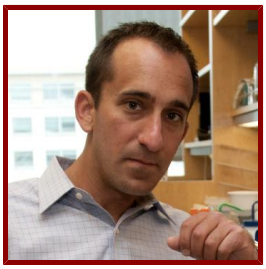
Stanford



Michael Fischbach

Associate Professor of Bioengineering

Bio

BIO

Michael Fischbach is an Associate Professor in the Departments of Bioengineering and Microbiology & Immunology at Stanford University, an Institute Scholar of Stanford ChEM-H, and the director of the Stanford Microbiome Therapies Initiative. Fischbach is a recipient of the NIH Director's Pioneer and New Innovator Awards, an HHMI-Simons Faculty Scholars Award, a Fellowship for Science and Engineering from the David and Lucille Packard Foundation, a Medical Research Award from the W.M. Keck Foundation, a Burroughs Wellcome Fund Investigators in the Pathogenesis of Infectious Disease award, and a Glenn Award for Research in Biological Mechanisms of Aging. His laboratory uses a combination of genomics and chemistry to identify and characterize small molecules from microbes, with an emphasis on the human microbiome. Fischbach received his Ph.D. as a John and Fannie Hertz Foundation Fellow in chemistry from Harvard in 2007, where he studied the role of iron acquisition in bacterial pathogenesis and the biosynthesis of antibiotics. After two years as an independent fellow at Massachusetts General Hospital, Fischbach joined the faculty at UCSF, where he founded his lab before moving to Stanford in 2017. Fischbach is a co-founder and director of Federation Bio and Kelonia, a co-founder of Revolution Medicines, a member of the scientific advisory boards of NGM Biopharmaceuticals and the Chan Zuckerberg Initiative, and an innovation partner at The Column Group.

ACADEMIC APPOINTMENTS

- Associate Professor, Bioengineering
- Member, Bio-X
- Member, Wu Tsai Human Performance Alliance
- Member, Maternal & Child Health Research Institute (MCHRI)
- Institute Scholar, Sarafan ChEM-H
- Director, Microbiome Therapies Initiative (MITI)
- Member, Stanford Cancer Institute

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

The microbiome carries out extraordinary feats of biology: it produces hundreds of molecules, many of which impact host physiology; modulates immune function potently and specifically; self-organizes biogeographically; and exhibits profound stability in the face of perturbations. Our lab studies the mechanisms of microbiome-host interactions. Our approach is based on two technologies we recently developed: a complex (119-member) defined gut community that serves as an analytically manageable but biologically relevant system for experimentation, and new genetic systems for common species from the microbiome. Using these systems, we investigate mechanisms at the community level and the strain level.

1) Community-level mechanisms. A typical gut microbiome consists of 200-250 bacterial species that span >6 orders of magnitude in relative abundance. As a system, these bacteria carry out extraordinary feats of metabolite consumption and production, elicit a variety of specific immune cell populations, self-organize geographically and metabolically, and exhibit profound resilience against a wide range of perturbations. Yet remarkably little is known about how the community functions as a system. We are exploring this by asking two broad questions: How do groups of organisms work together to influence immune function? What are the mechanisms that govern metabolism and ecology at the 100+ strain scale? Our goal is to learn rules that will enable us to design communities that solve specific therapeutic problems.

2) Strain-level mechanisms. Even though gut and skin colonists live in communities, individual strains can have an extraordinary impact on host biology. We focus on two broad (and partially overlapping) categories:

Immune modulation: Can we redirect colonist-specific T cells against an antigen of interest by expressing it on the surface of a bacterium? How do skin colonists induce high levels of Staphylococcus-specific antibodies in mice and humans?

Abundant microbiome-derived molecules: By constructing single-strain/single-gene knockouts in a complex defined community, we will ask: What are the effects of bacterially produced molecules on host metabolism and immunology? Can the molecular output of low-abundance organisms impact host physiology?

