

Personal Information:

Margaret R. Alexander

Assistant Professor
Microbial Sciences, 1550 Linden Dr, Room 6305
Madison, WI 53706
Office: (608) 265-5200
Cell: (503) 789-3417
Email: mralexander2@wisc.edu

Current Position:

University of Wisconsin - Madison

Assistant Professor
Department of Medical Microbiology and Immunology
2024-Present

Education:

University of Utah, Salt Lake City, Utah

PhD in Microbiology and Immunology
Mentor: Ryan O'Connell, Ph.D.
2012-2017

Carleton College, Northfield, Minnesota

B.A. in Biology
2008-2012

Past Positions:

Postdoctoral Fellow, UCSF 2017-2023

Department of Microbiology and Immunology

Exploring mechanisms of diet-microbiome-immune interactions and the functional consequences of these interactions on autoimmunity in Dr. Peter Turnbaugh's lab.

Graduate Student, University of Utah 2012-2017

Department of Pathology, Division of Microbiology and Immunology

Studied the functional transfer of miRNAs via exosomes in Dr. Ryan O'Connell's lab.

Research Assistant, Carleton College 2010-2012

Department of Biology

Investigated yeast mitochondrial DNA maintenance in Dr. Stephan Zweifel's lab.

Grants and Fellowships:

Current

- **NIH/NIAID R00 4R00AI159227-03** 2024-2026
Role: PI
Title: Deconstructing interactions between diet, microbiome, and immunity to gain mechanistic insight into health and disease

Total award amount: \$498,000

Past

- **NIH/NIAID K99/R00 1K99AI159227-01A1** 2022-2024
Role: PI
Title: Deconstructing interactions between diet, microbiome, and immunity to gain mechanistic insight into health and disease
- **NIH/NIAID F32 F32AI147456** 2019-2021
Role: PI
Title: Using diet to alter immune manipulation by *Eggerthella lenta* metabolites: eating away at autoimmunity
- **NIH T32 T32AI060537** 2018-2019
Microbial Pathogenesis and Host Defense Postdoctoral Training Grant, UCSF
- **NIH T32 T32HD007491** 2015-2017
Developmental Biology Training Program Predoctoral Training Grant, University of Utah

Publications:

1. **Alexander, M.**, Upadhyay, V., Rock, R., Ramirez, L., Puchalska, P., Orellana, D., Ang, Q.Y., Turnbaugh, J.A., Tian Y., Dumlao, D., Nayak, R.R., Patterson, A., Newman, J.C, Crawford, P.A, Turnbaugh, P.J. 2023. A diet-dependent host metabolite shapes the gut microbiota to protect from autoimmunity. *In Press Cell Reports* 2024.
2. Whelan, K., **Alexander, M.**, Gaiani, C., Lunken, G., Holmes, A., Staudacher, H.M., Theis, S., Marco, M.L. Design, conduct and reporting of prebiotic and probiotic clinical trials in the context of diet and the gut microbiome. *In press Nat. Microbiology* 2024.
3. Noecker, C., Sanchez, J., Bisanz, J.E., Escalante, V, **Alexander, M.**, Trepka, K., Heinken, A., Liu, Y., Dodd, D., Thiele, I., DeFelice, B., and Turnbaugh, P.J. 2023. Systems biology elucidates the distinctive metabolic niche filled by the human gut microbe *Eggerthella lenta*. *PLoS Bio*. <https://doi.org/10.1371/journal.pbio.3002125>
4. Dong, X., Guthrie, B.H.G., **Alexander, M.**, Noecker, C., Ramirez, L., Glasse, N.R., Turnbaugh, P.J., Balskus, E.P. 2022. Genetic manipulation of the human gut bacterium *Eggerthella lenta* reveals a widespread family of transcriptional regulators. *Nat Commun* 13, 7624. <https://doi.org/10.1038/s41467-022-33576-3>
5. Bauer, K.M., Nelson, M., Tang, W.W., Chiaro, T.R., Brown, D.G., Ghazaryan, A., Lee, S., Weis, A.M., Hill, J.H, Klag, K.A., Tran, V.B, Thompson, J.W., Ramstead, A., Monts, J., Marvin, J., **Alexander, M.**, Voth, W., Stephens, W., Ward, D.M., Petrey, A.C., Round, J., O'Connell, R.M. 2022. CD11c+ myeloid cell exosomes reduce intestinal inflammation during colitis. *JCI insight*. 7, e159469.
6. **Alexander, M.**, Ang, Q.Y., Nayak, R.R., Bustion, A.E., Sandy, M., Zhang, B., Upadhyay, V., Pollard, K.S., Lynch, S.V., and Turnbaugh, P.J. 2022. Human gut bacterial metabolism drives Th17 activation and colitis. *Cell Host & Microbe*. 30, 17 - 30.e9.

