

Литература к подразделу [III](#):

**Применение Метаболомики к пробиотическим и пребиотическим
вмешательствам в клинических исследованиях на людях**

Wanping Aw, Shinji Fukuda.

An Integrated Outlook on the Metagenome and Metabolome of Intestinal Diseases
Diseases 2015, 3(4), 341-359

1. Gibson, G.R.; Hutkins, R.; Sanders, M.E.; Prescott, S.L.; Reimer, R.A.; Salminen, S.J.; Scott, K.; Stanton, C.; Swanson, K.S.; Cani, P.D.; et al. Expert consensus document: The International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of prebiotics. *Nat. Rev. Gastroenterol. Hepatol.* 2017, 14, 491–502. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
2. Elie, M. *The Prolongation of Life: Optimistic Studies*; Putnam's Sons: New York, NY, USA, 1908. [[Google Scholar](#)]
3. Cheplin, H.A.; Rettger, L.F. Studies on the transformation of the intestinal flora, with special reference to the implantation of bacillus acidophilus: II. Feeding experiments on man. *Proc. Natl. Acad. Sci. USA* 1920, 6, 704–705. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
4. Clarke, G.; Stilling, R.M.; Kennedy, P.J.; Stanton, C.; Cryan, J.F.; Dinan, T.G. Minireview: Gut microbiota: The neglected endocrine organ. *Mol. Endocrinol.* 2014, 28, 1221–1238. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
5. Pedersen, H.K.; Gudmundsdottir, V.; Nielsen, H.B.; Hyotylainen, T.; Nielsen, T.; Jensen, B.A.; Forslund, K.; Hildebrand, F.; Prifti, E.; Falony, G.; et al. Human gut microbes impact host serum metabolome and insulin sensitivity. *Nature* 2016, 535, 376–381. [[Google Scholar](#)] [[CrossRef](#)]
6. Allison, S.D.; Martiny, J.B. Colloquium paper: Resistance, resilience, and redundancy in microbial communities. *Proc. Natl. Acad. Sci. USA* 2008, 105 (Suppl. 1), 11512–11519. [[Google Scholar](#)] [[CrossRef](#)]
7. Comte, J.; Fauteux, L.; Del Giorgio, P.A. Links between metabolic plasticity and functional redundancy in freshwater bacterioplankton communities. *Front. Microbiol.* 2013, 4, 112. [[Google Scholar](#)] [[CrossRef](#)]
8. Moya, A.; Ferrer, M. Functional Redundancy-Induced Stability of Gut Microbiota Subjected to Disturbance. *Trends Microbiol.* 2016, 24, 402–413. [[Google Scholar](#)] [[CrossRef](#)]
9. Ma, J.; Zhou, Q.; Li, H. Gut microbiota and nonalcoholic fatty liver disease: Insights on mechanisms and therapy. *Nutrients* 2017, 9, 1124. [[Google Scholar](#)] [[CrossRef](#)]
10. Mangiola, F.; Ianiro, G.; Franceschi, F.; Fagiuoli, S.; Gasbarrini, G.; Gasbarrini, A. Gut microbiota in autism and mood disorders. *World J. Gastroenterol.* 2016, 22, 361–368. [[Google Scholar](#)] [[CrossRef](#)]
11. Vallianou, N.G.; Stratigou, T.; Tsagarakis, S. Microbiome and diabetes: Where are we now? *Diabetes Res. Clin. Pract.* 2018, 146, 111–118. [[Google Scholar](#)] [[CrossRef](#)]
12. 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](#)]
13. Martin, F.P.; Sprenger, N.; Montoliu, I.; Rezzi, S.; Kochhar, S.; Nicholson, J.K. Dietary modulation of gut functional ecology studied by fecal metabonomics. *J. Proteome Res.* 2010, 9, 5284–5295. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
14. Vandeputte, D.; Falony, G.; Vieira-Silva, S.; Wang, J.; Sailer, M.; Theis, S.; Verbeke, K.; Raes, J. Prebiotic inulin-type fructans induce specific changes in the human gut microbiota. *Gut* 2017, 66, 1968–1974. [[Google Scholar](#)] [[CrossRef](#)]