3) Cell and gene therapy. We have begun two new efforts in mammalian cell and gene therapies. First, we are developing methods that enable cell-type specific delivery of genome editing payloads in vivo. We are especially interested in delivery vehicles that are customizable and easy to manufacture. Second, we have begun a comprehensive genome mining effort with an emphasis on understudied or entirely novel enzyme systems with utility in mammalian genome editing.

Teaching

COURSES

2023-24

- Problem choice and decision trees in science and engineering: BIOE 395 (Spr)
- Systems Physiology and Design: BIOE 103 (Spr)

2022-23

- Problem choice and decision trees in science and engineering: BIOE 395 (Spr)
- Systems Physiology and Design: BIOE 103 (Spr)
- Systems Physiology and Design: BIOE 103B (Spr)

2021-22

- Problem choice and decision trees in science and engineering: BIOE 395 (Spr)
- Systems Physiology and Design: BIOE 103 (Spr)

2020-21

- Problem choice and decision trees in science and engineering: BIOE 395 (Spr)
- Systems Physiology and Design: BIOE 103 (Spr)

STANFORD ADVISEES

Doctoral Dissertation Reader (AC)

Kaisha Benjamin, Alex Soohoo

Postdoctoral Faculty Sponsor

Kate Bauman, Djenet Bousbaine, Gabriel Filsinger, Nathan Johns, Martin McLaughlin, Xianfeng Zeng, Aishan Zhao

Doctoral Dissertation Advisor (AC)

Sriya Chitti, Elliot Hershberg

Undergraduate Major Advisor

Claudia Zimmerman

Doctoral (Program)

Elliot Hershberg, Jerry Yan, Xiaowei Zhang, Kyle Zolkin

Publications

PUBLICATIONS

- **Identification of human skin microbiome odorants that manipulate mosquito landing behavior.** *bioRxiv : the preprint server for biology*
  Coutinho-Abreu, I. V., Jamshidi, O., Raban, R., Atabakhsh, K., Merriman, J. A., Fischbach, M. A., Akbari, O. S.
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- **Mapping the T cell repertoire to a complex gut bacterial community.** *Nature*
  Nagashima, K., Zhao, A., Atabakhsh, K., Bae, M., Blum, J. E., Weakley, A., Jain, S., Meng, X., Cheng, A. G., Wang, M., Higginbottom, S., Dimas, A., Murugkar, et al
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- **Strain dropouts reveal interactions that govern the metabolic output of the gut microbiome.** *Cell*
  Wang, M., Osborn, L. J., Jain, S., Meng, X., Weakley, A., Yan, J., Massey, W. J., Varadharajan, V., Horak, A., Banerjee, R., Allende, D. S., Chan, E. R., Hajjar, et al
  2023; 186 (13): 2839-2852.e21
- **Atlas of gut microbe-derived products from aromatic amino acids and risk of cardiovascular morbidity and mortality.** *European heart journal*
  Nemet, I., Li, X. S., Haghikia, A., Li, L., Wilcox, J., Romano, K. A., Buffa, J. A., Witkowski, M., Demuth, I., König, M., Steinhagen-Thiessen, E., Bäckhed, F., Fischbach, et al
  2023
- **Engineered skin bacteria induce antitumor T cell responses against melanoma.** *Science (New York, N.Y.)*
  Chen, Y. E., Bousbaine, D., Veinbachs, A., Atabakhsh, K., Dimas, A., Yu, V. K., Zhao, A., Enright, N. J., Nagashima, K., Belkaid, Y., Fischbach, M. A.
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- **gutSMASH predicts specialized primary metabolic pathways from the human gut microbiota.** *Nature biotechnology*
  Pascal Andreu, V., Augustijn, H. E., Chen, L., Zhernakova, A., Fu, J., Fischbach, M. A., Dodd, D., Medema, M. H.
  2023
- **Host-microbe co-metabolism via MCAD generates circulating metabolites including hippuric acid.** *Nature communications*
  Pruss, K. M., Chen, H., Liu, Y., Van Treuren, W., Higginbottom, S. K., Jarman, J. B., Fischer, C. R., Mak, J., Wong, B., Cowan, T. M., Fischbach, M. A., Sonnenburg, J. L., Dodd, et al
  2023; 14 (1): 512
- **Retroviral Infection and Commensal Bacteria Dependently Alter the Metabolomic Profile in a Sterile Organ.** *Viruses*
  Spring, J., Beilinson, V., DeFelice, B. C., Sanchez, J. M., Fischbach, M., Chervonsky, A., Golovkina, T.
  2023; 15 (2)
- **A Limited Effect of Chronic Renal Insufficiency on the Colon Microbiome.** *Journal of the American Society of Nephrology : JASN*
  Guthrie, L., Sonnenburg, J. L., Fischbach, M. A., Meyer, T. W.
  2023
- **Two distinct gut microbial pathways contribute to meta-organismal production of phenylacetylglutamine with links to cardiovascular disease.** *Cell host & microbe*
  Zhu, Y., Dwidar, M., Nemet, I., Buffa, J. A., Sangwan, N., Li, X. S., Anderson, J. T., Romano, K. A., Fu, X., Funabashi, M., Wang, Z., Keranahalli, P., Battle, et al
  2022

