ELMER PRESS

Editorial

Clin Infect Immun. 2025;10(2):25-28

Collinsella and *Prevotella*: Mixed Systemic Actions of a Dynamic Duo

Victoria K. Nguyen[a], Jorge Cervantes[b, c]

The human microbiome is a complex and dynamic ecosystem with trillions of microorganisms that play a critical role in shaping our health. Among these, *Collinsella and Prevotella* are two significant genera of commensal bacteria with multifaceted roles that range from beneficial to harmful, depending on strain-specific traits, host physiology, and environmental influences [1]. Given the crucial roles of commensal bacteria in host metabolism, gut dysbiosis can lead to serious health implications in the host, including metabolic disorders and inflammatory diseases [2]. Understanding the duality of *Collinsella* and *Prevotella* is essential for advancing microbiome research and developing targeted therapies.

Members of the Clostridia class, organisms from the genus *Collinsella* are bacteria that play a role in the development of the intestinal microbiota. The genus *Prevotella* belongs to the order Bacteroidales, and is also considered beneficial due to its abundance in healthy intestinal microbiota and association with plant-rich diets [3]. *Collinsella* is abundant in the intestinal microbiota of Japanese [4], and along with *Prevotella* in Indian population [5]. In contrast, populations with westernized diets, characterized by low fiber and high fat, harbor lower levels of *Prevotella* [6, 7]. Fiber consumption increases the abundance of these bacteria in the gastrointestinal (GI) tract [8]. Intake of whole-grain and fiber-rich foods increases the relative abundance of *Collinsella* certain species of *Prevotella*, such as *P. tannerae* [9]. Additionally, specific dietary components can selectively influence microbial populations. For example, *Collinsella* has been found to be more abundant in groups consuming milk compared to yogurt [10].

In the GI tract, both *Collinsella* and *Prevotella* produce short-chain fatty acids, which play a critical role in gut health [11] (Table 1). *Collinsella* is a known degrader of common dietary fibers and has the ability to produce butyric acid [11, 12]. Butyrate promotes GI barrier integrity, reduces inflammation, and enhances resistance to pathogens [11]. The difference in metabolism is at the species levels for both of these genera, leading to divergent outcomes in different contexts [12, 13]. Certain strains, such as *Collinsella aerofaciens TF06-26*, produce butyrate and degrade dietary fibers, supporting gut health and reducing inflammation [14]. Other strains are associated with insulin resistance and cardiovascular complications (CVCs). For example, *Collinsella* abundance has been found to correlate positively with insulin levels, while showing a negative correlation with dietary fiber intake among pregnant women [15]. Additionally, *Collinsella* was found to be associated with CVC risk in type 2 diabetes patients [14]. In patients with CVCs, the abundance of butyrate-producing strains like *C. aerofaciens TF06-26* is reduced [14].

Alterations in commensal bacteria can contribute to the development of various diseases. Atherosclerosis is associated with the increased abundance of *Collinsella, Peptococcaceae,* and *Prevotella* [16, 17]. *Collinsella* is a TMA-producing bacterium that can contribute to atherogenic effects after being converted to TMA-oxide (TMAO) in the liver [14]. Similarly, atherosclerosis is associated with the increased abundance of *Prevotella* due to formation of TMAO [16, 17]. *Prevotella* is significantly decreased in diabetic patients [18], along with an increase of other genera like *Clostridium*, *Bacteroides*, and *Veillonella*. A recent study evaluating changes in gut microbiota during a weight loss program for obese individuals with type 2 diabetes observed a decrease in the levels of *Collinsella* [19]. An increase in *Collinsella* abundance could be used as a predictive marker of response to probiotic treatment efficacy in non-constipated irritable bowel syndrome [20].

The microbiota inhabiting the oral cavity is relatively identical to the microbiota that inhabits the lungs, with bacteria traveling from the oral cavity to the lungs through the respiratory tract via migration or microaspiration [21]. Alterations in the oral microbiota could affect the severity of coronavirus disease 2019 (COVID-19) [22]. They exert this action through immunomodulatory role of the oral microbiota in the response to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by alveolar macrophages [23]. Intestinal *Collinsella* was shown to mitigate SARS-CoV-2 infection and exacerbation of COVID-19 [24], as it was negatively correlated with COVID-19 mortality in 10 countries. *Prevotella* differentially regulates the inflammatory response of human monocytes to SARS-CoV-2 spike glycoproteins [25]. This exacerbated innate immune response translates clinically into severe COVID-19 [26].