15. De Preter, V.; van Staeyen, G.; Esser, D.; Rutgeerts, P.; Verbeke, K. Development of a screening method to determine the pattern of fermentation metabolites in faecal samples using on-line purge-and-trap gas chromatographic-mass spectrometric analysis. *J. Chromatogr. A* 2009, *1216*, 1476–1483. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
16. Burdock, G.A. *Encyclopedia of Food and Color Additives*; CRC Press: Boca Raton, FL, USA, 1996. [[Google Scholar](#)]
17. Lairon, D. Dietary fibres: Effects on lipid metabolism and mechanisms of action. *Eur. J. Clin. Nutr.* 1996, *50*, 125–133. [[Google Scholar](#)] [[PubMed](#)]
18. Windey, K.; de Preter, V.; Huys, G.; Broekaert, W.F.; Delcour, J.A.; Louat, T.; Herman, J.; Verbeke, K. Wheat bran extract alters colonic fermentation and microbial composition, but does not affect faecal water toxicity: A randomised controlled trial in healthy subjects. *Br. J. Nutr.* 2015, *113*, 225–238. [[Google Scholar](#)] [[CrossRef](#)]
19. Wasson, G.R.; McKelvey-Martin, V.J.; Downes, C.S. The use of the comet assay in the study of human nutrition and cancer. *Mutagenesis* 2008, *23*, 153–162. [[Google Scholar](#)] [[CrossRef](#)]
20. Lang, G.; Buchbauer, G. A review on recent research results (2008–2010) on essential oils as antimicrobials and antifungals. A review. *Flavor Fragr. J.* 2012, *27*, 13–39. [[Google Scholar](#)] [[CrossRef](#)]
21. Chen, V.L.; Kasper, D.L. Interactions between the intestinal microbiota and innate lymphoid cells. *Gut Microbes* 2014, *5*, 129–140. [[Google Scholar](#)] [[CrossRef](#)]
22. Vulevic, J.; Juric, A.; Walton, G.E.; Claus, S.P.; Tzortzis, G.; Toward, R.E.; Gibson, G.R. Influence of galacto-oligosaccharide mixture (B-GOS) on gut microbiota, immune parameters and metabolomics in elderly persons. *Br. J. Nutr.* 2015, *114*, 586–595. [[Google Scholar](#)] [[CrossRef](#)]
23. Dewulf, E.M.; Cani, P.D.; Claus, S.P.; Fuentes, S.; Puylaert, P.G.; Neyrinck, A.M.; Bindels, L.B.; de Vos, W.M.; Gibson, G.R.; Thissen, J.P.; et al. Insight into the prebiotic concept: Lessons from an exploratory, double blind intervention study with inulin-type fructans in obese women. *Gut* 2013, *62*, 1112–1121. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
24. Hibberd, A.A.; Yde, C.C.; Ziegler, M.L.; Honore, A.H.; Saarinen, M.T.; Lahtinen, S.; Stahl, B.; Jensen, H.M.; Stenman, L.K. Probiotic or synbiotic alters the gut microbiota and metabolism in a randomised controlled trial of weight management in overweight adults. *Benef. Microbes* 2019, *10*, 121–135. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
25. Han, J.; Liu, Y.; Wang, R.; Yang, J.; Ling, V.; Borchers, C.H. Metabolic profiling of bile acids in human and mouse blood by LC-MS/MS in combination with phospholipid-depletion solid-phase extraction. *Anal. Chem.* 2015, *87*, 1127–1136. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
26. Jie, Z.; Bang-Yao, L.; Ming-Jie, X.; Hai-Wei, L.; Zu-Kang, Z.; Ting-Song, W.; Craig, S.A. Studies on the effects of polydextrose intake on physiologic functions in Chinese people. *Am. J. Clin. Nutr.* 2000, *72*, 1503–1509. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
27. Heimann, E.; Nyman, M.; Palbrink, A.K.; Lindkvist-Petersson, K.; Degerman, E. Branched short-chain fatty acids modulate glucose and lipid metabolism in primary adipocytes. *Adipocyte* 2016, *5*, 359–368. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
