BIOGRAPHICAL SKETCH

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NAME: Andrew L. Goodman

eRA COMMONS USER NAME (credential, e.g., agency login): algoodman1

POSITION TITLE: C.N.H. Long Professor of Microbial Pathogenesis; Director, Yale Microbial Sciences Institute

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Princeton University, Princeton NJ	A.B.	06/1999	Ecology and Evolutionary Biology
Harvard Medical School and Harvard University, Boston MA	Ph.D.	05/2006	Microbiology and Molecular Genetics
Washington University School of Medicine, St. Louis MO	Postdoctoral training	12/2010	Genomics, Microbiome

A. Personal Statement

My lab uses microbial genetics, mass spectrometry, germfree animal models, and computational approaches to understand the mechanisms of host-microbiome interaction. I have a track record of developing new approaches for microbiology, including transposon insertion sequencing, personalized microbiota culture collections, and regulated control of microbiome gene expression in live animals. We have used these approaches to understand how commensal microbes recognize and modify small molecules in the gut, including vitamins and medical drugs.

a. Zimmermann, M.*, Zimmermann-Kogadeeva, M.*, Wegmann, R., and **Goodman, A.L.** Mapping human microbiome drug metabolism by gut bacteria and their genes. **Nature** 570(7762) p462-467 (2019). *equal contribution. PMCID: PMC6597290.

b. Zimmermann, M.*, Zimmermann-Kogadeeva, M.*, Wegmann, R., and **Goodman, A.L.** Separating host and microbiome contributions to drug metabolism and toxicity. **Science** 363(6427) (2019). *equal contribution. PMCID: PMC6533120.

c. Cullen, T.W., Schofield, W.B., Barry, N.A., Putnam, E.E., Rundell, E.A., Trent, M.S., Degnan, P.H., Booth, C.J., Yu, H., and **Goodman, A.L.** Antimicrobial peptide resistance mediates resilience of prominent gut commensals during inflammation. **Science** 347(6218) p170-175 (2015). PMCID: PMC4388331.

d. Lim, B., Zimmermann, M., Barry, N.A., and **Goodman, A.L.** Engineered regulatory systems modulate gene expression of human commensals in the gut. **Cell** 169(3) p547-558 (2017). PMCID: PMC5532740.

B. Positions and Honors

Positions and Employment

2000-2006 PhD student, laboratory of Stephen Lory, Harvard Medical School
2006-2010 Postdoctoral fellow, laboratory of Jeffrey Gordon, Washington University School of Medicine
2011-2015 Assistant Professor, Dept. of Microbial Pathogenesis and Microbial Sciences Institute, Yale University
2015-2018 Associate Professor, Yale University

2018-2019 Associate Professor with Tenure, Yale University
2019- C.N.H. Long Professor of Microbial Pathogenesis, Yale University
2019- Director, Yale Microbial Sciences Institute, Yale University
2022- Interim Chair, Department of Microbial Pathogenesis, Yale University School of Medicine

Other Experience and Professional Memberships

2012- Ad hoc study section participant for NCCIH, NIGMS, NIEHS, NIDDK, NIMH, NIAID, NIH Office of the Director, NSF, NASA
2018- Editorial Board Member, Annual Review of Microbiology
2019- Standing study section member, NIH XNDA
2021- Associate Editor, Annual Review of Microbiology

Honors

1999 Magna Cum Laude, Princeton University
1999 Charles M. Cannon Thesis Prize in Ecology and Evolutionary Biology, Princeton University
2000 HHMI Predoctoral Fellowship
2004 Finkelstein Award, American Society for Microbiology
2008 NIH/NIAID Ruth L. Kirschstein postdoctoral fellowship (NRSA/F32)
2010 NIH/NIDDK Mentored Research Science Development Award (K01)
2011 Robert T. McCluskey, MD, Yale Scholar
2012 Yale Center for Clinical Investigation Junior Faculty Scholar
2012 NIH Director's New Innovator Award (DP2)
2013 Pew Scholar in the Biomedical Sciences
2013 Presidential Early Career Award for Scientists and Engineers (PECASE)
2015 DuPont Young Professor
2015 Burroughs Wellcome Fund Investigator in the Pathogenesis of Infectious Disease
2016 HHMI Faculty Scholar
2019 C.N.H. Long Professor, Yale University
2020 John J. Abel Award, American Society for Pharmacology and Experimental Therapeutics
2020 Finalist, Yale Postdoc Mentoring Award
2022 Fellow, American Academy of Microbiology