One important aspect to consider is that the risks and benefits from these two genera come from differences at the spe-

Manuscript submitted April 1, 2025, accepted April 9, 2025
Published online April 16, 2025

[a]Medical City Fort Worth, Fort Worth, TX, USA
[b]Dr. Kiran C. Patel College of Allopathic Medicine, Nova Southeastern University, Fort Lauderdale, FL, USA
[c]Corresponding Author: Jorge Cervantes, Dr. Kiran C. Patel College of Allopathic Medicine, Nova Southeastern University, Fort Lauderdale, FL, USA. Email: jcervan1@nova.edu

doi: https://doi.org/10.14740/cii506

Table 1. Microbiological Characteristics of *Collinsella* and *Prevotella*

Feature	*Collinsella*	*Prevotella*
Gram stain	Gram-positive	Gram-negative
Shape	Rod-shaped	Rod-shaped
Spore formation	Non-spore-forming	Non-spore-forming
Motility	Non-motile	Non-motile
Oxygen requirement	Anaerobic	Anaerobic, some species are aerotolerant
Habitat	Human gut microbiota	Oral cavity, gastrointestinal tract, female genital tract
Temperature	Optimal growth at 37 °C	Optimal growth at 37 °C
pH	Thrives at pH 7	Thrives at 6.5 to 7.5
Metabolism	Breaks down complex carbohydrates and proteins, producing SCFAs and ammonia	Fermentative, producing SCFAs such as acetate and propionate
Lipids	Major fatty acids: C16:0, C18:1n9, C18:2n6	Branched-chain fatty acids, methyl-branched fatty acids, straight-chain saturated and unsaturated fatty acids
Pigmentation	Not typically pigmented	Some species produce brown or black pigmented colonies on blood agar

SCFAs: short-chain fatty acids.

cies level [27, 28]. *Prevotella* species are found at multiple mucosal sites, including the respiratory system, oral cavity, and GI tract. Evidence revealed beneficial effects of some *Prevotella* strains in the gut such as not only improving cardiovascular disease (CVD) risk factor profile and glucose metabolism, but also pathobiontic properties of some strains which promoted diseases like metabolic syndrome, obesity, inflammatory bowel disease or other inflammatory diseases such as rheumatoid arthritis [29]. Oral administration of *Prevotella histicola* to arthritis-susceptible mice reduced the incidence and severity of the disease [30]. This same species suppresses multiple sclerosis in animal models through modulation of systemic immune responses [31, 32]. *P. histicola* decreases the inflammatory activity of Th17 cells and increases the activity of regulatory T cells. On the other hand, patients with rheumatoid arthritis (RA) show increased level of enteric *Prevotella copri* [33], and autoantigens in these patients exhibit high homology to *Prevotella*-associated peptides [34]. This phenomenon of molecular mimicry of RA-associated antigens by the gut microbiota has also been reported in a metagenomic study of RA patients [35].

Three mechanisms by which microbiota might contribute to RA pathogenesis are proposed: inflammatory responses (*P. copri* and *Lactobacillus*), molecular mimicry (*P. copri*), and loss of intestinal barrier integrity (*Collinsella*) [36]. The abundance of *Collinsella* and *Bifidobacterium* is increased in RA patients compared with controls [37]. Another study showed that *Collinsella*, along with *Eggerthella*, and *Faecalibacterium*, segregated with RA. The abundance of *Collinsella* correlated strongly with high levels of alpha-aminoadipic acid and asparagine as well as production of the proinflammatory cytokine interleukin (IL)-17A [38]. A role for *Collinsella* in altering gut permeability and disease severity was confirmed in experimental arthritis. *C. aerofaciens* can aggravate arthritis in a collagen-induced arthritis model [38]. *Collinsella sp* could participate in the development of RA through molecular mimicry as well.

C. aerofaciens has been associated with increased ethanol production and liver inflammation. *C. aerofaciens* has shown an increased abundance in the gut of obese patients living in India [39]. *Collinsella aerofaciens* was increased in non-constipated irritable bowel syndrome [20]. This bacterium contributes to pro-inflammatory immune states, and is associated with markers of increased endothelial permeability and liver functionality, suggesting an involvement of the gut-liver axis in this condition.