- **Bacteroides thetaiotaomicron rough-type lipopolysaccharide: The chemical structure and the immunological activity** *CARBOHYDRATE POLYMERS*
  Pither, M., Illiano, A., Pagliuca, C., Jacobson, A., Mantova, G., Stornaiuolo, A., Colicchio, R., Vitiello, M., Pinto, G., Silipo, A., Fischbach, M. A., Salvatore, P., Amoresano, et al
  2022; 297: 120040

- **Gut commensal bacteria enhance pathogenesis of a tumorigenic murine retrovirus.** *Cell reports*
  Spring, J., Khan, A. A., Lara, S., O'Grady, K., Wilks, J., Gurbuxani, S., Erickson, S., Fischbach, M., Jacobson, A., Chervonsky, A., Golovkina, T.
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- **Design, construction, and invivo augmentation of a complex gut microbiome.** *Cell*
  Cheng, A. G., Ho, P., Aranda-Diaz, A., Jain, S., Yu, F. B., Meng, X., Wang, M., Iakiviak, M., Nagashima, K., Zhao, A., Murugkar, P., Patil, A., Atabakhsh, et al
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- **Gut Microbe-derived Short-Chain Fatty Acids Regulate Arthritis and Myositis During Chikungunya Virus Infection**
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- **A gut-derived metabolite alters brain activity and anxiety behaviour in mice.** *Nature*
  Needham, B. D., Funabashi, M., Adame, M. D., Wang, Z., Boktor, J. C., Haney, J., Wu, W., Rabut, C., Ladinsky, M. S., Hwang, S., Guo, Y., Zhu, Q., Griffiths, et al
  2022

- **Novel bile acid biosynthetic pathways are enriched in the microbiome of centenarians.** *Nature*
  Sato, Y., Atarashi, K., Plichta, D. R., Arai, Y., Sasajima, S., Kearney, S. M., Suda, W., Takeshita, K., Sasaki, T., Okamoto, S., Skelly, A. N., Okamura, Y., Vlamakis, et al
  2021

- **Metagenomic compendium of 189,680 DNA viruses from the human gut microbiome.** *Nature microbiology*
  Nayfach, S., Paez-Espino, D., Call, L., Low, S. J., Sberro, H., Ivanova, N. N., Proal, A. D., Fischbach, M. A., Bhatt, A. S., Hugenholtz, P., Kyrpides, N. C.
  2021

