




Editorial

The Relation of Diet and Health: You Are What You Eat

Ann-Kathrin Lederer ^{1,2,*}  and Roman Huber ¹

¹ Center for Complementary Medicine, Department of Medicine II, Medical Center—University of Freiburg, Faculty of Medicine, University of Freiburg, 79106 Freiburg, Germany; roman.huber@uniklinik-freiburg.de

² Department of General, Visceral and Transplantation Surgery, University Medical Center, 55131 Mainz, Germany

* Correspondence: ann-kathrin.lederer@uniklinik-freiburg.de

The intake of food is more than just a necessary process for ensuring the functionality of the human body. Nutritional components become a part of us, interacting with our gut microbiota, immune system and metabolism. For decades, it has been known that the occurrence and the course of a variety of typical Western diseases such as cancer, stroke and myocardial infarction are affected by diet [1–4]. The common Western diet consists of highly processed foods and is rich of animal protein, trans-fatty acids and sugar [5,6]. Recent research shows that a diet rich in red meat and processed meat leads to a high risk of cancer, especially colorectal cancer [7,8]. Substantial evidence indicates that eating more vegetables and fruits and less meat is able to decrease overall cancer risk and improve health [4,9–11]. Plant-based diets, in particular, are reported to be beneficial for health [12,13]. Remarkably, the definition of a “plant-based diet” is sometimes inconsistent across publications, which must be considered when evaluating results of nutritional trials [12].

Diet does not only affect the risk of cancer occurrence; it appears that it might also play a pivotal role in the prognosis and outcomes of cancer patients [14–18]. The gut microbiota might be a key contributor to these observations as animal models and observational human cohort trials emphasize the impact of gut microbiota on the toxicity and efficacy of anticancer immunotherapy and chemotherapy [19,20]. CTLA-4-specific antibodies are able to control the progression of sarcoma in specific pathogen-free mice, but not in germ-free mice or those treated with broad-spectrum antibiotics [19]. The interplay between gut microbiota and the immune system constitutes a sensitive equilibrium controlling billions of gastrointestinal inhabitants. The existence of these commensals is essential for the function of the immune system, for digesting foods and processing nutrients in a healthy human being [21,22]. The composition of gut microbiota is affected by a variety of external factors such as diet. In general, research emphasizes a high intra-individual stability of human microbial communities, but they can rapidly be individually altered by external factors [23–25]. Faith et al. were able to show that 60% of bacterial strains, which were isolated from the stool of 37 healthy individuals, remained stable for up to 5 years [23]. Even in the case of antibiotic treatment, the gut microbiota of healthy individuals is able to recover rapidly [26]. Nevertheless, several publications indicate associations between the gut microbiota composition and occurrence and development of diseases, but the distinction of potentially beneficial and potentially harmful gut microbiota is challenging [27–29]. The results of human microbiome trials are mostly population-based, showing a great variance of microbiota results, implying that the gut microbiome is as individual as its owner [27,30]. In 2020, Shanahan et al. postulated that the microbiome “is a reflection, in part, of host genetics, but mainly environmental and lifestyle factors, including ethnicity, geographic location, and diet” [30].

The underlying mechanism, how food affects the human body, is complex and not only explained by the composition of gut microbiota. Recent research also emphasizes (chronic) inflammation, e.g., caused by the disturbed interplay of diet and gut microbiota, as a driver of diseases [31–34]. In 2022, Tan et al. postulated that “diet appears to be one of the most



Citation: Lederer, A.-K.; Huber, R. The Relation of Diet and Health: You Are What You Eat. *Int. J. Environ. Res. Public Health* **2022**, *19*, 7774. <https://doi.org/10.3390/ijerph19137774>

Received: 21 June 2022

Accepted: 23 June 2022

Published: 24 June 2022

Publisher’s Note: MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.



Copyright: © 2022 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

influential environmental factors regulating regulatory T cell biology” [35]. This axis might also be responsible for the development of inflammatory bowel diseases [36]. Nutritional components such as dietary fibers and also the gut microbiota affect the differentiation and the survival of intestinal regulatory T cells [37,38]. Different nutritional components are able to provoke variable immune-modulating effects [34,39]. For example, Christ et al. reported sugar and saturated fatty acids to be pro-inflammatory, whereas omega-3-fatty acids and polyphenols are able to decrease inflammation [34]. Even plant-based diets can be healthy or harmful depending on composition [12,40]. Different plant-based diets differed significantly regarding cardiovascular risk reduction [41]. Furthermore, it is assumable that the interplay of different food compounds might be responsible for the observed beneficial effects of diet [31,35].