28. Koenig, J.E.; Spor, A.; Scalfone, N.; Fricker, A.D.; Stombaugh, J.; Knight, R.; Angenent, L.T.; Ley, R.E. Succession of microbial consortia in the developing infant gut microbiome. *Proc. Natl. Acad. Sci. USA* 2011, *108* (Suppl. 1), 4578–4585. [[Google Scholar](#)] [[CrossRef](#)]
29. Backhed, F.; Roswall, J.; Peng, Y.; Feng, Q.; Jia, H.; Kovatcheva-Datchary, P.; Li, Y.; Xia, Y.; Xie, H.; Zhong, H.; et al. Dynamics and stabilization of the human gut microbiome during the first year of life. *Cell Host Microbe* 2015, *17*, 852. [[Google Scholar](#)] [[CrossRef](#)]
30. Guaraldi, F.; Salvatori, G. Effect of breast and formula feeding on gut microbiota shaping in newborns. *Front. Cell. Infect. Microbiol.* 2012, *2*, 94. [[Google Scholar](#)] [[CrossRef](#)]
31. Tannock, G.W.; Lawley, B.; Munro, K.; Gowri Pathmanathan, S.; Zhou, S.J.; Makrides, M.; Gibson, R.A.; Sullivan, T.; Prosser, C.G.; Lowry, D.; et al. Comparison of the compositions of

- the stool microbiotas of infants fed goat milk formula, cow milk-based formula, or breast milk. *Appl. Environ. Microbiol.* 2013, 79, 3040–3048. [[Google Scholar](#)] [[CrossRef](#)]
32. Bazanella, M.; Maier, T.V.; Clavel, T.; Lagkouvardos, I.; Lucio, M.; Maldonado-Gomez, M.X.; Autran, C.; Walter, J.; Bode, L.; Schmitt-Kopplin, P.; et al. Randomized controlled trial on the impact of early-life intervention with bifidobacteria on the healthy infant fecal microbiota and metabolome. *Am. J. Clin. Nutr.* 2017, 106, 1274–1286. [[Google Scholar](#)] [[CrossRef](#)]
 33. Lucassen, P.L.; Assendelft, W.J. Systematic review of treatments for infant colic. *Pediatrics* 2001, 108, 1047–1048. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
 34. Camilleri, M.; Park, S.Y.; Scarpato, E.; Staiano, A. Exploring hypotheses and rationale for causes of infantile colic. *Neurogastroenterol. Motil.* 2017, 29. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
 35. Baldassarre, M.E.; Di Mauro, A.; Tafuri, S.; Rizzo, V.; Gallone, M.S.; Mastromarino, P.; Capobianco, D.; Laghi, L.; Zhu, C.; Capozza, M.; et al. Effectiveness and safety of a probiotic-mixture for the treatment of infantile colic: A double-blind, randomized, placebo-controlled clinical trial with fecal real-time pcr and nmr-based metabolomics Analysis. *Nutrients* 2018, 10, 195. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
 36. Bozzetto, S.; Pirillo, P.; Carraro, S.; Berardi, M.; Cesca, L.; Stocchero, M.; Giordano, G.; Zanconato, S.; Baraldi, E. Metabolomic profile of children with recurrent respiratory infections. *Pharmacol. Res.* 2017, 115, 162–167. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
 37. Santamaria, F.; Montella, S.; Stocchero, M.; Pirillo, P.; Bozzetto, S.; Giordano, G.; Poeta, M.; Baraldi, E. Effects of pidotimod and bifidobacteria mixture on clinical symptoms and urinary metabolomic profile of children with recurrent respiratory infections: A randomized placebo-controlled trial. *Pulm. Pharmacol. Ther.* 2019, 58, 101818. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
 38. Gaul, J. Probiotics for the prevention of necrotizing enterocolitis. *Neonatal. Netw.* 2008, 27, 75–80. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
 39. Ofek Shlomai, N.; Deshpande, G.; Rao, S.; Patole, S. Probiotics for preterm neonates: What will it take to change clinical practice? *Neonatology* 2014, 105, 64–70. [[Google Scholar](#)] [[CrossRef](#)]