- **Gut microbes impact stroke severity via the trimethylamine N-oxide pathway.** *Cell host & microbe*
  Zhu, W., Romano, K. A., Li, L., Buffa, J. A., Sangwan, N., Prakash, P., Tittle, A. N., Li, X. S., Fu, X., Androjna, C., DiDonato, A. J., Brinson, K., Trapp, et al
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- **The gutSMASH web server:automated identification of primary metabolic gene clusters from the gut microbiota.** *Nucleic acids research*
  Pascal Andreu, V., Roel-Touris, J., Dodd, D., Fischbach, M. A., Medema, M. H.
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- **CRISPR-based functional genomics in human dendritic cells.** *eLife*
  Jost, M., Jacobson, A. N., Hussmann, J. A., Cirolia, G., Fischbach, M. A., Weissman, J. S.
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- **A method for detection of SARS-CoV-2 RNA in healthy human stool: a validation study.** *The Lancet. Microbe*
  Coryell, M. P., Iakiviak, M., Pereira, N., Murugkar, P. P., Rippe, J., Williams, D. B., Heald-Sargent, T., Sanchez-Pinto, L. N., Chavez, J., Hastie, J. L., Sava, R. L., Lien, C. Z., Wang, et al
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- **Role of dietary fiber in the recovery of the human gut microbiome and its metabolome.** *Cell host & microbe*
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- **A metabolomics pipeline for the mechanistic interrogation of the gut microbiome.** *Nature*
  Han, S., Van Treuren, W., Fischer, C. R., Merrill, B. D., DeFelice, B. C., Sanchez, J. M., Higginbottom, S. K., Guthrie, L., Fall, L. A., Dodd, D., Fischbach, M. A., Sonnenburg, J. L.
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- **Endogenous retroviruses promote homeostatic and inflammatory responses to the microbiota.** *Cell*
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- **BiG-MAP: an Automated Pipeline To Profile Metabolic Gene Cluster Abundance and Expression in Microbiomes.** *mSystems*
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- **Bacterially Derived Tryptamine Increases Mucus Release by Activating a Host Receptor in a Mouse Model of Inflammatory Bowel Disease.** *iScience*
  Bhattarai, Y., Jie, S., Linden, D. R., Ghatak, S., Mars, R. A., Williams, B. B., Pu, M., Sonnenburg, J. L., Fischbach, M. A., Farrugia, G., Sha, L., Kashyap, P. C.
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- **A Cutibacterium acnes antibiotic modulates human skin microbiota composition in hair follicles.** *Science translational medicine*
  Claesen, J., Spagnolo, J. B., Ramos, S. F., Kurita, K. L., Byrd, A. L., Aksenov, A. A., Melnik, A. V., Wong, W. R., Wang, S., Hernandez, R. D., Donia, M. S., Dorrestein, P. C., Kong, et al
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- **Bifidobacterium alters the gut microbiota and modulates the functional metabolism of T regulatory cells in the context of immune checkpoint blockade.** *Proceedings of the National Academy of Sciences of the United States of America*
  Sun, S., Luo, L., Liang, W., Yin, Q., Guo, J., Rush, A. M., Lv, Z., Liang, Q., Fischbach, M. A., Sonnenburg, J. L., Dodd, D., Davis, M. M., Wang, et al
  2020

- **Computational genomic discovery of diverse gene clusters harbouring Fe-S flavoenzymes in anaerobic gut microbiota.** *Microbial genomics*
  Pascal Andreu, V., Fischbach, M. A., Medema, M. H.
  2020

- **MAIT cells are imprinted by the microbiota in early life and promote tissue repair**
  Constantinides, M. G., Link, V. M., Tamoutounour, S., Wong, A. C., Perez-Chaparro, P., Han, S., Chen, Y., Li, K., Farhat, S., Weckel, A., Krishnamurthy, S. R., Vujkovic-Cvijin, I., Linehan, et al
  AMER ASSOC IMMUNOLOGISTS.2020

- **Bile acid metabolites control Th17 and Treg cell differentiation**
  Hang, S., Paik, D., Yao, L., Jamma, T., Lu, J., Ha, S., Nelson, B. N., Kelly, S. P., Wu, L., Zheng, Y., Longman, R. S., Rastinejad, F., Devlin, et al
  AMER ASSOC IMMUNOLOGISTS.2020

