



Potentials of Microorganisms in Human Health

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Author's contribution

The sole author designed analyzed, interpreted and prepared the manuscript.

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Short Communication

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ABSTRACT

There are large numbers of powerful species of microorganisms present within our bodies that make up the diverse human microbiomes. Microbiomes, the collective genomes of the microorganisms in a particular environment, support and maintain our health, but they are disturbed in some fashion in case of the presence of some diseases such as autoimmune diseases and cancer. Different food products provide different growth conditions for microorganisms. Microbial growth is also controlled by some factors such as pH, nutrients, moisture content, temperature, relative humidity, and gases. Thus the growth of microorganisms in optimum conditions results in spoilage and degradation of food products resulting in a sour or foul-smelling, in addition to a visible change in color, effervescences on the food surface, etc. Microbial contamination of food can occur at any point in the food production process starting from growth, harvesting, transport, storage, or final preparation. A variety of environmental factors can influence intestinal microbial imbalance, which has a close relationship with human health and disease. There are many numerous potential probiotics or beneficial bacteria that may prevent or treat certain diseases such as *Lactobacillus* and *Bifidobacterium*. On the other hand, a few destructive microorganisms play a major role in the development and progression of major human diseases such as infectious diseases, liver diseases, gastrointestinal cancers, metabolic diseases, respiratory diseases, mental or psychological diseases, and autoimmune diseases. With the increased understanding of the relationship between the human microbiome and a variety of diseases, the use of these findings to predict or diagnose diseases has attracted a great deal of attention. Thus, the aim of the present work was to review

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briefly the role of microorganisms in human health, during the development of autoimmune and tumor diseases. This review article also includes microbiota diversity, colonization, and normalization of perturbed intestinal microbial communities, the safety of gastrointestinal tract, and the beneficial role of probiotics.

Keywords: Microorganisms; human health; probiotics; nutrition; microbiota.

1. ROLE OF MICROORGANISMS IN THE SAFETY OF GASTROINTESTINAL TRACT

Around a hundred trillion microorganisms (such as, bacteria, fungi, viruses, and protozoa) exist within the human gastrointestinal tract [1,2]. The microbiome encodes over three million genes producing thousands of metabolites, which replace numerous of the capacities of the host [3], consequently affecting the host's fitness, phenotype, and health [4]. Gut microbes are key to various aspects of human health including metabolic, immune, and neuro-behavioral traits [5-7]. Different levels of evidence support the role of gut microbiota in human health, from animal models [8] and human studies [9]. The gut microbiota gives essential capacities for the fermentation of non-digestible substrates like dietary fibers and endogenous intestinal mucus. This fermentation supports the growth of microbes that produce short-chain fatty acids (such as acetate, propionate, and butyrate), and gases [10]. In this connection, butyrate is the most vitality source for human colonocytes can start apoptosis of colon cancer cells and can activate intestinal gluconeogenesis, having beneficial impacts on glucose and energy homeostasis [11]. Butyrate is fundamental for epithelial cells to expend expansive amounts of oxygen through β oxidation, creating a state of hypoxia that keeps up oxygen balance within the gut, preventing gut microbiota dysbiosis [12]. There is growing evidence that any change in microbiota composition leads to several metabolic diseases including diabetes, obesity, and cardiovascular. Different parts of the intestinal tract have different compositions of microbes and it varies according to age, weight, site, and diet [13-16]. Most studies of overweight and obese people show a dysbiosis characterized by a lower diversity. For example the microbes that live inside our intestines influence our health in beneficial and harmful ways (Fig. 1). A variety of mechanisms including immune dysregulation and alter gut hormone and energy regulation promote diet-induced obesity and metabolic complications [17].