Several bacterial genera, including *Prevotella*, *Bacteroides*, *Ruminococcus*, *Blautia*, and *Collinsella* have been reported in association with brain connectivity [40]. The autistic spectrum disorder (ASD)-associated intestinal microbiota exhibits an increased bacterial diversity [41] with enrichment of *Collinsella*, *Corynebacterium*, and *Lactobacillus*.

The associations of *C. aerofaciens* with pro-inflammatory responses and undesirable outcomes can be leveraged to induce beneficial responses in programmed cell death 1 (PD-1)/programmed death-ligand 1 (PD-L1) cancer immunotherapy [42]. Enrichment of certain commensal such as *Bifidobacterium longum*, *Bifidobacterium adolescentis*, *Collinsella aerofaciens*, and *Enterococcus faecium* in patients with metastatic melanoma have been associated with anti-PD-1 treatment efficacy [43].

Further research will elucidate the advantages and broaden the applications of these bacteria across a range of conditions.

Acknowledgments

None to declare.

Financial Disclosure

None to declare.

Conflict of Interest

None to declare.

Author Contributions

VN and JC wrote the manuscript.

Data Availability

The authors declare that data supporting the findings of this study are available within the article.

References

1. Sharma G, Garg N, Hasan S, Shirodkar S. Prevotella: An insight into its characteristics and associated virulence factors. Microb Pathog. 2022;169:105673. doi pubmed
2. Krishnamurthy HK, Pereira M, Bosco J, George J, Jayaraman V, Krishna K, Wang T, et al. Gut commensals and their metabolites in health and disease. Front Microbiol. 2023;14:1244293. doi pubmed
3. Sun W, Zhang Y, Guo R, Sha S, Chen C, Ullah H, Zhang Y, et al. A population-scale analysis of 36 gut microbiome studies reveals universal species signatures for common diseases. NPJ Biofilms Microbiomes. 2024;10(1):96. doi pubmed
4. Nishijima S, Suda W, Oshima K, Kim SW, Hirose Y, Morita H, Hattori M. The gut microbiome of healthy Japanese and its microbial and functional uniqueness. DNA Res. 2016;23(2):125-133. doi pubmed
5. Bhute S, Pande P, Shetty SA, Shelar R, Mane S, Kumbhare SV, Gawali A, et al. Molecular characterization and meta-analysis of gut microbial communities illustrate enrichment of Prevotella and Megasphaera in Indian subjects. Front Microbiol. 2016;7:660. doi pubmed
6. Nakayama J, Yamamoto A, Palermo-Conde LA, Higashi K, Sonomoto K, Tan J, Lee YK. Impact of westernized diet on gut microbiota in children on Leyte island. Front Microbiol. 2017;8:197. doi pubmed
7. De Filippo C, Di Paola M, Ramazzotti M, Albanese D, Pieraccini G, Banci E, Miglietta F, et al. Diet, environments, and gut microbiota. a preliminary investigation in children living in rural and urban Burkina Faso and Italy. Front Microbiol. 2017;8:1979. doi pubmed
8. Matsuoka T, Hosomi K, Park J, Goto Y, Nishimura M, Maruyama S, Murakami H, et al. Relationships between barley consumption and gut microbiome characteristics in a healthy Japanese population: a cross-sectional study. BMC Nutr. 2022;8(1):23. doi pubmed