- a. Featured on cover and previewed by: Rodriguez-Marino, N. and Cervantes-Barragan, L. 2022. Microbial Cgr2 will let your Th17 cells ROR(gT). *Cell Host & Microbe*. 30, 10-12.
7. Lam, K.N., Spanogiannopoulos, P., Soto-Perez, P., **Alexander, M.**, Nalley, M.J., Bisanz, J.E., Yu, F.B., Turnbaugh P.J. 2021. Phage-delivered CRISPR-Cas9 for strain-specific depletion and genomic deletions in the gut microbiota. *Cell Reports* 37, 109930.
8. Nayak, R.R., **Alexander, M.**, Deshpande, I., Stapleton-Gray, K., Rimal, B., Patterson, A.D., Ubeda, C., Scher, J.U., and Turnbaugh, P.J. 2021. Methotrexate impacts conserved pathways in diverse human gut bacteria leading to decreased host immune activation. *Cell Host & Microbe* 29, 362-377.e11.
9. Artacho, A., Isaac, S., Nayak, R.R., Flor-Duro, A., **Alexander, M.**, Koo, I., Manasson, J., Smith, P.B., Rosenthal, P., Homsy, Y., Gulko, P., Pons, J., Puchades-Carrasco, L., Izmirly, P., Patterson, A., Abramson, S.B., Pineda-Lucena, A., Turnbaugh, P.J., Ubeda, C., Scher, J.U. 2021. The pretreatment gut microbiome is associated with lack of response to methotrexate in new-onset rheumatoid arthritis. *Arthritis Rheumatol*. 73, 931-942.
10. **Alexander, M.**, Turnbaugh P.J. 2020. Stressed out gut bacteria are pterin up gut inflammation. *Nature Microbiology*. 11, 1316-1318.
11. **Alexander, M.** and Turnbaugh, P.J. 2020. Deconstructing mechanisms of diet-microbiome-immune interactions. *Immunity* 53, 264-276.
12. Ang, Q.Y., **Alexander, M.**, Newman, J.C., Tian, Y., Cai, J., Upadhyay, V., Turnbaugh, J.A., Verdin, E., Hall, K.D., Leibel, L.L., Ravussin, E., Rosenbaum, M., Patterson, A.D., and Turnbaugh, P.J. 2020. Ketogenesis alters the gut microbiome resulting in decreased intestinal Th17 levels. *Cell* 181, 1263-1275.E16.
13. Lam, K.N.*, **Alexander, M.***, and Turnbaugh, P.J. 2019. Precision medicine goes microscopic: engineering the microbiome to improve drug outcomes. *Cell Host & Microbe* 26, 22-34.
14. Runtsch, M.C., Nelson, M.C, Lee, S., **Alexander, M.**, Hu, R., Wallace, J.A., Petersen, C., Mosbrugger, T.L, Boudina, S., Bronner, M.P., Round, J.L., Drummond, M., O'Connell, R.M. 2018. Anti-inflammatory microRNA-146a protects mice from diet-induced metabolic disease. *PLOS Genet*. 15, e1007970.
15. **Alexander, M.**, Ramstead, A.G., Bauer, K.M., Lee, S.H., Runtsch, M.C., Wallace, J., Huffaker, T.B., Larsen, D.K., Tolmachova, T., Seabra, M.C., Round, J.L., Ward, D.M., and O'Connell, R.M. 2017. Rab27-dependent exosome production inhibits chronic inflammation and enables acute responses to inflammatory stimuli. *J. Immunol*. 199, 3559-3570.
16. Huffaker, T.B., Lee, S., Tang, W.W., Wallace, J.A., **Alexander, M.**, Runtsch, M.C., Larsen, D.K., Thompson, J., Ramstead, A.G., Voth, W.P., Hu, R., Round, J.L., Williams, M.A., and O'Connell, R.M. 2017. Antitumor immunity is defective in T cell-specific microRNA-155-deficient mice and is rescued by immune checkpoint blockade. *J. Cell Biol*. 292, 18530-18541.
17. Wallace, J., Kagele, D.A., Hu, R., Runtsch, M.C., **Alexander, M.**, Huffaker, T.B, Mosbrugger, T.L., Rao, D.S., Miles, R.R, Round, J.L., and O'Connell, R.M. 2017. MiR-155 promotes FLT3-ITD-induced myeloproliferative disease through inhibition of interferon signaling. *Blood* 22, 3074-3086.