2. DETERIORATION OF FOOD BY CONTAMINANTS

During the past 30 years, the problem of food contamination has received considerable attention. Generally, foods may spoil through the action of several agents including microorganisms (fungi, molds, yeasts, and bacteria), enzymes, insect and animal contamination. The character of the food material will determine largely which type of spoilage occurs. An acid condition is favorable to yeasts and molds but unfavorable to bacteria. Thus, fruit products and acid vegetables are susceptible primarily to yeast fermentation or mold growth, and nonacid vegetables and meats are susceptible to the action of bacteria. A proper evaluation of these factors involved in food spoilage is essential to the proper processing, transportation, storage, handling, and merchandising of food products. The preservation of foods is intended to reduce or inhibit microbial growth, enzymatic activity, and atmospheric oxidation. These factors responsible for food spoilage may be controlled by food processing procedures or by chemical additives (food additives). Only a relatively few chemical additives are used in food preservation and their use must comply with FDA regulations [18-20].

The following methods are applicable in the preservation of foods:-

- a) Removal of water: Dehydration or drying is effective as method of preservation because bacteria must obtain their nutrients in soluble form and thus require the presence of water.
- b) Refrigeration: The effectiveness of refrigeration as a preservation method requires maintaining food at a sufficiently low temperature (usually 0°_4°C) to retard microbial growth, enzymatic activity, and atmospheric oxidation.
- c) Freezing: The effectiveness of refrigeration as a preservation method requires maintaining food at a sufficiently low temperature (usually 0°_4°C) to retard

- microbial growth, enzymatic activity, and atmospheric oxidation.
- d) Heating: The application of heat to kill microorganisms and inactivate enzymes by denaturation is a very common form of food preservation.
 - e) Exclusion of air: Certain types of deterioration are prevented by excluding air from food products. This is achieved by various means depending upon the type of product involved.
 - f) Exclusion of light: Atmospheric oxidation of fats themselves and of products containing fats, essential oils, and pigments is retarded by the exclusion of light. This is true because blue and ultraviolet light materially accelerates the atmospheric oxidation of food products containing fats.
 - g) Radiation: Both ultraviolet and ionizing radiations are used to a limited extent for food preservation. Ultraviolet irradiation as a method of food preservation has found application in the meat, baking, beverage, dairy, fresh fruit and vegetable, and frozen food industries.
 - h) Sugaring: Sugar solutions of high concentration exert a high osmotic pressure and withdraw water from microorganisms, thereby preventing their growth. This method of food preservation is limited to those products in which a large quantity of sugar can be used.
 - i) Salting: Salt functions as a preservative through its effect on osmotic pressure and the destructive effect of the chloride ion itself on microorganisms. Gram-negative bacteria are more sensitive to sodium chloride (8%) than gram-positive bacteria.
 - j) Smoking: Food products are usually smoked by subjecting them to the action of smoke in a closed room. Few meat products are produced in which smoke constituents exert an important effect in protecting the product against microbial spoilage.
 - k) Spicing: Spices were once considered to have an appreciable preservative action due to the volatile oils they contained.
 - l) Pickling and souring: The acidity associated with pickling or souring is unfavorable to bacterial growth and thereby acts as a preservative.
- Foods may be contaminated with a number of microorganisms or toxic products that are potentially toxic to humans or that otherwise make food unfit or undesirable for consumption. Among the important contaminants are botulinum toxins, mycotoxins, and aflatoxins.
- a) Botulinum Toxins: Botulism is a food-borne disease that afflicts man and several species of animals with a high fatality rate. The cause is the contamination of food materials by a specific group of spore-forming bacteria found in the soil and aquatic environments. The rate of mortality in botulism varies according to the immunological type of toxin involved. The causative agent of botulism is the gram-positive, anaerobic bacillus *Clostridium botulinum*. These endospore-forming bacteria possess a heat-resistant form, which under suitable growth conditions germinate to form the rod-shaped vegetative form. The vegetative form is capable of active proliferation and exotoxin formation in substrates such as canned foods or other food products that have the required low oxygen tension [21].
 - b) Mycotoxins: The term mycotoxin refers to all toxic metabolites of the true fungi, Eumycetes. Mycotoxicosis is the general term used to describe the diseases caused by mycotoxins. Ergotism, caused by the parasitic fungus *Claviceps purpurea*, is a well-known disease of this type. The term mycotoxin is usually restricted to the filamentous fungi called molds. In nature, these molds are both parasitic and saprophytic and are widely distributed over the earth's surface [22].
 - c) Aflatoxins: They are hepatotoxic carcinogenic metabolites of *Aspergillus flavus*, which grows on many different foodstuffs when sufficient moisture is present. In the laboratory, aflatoxins have been produced on many foods by growing *Aspergillus flavus* on the food [23].