Our own experiences and the results of further clinical trials showed that plant-based diets are able to relieve the symptoms of patients with autoimmune diseases [42–45]. In a randomized-controlled pilot trial conducted in 2017 comparing healthy, young, previously omnivore participants, who were assigned to either a vegan diet or a meat-rich diet for 4 weeks, we were able to show a significant difference of leukocytes, thrombocytes and monocytes between vegan participants and meat-rich participants [46,47]. Interestingly, we did not observe a difference in FoxP3, a potential master regulator for the development and function of regulatory T cells, between a vegan diet and meat-rich diet in our trial.

In 2018, Witkamp et al. underlined that the effect of nutritional components is not comparable to the effect of drugs [48]. Nutritional therapies are not a pill to relieve symptoms, but a holistic approach to help the whole human body recover. It is said that, more than 2000 years ago, Hippocrates postulated nutrition as a remedy. Changing diet appears to be a simple and inexpensive way to improve a patient’s life. There is evidence for nutritional therapies to treat a broad spectrum of diseases, not only for Western diseases such as diabetes and hypertension, but also for critical ill patients and psychiatric patients [49,50]. In 2017, Kahleova et al. postulated that plant-based diets could be able to reduce the risk of coronary heart disease events by 40% and the risk of cerebral vascular disease events by almost 30% [51]. Therefore, it is justified to discuss whether it is ethically reasonable to neglect nutrition in medical training and everyday medical life [40]. Although the research of the recent decades has accentuated the overwhelming role of diet in health and disease, recent publications indicate many physicians’ just basic knowledge of diet [52,53]. In the future, we have to pay more attention to the diets of patients as nutrition appears to be a key contributor to health, longevity and delayed ageing [3,54,55].

Author Contributions: Writing—original draft preparation, A.-K.L.; writing—review and editing, R.H. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Shah, B.; Newman, J.D.; Woolf, K.; Ganguzza, L.; Guo, Y.; Allen, N.; Zhong, J.; Fisher, E.A.; Slater, J. Anti-Inflammatory Effects of a Vegan Diet Versus the American Heart Association–Recommended Diet in Coronary Artery Disease Trial. *J. Am. Heart Assoc.* **2018**, *7*, e011367. [[CrossRef](#)] [[PubMed](#)]
2. Spence, J.D. Diet for stroke prevention. *Stroke Vasc. Neurol.* **2018**, *3*, 44–50. [[CrossRef](#)] [[PubMed](#)]
3. Kahleova, H.; Levin, S.; Barnard, N.D. Vegetarian Dietary Patterns and Cardiovascular Disease. *Prog. Cardiovasc. Dis.* **2018**, *61*, 54–61. [[CrossRef](#)]
4. Dinu, M.; Abbate, R.; Gensini, G.F.; Casini, A.; Sofi, F. Vegetarian, vegan diets and multiple health outcomes: A systematic review with meta-analysis of observational studies. *Crit. Rev. Food Sci. Nutr.* **2017**, *57*, 3640–3649. [[CrossRef](#)]
5. Tonsor, G.T.; Lusk, J.L. U.S. perspective: Meat demand outdoes meat avoidance. *Meat Sci.* **2022**, *190*, 108843. [[CrossRef](#)]
6. Azzam, A. Is the world converging to a ‘Western diet’? *Public Health Nutr.* **2021**, *24*, 309–317. [[CrossRef](#)]
7. Bultman, S.J. Interplay between diet, gut microbiota, epigenetic events, and colorectal cancer. *Mol. Nutr. Food Res.* **2017**, *61*, 1500902. [[CrossRef](#)]