18. Runtsch, M.C., Hu, R., **Alexander, M.**, Wallace, J., Kagele, D., Petersen, C., Valentine, J.F., Welker, J.F., Bronner, M.P., Chen, X., Smith, D.P., Ajami, N.J., Petrosino, J.F., Round, J.L., and O'Connell, R.M. 2015. MicroRNA-146a constrains multiple parameters of intestinal immunity and increases susceptibility to DSS colitis. *Oncotarget* 6, 28556-72.
19. **Alexander, M.**, O'Connell, R.M. 2015. Noncoding RNAs and chronic inflammation: Micro-managing the fire within. *Bioessays* 9, 1005-15.
20. **Alexander, M.**, Hu, R., Runtsch, M.C., Kagele, D.A., Mosbrugger, T.L., Tolmachova, T., Seabra, M.C., Round, J.L., Ward, D.M., and O'Connell, R.M. 2015. Exosome-delivered microRNAs modulate the inflammatory response to endotoxin. *Nature Communications* 6, 7321.
21. Gu, Y., Shea, J., Slattum, G., Firpo, M., **Alexander, M.**, Mulvihill, S.J., Golubovskaya, V.M., and Rosenblatt, J. 2015. Defective apical extrusion signaling contributes to aggressive tumor hallmarks. *Elife* 4, 1-17.
22. Hu, R., Kagele, D.A., Huffaker, T.B., Runtsch, M.C., **Alexander, M.**, Liu, J., Bake, E., Su, W., Williams, M.A., Rao, D.S., et al. 2014. miR-155 promotes T follicular helper cell accumulation during chronic, low-grade inflammation. *Immunity* 41, 605-619.

*Authors contributed equally

Educational Activities & Presentations:

- **How to be(come) a PI Mini-course lecturer.** UCSF, CA. May 2023
- **Inquiry Mini-course Lecturer.** UCSF, CA. January 2021
Can we leverage diet to alter microbiome immunomodulation?
- **Nurse Practitioner Continuing Education Conference.** *Crosstalk between diet, microbiota, the immune system, and autoimmunity.* San Francisco, CA. 2019
- **Biomedical Sciences Mini-course Lecturer.** UCSF, CA. May 2019
Gut immune-microbiome interactions.
- **Teaching Assistant.** University of Utah. Spring 2014
Cellular Biology I and II
- **Genetics Lab Teaching Assistant.** Carleton College. 2011-2012
Biology department
- **Biology Lab Teaching Assistant.** Carleton College. 2009-2012
Biology department

Mentoring Experience:

University of Wisconsin - Madison:

- **Chi Yan**, Postdoctoral Scholar 2024-present
Mentor on project focus on understanding the microbiota-dependent protective effect of dietary arginine.
- **Theodora Osborne**, MSTP Summer Scholars Program 2024
Summer project focused on the impact of host genetic variation on host response to a ketogenic diet.
- **Wenxuan Dong**, Biophysics Ph.D. student 2024-present

Thesis mentor in a project focused on understanding how diet-responsive host metabolites influence microbial metabolism and downstream immune responses during colitis.