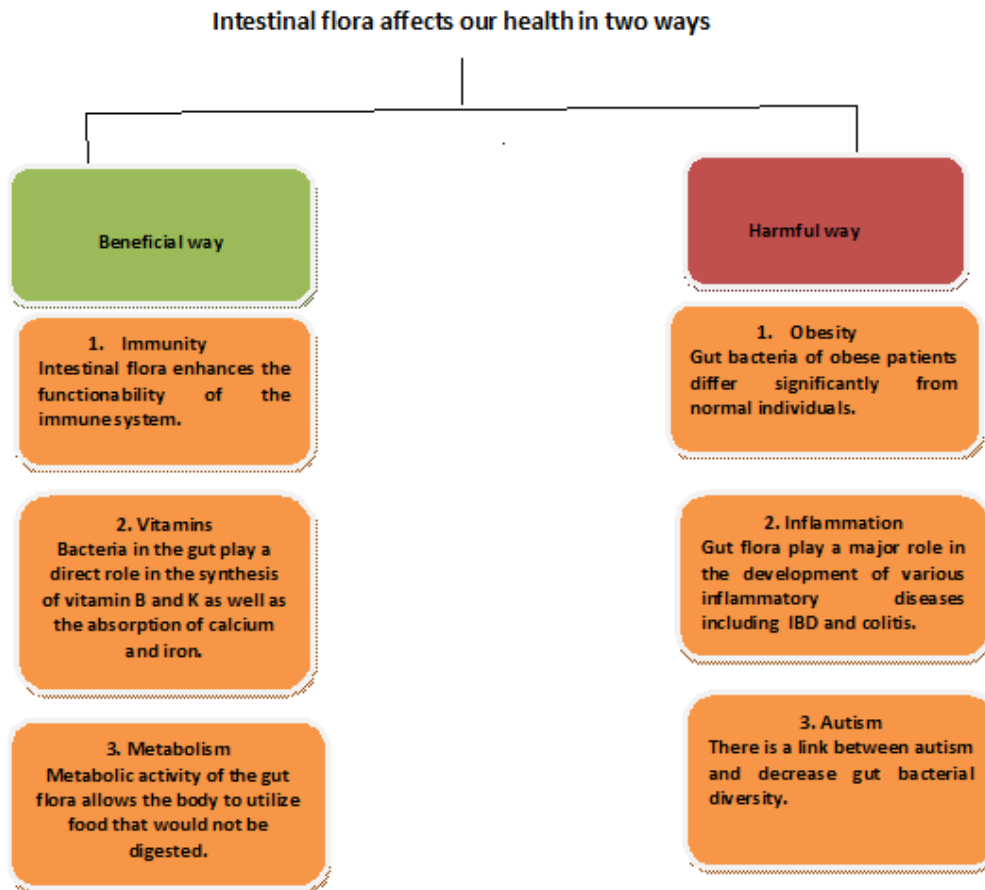


Fig. 1. Intestinal flora affects our health by two ways

3. THE ROLE OF MICROORGANISMS DURING THE DEVELOPMENT OF AUTOIMMUNE AND TUMOR DISEASES

Recently, it has been reported that microbial imbalance may play a critical role in the development of multiple diseases, such as autoimmune conditions, cancer, and increased susceptibility to infection. Oncogenic viruses, seven of which are known to be associated with human cancer, represent an important infectious cause of cancer [24]. Two of the human oncogenic viruses are herpes viruses: Epstein-Barr virus (EBV), which is associated with Burkitt's lymphoma, nasopharyngeal carcinoma, and a subset of gastric carcinoma, and Kaposi's sarcoma-associated herpesvirus/human herpesvirus type 8, which causes Kaposi's sarcoma and other pathologies in immune-suppressed individuals [24]. The two hepatitis viruses among the tumorigenic viruses, hepatitis