8. Diallo, A.; Deschasaux, M.; Latino-Martel, P.; Hercberg, S.; Galan, P.; Fassier, P.; Allès, B.; Guéraud, F.; Pierre, F.H.; Touvier, M. Red and processed meat intake and cancer risk: Results from the prospective NutriNet-Santé cohort study. *Int. J. Cancer* **2018**, *142*, 230–237. [[CrossRef](#)]
9. Key, T.J.; Bradbury, K.E.; Perez-Cornago, A.; Sinha, R.; Tsilidis, K.K.; Tsugane, S. Diet, nutrition, and cancer risk: What do we know and what is the way forward? *BMJ* **2020**, *368*, m511. [[CrossRef](#)]
10. Mayne, S.T.; Playdon, M.C.; Rock, C.L. Diet, nutrition, and cancer: Past, present and future. *Nat. Rev. Clin. Oncol.* **2016**, *13*, 504–515. [[CrossRef](#)]
11. Samraj, A.N.; Pearce, O.M.T.; Läubli, H.; Crittenden, A.N.; Bergfeld, A.K.; Banda, K.; Gregg, C.J.; Bingman, A.E.; Secrest, P.; Diaz, S.L.; et al. A red meat-derived glycan promotes inflammation and cancer progression. *Proc. Natl. Acad. Sci. USA* **2015**, *112*, 542–547. [[CrossRef](#)]
12. Storz, M.A. What makes a plant-based diet? A review of current concepts and proposal for a standardized plant-based dietary intervention checklist. *Eur. J. Clin. Nutr.* **2022**, *76*, 789–800. [[CrossRef](#)]
13. Craig, W.J.; Mangels, A.R.; Fresán, U.; Marsh, K.; Miles, F.L.; Saunders, A.V.; Haddad, E.H.; Heskey, C.E.; Johnston, P.; Larson-Meyer, E.; et al. The Safe and Effective Use of Plant-Based Diets with Guidelines for Health Professionals. *Nutrients* **2021**, *13*, 4144. [[CrossRef](#)]
14. Mann, S.; Sidhu, M.; Gowin, K. Understanding the Mechanisms of Diet and Outcomes in Colon, Prostate, and Breast Cancer; Malignant Gliomas; and Cancer Patients on Immunotherapy. *Nutrients* **2020**, *12*, 2226. [[CrossRef](#)]
15. Xu, L.; Peterson, L.L. The Impact of Diet on Breast Cancer Outcomes. *Curr. Nutr. Rep.* **2019**, *8*, 212–221. [[CrossRef](#)]
16. Jochems, S.H.J.; Van Osch, F.H.M.; Bryan, R.T.; Wesselius, A.; van Schooten, F.J.; Cheng, K.K.; Zeegers, M.P. Impact of dietary patterns and the main food groups on mortality and recurrence in cancer survivors: A systematic review of current epidemiological literature. *BMJ Open* **2018**, *8*, e014530. [[CrossRef](#)]
17. Mahumud, R.A.; Sultana, M.; Gow, J.; Rahman, M.A.; Uddin, K.F.; Kamal, M.; Alam, K.; Dawson, A.; Law, C.K. Association of dietary risks, behavioural and lifestyle factors, and the magnitude of disability burden among Australian cancer patients: An observational epidemiology study. *Cancer Epidemiol.* **2022**, *78*, 102161. [[CrossRef](#)]
18. Mittelman, S.D. The Role of Diet in Cancer Prevention and Chemotherapy Efficacy. *Annu. Rev. Nutr.* **2020**, *40*, 273–297. [[CrossRef](#)]
19. Vétizou, M.; Pitt, J.M.; Daillère, R.; Lepage, P.; Waldschmitt, N.; Flament, C.; Rusakiewicz, S.; Routy, B.; Roberti, M.P.; Duong, C.P.M.; et al. Anticancer immunotherapy by CTLA-4 blockade relies on the gut microbiota. *Science* **2015**, *350*, 1079–1084. [[CrossRef](#)]
