Lecture Section

Class 1:

Intro to the Human Microbiome

Bacteria fundamentals:

Phyla, locations and abundance; bacterial metabolism and biosynthesis; GI tract basics

Host fundamentals:

Immunology Crash Course

Class 2:

Tools for studying the microbiome:

Mouse models (germ-free mice, humanized mice)

Stats, Bioinformatics, and Sequencing Technology; Metagenomic Analysis

To read prior to class #2: Chaudhari SN, McCurry MD, Devlin AS. Chains of evidence from correlations to causal molecules in microbiome-linked diseases. Nat Chem Biol. 2021, 17(10), 1046-1056.

Devlin, A.S. â€œLessons learned by an organic chemist entering the microbiome field.â€ Cell Host Microbe 2022, 30, 435.

Paper Discussion Section

Class 3: Determinants of the Composition of the Human Microbiota

1. Rothschild, Daphna, Omer Weissbrod, Elad Barkan, Alexander Kurilshikov, Tal Korem, David Zeevi, Paul I. Costea, et al. 2018. â€œEnvironment Dominates over Host Genetics in Shaping Human Gut Microbiota.â€ Nature 555 (7695): 210â€“15.
2. Vatanen, T., Jabbar, K.S., Ruohtula, T., Honkanen, J., Avila-Pacheco, J., Siljander, H., StraÅ¾ar, M., Oikarinen, S., HyÃ¶ty, H., Ilonen, J., et al. (2022). Mobile genetic elements from the maternal microbiome shape infant gut microbial assembly and metabolism. Cell *185*, 4921â€“4936.e15.

Class 4: The Gut Microbiome Transfers Phenotypes

3. Ridaura, K. et al. Gut microbiota from twins discordant for obesity modulate metabolism in mice. Science 341, 1241214 (2013).
4. Kimura, Ikuo, Junki Miyamoto, Ryuji Ohue-Kitano, Keita Watanabe, Takahiro Yamada, Masayoshi Onuki, Ryo Aoki, et al. 2020. â€œMaternal Gut Microbiota in Pregnancy Influences Offspring Metabolic Phenotype in Mice.â€ *Science* 367 (6481).

Class 5: The Gut Microbiota Shapes the Immune System, and vice versa

5. Shen, Y., Giardino Torchia, M.L., Lawson, G.W., Karp, C.L., Ashwell, J.D., and Mazmanian, S.K. (2012). Outer membrane vesicles of a human commensal mediate immune regulation and disease protection. Cell Host Microbe *12*, 509â€“520.
6. Lima-Junior, D.S., Krishnamurthy, S.R., Bouladoux, N., Collins, N., Han, S.-J., Chen, E.Y., Constantinides, M.G., Link, V.M., Lim, A.I., Enamorado, M., et al. (2021). Endogenous retroviruses promote homeostatic and inflammatory responses to the microbiota. Cell *184*, 3794â€“3811.e19.

Class 6: Commensal-Pathogen Interactions

7. Li, Y., Watanabe, E., Kawashima, Y. *et al*.Identification of trypsin-degrading commensals in the large intestine. *Nature* **609**, 582â€“589 (2022). https://doi.org/10.1038/s41586-022-05181-3.
8. Stacy, A., Andrade-Oliveira, V., McCulloch, J.A., Hild, B., Oh, J.H., Perez-Chaparro, P.J., Sim, C.K., Lim, A.I., Link, V.M., Enamorado, M., et al. (2021). Infection trains the host for microbiota-enhanced

resistance to pathogens. Cell *184*, 615â€“627.e17.

Class 7: Diet and the Gut Microbiome

9. Wang, Z. et al. Gut flora metabolism of phosphatidylcholine promotes cardiovascular disease. Nature 472, 57â€“63 (2011).
10. Spencer, C.N., McQuade, J.L., Gopalakrishnan, V., McCulloch, J.A., Vetizou, M., Cogdill, A.P., Khan, M.A.W., Zhang, X., White, M.G., Peterson, C.B., et al. (2021). Dietary fiber and probiotics influence the gut microbiome and melanoma immunotherapy response. Science *374*, 1632â€“1640.