- **Dysbiosis-Induced Secondary Bile Acid Deficiency Promotes Intestinal Inflammation.** *Cell host & microbe*
  Sinha, S. R., Haileselassie, Y., Nguyen, L. P., Tropini, C., Wang, M., Becker, L. S., Sim, D., Jarr, K., Spear, E. T., Singh, G., Namkoong, H., Bittinger, K., Fischbach, et al
  2020

- **Michael Fischbach: Homing in on the molecules from microbes** *NATURE*
  Scott, A., Fischbach, M.
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- **Michael Fischbach: Homing in on the molecules from microbes** *NATURE*
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- **Bile acids profile, histopathological indices and genetic variants for non-alcoholic fatty liver disease progression.** *Metabolism: clinical and experimental*
  Nimer, N. n., Choucair, I. n., Wang, Z. n., Nemet, I. n., Li, L. n., Gukasyan, J. n., Weeks, T. L., Alkhouri, N. n., Zein, N. n., Tang, W. H., Fischbach, M. A., Brown, J. M., Allayee, et al
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- **A Cardiovascular Disease-Linked Gut Microbial Metabolite Acts via Adrenergic Receptors.** *Cell*
  Nemet, I. n., Saha, P. P., Gupta, N. n., Zhu, W. n., Romano, K. A., Skye, S. M., Cajka, T. n., Mohan, M. L., Li, L. n., Wu, Y. n., Funabashi, M. n., Ramer-Tait, A. E., Naga Prasad, et al
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- **Characterization of Serine Hydrolases Across Clinical Isolates of Commensal Skin Bacteria Staphylococcus epidermidis Using Activity-Based Protein Profiling.** *ACS infectious diseases*

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2020

- **Author Correction: Bile acid metabolites control TH17 and Treg cell differentiation.** *Nature*
  Hang, S. n., Paik, D. n., Yao, L. n., Kim, E. n., Trinath, J. n., Lu, J. n., Ha, S. n., Nelson, B. N., Kelly, S. P., Wu, L. n., Zheng, Y. n., Longman, R. S., Rastinejad, et al
  2020
- **Expansion of RiPP biosynthetic space through integration of pan-genomics and machine learning uncovers a novel class of lantibiotics.** *PLoS biology*
  Kloosterman, A. M., Cimermancic, P. n., Elsayed, S. S., Du, C. n., Hadjithomas, M. n., Donia, M. S., Fischbach, M. A., van Wezel, G. P., Medema, M. H.
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- **A metabolic pathway for bile acid dehydroxylation by the gut microbiome.** *Nature*
  Funabashi, M. n., Grove, T. L., Wang, M. n., Varma, Y. n., McFadden, M. E., Brown, L. C., Guo, C. n., Higginbottom, S. n., Almo, S. C., Fischbach, M. A.
  2020
- **Depletion of microbiome-derived molecules in the host using Clostridium genetics.** *Science (New York, N.Y.)*
  Guo, C., Allen, B. M., Hiam, K. J., Dodd, D., Van Treuren, W., Higginbottom, S., Nagashima, K., Fischer, C. R., Sonnenburg, J. L., Spitzer, M. H., Fischbach, M. A.
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- **Quantification of bile acids: A mass spectrometry platform for studying gut microbe connection to metabolic diseases.** *Journal of lipid research*
  Choucair, I., Nemet, I., Li, L., Cole, M. A., Skye, S. M., Kirsop, J. D., Fischbach, M., Gogonea, V., Brown, J. M., Tang, W. H., Hazen, S. L.
  2019
- **Bile acid metabolites control TH17 and Treg cell differentiation.** *Nature*
  Hang, S. n., Paik, D. n., Yao, L. n., Kim, E. n., Jamma, T. n., Lu, J. n., Ha, S. n., Nelson, B. N., Kelly, S. P., Wu, L. n., Zheng, Y. n., Longman, R. S., Rastinejad, et al
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  2019; 366 (6464)
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  2019; 26 (5): 650–65.e4
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  Skye, S. M., Zhu, W., Romano, K. A., Guo, C., Wang, Z., Jia, X., Kirsop, J., Haag, B., Lang, J. M., DiDonato, J. A., Tang, W. H., Lusis, A. J., Rey, et al
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- **Microbial Transplantation With Human Gut Commensals Containing CutC Is Sufficient to Transmit Enhanced Platelet Reactivity and Thrombosis Potential** *CIRCULATION RESEARCH*
  Skye, S. M., Zhu, W., Romano, K. A., Guo, C., Wang, Z., Jia, X., Kirsop, J., Haag, B., Lang, J. M., DiDonato, J. A., Tang, W., Lusis, A. J., Rey, et al
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  Fischbach, M. A.
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- **Mapping the Genetic Landscape of Human Cells** *CELL*
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- **Contextual control of skin immunity and inflammation byCorynebacterium.** *The Journal of experimental medicine*
  Ridaura, V. K., Bouladoux, N. n., Claesen, J. n., Chen, Y. E., Byrd, A. L., Constantinides, M. G., Merrill, E. D., Tamoutounour, S. n., Fischbach, M. A., Belkaid, Y. n.
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- **A Pressure Test to Make 10 Molecules in 90 Days: External Evaluation of Methods to Engineer Biology.** *Journal of the American Chemical Society*
  Casini, A. n., Chang, F. Y., Eluere, R. n., King, A. M., Young, E. M., Dudley, Q. M., Karim, A. n., Pratt, K. n., Bristol, C. n., Forget, A. n., Ghodasara, A. n., Warden-Rothman, R. n., Gan, et al
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  Jacobson, A. N., Choudhury, B. P., Fischbach, M. A.
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- **Skin microbiota-host interactions.** *Nature*
  Chen, Y. E., Fischbach, M. A., Belkaid, Y. n.
  2018; 553 (7689): 427–36