C. Contributions to Science

1. Metabolism of xenobiotics by the gut microbiome

Although the gut microbiome encodes a rich repository of enzymes with the potential to modify small molecules, how these activities impact clinically relevant compounds such as dietary vitamins and medical drugs is unknown. Progress in this area could benefit drug development and could enable co-therapies (probiotics, prebiotics, antibiotics, fecal transplant) that transiently alter an individual's microbiome to improve their response to a drug. We combined microbial genetics, gnotobiotics, and pharmacokinetic modeling to discover and characterize human microbiome-encoded drug- and vitamin- metabolizing enzymes in vitro and in mice. These studies provided three conceptual advances. First, we learned that gut microbes target xenobiotics far more broadly than previous anecdotal examples suggested. For two-thirds of the tested medical drugs, we identified at least one human gut bacterium with the capacity to significantly metabolize the drug; unexpected transformations include *O*-propionylation, sulfoxide excision, defluorination, and large mass increases. Second, we identified microbiome-encoded enzymes that mediate these activities and demonstrated that these enzymes can predict interpersonal differences in microbiome drug metabolism. Third, we developed physiologically-based pharmacokinetic models of host-microbiome xenobiotic metabolism that quantify the impact of microbiome activities and other parameters on drug and metabolite exposure. I am the PI and corresponding author for the representative publications below.

a. Zimmermann, M.*, Zimmermann-Kogadeeva, M.*, Wegmann, R., and **Goodman, A.L.** Mapping human microbiome drug metabolism by gut bacteria and their genes. **Nature** 570(7762) p462-467 (2019). *equal contribution. PMCID: PMC6597290.

b. Zimmermann, M.*, Zimmermann-Kogadeeva, M.*, Wegmann, R., and **Goodman, A.L.** Separating host and microbiome contributions to drug metabolism and toxicity. **Science** 363(6427) (2019). *equal contribution. PMCID: PMC6533120.

c. Wexler, A.G., Schofield, W.B., Degnan, P.H., Folta-Stogniew, E., Barry, N.A., and **Goodman, A.L.** Human gut Bacteroides capture vitamin B12 via cell surface-exposed lipoproteins. **eLife** 37138 (2018). PMCID: PMC6143338.

d. Degnan, P.H., Barry, N.A., Mok, K.C., Taga, M.E., and **Goodman, A.L.** Human gut microbes use multiple transporters to distinguish vitamin B_{12} analogs and compete in the gut. **Cell Host & Microbe** 15 p47-57 (2014). PMCID: PMC3923405.

2. Mechanisms of host-pathogen-microbiome interaction

These studies provide examples of our contributions to understanding the molecular mechanisms that dictate the interactions between human gut commensal bacteria, invading enteropathogens, and their host. For example, we have uncovered commensal-encoded mechanisms for resilience during infection with gastrointestinal bacterial pathogens. We established the underlying genes and biochemical activities, demonstrated their importance in a range of animal models, and completed an IRB-approved human study with complementary results. These studies suggest that commensal-encoded mechanisms for resilience during infection are a counterpart to host-encoded mechanisms for tolerance of the microbiota. I am the Primary Investigator for the microbiome resilience and inflammation studies.

a. Cullen, T.W., Schofield, W.B., Barry, N.A., Putnam, E.E., Rundell, E.A., Trent, M.S., Degnan, P.H., Booth, C.J., Yu, H., and **Goodman, A.L.** Antimicrobial peptide resistance mediates resilience of prominent gut commensals during inflammation. **Science** 347(6218) p170-175 (2015). PMCID: PMC4388331.