 40. Abdulkadir, B.; Nelson, A.; Skeath, T.; Marrs, E.C.; Perry, J.D.; Cummings, S.P.; Embleton, N.D.; Berrington, J.E.; Stewart, C.J. Routine use of probiotics in preterm infants: Longitudinal impact on the microbiome and metabolome. *Neonatology* 2016, 109, 239–247. [[Google Scholar](#)] [[CrossRef](#)]
 41. Canavan, C.; West, J.; Card, T. The epidemiology of irritable bowel syndrome. *Clin. Epidemiol.* 2014, 6, 71–80. [[Google Scholar](#)] [[CrossRef](#)]
 42. Hong, Y.S.; Hong, K.S.; Park, M.H.; Ahn, Y.T.; Lee, J.H.; Huh, C.S.; Lee, J.; Kim, I.K.; Hwang, G.S.; Kim, J.S. Metabonomic understanding of probiotic effects in humans with irritable bowel syndrome. *J. Clin. Gastroenterol.* 2011, 45, 415–425. [[Google Scholar](#)] [[CrossRef](#)]
 43. Kochhar, S.; Jacobs, D.M.; Ramadan, Z.; Berruex, F.; Fuerholz, A.; Fay, L.B. Probing gender-specific metabolism differences in humans by nuclear magnetic resonance-based metabonomics. *Anal. Biochem.* 2006, 352, 274–281. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
 44. Levine, R.J.; Conn, H.O. Tyrosine metabolism in patients with liver disease. *J. Clin. Investig.* 1967, 46, 2012–2020. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
 45. Greenstein, A.J.; Janowitz, H.D.; Sachar, D.B. The extra-intestinal complications of Crohn's disease and ulcerative colitis: A study of 700 patients. *Medicine* 1976, 55, 401–412. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
 46. Noorbakhsh, H.; Yavarmanesh, M.; Mortazavi, S.A.; Adibi, P.; Moazzami, A.A. Metabolomics analysis revealed metabolic changes in patients with diarrhea-predominant irritable bowel syndrome and metabolic responses to a synbiotic yogurt intervention. *Eur. J. Nutr.* 2019, 58, 3109–3119. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
 47. Sobel, J.D. Is there a protective role for vaginal flora? *Curr. Infect Dis. Rep.* 1999, 1, 379–383. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]

48. Yamamoto, T.; Zhou, X.; Williams, C.J.; Hochwalt, A.; Forney, L.J. Bacterial populations in the vaginas of healthy adolescent women. *J. Pediatr. Adolesc. Gynecol.* 2009, *22*, 11–18. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
49. Bisanz, J.E.; Seney, S.; McMillan, A.; Vongsa, R.; Koenig, D.; Wong, L.; Dvoracek, B.; Gloor, G.B.; Sumarah, M.; Ford, B.; et al. A systems biology approach investigating the effect of probiotics on the vaginal microbiome and host responses in a double blind, placebo-controlled clinical trial of post-menopausal women. *PLoS ONE* 2014, *9*, e104511. [[Google Scholar](#)] [[CrossRef](#)]
50. McMillan, A.; Rulisa, S.; Gloor, G.B.; Macklaim, J.M.; Sumarah, M.; Reid, G. Pilot assessment of probiotics for pregnant women in Rwanda. *PLoS ONE* 2018, *13*, e0195081. [[Google Scholar](#)] [[CrossRef](#)]
51. Reid, G.; Kumar, H.; Khan, A.I.; Rautava, S.; Tobin, J.; Salminen, S. The case in favour of probiotics before, during and after pregnancy: Insights from the first 1500 days. *Benef. Microbes* 2016, *7*, 353–362. [[Google Scholar](#)] [[CrossRef](#)]
52. Smid, M.C.; Stringer, E.M.; Stringer, J.S. A Worldwide epidemic: The problem and challenges of preterm birth in low- and middle-income countries. *Am. J. Perinatol.* 2016, *33*, 276–289. [[Google Scholar](#)] [[CrossRef](#)]
