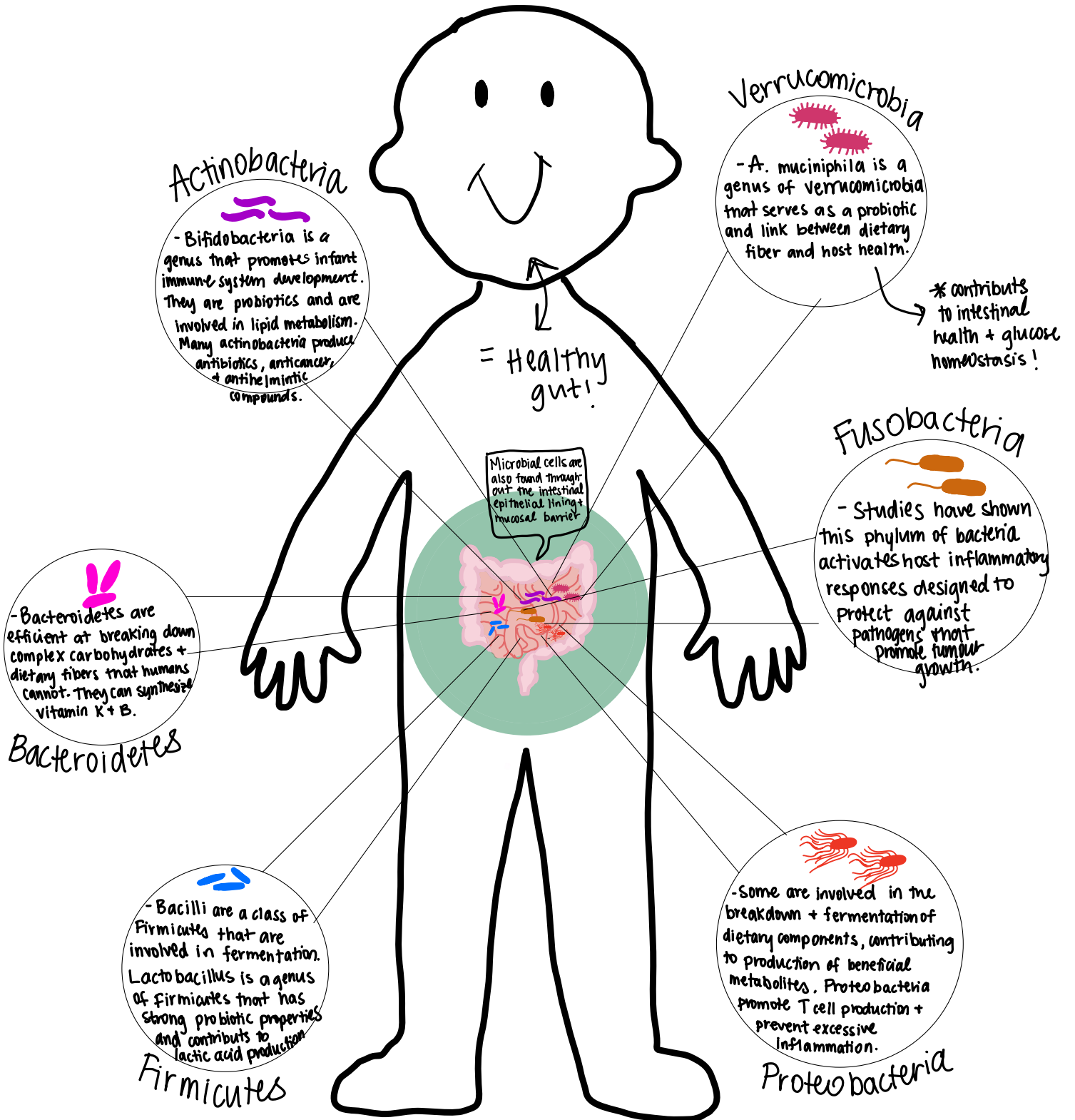


Fun Fact: The human body has 10^{14} microbial cells, that exceeds the number of stars in the milky way!



We have known that microbes exist and are present in our everyday environment since the microscope was invented in the 17th century, but it was not until the 19th century that microbes were identified as agents of infectious diseases. As improvements in human hygiene were made and microbial studies advanced, researchers started to make connections between microorganisms and human health, as well as identify ways to prevent disease. The hygiene hypothesis, first proposed by Dr. David Strachan in 1958, states that exposure to diverse microorganisms in the early years of life can contribute to a strong immune system that can differentiate between harmful and harmless substances. This led to an understanding of the symbiotic relationship between the host and microbiota where the microbes are given a habitat and nutrients while the host is provided with resistance to infection. (Okada, 2010).

