scholar] [CrossRef] [PubMed]
64. Maslowski, K.M.; Vieira, A.T.; Ng, A.; Kranich, J.; Sierro, F.; Yu, D.; Schilter, H.C.; Rolph, M.S.; Mackay, F.; Artis, D.; *et al.* Regulation of inflammatory responses by gut microbiota and chemoattractant receptor gpr43. *Nature* 2009, *461*, 1282–1286. [Google Scholar] [PubMed]
65. Ganapathy, V.; Thangaraju, M.; Prasad, P.D.; Martin, P.M.; Singh, N. Transporters and receptors for short-chain fatty acids as the molecular link between colonic bacteria and the host. *Curr. Opin. Pharmacol.* 2013, *13*, 869–874. [Google Scholar] [CrossRef] [PubMed]
66. Buda, A.; Qualtrough, D.; Jepson, M.A.; Martines, D.; Paraskeva, C.; Pignatelli, M. Butyrate downregulates alpha2beta1 integrin: A possible role in the induction of apoptosis in colorectal cancer cell lines. *Gut* 2003, *52*, 729–734. [Google Scholar] [CrossRef] [PubMed]
67. Clarke, J.M.; Topping, D.L.; Bird, A.R.; Young, G.P.; Cobiac, L. Effects of high-amylose maize starch and butyrylated high-amylose maize starch on azoxymethane-induced intestinal cancer in rats. *Carcinogenesis* 2008, *29*, 2190–2194. [Google Scholar] [CrossRef] [PubMed]
68. Blachier, F.; Nepelska, M.; Cultrone, A.; Béguet-Crespel, F.; Le Roux, K.; Doré, J.; Arulampalam, V.; Blottière, H.M. Butyrate produced by commensal bacteria potentiates phorbol esters induced ap-1 response in human intestinal epithelial cells. *PLoS ONE* 2012, *7*, e52869. [Google Scholar] [CrossRef]
69. Ou, J.; Carbonero, F.; Zoetendal, E.G.; DeLany, J.P.; Wang, M.; Newton, K.; Gaskins, H.R.; O'Keefe, S.J. Diet, microbiota, and microbial metabolites in colon cancer risk in rural africans and african americans. *Am. J. Clin. Nutr.* 2013, *98*, 111–120. [Google Scholar] [CrossRef] [PubMed]
70. Russell, W.R.; Gratz, S.W.; Duncan, S.H.; Holtrop, G.; Ince, J.; Scobbie, L.; Duncan, G.; Johnstone, A.M.; Lobley, G.E.; Wallace, R.J.; *et al.* High-protein, reduced-carbohydrate weight-loss diets promote metabolite profiles likely to be detrimental to colonic health. *Am. J. Clin. Nutr.* 2011, *93*, 1062–1072. [Google Scholar] [CrossRef] [PubMed]
71. Windey, K.; de Preter, V.; Verbeke, K. Relevance of protein fermentation to gut health. *Mol. Nutr. Food Res.* 2012, *56*, 184–196. [Google Scholar] [CrossRef] [PubMed]
72. Russell, W.R.; Duncan, S.H.; Scobbie, L.; Duncan, G.; Cantlay, L.; Calder, A.G.; Anderson, S.E.; Flint, H.J. Major phenylpropanoid-derived metabolites in the human gut can arise from microbial fermentation of protein. *Mol. Nutr. Food Res.* 2013, *57*, 523–535. [Google Scholar] [CrossRef] [PubMed]
73. Loh, Y.H.; Jakszyn, P.; Luben, R.N.; Mulligan, A.A.; Mitrou, P.N.; Khaw, K.T. N-nitroso compounds and cancer incidence: The european prospective investigation into cancer and nutrition (epic)-norfolk study. *Am. J. Clin. Nutr.* 2011, *93*, 1053–1061. [Google Scholar] [CrossRef] [PubMed]
74. Hughes, R. Metabolic activities of the gut microflora in relation to cancer. *Microb. Ecol. Health Dis.* 2000, *12*, 179–185. [Google Scholar] [CrossRef]
75. Di Martino, M.L.; Campilongo, R.; Casalino, M.; Micheli, G.; Colonna, B.; Prosseda, G. Polyamines: Emerging players in bacteria-host interactions. *Int. J. Med. Microbiol. IJMM* 2013, *303*, 484–491. [Google Scholar] [CrossRef] [PubMed]
76. Pegg, A.E. Toxicity of polyamines and their metabolic products. *Chem. Res. Toxicol.* 2013, *26*, 1782–1800. [Google Scholar] [CrossRef] [PubMed]
77. Hanfrey, C.C.; Pearson, B.M.; Hazeldine, S.; Lee, J.; Gaskin, D.J.; Woster, P.M.; Phillips, M.A.; Michael, A.J. Alternative spermidine biosynthetic route is critical for growth of campylobacter jejuni and is the dominant polyamine pathway in human gut microbiota. *J. Biol. Chem.* 2011, *286*, 43301–43312. [Google Scholar] [CrossRef] [PubMed]