9. Lappi J, Salojarvi J, Kolehmainen M, Mykkanen H, Poutanen K, de Vos WM, Salonen A. Intake of wholegrain and fiber-rich rye bread versus refined wheat bread does not differentiate intestinal microbiota composition in Finnish adults with metabolic syndrome. J Nutr. 2013;143(5):648-655. doi pubmed
10. Rettedal EA, Altermann E, Roy NC, Dalziel JE. The effects of unfermented and fermented cow and sheep milk on the gut microbiota. Front Microbiol. 2019;10:458. doi pubmed
11. Holmes ZC, Villa MM, Durand HK, Jiang S, Dallow EP, Petrone BL, Silverman JD, et al. Microbiota responses to different prebiotics are conserved within individuals and associated with habitual fiber intake. Microbiome. 2022;10(1):114. doi pubmed
12. Qin P, Zou Y, Dai Y, Luo G, Zhang X, Xiao L. Characterization a novel butyric acid-producing bacterium Collinsella aerofaciens Subsp. Shenzhenensis Subsp. Nov. Microorganisms. 2019;7(3):78. doi pubmed
13. Kordahi MC, DePaolo RW. Commensal bacteria decontaminating your diet. Cell Host Microbe. 2019;26(4):446-448. doi pubmed
14. Siegel EL, Lane K, Yuan A, Smalls-Mantey LA, Laird J, Olson C, Hernandez D. Energy insecurity indicators associated with increased odds of respiratory, mental health, and cardiovascular conditions. Health Aff (Millwood). 2024;43(2):260-268. doi pubmed
15. Gomez-Arango LF, Barrett HL, Wilkinson SA, Callaway LK, McIntyre HD, Morrison M, Dekker Nitert M. Low dietary fiber intake increases Collinsella abundance in the gut microbiota of overweight and obese pregnant women. Gut Microbes. 2018;9(3):189-201. doi pubmed
16. Novakovic M, Rout A, Kingsley T, Kirchoff R, Singh A, Verma V, Kant R, et al. Role of gut microbiota in cardiovascular diseases. World J Cardiol. 2020;12(4):110-122. doi pubmed
17. Ahmadmehrabi S, Tang WHW. Gut microbiome and its role in cardiovascular diseases. Curr Opin Cardiol. 2017;32(6):761-766. doi pubmed
18. Murri M, Leiva I, Gomez-Zumaquero JM, Tinahones FJ, Cardona F, Soriguer F, Queipo-Ortuno MI. Gut microbiota in children with type 1 diabetes differs from that in healthy children: a case-control study. BMC Med. 2013;11:46. doi pubmed
19. Frost F, Storck LJ, Kacprowski T, Gartner S, Ruhlemann M, Bang C, Franke A, et al. A structured weight loss program increases gut microbiota phylogenetic diversity and reduces levels of Collinsella in obese type 2 diabetics: A pilot study. PLoS One. 2019;14(7):e0219489. doi pubmed
20. Gargari G, Mantegazza G, Cremon C, Taverniti V, Valenza A, Barbaro MR, Marasco G, et al. Collinsella aerofaciens as a predictive marker of response to probiotic treatment in non-constipated irritable bowel syndrome. Gut Microbes. 2024;16(1):2298246. doi pubmed
21. Bassis CM, Erb-Downward JR, Dickson RP, Freeman CM, Schmidt TM, Young VB, Beck JM, et al. Analysis of the upper respiratory tract microbiotas as the source of the lung and gastric microbiotas in healthy individuals. mBio. 2015;6(2):e00037. doi pubmed
22. Bao L, Zhang C, Dong J, Zhao L, Li Y, Sun J. Oral Microbiome and SARS-CoV-2: Beware of Lung Co-infection. Front Microbiol. 2020;11:1840. doi pubmed