B virus and hepatitis C virus (HBV and HCV), are associated with hepatocellular carcinoma (HCC) [25]. High-risk oncogenic strains of human papilloma viruses are associated with anogenital cancers, a subset of head and neck cancers and skin cancers [26]. The human T-cell lymphoma virus is the pathogenic determinant of the T-cell lymphomas prevalent in certain geographical regions [27]. Although commensal bacteria may likely also play a role in human and animal carcinogenesis, *Helicobacter pylori* is the only bacterial species that has been defined as a class I human carcinogen by the International Agency for Research on Cancer, by virtue of its certain association with gastric carcinoma and lymphoma. Dysbiosis of the intestinal microbiota or its physical interaction with hematopoietic cells following barrier damage can both regulate inflammation [28] and be a cause of cancer [29]. There is now a considerable body of evidence, both in humans and in experimental animals, that the commensal microbiota (bacteria, fungi, and viruses) exerts important effects on

carcinogenesis, tumor progression, and the response to therapy. The effect of the microbiota on cancer can be local, situated at the level of the organism barriers in which cancer originates, or can be systemic, through the physiological communication of the organism and the microbiota through an intact membrane or following alteration of barrier permeability in pathology. While many mechanisms of the local effects have been characterized in recent years, our understanding of the systemic effects is currently much more rudimentary [30]. A detailed understanding of these mechanisms both in experimental animals and in humans will teach us how to target them therapeutically and could bring much progress in cancer prevention and treatment. A recent report showed that in mice a reduction of colon polyps incidence could be achieved by either antibiotics treatment, or a diet reduced in carbohydrates that induced changes in the microbiota composition and reduced the production of SCFAs [31]. While that report indicates the possibility to somehow influence the outcome of cancer with modifications in the microbiota, it also indicates the importance of a full understanding of the role of different microbial species and functions in cancer, because, in other experimental models, SCFAs have been shown to be protective against colon and mammary cancer [32]. Clinically, different therapeutic approaches are potentially available, including the use of probiotics, diet modification and prebiotics, fecal or defined microbiota transfer, which could be used for cancer prevention; supportive therapy for cancer and cancer comorbidities treatment; and enhancement of the response to cancer immune, chemo, and radiation therapy [33]. Fecal transplant has been shown to be very successful in the treatment of *Clostridium difficile* infections in humans and has been proposed as a treatment for IBD and metabolic disorders, although several safety and consistency concerns remain, which may suggest the usefulness of developing better-defined and safer microbial replacement therapeutic procedures [34,35].

4. MICROBIOTA DIVERSITY

Studies reported on the microbiota diversity and health indicate that Lower bacterial diversity has been reproducibly observed in people with type 1 diabetes [36,37], type 2 diabetes [38], Inflammatory bowel disease [39], coeliac disease [40], psoriatic arthritis [41], atopic eczema [42],

arterial stiffness [43] and obesity [44] than in healthy controls.