53. Vos, T.; Barber, R.M.; Bell, B.; Bertozzi-Villa, A.; Biryukov, S.; Bolliger, I.; Charlson, F.; Davis, A.; Degenhardt, L.; Dicker, D.; et al. Global, regional and national incidence, prevalence and years live with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990–2013: A systematic analysis for the Global Burden of Disease Study. *Lancet* 2015, *386*, 743–800. [[Google Scholar](#)]
54. McMillan, A.; Rulisa, S.; Sumarah, M.; Macklaim, J.M.; Renaud, J.; Bisanz, J.E.; Gloor, G.B.; Reid, G. A multi-platform metabolomics approach identifies highly specific biomarkers of bacterial diversity in the vagina of pregnant and non-pregnant women. *Sci. Rep.* 2015, *5*, 14174. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
55. Tankou, S.K.; Regev, K.; Healy, B.C.; Tjon, E.; Laghi, L.; Cox, L.M.; Kivisakk, P.; Pierre, I.V.; Hrishikesh, L.; Gandhi, R.; et al. A probiotic modulates the microbiome and immunity in multiple sclerosis. *Ann. Neurol.* 2018, *83*, 1147–1161. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
56. Jangi, S.; Gandhi, R.; Cox, L.M.; Li, N.; von Glehn, F.; Yan, R.; Patel, B.; Mazzola, M.A.; Liu, S.; Glanz, B.L.; et al. Alterations of the human gut microbiome in multiple sclerosis. *Nat. Commun.* 2016, *7*, 12015. [[Google Scholar](#)] [[CrossRef](#)] [[PubMed](#)]
57. Zhang, X.; Zhang, D.; Jia, H.; Feng, Q.; Wang, D.; Liang, D.; Wu, X.; Li, J.; Tang, L.; Li, Y.; et al. The oral and gut microbiomes are perturbed in rheumatoid arthritis and partly normalized after treatment. *Nat. Med.* 2015, *21*, 895–905. [[Google Scholar](#)] [[CrossRef](#)]
58. Miyake, S.; Kim, S.; Suda, W.; Oshima, K.; Nakamura, M.; Matsuoka, T.; Chihara, N.; Tomita, A.; Sato, W.; Kim, S.W.; et al. Dysbiosis in the gut microbiota of patients with multiple sclerosis, with a striking depletion of species belonging to clostridia XIVA and IV clusters. *PLoS ONE* 2015, *10*, e0137429. [[Google Scholar](#)] [[CrossRef](#)]
59. Chen, J.; Chia, N.; Kalari, K.R.; Yao, J.Z.; Novotna, M.; Paz Soldan, M.M.; Luckey, D.H.; Marietta, E.V.; Jeraldo, P.R.; Chen, X.; et al. Multiple sclerosis patients have a distinct gut microbiota compared to healthy controls. *Sci. Rep.* 2016, *6*, 28484. [[Google Scholar](#)] [[CrossRef](#)]
60. Matsumoto, M.; Ebata, T.; Hirooka, J.; Hosoya, R.; Inoue, N.; Itami, S.; Tsuji, K.; Yaginuma, T.; Muramatsu, K.; Nakamura, A.; et al. Antipruritic effects of the probiotic strain LKM512 in adults with atopic dermatitis. *Ann. Allergy Asthma Immunol.* 2014, *113*, 209–216. [[Google Scholar](#)] [[CrossRef](#)]
61. Bjorksten, B.; Naaber, P.; Sepp, E.; Mikelsaar, M. The intestinal microflora in allergic Estonian and Swedish 2-year-old children. *Clin. Exp. Allergy* 1999, *29*, 342–346. [[Google Scholar](#)] [[CrossRef](#)]

62. Kalliomaki, M.; Kirjavainen, P.; Eerola, E.; Kero, P.; Salminen, S.; Isolauri, E. Distinct patterns of neonatal gut microflora in infants in whom atopy was and was not developing. *J. Allergy Clin. Immunol.* 2001, *107*, 129–134. [[Google Scholar](#)] [[CrossRef](#)]
63. Penders, J.; Thijs, C.; van den Brandt, P.A.; Kummeling, I.; Snijders, B.; Stelma, F.; Adams, H.; van Ree, R.; Stobberingh, E.E. Gut microbiota composition and development of atopic manifestations in infancy: The KOALA Birth Cohort Study. *Gut* 2007, *56*, 661–667. [[Google Scholar](#)] [[CrossRef](#)]
64. Abrahamsson, T.R.; Jakobsson, H.E.; Andersson, A.F.; Bjorksten, B.; Engstrand, L.; Jenmalm, M.C. Low diversity of the gut microbiota in infants with atopic eczema. *J. Allergy Clin. Immunol.* 2012, *129*, 434–440. [[Google Scholar](#)] [[CrossRef](#)]