78. Kibe, R.; Kurihara, S.; Sakai, Y.; Suzuki, H.; Ooga, T.; Sawaki, E.; Muramatsu, K.; Nakamura, A.; Yamashita, A.; Kitada, Y.; *et al*. Upregulation of colonic luminal polyamines produced by intestinal microbiota delays senescence in mice. *Sci. Rep.* 2014, *4*, 4548. [Google Scholar] [CrossRef] [PubMed]
79. Matsumoto, M.; Kurihara, S.; Kibe, R.; Ashida, H.; Benno, Y. Longevity in mice is promoted by probiotic-induced suppression of colonic senescence dependent on upregulation of gut bacterial polyamine production. *PLoS ONE* 2011, *6*, e23652. [Google Scholar] [CrossRef] [PubMed]
80. Swann, J.R.; Want, E.J.; Geier, F.M.; Spagou, K.; Wilson, I.D.; Sidaway, J.E.; Nicholson, J.K.; Holmes, E. Systemic gut microbial modulation of bile acid metabolism in host tissue compartments. *Proc. Natl. Acad. Sci. USA* 2011, *108* (Suppl. S1), 4523–4530. [Google Scholar] [CrossRef] [PubMed]
81. Ridlon, J.M.; Kang, D.J.; Hylemon, P.B. Bile salt biotransformations by human intestinal bacteria. *J. Lipid Res.* 2006, *47*, 241–259. [Google Scholar] [CrossRef] [PubMed]
82. Watanabe, M.; Houten, S.M.; Mataki, C.; Christoffolete, M.A.; Kim, B.W.; Sato, H.; Messaddeq, N.; Harney, J.W.; Ezaki, O.; Kodama, T.; *et al*. Bile acids induce energy expenditure by promoting intracellular thyroid hormone activation. *Nature* 2006, *439*, 484–489. [Google Scholar] [CrossRef] [PubMed]
83. Barrasa, J.I.; Olmo, N.; Lizarbe, M.A.; Turnay, J. Bile acids in the colon, from healthy to cytotoxic molecules. *Toxicol. Vitro Int. J. Publ. Assoc. BIBRA* 2013, *27*, 964–977. [Google Scholar] [CrossRef] [PubMed]
84. Bernstein, H. Bile acids as endogenous etiologic agents in gastrointestinal cancer. *World J. Gastroenterol.* 2009, *15*, 3329. [Google Scholar] [CrossRef] [PubMed]
85. Ou, J.; DeLany, J.P.; Zhang, M.; Sharma, S.; O'Keefe, S.J. Association between low colonic short-chain fatty acids and high bile acids in high colon cancer risk populations. *Nutr. Cancer* 2012, *64*, 34–40. [Google Scholar] [CrossRef] [PubMed]
86. Islam, K.B.; Fukiya, S.; Hagio, M.; Fujii, N.; Ishizuka, S.; Ooka, T.; Ogura, Y.; Hayashi, T.; Yokota, A. Bile acid is a host factor that regulates the composition of the cecal microbiota in rats. *Gastroenterology* 2011, *141*, 1773–1781. [Google Scholar] [CrossRef] [PubMed]
87. David, L.A.; Maurice, C.F.; Carmody, R.N.; Gootenberg, D.B.; Button, J.E.; Wolfe, B.E.; Ling, A.V.; Devlin, A.S.; Varma, Y.; Fischbach, M.A.; *et al*. Diet rapidly and reproducibly alters the human gut microbiome. *Nature* 2014, *505*, 559–563. [Google Scholar] [CrossRef] [PubMed]
88. Magee, E.A.; Richardson, C.J.; Hughes, R.; Cummings, J.H. Contribution of dietary protein to sulfide production in the large intestine: An *in vitro* and a controlled feeding study in humans. *Am. J. Clin. Nutr.* 2000, *72*, 1488–1494. [Google Scholar] [PubMed]
89. Attene-Ramos, M.S.; Nava, G.M.; Muellner, M.G.; Wagner, E.D.; Plewa, M.J.; Gaskins, H.R. DNA damage and toxicogenomic analyses of hydrogen sulfide in human intestinal epithelial fhs 74 int cells. *Environ. Mol. Mutagen.* 2010, *51*, 304–314. [Google Scholar] [CrossRef] [PubMed]
90. Attene-Ramos, M.S.; Wagner, E.D.; Gaskins, H.R.; Plewa, M.J. Hydrogen sulfide induces direct radical-associated DNA damage. *Mol. Cancer Res. MCR* 2007, *5*, 455–459. [Google Scholar] [CrossRef] [PubMed]
91. Health and nutritional properties and guidelines for evaluation. Available online: ftp://ftp.fao.org/docrep/fao/009/a0512e/a0512e00.pdf (accessed on 5 November 2015).