5. THE BENEFICIAL ROLE OF PROBIOTICS

The other brilliant portion of the relationship between microorganisms and human health incorporates probiotics which are defined as live microorganisms that are similar to the beneficial microorganisms found in humans and are hence "Generally Regarded As Safe" (GRAS). Their activities have demonstrated their effectiveness in cases of antibiotic-associated diarrhea, irritable bowel syndrome, lactose intolerance, oral health, etc. Probiotics are commonly consumed as part of fermented foods with specially added active live cultures such as in yogurt soy and yogurt or as dietary supplements [45]. A probiotic contains thousands of genes that may potentially influence the clinical effects. Furthermore, interaction with the host, food components or endogenous substrates, or the endogenous microbiota inside the gastrointestinal lumen may generate by-products or end-products with functional properties. The intestinal microflora likely plays a basic part in inflammatory conditions in the gut and potentially probiotics could remediate such conditions through modulation of the microflora. Some probiotic strains were shown to inhibit the growth of enteropathogens, such as *Salmonella enteritidis*, enterotoxigenic *Escherichia coli*, and *Serratia marcescens* in vitro. This finding together with more recent evidence showing that Lactobacillus exerts antagonist activity against *Salmonella typhimurium* infection both in vitro and in vivo [46]. There is some clinical evidence to suggest that oral and vaginal administration of lactobacilli can eradicate asymptomatic [47,48] and symptomatic bacterial vaginosis [49].

6. BENEFITS OF MICROORGANISMS FOR HUMAN HEALTH

There are many other benefits of microorganisms for human health in many sectors [50] as follows:-

1. In medicine: Microorganisms have a significant role in the production of antibiotics, insulin, and vaccines. They are also used in the diagnosis of certain diseases.

2. In the food industry: Microorganisms are essential in the production of fermented foods and beverages. For example Lactobacilli. Foods like cheese, bread, beer, sauce, olives and sausages are made using different species of bacteria and yeasts.
3. In waste treatment: Microorganisms play a major role in the handling and disposal of domestic and industrial wastes through biological processes of decomposition producing compost.
4. In microflora: There are billions of bacteria that inhabit the digestive tract of humans. The microflora is responsible for defending the body from bacteria and fungi harmful to human health. It produces vitamin k, which is necessary to regulate blood clotting processes.
5. In Biotechnology: Biotechnology is the branch of science that deals with the manipulation of living organisms through genetic engineering which depends directly on microorganisms. In addition, microorganisms are used recently to produce alternative energy sources such as biofuels and bio-alcohol.
6. In agriculture: Some microorganisms that live in the soil allow improving agriculture productivity. Humans naturally use microorganisms to develop biopesticides and biofertilizers.
7. In the environment: Microorganisms are present in the biosphere and their presence affects beneficially the environment in which they coexist.
8. In body balance: The complex communities of microorganisms located in the human body have the power to balance or unbalance. For this reason administration of probiotics allow the regulation of internal processes of the body.

7. CONCLUSION

Microorganisms have been distinguished to play an important role in human health and illnesses. Physiological characterization of these microorganisms and characterizing their functional molecular machinery might empower

us to create potential diagnostic and therapeutic targets. For this reason, the study of the human microbiome is important, and it gives an in-depth understanding of the interplay between humans and their indigenous microbiota. This gives valuable insight into further research studies in optimizing these microorganisms to combating life-threatening diseases. Most of the recent studies indicate that continuous use of broad-spectrum antibiotics may disrupt the human microbiota. This results in an imbalance of the indigenous microbial community paving way for invading pathogens. However, further studies should be focused on the use of new therapeutic medicine, prebiotics, and probiotics in the treatments of human infectious diseases.

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COMPETING INTERESTS

Author has declared that no competing interests exist.