20. Alexander, J.L.; Wilson, I.D.; Teare, J.; Marchesi, J.R.; Nicholson, J.K.; Kinross, J.M. Gut microbiota modulation of chemotherapy efficacy and toxicity. *Nat. Rev. Gastroenterol. Hepatol.* **2017**, *14*, 356–365. [[CrossRef](#)]
21. Lederberg, J. Infectious History. *Science* **2000**, *288*, 287–293. [[CrossRef](#)]
22. De Vos, W.M.; Tilg, H.; Van Hul, M.; Cani, P.D. Gut microbiome and health: Mechanistic insights. *Gut* **2022**, *71*, 1020–1032. [[CrossRef](#)]
23. Faith, J.J.; Guruge, J.L.; Charbonneau, M.; Subramanian, S.; Seedorf, H.; Goodman, A.L.; Clemente, J.C.; Knight, R.; Heath, A.C.; Leibel, R.L.; et al. The Long-Term Stability of the Human Gut Microbiota. *Science* **2013**, *341*, 6141. [[CrossRef](#)]
24. Kohnert, E.; Kreutz, C.; Binder, N.; Hannibal, L.; Gorkiewicz, G.; Müller, A.; Storz, M.A.; Huber, R.; Lederer, A.-K. Changes in Gut Microbiota after a Four-Week Intervention with Vegan vs. Meat-Rich Diets in Healthy Participants: A Randomized Controlled Trial. *Microorganisms* **2021**, *9*, 727. [[CrossRef](#)]
25. David, L.A.; Materna, A.C.; Friedman, J.; Campos-Baptista, M.I.; Blackburn, M.C.; Perrotta, A.; Erdman, S.E.; Alm, E.J. Host lifestyle affects human microbiota on daily timescales. *Genome Biol.* **2014**, *15*, R89. [[CrossRef](#)]
26. Anthony, W.E.; Wang, B.; Sukhum, K.V.; D’Souza, A.W.; Hink, T.; Cass, C.; Seiler, S.; Reske, K.A.; Coon, C.; Dubberke, E.R.; et al. Acute and persistent effects of commonly used antibiotics on the gut microbiome and resistome in healthy adults. *Cell Rep.* **2022**, *39*, 110649. [[CrossRef](#)]
27. Gomma, E.Z. Human gut microbiota/microbiome in health and diseases: A review. *Antonie Van Leeuwenhoek* **2020**, *113*, 2019–2040. [[CrossRef](#)]
28. Scotti, E.; Boué, S.; Sasso, G.L.; Zanetti, F.; Belcastro, V.; Poussin, C.; Sierro, N.; Battey, J.; Gimalac, A.; Ivanov, N.V.; et al. Exploring the microbiome in health and disease. *Toxicol. Res. Appl.* **2017**, *1*, 239784731774188. [[CrossRef](#)]
29. Lynch, S.V.; Pedersen, O. The Human Intestinal Microbiome in Health and Disease. *N. Engl. J. Med.* **2016**, *375*, 2369–2379. [[CrossRef](#)]
30. Shanahan, F.; Ghosh, T.S.; O’Toole, P.W. The Healthy Microbiome—What Is the Definition of a Healthy Gut Microbiome? *Gastroenterology* **2021**, *160*, 483–494. [[CrossRef](#)]
31. Lee, A.H.; Dixit, V.D. Dietary Regulation of Immunity. *Immunity* **2020**, *53*, 510–523. [[CrossRef](#)]
32. Hardman, W.E. Diet components can suppress inflammation and reduce cancer risk. *Nutr. Res. Pract.* **2014**, *8*, 233. [[CrossRef](#)]
33. Klement, R.; Paziienza, V. Impact of Different Types of Diet on Gut Microbiota Profiles and Cancer Prevention and Treatment. *Medicina* **2019**, *55*, 84. [[CrossRef](#)]
34. Christ, A.; Lauterbach, M.; Latz, E. Western Diet and the Immune System: An Inflammatory Connection. *Immunity* **2019**, *51*, 794–811. [[CrossRef](#)]
35. Tan, J.; Taitz, J.; Sun, S.M.; Langford, L.; Ni, D.; Macia, L. Your Regulatory T Cells Are What You Eat: How Diet and Gut Microbiota Affect Regulatory T Cell Development. *Front. Nutr.* **2022**, *9*, 717. [[CrossRef](#)]