92. Kostic, A.D.; Xavier, R.J.; Gevers, D. The microbiome in inflammatory bowel disease: Current status and the future ahead. *Gastroenterology* 2014, *146*, 1489–1499. [Google Scholar] [CrossRef] [PubMed]
93. Rembacken, B.J.; Snelling, A.M.; Hawkey, P.M.; Chalmers, D.M.; Axon, A.T.R. Non-pathogenic escherichia coli *versus* mesalazine for the treatment of ulcerative colitis: A randomised trial. *Lancet* 1999, *354*, 635–639. [Google Scholar] [CrossRef]
94. Matthes, H.; Krummenerl, T.; Giensch, M.; Wolff, C.; Schulze, J. Clinical trial: Probiotic treatment of acute distal ulcerative colitis with rectally administered escherichia coli nissle 1917 (ecn). *BMC Complement. Altern. Med.* 2010, *10*. [Google Scholar] [CrossRef] [PubMed]

95. Zocco, M.A.; dal Verme, L.Z.; Cremonini, F.; Piscaglia, A.C.; Nista, E.C.; Candelli, M.; Novi, M.; Rigante, D.; Cazzato, I.A.; Ojetti, V.; *et al.* Efficacy of lactobacillus gg in maintaining remission of ulcerative colitis. *Aliment. Pharmacol. Ther.* 2006, *23*, 1567–1574. [Google Scholar] [CrossRef] [PubMed]
96. Veiga, P.; Gallini, C.A.; Beal, C.; Michaud, M.; Delaney, M.L.; DuBois, A.; Khlebnikov, A.; van Hylckama Vlieg, J.E.; Punit, S.; Glickman, J.N.; *et al.* Bifidobacterium animalis subsp. Lactis fermented milk product reduces inflammation by altering a niche for colitogenic microbes. *Proc. Natl. Acad. Sci. USA* 2010, *107*, 18132–18137. [Google Scholar] [CrossRef] [PubMed]
97. Guarner, F. Prebiotics, probiotics and helminths: The “natural” solution? *Dig. Dis.* 2009, *27*, 412–417. [Google Scholar] [CrossRef] [PubMed]
98. Fukuda, S.; Furuya, H.; Suzuki, Y.; Asanuma, N.; Hino, T. A new strain of butyrivibrio fibrisolvens that has high ability to isomerize linoleic acid to conjugated linoleic acid. *J. Gen. Appl. Microbiol.* 2005, *51*, 105–113. [Google Scholar] [CrossRef] [PubMed]
99. West, D.; Delany, J.; Camet, P.; Blohm, F.; Truett, A.; Scimeca, J. Effects of conjugated linoleic acid on body fat and energy metabolism in the mouse. *Am. J. Physiol.* 1998, *275*, R667–R672. [Google Scholar] [PubMed]
100. Fukuda, S.; Suzuki, Y.; Murai, M.; Asanuma, N.; Hino, T. Isolation of a novel strain of butyrivibrio fibrisolvens that isomerizes linoleic acid to conjugated linoleic acid without hydrogenation, and its utilization as a probiotic for animals. *J. Appl. Microbiol.* 2006, *100*, 787–794. [Google Scholar] [CrossRef] [PubMed]
101. Sugahara, H.; Odamaki, T.; Fukuda, S.; Kato, T.; Xiao, J.Z.; Abe, F.; Kikuchi, J.; Ohno, H. Probiotic bifidobacterium longum alters gut luminal metabolism through modification of the gut microbial community. *Sci. Rep.* 2015, *5*, 13548. [Google Scholar] [CrossRef]
102. Kanauchi, O.; Agata, K. Protein, and dietary fiber-rich new foodstuff from brewer’s spent grain increased excretion of feces and jejunum mucosal protein content in rats. *Biosci. Biotechnol. Biochem.* 1997, *61*, 29–33. [Google Scholar] [CrossRef] [PubMed]
103. Kanauchi, O.; Iwanaga, T.; Andoh, A.; Araki, Y.; Nakamura, T.; Mitsuyama, K.; Suzuki, A.; Hibi, T.; Bamba, T. Dietary fiber fraction of germinated barley foodstuff attenuated mucosal damage and diarrhea, and accelerated the repair of the colonic mucosa in an experimental colitis. *J. Gastroenterol. Hepatol.* 2001, *16*, 160–168. [Google Scholar] [CrossRef]