b. Tawk, C., Lim, B., Bencivenga-Barry, N.A., Lees, H.J., Ramos, R.J., Cross, J., and **Goodman, A.L.** Infection leaves a genetic and functional mark on the gut population of a commensal bacterium. **Cell Host & Microbe** (in press).

c. Vieira, S. M., Hiltensperger, M., Kumar, V., Dehner, C., Zegarra-Ruiz, D., Khan, N., Costa, F. R., Greiling, T., Ruff, W., Barbieri, A., Kim, W., Kriegel, C., Erkan, D., Jain, D., **Goodman, A. L.**, and Kriegel, M. A. Translocation of a gut pathobiont drives autoimmunity in mice and humans. **Science** 359(6380) p1156-61 (2018). PMCID: PMC5969731.

d. Palm, N.W.*, de Zoete, M.R.*, Cullen, T.W., Barry, N.A., Stefanowski, J., Hao, L., Degnan, P.H., Hu, J., Peter, I., Zhang, W., Ruggiero, E., Cho, J.H., **Goodman, A.L.**, and Flavell, R.A. Immunoglobulin A coating identifies colitogenic bacteria in inflammatory bowel disease. **Cell** 158(5) p1000-1010 (2014). PMCID: PMC4174347. (*equal contribution)

3. Cooperation and competition in the gut microbiome

My lab works to understand the mechanisms of interaction between commensal microbes in the human gut, including nutrient competition and the production of antibacterial factors that shape the microbiome. For example, we recently identified a pathway that gut microbes use to activate antibacterial proteins. Notably, this pathway is also required for activation of host-targeting toxins. Together, these studies reveal critical factors that shape microbiome dynamics and highlight avenues for therapeutic manipulation of these communities. I am the Principal Investigator for the current work.

a. Wexler, A.G., Bao, Y., Whitney, J.C., Bobay, L-M., Xavier, J.B., Schofield, W.B., Barry, N.A., Russell, A.B., Tran, B.Q., Goo, Y., Goodlett, D.R., Ochman, H.O., Mougous, J.D., and **Goodman, A.L.** Human symbionts inject and neutralize antibacterial toxins to persist in the gut. **Proceedings of the National Academy of Sciences** 113(13) p3639-44 (2016). PMCID: PMC4822603.

b. Russell, A.B., Wexler, A.G., Harding, B.N., Whitney, J.C., Bohn, A.J., Goo, A.Y., Tran, B.Q., Barry, N.A., Zheng, H., Peterson, S.B., Chou, S., Gonen, T., Goodlett, D.R., **Goodman, A.L.***, and Mougous, J.D.* A Type VI secretion-related pathway in Bacteroidetes mediates interbacterial antagonism. **Cell Host & Microbe** 16 p1-10 (2014). PMCID: PMC4136423. (*co-corresponding authors).

c. Bao, Y., Verdegaal, A.A., Anderson, B.W., Barry, N.A., He, J., Gao, X., and **Goodman, A.L.** A common pathway for activation of host-targeting and bacteria-targeting toxins in human intestinal bacteria. **mBio** 12(4): e0056621. PMCID: PMC8406203.

d. Putnam, E.E., Abellon-Ruiz, J., Killinger, B.J., Rosnow, J.J., Wexler, A.G., Folta-Stogniew, E., Wright, A.T., van den Berg, B., and **Goodman, A.L.** Gut commensal *Bacteroidetes* encode a novel class of vitamin-B_{12} binding proteins. **mBio** 13(2) e0284521 (2022). PMCID: PMC8941943.