Microbes that inhabit the human body are critical to the development of the immune system and maintaining health within the body. The immune system is a complex system with numerous components that works to maintain the body's ability to fight off pathogenic microorganisms including bacteria, viruses, fungi, and parasites. The innate immune system provides protection via physical barriers such as skin and mucosal membranes, as well as chemical barriers in the form of antimicrobial proteins and innate immune cells, including granulocytes, macrophages, and natural killer cells. The human body harbors 10^{14} microbial cells each with different genetic makeup that can influence the immune system. Every human has their own personal microbiome that begins accumulating microbes from the very first day of life. Our microbiomes within us reflect how our bodies perform physiological processes and fight off infection. Microbiomes with high diversity correlate with high metabolic health and strong immune systems, which is consistent with the hygiene hypothesis (Colella, 2023).

The large intestine and colon are two regions that contain a functionally and metabolically diverse collection of phyla, including Firmicutes, Bacteroidetes, Actinobacteria, Proteobacteria, Fusobacteria, Verrucomicrobia, with Firmicutes and Bacteroidetes representing 90% of the microbial composition (Rinninella, 2019). Culture-independent mechanisms such as sequencing of genes that are conserved across many phyla allow for a deeper analysis of microbial function and composition (Dekaboruah, 2020). The collection of microbes that inhabit the gastrointestinal tract provide many benefits to the host health such as digestion of macromolecules, production of nutrients, detoxification, protections against pathogens, and immune system maintenance (Hsin-Jung, 2012). (Wiertsema, 2021). With immune cells, such as B and T lymphocytes, and intestinal microbiota sharing the gut environment, it establishes interplay between the microbes, the intestinal epithelial layer, and the local mucosal immune system. Studies have shown the gut microbiome can influence the immune system via promotion of differentiation of the T cell population. In germ free animals, T lymphocytes that typically provide cellular-level immunity by attacking foreign cells, were absent. Recolonization of microbes showed establishment of T cells and immune responses. (Hsin-Jung, 2012).

Upon the introduction of the hygiene hypothesis to society and science, an understanding emerged that a diverse gut microbiome can help maintain immune homeostasis and maturation and development of various immune cell types in the gut. Overall, the intricate connections made between immune system health and a microbiologically diverse gut should be emphasized in our community so that everyone is aware of the implications and benefits microorganisms pose to our immune system and overall health.

References:

Colella M, Charitos IA, Ballini A, Cafiero C, Topi S, Palmirotta R, Santacroce L. Microbiota revolution: How gut microbes regulate our lives. *World J Gastroenterol*. 2023 Jul 28;29(28):4368-4383. doi: 10.3748/wjg.v29.i28.4368. PMID: 37576701; PMCID: PMC10415973.

Dekaboruah, E., Suryavanshi, M., Chettri, D. et al. Human microbiome: an academic update on human body site specific surveillance and its possible role. *Arch Microbiol* 202, 2147–2167 (2020). <https://doi.org/10.1007/s00203-020-01931-x>

Okada H, Kuhn C, Feillet H, Bach JF. The 'hygiene hypothesis' for autoimmune and allergic diseases: an update. *Clin Exp Immunol*. 2010 Apr;160(1):1-9. doi: 10.1111/j.1365-2249.2010.04139.x. PMID: 20415844; PMCID: PMC2841828.

Rinninella E, Raoul P, Cintoni M, Franceschi F, Miggiano GAD, Gasbarrini A, Mele MC. What is the Healthy Gut Microbiota Composition? A Changing Ecosystem across Age, Environment, Diet, and Diseases. *Microorganisms*. 2019 Jan 10;7(1):14. doi: 10.3390/microorganisms7010014. PMID: 30634578; PMCID: PMC6351938.

Ursell LK, Metcalf JL, Parfrey LW, Knight R. Defining the human microbiome. *Nutr Rev*. 2012 Aug;70 Suppl 1(Suppl 1):S38-44. doi: 10.1111/j.1753-4887.

Wiertsema SP, van Bergenhenegouwen J, Garssen J, Knippels LMJ. The Interplay between the Gut Microbiome and the Immune System in the Context of Infectious Diseases throughout Life and the Role of Nutrition in Optimizing Treatment Strategies. *Nutrients*. 2021 Mar 9;13(3):886. doi: 10.3390/nu13030886. PMID: 33803407; PMCID: PMC8001875.

Wu HJ, Wu E. The role of gut microbiota in immune homeostasis and autoimmunity. *Gut Microbes*. 2012 Jan-Feb;3(1):4-14. doi: 10.4161/gmic.19320. Epub 2012 Jan 1. PMID: 22356853; PMCID: PMC3337124.2012.00493.x. PMID: 22861806; PMCID: PMC3426293.