REFERENCES

1. Motta J, Wallace JL, Buret AG, Deraison C, Vergnolle N. Gastrointestinal biofilms in health and disease. *Nature Reviews Gastroenterology and Hepatology*. 2021;18(5):314-334.
2. Bull MJ, Plummer NT. Part 1: The human gut microbiome in health and disease. *Integr Med (Encinitas)*. 2014;13:17-22.
3. Vyas U, Ranganathan N. Probiotics, prebiotics, and synbiotics: Gut and beyond. *Gastroenterol Res Pract*. 2012;872716. DOI:10.1155/2012/872716.
4. Rath CM, Dorrestein PC. The bacterial chemical repertoire mediates metabolic exchange within gut microbiomes. *Curr Opin Microbiol*. 2012;15:147-54. DOI:10.1016/j.mib.2011.12.009.
5. Zhang H, Sparks JB, Karyala SV, Settlege R, Luo XM. Host adaptive immunity alters gut microbiota. *ISME J*. 2015 9:770-81. DOI:10.1038/ismej.2014.165.
6. Rothschild D, Weissbrod O, Barkan E, et al. Environment dominates over host genetics in shaping human gut microbiota. *Nature*. 2018;555:210-5. DOI:10.1038/nature25973.

7. Levy M, Kolodziejczyk AA, Thaiss CA, Elinav E. Dysbiosis and the immune system. *Nat Rev Immunol.* 2017;17:219-32. DOI:10.1038/nri.2017.7.
8. De Palma G, Lynch MD, Lu J, et al. Transplantation of fecal microbiota from patients with irritable bowel syndrome alters gut function and behavior in recipient mice. *Sci Transl Med.* 2017;9:9. DOI:10.1126/scitranslmed.aaf6397.
9. Beaumont M, Goodrich JK, Jackson MA, et al. Heritable components of the human fecal microbiome are associated with visceral fat. *Genome Biol.* 2016;17:189. DOI:10.1186/s13059-016-1052-7.
10. Wong JM, de Souza R, Kendall CW, Emam A, Jenkins DJ. Colonic health: Fermentation and short-chain fatty acids. *J Clin Gastroenterol.* 2006;40:235-43. DOI:10.1097/00004836-200603000-00015.
11. De Vadder F, Kovatcheva-Datchary P, Goncalves D, Vinera J, Zitoun C, Duchamp A, Backhed F, Mithieux G. Microbiota-generated metabolites promote metabolic benefits via gut-brain neural circuits. *Cell.* 2014;156:84-96. DOI:10.1016/j.cell.2013.12.016.
12. Byndloss MX, Olsan EE, Rivera-Chavez F, et al. Microbiota-activated PPAR- γ signaling inhibits dysbiotic Enterobacteriaceae expansion. *Science.* 2017;357:570-5. DOI:10.1126/science.aam9949.
13. Stecher B. The roles of inflammation, nutrient availability and the commensal microbiota in enteric pathogen infection. *Microbiol Spectr.* 2015;3(3). DOI:10.1128/microbiolspec.MBP-0008-2014. PMID: 26185088 .