Class 8: Bacteria Making Molecules

11. Sugimoto, Yuki, Francine R. Camacho, Shuo Wang, Pranatchareeya Chankhamjon, Arman Odabas, Abhishek Biswas, Philip D. Jeffrey, and Mohamed S. Donia. 2019. â€œA Metagenomic Strategy for Harnessing the Chemical Repertoire of the Human Microbiome.â€ Science, October 2019, 366 (6471): eaax9176.
12. Bae, M., Cassilly, C.D., Liu, X. et al. Akkermansia muciniphila phospholipid induces homeostatic immune responses. Nature 608, 168â€“173 (2022). https://doi.org/10.1038/s41586-022-04985-7.

Class 9: Bacterial Manipulations: Small Molecules and Genetic Engineering

13. Roberts, A.B., Gu, X., Buffa, J.A. et al. Development of a gut microbeâ€“targeted nonlethal therapeutic to inhibit thrombosis potential. Nat Med 24, 1407â€“1417 (2018). https://doi.org/10.1038/s41591-018-0128-1.
14. Canale, F.P., Basso, C., Antonini, G., Perotti, M., Li, N., Sokolovska, A., Neumann, J., James, M.J., Geiger, S., Jin, W., et al. (2021). Metabolic modulation of tumours with engineered bacteria for immunotherapy. Nature 2021, 598, 662.

Class 10: Microbes and the Gut-Brain Axis: neurodevelopment and nerve regeneration

15. Chu, Coco, Mitchell H. Murdock, Deqiang Jing, Tae Hyung Won, Hattie Chung, Adam M. Kressel, Tea Tsaava, et al. 2019. â€œThe Microbiota Regulate Neuronal Function and Fear Extinction Learning.â€ Nature 574 (7779): 543â€“48.
16. Serger, E., Luengo-Gutierrez, L., Chadwick, J.S. et al. The gut metabolite indole-3 propionate promotes nerve regeneration and repair. Nature 607, 585â€“592 (2022). https://doi.org/10.1038/s41586-022-04884-x.

Class 11: Microbes and the Gut-Brain Axis: Human Disease

17. Sharon G, Cruz NJ, Kang DW, Gandal MJ, et al. Human Gut Microbiota from Autism Spectrum Disorder Promote Behavioral Symptoms in Mice. Cell. 2019, 177(6), 1600-1618.e17.
18. Blacher E, Bashiardes S, Shapiro H, et al. Potential roles of gut microbiome and metabolites in modulating ALS in mice. Nature. 2019, 572(7770), 474-480.

Class 12: â€˜omics drives mechanistic microbiome discovery

19. Han, S., Van Treuren, W., Fischer, C.R. *et al*.A metabolomics pipeline for the mechanistic interrogation of the gut microbiome. *Nature***595**, 415â€“420 (2021). https://doi.org/10.1038/s41586-021-03707-9.
20. DohnalovÃ¡, L., Lundgren, P., Carty, J.R.E. *et al*.A microbiome-dependent gutâ€“brain pathway regulates motivation for exercise. *Nature***612**, 739â€“747 (2022). https://doi.org/10.1038/s41586-022-05525-z

Class 13: The microbiome: beyond bacterial cells

21. Aykut, Berk, Smruti Pushalkar, Ruonan Chen, Qianhao Li, Raquel Abengozar, Jacqueline I. Kim, Sorin A. Shadaloey, et al. 2019. â€œThe Fungal Mycobiome Promotes Pancreatic Oncogenesis via Activation of MBL.â€ Nature 574 (7777): 264â€“67.
22. Bittel, M., Reichert, P., Sarfati, I., Dressel, A., Leikam, S., Uderhardt, S., Stolzer, I., Phu, T.A., Ng, M., Vu, N.K., et al. (2021). Visualizing transfer of microbial biomolecules by outer membrane vesicles in microbe-host-communication in vivo. J Extracell Vesicles *10*, e12159.

Term Paper

Write an NIH-style 4 page proposal on a topic of choice related to the microbiome.

Due date: Wed March 22

Please see post under "Announcements" for format.