104. Mitsuyama, K.; Saiki, T.; Kanauchi, O.; Iwanaga, T.; Tomiyasu, N.; Nishiyama, T.; Tateishi, H.; Shirachi, A.; Ide, M.; Suzuki, A.; *et al.* Treatment of ulcerative colitis with germinated barley foodstuff feeding: A pilot study. *Aliment. Pharmacol. Ther.* 1998, *12*, 1225–1230. [Google Scholar] [CrossRef] [PubMed]
105. Faghfoori, Z.; Navai, L.; Shakerhosseini, R.; Somi, M.H.; Nikniaz, Z.; Norouzi, M.F. Effects of an oral supplementation of germinated barley foodstuff on serum tumour necrosis factor-alpha, interleukin-6 and -8 in patients with ulcerative colitis. *Ann. Clin. Biochem.* 2011, *48*, 233–237. [Google Scholar] [CrossRef] [PubMed]
106. Joossens, M.; de Preter, V.; Ballet, V.; Verbeke, K.; Rutgeerts, P.; Vermeire, S. Effect of oligofructose-enriched inulin (of-in) on bacterial composition and disease activity of patients with crohn's disease: Results from a double-blinded randomised controlled trial. *Gut* 2012, *61*, 958. [Google Scholar] [CrossRef] [PubMed]
107. Verghese, M.; Rao, D.R.; Chawan, C.B.; Williams, L.L.; Shackelford, L. Dietary inulin suppresses azoxymethane-induced aberrant crypt foci and colon tumors at the promotion stage in young fisher 344 rat. *J. Nutr.* 2002, *132*, 2809–2813. [Google Scholar] [PubMed]
108. Hsu, C.K.; Liao, J.W.; Chung, Y.C.; Hsieh, C.P.; Chan, Y.C. Xylooligosaccharides and fructooligosaccharides affect the intestinal microbiota and precancerous colonic lesion development in rats. *J. Nutr.* 2004, *134*, 1523–1528. [Google Scholar] [PubMed]
109. Smits, L.; Bouter, K.; de Vos, W.; Borody, T.; Nieuwdorp, M. Therapeutic potential of fecal microbiota transplantation. *Gastroenterology* 2013, *145*, 946–953. [Google Scholar] [CrossRef] [PubMed]

110. Borody, T. “Flora power”—Fecal bacteria cure chronic c. Difficile diarrhea. *Am. J. Gastroenterol.* 2000, *95*, 3028–3029. [Google Scholar] [PubMed]
111. Khoruts, A.; Dicksved, J.; Jansson, J.; Sadowsky, M. Changes in the composition of the human fecal microbiome after bacteriotherapy for recurrent clostridium difficile-associated diarrhea. *J. Clin. Gastroenterol.* 2010, *44*, 354–360. [Google Scholar] [CrossRef] [PubMed]
112. Van Nood, E.; Vrieze, A.; Nieuwdorp, M.; Fuentes, S.; Zoetendal, E.G.; de Vos, W.M.; Visser, C.E.; Kuijper, E.J.; Bartelsman, J.F.; Tijssen, J.G.; *et al.* Duodenal infusion of donor feces for recurrent clostridium difficile. *N. Engl. J. Med.* 2013, *368*, 407–415. [Google Scholar] [CrossRef] [PubMed]
113. Wei, Y.; Zhu, W.; Gong, J.; Guo, D.; Gu, L.; Li, N.; Li, J. Fecal microbiota transplantation improves the quality of life in patients with inflammatory bowel disease. *Gastroenterol. Res. Pract.* 2015, *2015*, 517597. [Google Scholar] [CrossRef] [PubMed]
114. Kellermayer, R.; Nagy-Szakal, D.; Harris, R.A.; Luna, R.A.; Pitashny, M.; Schady, D.; Mir, S.A.; Lopez, M.E.; Gilger, M.A.; Belmont, J.; *et al.* Serial fecal microbiota transplantation alters mucosal gene expression in pediatric ulcerative colitis. *Am. J. Gastroenterol.* 2015, *110*, 604–606. [Google Scholar] [CrossRef] [PubMed]