14. Roberfroid M, Gibson GR, Hoyles L, McCartney AL, Rastall R, Rowland I, Wolvers D, Watzl B, Szajewska H, Stahl B, Guarner F, Respondek F, Whelan K, Coxam V, Davicco MJ, Léotoing L, Wittrant Y, Delzenne NM, Cani PD, Neyrinck AM, Meheust A. Prebiotic effects: Metabolic and health benefits. *Br J Nutr.* 2010;104(2):1-63. DOI:10.1017/S0007114510003363. PMID: 20920376.
15. Sirisinha S. The potential impact of gut microbiota on your health: Current status and future challenges. *Asian Pac J Allergy Immunol.* 2016;34(4):249-264. DOI:10.12932/AP0803. PMID: 28042926 Review.
16. Tomasello G, Tralongo P, Damiani P, Sinagra E, Di Trapani B, Zeenny MN, Hussein IH, Jurjus A, Leone A. Dismicrobism in inflammatory bowel disease and colorectal cancer: Changes in response of colocytes. *World J Gastroenterol.* 2014;20(48):18121-30. DOI:10.3748/wjg.v20.i48.18121.
17. Baothman OA, Zamzami MA, Taher I, Abubaker J, Abu-Farha M. The role of gut microbiota in the development of obesity and diabetes. *Lipids Health Dis.* 2016;15:108. DOI:10.1186/s12944-016-0278-4.
18. Sankaran S. "Development and evaluation of novel sensing materials for detecting food contamination." Doctoral dissertation, North Dakota State University of Agriculture and Applied Science; 2009.
19. Nerin C, Aznar M, Carrizo D. "Food contamination during food process." *Trends in Food Science and Technology.* 2016;48:63-68.
20. Yeleliere E, Cobbina SJ, Abubakari ZI. "Review of microbial food contamination and food hygiene in selected capital cities of Ghana." *Cogent Food and Agriculture.* 2017;3(1).
21. Rasetti-Escargueil C, Lemichez E, Popoff MR. Public health risk associated with botulism as foodborne zoonoses. *Toxins.* 2019;12:17.
22. Obida MG, Stephen SH, Goni AD, James AA. Assessment of mycotoxins (Total Aflatoxins and Ochratoxin – A) contamination of staple cereals. *International Journal of Chemical and Biochemical Sciences.* 2012;2:1-6.
23. Kata K, Paolo B, Andrea S, Federica G, Silvia P, Vittorio Z, Alessandra C, Zsuzsa F, Árpád A. An effective self-control strategy for the reduction of aflatoxin M1 content in milk and to decrease the exposure of consumers. *Food Additives and Contaminants. Part A;* 2016. DOI:10.1080/19440049.2016.1241895.
24. Zhang X, Zhang Z, Zheng B, He Z, Winberg G, Ernberg I. An update on viral association of human cancers. *Arch. Virol.* 2013;158:1433–1443.
25. Ng J, Wu J. Hepatitis B- and hepatitis C-related hepatocellular carcinomas in the United States: Similarities and differences. *Hepat. Mon.* 2012;12:7635.