65. Matsumoto, M.; Aranami, A.; Ishige, A.; Watanabe, K.; Benno, Y. LKM512 yogurt consumption improves the intestinal environment and induces the T-helper type 1 cytokine in adult patients with intractable atopic dermatitis. *Clin. Exp. Allergy* 2007, *37*, 358–370. [[Google Scholar](#)] [[CrossRef](#)]
66. Dufour, C.; Dandrifosse, G.; Forget, P.; Vermesse, F.; Romain, N.; Lepoint, P. Spermine and spermidine induce intestinal maturation in the rat. *Gastroenterology* 1988, *95*, 112–116. [[Google Scholar](#)] [[CrossRef](#)]
67. Wang, J.Y.; McCormack, S.A.; Viar, M.J.; Johnson, L.R. Stimulation of proximal small intestinal mucosal growth by luminal polyamines. *Am. J. Physiol.* 1991, *261*, G504–G511. [[Google Scholar](#)] [[CrossRef](#)]
68. Buts, J.P.; de Keyser, N.; Kolanowski, J.; Sokal, E.; Van Hoof, F. Maturation of villus and crypt cell functions in rat small intestine. Role of dietary polyamines. *Dig. Dis. Sci.* 1993, *38*, 1091–1098. [[Google Scholar](#)] [[CrossRef](#)]
69. Deloyer, P.; Peulen, O.; Dandrifosse, G. Dietary polyamines and non-neoplastic growth and disease. *Eur. J. Gastroenterol. Hepatol.* 2001, *13*, 1027–1032. [[Google Scholar](#)] [[CrossRef](#)]
70. Kanauchi, O.; Iwanaga, T.; Mitsuyama, K.; Saiki, T.; Tsuruta, O.; Noguchi, K.; Toyonaga, A. Butyrate from bacterial fermentation of germinated barley foodstuff preserves intestinal barrier function in experimental colitis in the rat model. *J. Gastroenterol. Hepatol.* 1999, *14*, 880–888. [[Google Scholar](#)] [[CrossRef](#)]
71. Mariadason, J.M.; Barkla, D.H.; Gibson, P.R. Effect of short-chain fatty acids on paracellular permeability in Caco-2 intestinal epithelium model. *Am. J. Physiol.* 1997, *272*, G705–G712. [[Google Scholar](#)] [[CrossRef](#)]
72. Venkatraman, A.; Ramakrishna, B.S.; Pulimood, A.B. Butyrate hastens restoration of barrier function after thermal and detergent injury to rat distal colon In Vitro. *Scand. J. Gastroenterol.* 1999, *34*, 1087–1092. [[Google Scholar](#)] [[CrossRef](#)]
73. Pinu, F.R.; Goldansaz, S.A.; Jaïne, J. Translational metabolomics: Current challenges and future opportunities. *Metabolites* 2019, *9*, 108. [[Google Scholar](#)] [[CrossRef](#)]
74. Karu, N.; Deng, L.; Slae, M.; Guo, A.C.; Sajed, T.; Huynh, H.; Wine, E.; Wishart, D.S. A review on human fecal metabolomics: Methods, applications and the human fecal metabolome database. *Anal. Chim. Acta* 2018, *1030*, 1–24. [[Google Scholar](#)] [[CrossRef](#)]
75. Gratton, J.; Phetcharaburanin, J.; Mullish, B.H.; Williams, H.R.; Thursz, M.; Nicholson, J.K.; Holmes, E.; Marchesi, J.R.; Li, J.V. Optimized sample handling strategy for metabolic profiling of human feces. *Anal. Chem.* 2016, *88*, 4661–4668. [[Google Scholar](#)] [[CrossRef](#)]
76. Bliss, D.Z.; Savik, K.; Jung, H.; Jensen, L.; LeMoine, M.; Lowry, A. Comparison of subjective classification of stool consistency and stool water content. *J. Wound Ostomy Cont. Nurs* 1999, *26*, 137–141. [[Google Scholar](#)] [[CrossRef](#)]
77. Dieterle, F.; Ross, A.; Schlotterbeck, G.; Senn, H. Probabilistic quotient normalization as robust method to account for dilution of complex biological mixtures. Application in ¹H NMR metabonomics. *Anal. Chem.* 2006, *78*, 4281–4290. [[Google Scholar](#)] [[CrossRef](#)]