23. Rodriguez Y, et al. Immunomodulation of human alveolar macrophage response to the SARS-CoV-2 S protein by oral microbiota. Clinical Infection and Immunity. 2024;9(1):16-19.
24. Hirayama M, Nishiwaki H, Hamaguchi T, Ito M, Ueyama J, Maeda T, Kashihara K, et al. Intestinal Collinsella may mitigate infection and exacerbation of COVID-19 by producing ursodeoxycholate. PLoS One. 2021;16(11):e0260451. doi pubmed
25. Cervantes JR, Barragan J, Dempsey KB, and Palfreeman M. Prevotella differentially regulates the inflammatory response of human monocytes to SARS-CoV-2 spike glycoproteins. J Investig Med. 2021;69(2):1114-1115.
26. Utrero-Rico A, Gonzalez-Cuadrado C, Chivite-Lacaba M, Cabrera-Marante O, Laguna-Goya R, Almendro-Vazquez P, Diaz-Pedroche C, et al. Alterations in circulating monocytes predict COVID-19 severity and include chromatin modifications still detectable six months after recovery. Biomedicines. 2021;9(9):1253. doi pubmed
27. Ley RE. Gut microbiota in 2015: Prevotella in the gut: choose carefully. Nat Rev Gastroenterol Hepatol. 2016;13(2):69-70. doi pubmed
28. Wang L, Wang Y, Zhang P, Song C, Pan F, Li G, Peng L, et al. Gut microbiota changes in patients with spondyloarthritis: A systematic review. Semin Arthritis Rheum. 2022;52:151925. doi pubmed
29. Precup G, Vodnar DC. Gut Prevotella as a possible biomarker of diet and its eubiotic versus dysbiotic roles: a comprehensive literature review. Br J Nutr. 2019;122(2):131-140. doi pubmed
30. Marietta EV, Murray JA, Luckey DH, Jeraldo PR, Lamba A, Patel R, Luthra HS, et al. Suppression of inflammatory arthritis by human gut-derived prevotella histicola in humanized mice. Arthritis Rheumatol. 2016;68(12):2878-2888. doi pubmed
31. Mangalam A, Shahi SK, Luckey D, Karau M, Marietta E, Luo N, Choung RS, et al. Human gut-derived commensal bacteria suppress CNS inflammatory and demyelinating disease. Cell Rep. 2017;20(6):1269-1277. doi pubmed
32. Shahi SK, Freedman SN, Murra AC, Zarei K, Sompallae R, Gibson-Corley KN, Karandikar NJ, et al. Prevotella histicola, a human gut commensal, is as potent as COPAXONE(R) in an animal model of multiple sclerosis. Front Immunol. 2019;10:462. doi pubmed
33. Scher JU, Sczesnak A, Longman RS, Segata N, Ubeda C, Bielski C, Rostron T, et al. Expansion of intestinal Prevotella copri correlates with enhanced susceptibility to arthritis. Elife. 2013;2:e01202. doi pubmed
34. Pianta A, Arvikar S, Strle K, Drouin EE, Wang Q, Costello CE, Steere AC. Evidence of the immune relevance of prevotella copri, a gut microbe, in patients with rheumatoid arthritis. Arthritis Rheumatol. 2017;69(5):964-975. doi pubmed
35. Zhang X, Zhang D, Jia H, Feng Q, Wang D, Liang D, Wu X, et al. The oral and gut microbiomes are perturbed in rheumatoid arthritis and partly normalized after treatment. Nat Med. 2015;21(8):895-905. doi pubmed
36. Tsetseri MN, Silman AJ, Keene DJ, Dakin SG. The role of the microbiome in rheumatoid arthritis: a review. Rheumatol Adv Pract. 2023;7(2):rkad034. doi pubmed
37. Ruiz-Limon P, Mena-Vazquez N, Moreno-Indias I, Manrique-Arija S, Lisbona-Montanez JM, Cano-Garcia L, Tinahones FJ, et al. Collinsella is associated with cumulative inflammatory burden in an established rheumatoid arthritis cohort. Biomed Pharmacother. 2022;153:113518. doi pubmed
38. Chen J, Wright K, Davis JM, Jeraldo P, Marietta EV, Murray J, Nelson H, et al. An expansion of rare lineage intestinal microbes characterizes rheumatoid arthritis. Genome Med. 2016;8(1):43. doi pubmed
39. Purohit A, Kandiyal B, Kumar S, Pragasam AK, Kamboj P, Talukdar D, Verma J, et al. Collinsella aerofaciens linked with increased ethanol production and liver inflammation contribute to the pathophysiology of NAFLD. iScience. 2024;27(2):108764. doi pubmed
40. Mulder D, Aarts E, Arias Vasquez A, Bloemendaal M. A systematic review exploring the association between the human gut microbiota and brain connectivity in health and disease. Mol Psychiatry. 2023;28(12):5037-5061. doi pubmed
41. Finegold SM, Dowd SE, Gontcharova V, Liu C, Henley KE, Wolcott RD, Youn E, et al. Pyrosequencing study of fecal microflora of autistic and control children. Anaerobe. 2010;16(4):444-453. doi pubmed
42. Kwon J, Bae M, Szamosvari D, Cassilly CD, Bolze AS, Jackson DR, Xavier RJ, et al. Collinsella aerofaciens Produces a pH-responsive lipid immunogen. J Am Chem Soc. 2023;145(13):7071-7074. doi pubmed
43. Matson V, Fessler J, Bao R, Chongsuwat T, Zha Y, Alegre ML, Luke JJ, et al. The commensal microbiome is associated with anti-PD-1 efficacy in metastatic melanoma patients. Science. 2018;359(6371):104-108. doi pubmed