26. Psyrrri A, Rampia T, Vermorken JB. The current and future impact of human papillomavirus on treatment of squamous cell carcinoma of the head and neck. *Ann. Oncol.* 2014;25:2101–2115.
27. Ciminale V, Rende, F, Bertazzoni U, Romanelli MG. HTLV-1 and HTLV-2: Highly similar viruses with distinct oncogenic properties. *Front Microbiol.* 2014;5:398.
28. Richard M, Peek Jr, Blaser JB. *Helicobacter pylori* and gastrointestinal tract adenocarcinomas. *Nat. Rev. Cancer.* 2002;2:28–37.
29. Rao VP, Poutahidis T, Ge Z, Nambiar PR, Bousahmain C, Wang YY, Horwitz BH, et al. Innate immune inflammatory response against enteric bacteria *Helicobacter hepaticus* induces mammary adenocarcinoma in mice. *Cancer Res.* 2006;66:7395–7400.
30. Dzutsev A, Goldszmid RS, Viaud S, Zitvogel L, Trinchieri G. The role of the microbiota in inflammation, carcinogenesis, and cancer therapy. *Eur. J. Immunol.* 2015;45:17–31. DOI: 10.1002/eji.201444972.
31. Belcheva A, Irrazabal T, Robertson SJ, Streutker C, Maughan H, Rubino S, Moriyama EH, et al. Gut microbial metabolism drives transformation of *msh2*-deficient colon epithelial cells. *Cell.* 2014;158:288–299.
32. Elangovan S, Pathania R, Ramachandran S, Ananth S, Padia RN, Lan L, Singh N, et al. The niacin / butyrate receptor GPR109A suppresses mammary tumorigenesis by inhibiting cell survival. *Cancer Res.* 2014;74:1166–1178.
33. Ursell LK, Van Treuren W, Metcalf JL, Pirrung M, Gewirtz A, Knight R. Replenishing our defensive microbes. *Bioessays.* 2013;35:810–817.
34. Van Nood E, Vriese A, Nieuwdorp M, Fuentes S, Zoetendal EG, de Vos WM, Visser CE, et al. Duodenal infusion of donor feces for recurrent *Clostridium difficile*. *N. Engl. J. Med.* 2013;368:407–415.
35. Vriese A, Van Nood E, Holleman F, Salojarvi J, Kootte RS, Bar-telsman JF, Dallinga-Thie GM, et al. Transfer of intestinal micro-biota from lean donors increases insulin sensitivity in individuals with metabolic syndrome. *Gastroenterology.* 2012;143:913–916.
36. Keskitalo A, Aatsinki AK, Kortelainen S, Pelto J, Korhonen L, Lahti L, Lukkarinen M, Munukka E, Karlsson H, Karlsson L. Gut microbiota diversity but not composition is related to saliva cortisol stress response at the age of 2.5 months. *Stress.* 2021;17:1-10. DOI: 10.1080/10253890.2021.1895110. Epub ahead of print. PMID: 33729084.
37. De Goffau MC, Luopajarvi K, Knip M, et al. Fecal microbiota composition differs between children with β -cell autoimmunity and those without diabetes. 2013;62:1238-44. DOI:10.2337/db12-0526.
38. Lambeth SM, Carson T, Lowe J, et al. Composition, diversity and abundance of gut microbiome in prediabetes and type 2 diabetes. *J Diabetes Obes.* 2015;2:1-7.
39. Manichanh C, Rigottier-Gois L, Bonnaud E, et al. Reduced diversity of faecal microbiota in Crohn's disease revealed by a metagenomic approach. *Gut.* 2006;55:205-11. DOI:10.1136/gut.2005.073817.
40. Schippa S, Iebba V, Barbato M, et al. A distinctive 'microbial signature' in celiac pediatric patients. *BMC Microbiol.* 2010;10:175. DOI:10.1186/1471-2180-10-175.
41. Scher JU, Ubeda C, Artacho A, et al. Decreased bacterial diversity characterizes the altered gut microbiota in patients with psoriatic arthritis, resembling dysbiosis in inflammatory bowel disease. *Arthritis Rheumatol.* 2015;67:128-39. DOI:10.1002/art.38892.
42. Wang M, Karlsson C, Olsson C, et al. Reduced diversity in the early fecal microbiota of infants with atopic eczema. *J Allergy Clin Immunol.* 2008;121:129-34. DOI:10.1016/j.jaci.2007.09.011.
43. Menni C, Lin C, Cecelja M, et al. Gut microbial diversity is associated with lower arterial stiffness in women. *Eur Heart J.* 2018;39(25):2390–2397. Available: <https://doi.org/10.1093/eurheartj/ehy226>.
44. Turnbaugh PJ, Hamady M, Yatsunenko T, et al. A core gut microbiome in obese and lean twins. *Nature.* 2009;457:480-484. DOI:10.1038/nature07540.
45. Vijayaram S, Kannan S. Probiotics: The marvelous factor and health benefits. *Biomedical, Biotechnology Research Journal (BBRJ).* 2018;2(1):1-8.

46. Hudault S, Lievin V, Bernet-Camard MF, Servin AL. Antagonistic activity exerted *in vitro* and *in vivo* by *Lactobacillus casei* (strain GG) against *Salmonella typhimurium* C5 infection. *Appl Environ Microbiol.* 1997;63:513–8.
47. Reid G, Bruce AW, Taylor M. Instillation of lactobacillus and stimulation of indigenous organisms to prevent recurrence of urinary tract infections. *Microecol Ther.* 1995;23:32–45.
48. Reid G, Bruce AW, Fraser N, Heinemann C, Owen J, Henning B. Oral probiotics can resolve urogenital infections. *FEMS Immunol Med Microbiol.* 2001;30:49–52.
DOI:10.1111/j.1574-695X.2001.tb01549.x.
49. Hamilton-Miller JMT, Fuller R. Probiotics panacea or nostrum. *BNF Nutr Bull.* 1996;21:199–208.
50. Marco ML. Defining how microorganisms benefit human health. *Microbial Biotechnology.* 2020;14:35-40.
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