- **Discovery of Reactive Microbiota-Derived Metabolites that Inhibit Host Proteases** *CELL*
  Guo, C., Chang, F., Wyche, T. P., Backus, K. M., Acker, T. M., Funabashi, M., Taketani, M., Donia, M. S., Nayfach, S., Pollard, K. S., Craik, C. S., Cravatt, B. F., Clardy, et al
  2017; 168 (3): 517-?

- **A gut bacterial pathway metabolizes aromatic amino acids into nine circulating metabolites.** *Nature*
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  2017; 551 (7682): 648–52

- **Modulation of a Circulating Uremic Solute via Rational Genetic Manipulation of the Gut Microbiota** *CELL HOST & MICROBE*
  Devlin, A. S., Marcobal, A., Dodd, D., Nayfach, S., Plummer, N., Meyer, T., Pollard, K. S., Sonnenburg, J. L., Fischbach, M. A.
  2016; 20 (6): 709-715

- **Signaling in Host-Associated Microbial Communities** *CELL*
  Fischbach, M. A., Segre, J. A.
  2016; 164 (6): 1288-1300

- **Synthetic biology to access and expand nature's chemical diversity** *NATURE REVIEWS MICROBIOLOGY*
  Smanski, M. J., Zhou, H., Claesen, J., Shen, B., Fischbach, M. A., Voigt, C. A.
  2016; 14 (3): 135-149

- **A Wave of Regulatory T Cells into Neonatal Skin Mediates Tolerance to Commensal Microbes** *IMMUNITY*
  Scharschmidt, T. C., Vasquez, K. S., Truong, H., Gearty, S. V., Pauli, M. L., Nosbaum, A., Gratz, I. K., Otto, M., Moon, J. J., Liese, J., Abbas, A. K., Fischbach, M. A., Rosenblum, et al
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  Wilks, J., Lien, E., Jacobson, A. N., Fischbach, M. A., Qureshi, N., Chervonsky, A. V., Golovkina, T. V.
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