36. Tracy, M.; Khalili, H. You Are What You Eat? Growing Evidence That Diet Influences the Risk of Inflammatory Bowel Disease. *J. Crohn's Colitis* **2022**, *jjac025*. [[CrossRef](#)]
37. Tanoue, T.; Atarashi, K.; Honda, K. Development and maintenance of intestinal regulatory T cells. *Nat. Rev. Immunol.* **2016**, *16*, 295–309. [[CrossRef](#)]
38. Hori, S.; Nomura, T.; Sakaguchi, S. Control of regulatory T cell development by the transcription factor Foxp3. *Science* **2003**, *299*, 1057–1061. [[CrossRef](#)]
39. Christ, A.; Latz, E. The Western lifestyle has lasting effects on metaflammation. *Nat. Rev. Immunol.* **2019**, *19*, 267–268. [[CrossRef](#)]
40. Storz, M.A. Will the plant-based movement redefine physicians' understanding of chronic disease? *New Bioeth.* **2020**, *26*, 141–157. [[CrossRef](#)]
41. Satija, A.; Bhupathiraju, S.N.; Spiegelman, D.; Chiuve, S.E.; Manson, J.E.; Willett, W.; Rexrode, K.M.; Rimm, E.B.; Hu, F.B. Healthful and Unhealthful Plant-Based Diets and the Risk of Coronary Heart Disease in U.S. Adults. *J. Am. Coll. Cardiol.* **2017**, *70*, 411–422. [[CrossRef](#)]
42. Huber, R.; Herdrich, A.; Rostock, M.; Vogel, T. Clinical remission of an HLA B27-positive sacroiliitis on vegan diet. *Forsch. Komplementarmed. Klass. Naturheilkd.* **2001**, *8*, 228–231.
43. Kjeldsen-Kragh, J.; Mellbye, O.J.; Haugen, M.; Mollnes, T.E.; Hammer, H.B.; Sioud, M.; Førre, Ø. Changes in Laboratory Variables in Rheumatoid Arthritis Patients During a Trial of Fasting and One-year Vegetarian Diet. *Scand. J. Rheumatol.* **1995**, *24*, 85–93. [[CrossRef](#)]
44. Kjeldsen-Kragh, J. Rheumatoid arthritis treated with vegetarian diets. *Am. J. Clin. Nutr.* **1999**, *70*, 594S–600S. [[CrossRef](#)]
45. Alwarith, J.; Kahleova, H.; Rembert, E.; Yonas, W.; Dort, S.; Calcagno, M.; Burgess, N.; Crosby, L.; Barnard, N.D. Nutrition Interventions in Rheumatoid Arthritis: The Potential Use of Plant-Based Diets. A Review. *Front. Nutr.* **2019**, *6*, 141. [[CrossRef](#)]
46. Lederer, A.-K.; Maul-Pavicic, A.; Hannibal, L.; Hettich, M.; Steinborn, C.; Gründemann, C.; Zimmermann-Klemd, A.M.; Müller, A.; Sehnert, B.; Salzer, U.; et al. Vegan diet reduces neutrophils, monocytes and platelets related to branched-chain amino acids—A randomized, controlled trial. *Clin. Nutr.* **2020**, *39*, 3241–3250. [[CrossRef](#)]
47. Lederer, A.-K.; Huber, R. Reply-Letter to the editor: Comment on “Vegan diet reduces neutrophils, monocytes and platelets related to branched-chain amino acids—A randomized, controlled trial. ” *Clin. Nutr.* **2022**, *41*, 567–568. [[CrossRef](#)]
48. Witkamp, R.F.; van Norren, K. Let thy food be thy medicine . . . when possible. *Eur. J. Pharmacol.* **2018**, *836*, 102–114. [[CrossRef](#)]
49. Vartanian, C. *Overview of Nutritional Therapy for Autism Spectrum Disorder*; Springer: Berlin/Heidelberg, Germany, 2020; pp. 527–534.
50. Lambell, K.J.; Tatu-Babet, O.A.; Chapple, L.; Gantner, D.; Ridley, E.J. Nutrition therapy in critical illness: A review of the literature for clinicians. *Crit. Care* **2020**, *24*, 35. [[CrossRef](#)]
51. Kahleova, H.; Levin, S.; Barnard, N. Cardio-Metabolic Benefits of Plant-Based Diets. *Nutrients* **2017**, *9*, 848. [[CrossRef](#)]
52. Sutherland, M.; McKenney, K.; Shanahan, H.; McKenney, M.; Elkbuli, A. The Need for Nutritional Education Reform in US Medical Education System. *Am. Surg.* **2021**, *87*, 1032–1038. [[CrossRef](#)]
53. Crowley, J.; Ball, L.; Hiddink, G.J. Nutrition in medical education: A systematic review. *Lancet Planet. Health* **2019**, *3*, e379–e389. [[CrossRef](#)]
54. Green, C.L.; Lamming, D.W.; Fontana, L. Molecular mechanisms of dietary restriction promoting health and longevity. *Nat. Rev. Mol. Cell Biol.* **2022**, *23*, 56–73. [[CrossRef](#)]
55. Kahleova, H.; Levin, S.; Barnard, N.D. Plant-Based Diets for Healthy Aging. *J. Am. Coll. Nutr.* **2021**, *40*, 478–479. [[CrossRef](#)]