4. New tools for genetic analysis of human gut microbiomes

We have a track record of innovative approaches for microbiome and microbiology research. For example, we developed transposon sequencing (TN-seq; named Insertion Sequencing or INSeq in our publications), which we applied to conduct the first genomewide screen for fitness determinants of a human commensal in a mammalian host. We also developed approaches for creating personalized human gut microbiota culture collections that capture the majority of an individual's gut microbiota. This strategy is now widely used to directly establish specific contributions of individual species in microbial communities. In another example, we established the first genetic system for controlling microbiome gene expression in the mouse gut through a synthetic inducer provided in drinking water. Recently, we established new techniques for genetic manipulation of diverse human gut Bacteroides, including type strains and direct patient isolates. We have used this approach to study antimicrobial peptide resistance in *Bacteroides vulgatus.* I am the Principal Investigator of the recent studies and first author of the earlier work.

a. Lim, B., Zimmermann, M., Barry, N.A., and **Goodman, A.L.** Engineered regulatory systems modulate gene expression of human commensals in the gut. **Cell** 169(3) p547-558 (2017). PMCID: PMC5532740.

b. Bencivenga-Barry, N.A., Lim, B., Herrara, C.M., Trent, M.S., and **Goodman, A.L.** Genetic manipulation of wild human gut *Bacteroides.* **Journal of Bacteriology** 202(3) e00544-19 (2020). PMCID: PMC6964735.

c. Zimmermann-Kogadeeva, M., Zimmermann, M., and **Goodman, A.L.** Insights from pharmacokinetic models of host-microbiome drug metabolism. **Gut Microbes** (2019).

d. **Goodman, A.L.**, Kallstrom, G., Faith, J.J., Reyes, A., Moore, A., Dantas, G., and Gordon, J.I. Extensive personal human gut microbiota culture collections characterized and manipulated in gnotobiotic mice. **Proceedings of the National Academy of Sciences** 108(15) p6252-6257 (2011). PMCID: PMC3076821.

5. Metabolic interactions between microbiome and host

We are involved in multiple studies aimed at understanding how endogenous and dietary small molecules mediate host-microbiome metabolic interactions. For example, we combined microbiome transcriptomics, metabolomics, and stable isotope metabolic flux analyses of anaerobic human gut commensals to understand how these microbes use the intracellular signaling molecule (p)ppGpp to modulate central metabolism in order to persist in the gut. We identified alpha-ketoglutarate as a central target of these signals, determined the underlying metabolic route, and demonstrated that alpha-ketoglutarate supplementation rescues fitness defects of mutants that lack (p)ppGpp. This revealed that how the ability to halt rather than accelerate growth can be a determining factor for membership in the gut microbiome. In other studies, we have worked to understand how microbial and dietary small molecules impact host physiology and commensal fitness in the gut. I am the Principal Investigator for the microbial metabolism and physiology studies and contributed microbiome and gnotobiotic expertise to the other projects.

a. Schofield, W.B.*, Zimmermann-Kogadeeva, M.*, Zimmermann, M., Barry, N.A., and **Goodman, A.L.** The stringent response determines the ability of a commensal bacterium to survive starvation and to persist in the gut. **Cell Host & Microbe** 24(1) p120-132 (2018). (*equal contribution) PMCID: PMC6086485.

b. Perry, R.J., Peng, L., Barry, N.A., Cline, G.W. Zhang, D., Cardone, R.L. Peterson, K., Kibbey, R.G., **Goodman, A.L.**, and Shulman, G.I. Acetate mediates a gut microbiota-brain-beta-cell axis to promote obesity and the metabolic syndrome. **Nature** 534 p213-217 (2016). PMCID: PMC4922538.

c. Townsend, G.E., Han, W., Schwalm, N.D., Raghavan, V., Barry, N.A., **Goodman, A.L.**, and Groisman, E.A. Dietary sugar silences a colonization factor in a mammalian gut symbiont. **Proceedings of the National Academy of Sciences** 116(1) p233-238 (2019). PMCID: PMC6320540.

d. **Goodman, A.L.**, McNulty, N.P., Zhao, Y., Leip, D., Mitra, R.D., Lozupone, C.A., Knight, R., and Gordon, J.I. Identifying genetic determinants needed to establish a human gut symbiont in its habitat. **Cell Host & Microbe** 6(3) p279-289 (2009). PMCID: PMC2895552.

Complete List of Published Work:
https://www.ncbi.nlm.nih.gov/myncbi/andrew.goodman.1/bibliography/public/