- **Gillian Hughes**, MDTP Ph.D. student 2024-present
Thesis mentor in a project focused on understanding the mechanisms by which diet-responsive microbial signals influence immune responses in the context of multiple sclerosis.
- **Kate Stack**, Undergraduate researcher 2024-present
Researching the ways by which diet, microbiota, and immune responses interact and the consequences of these interactions for autoimmunity. Our goal is to uncover the mechanisms by which complex diets influence diseases, as well as how disease-associated microbiota members affect immune responses during disease.

University of Wisconsin - Madison Thesis Committees:

- Tahliyah Mims - Joseph Pierre Lab
- Avery Imes - Mark Mandel Lab
- Ebru Guver - Vanessa Sperandio Lab
- Joie Ling - Andrew Hryckowian Lab
- Shawn Portwood - Joseph Pierre Lab

University of California, San Francisco:

- **Lorenzo Ramirez**, Post-bac researcher, SF BUILD & PROPEL programs 2022-2024
Mentored in a project focused on identifying bioactive compounds metabolized by *E. lenta*. Working toward the goal of gaining experience in a research environment.
- **Caroline Whitty**, Ph.D. student: 2021
Primary rotation mentor on a project focused on the role of the microbiota in intestinal and adipose immune regulation during a high fat diet.
- **Rachel Rock**, Ph.D. student: 2020-2024
Primary rotation mentor and mentor for first 4 years of graduate school on a project focused on the sex-specific impacts of an autoimmune-associated microbe in a mouse model of multiple sclerosis.
- **Qi Yan Ang**, Ph.D. candidate: 2018-2020
Mentored in her final PhD years focusing on understanding how dietary changes to the microbiome impact immunity.
- **Vincent Dimassa**, Undergraduate researcher: 2018
Mentored during summer internship working to identify bioactive bacterial metabolites.

University of Utah:

- **Kaylyn Bauer**, Ph.D. student: 2016-2017
Primary mentor during her rotation and first year of her Ph.D. in the O'Connell lab in a project focused on investigating the role of exosomal miRNAs in immune cell communication.
- **Gabriela Furukawa**, Ph.D. student: 2016
Rotation mentor in the O'Connell lab.
- **Gurkan Mollaoglu**, Ph.D. student: 2014
Rotation mentor in the O'Connell lab.

Contributions to Diversity, Equity and Inclusion:

Training:

- Conducting Inclusive and Effective Interviews, UCSF. 2021
Training in understanding and recognizing bias in interviewing and how to design checks and balances to mitigate biases in interviewing.
- UCSF Diversity, Equity, and Inclusion Champion Training. 2021
Educated to recognize and address bias and discrimination.
- UCSF Inclusive Mentoring Course. 2020
Trained to effectively hire, train, supervise, and mentor a diverse research team.

Mentoring:

- *Formal:* Served as a primary mentor to graduate students and undergraduates under-represented in scientific research including first-generation college students, racial minorities, women, and LGBTQ+ mentees.
Programs: Building Infrastructure Leading to Diversity (BUILD); Post-baccalaureate Research Opportunities to Promote Equity in Learning (PROPEL); Medical Scientist Training Program (MSTP) Summer Scholars
- *Informal:* Provided *ad hoc* guidance to under-represented postdocs, undergraduate, and graduate students, from my lab and other labs at UW-Madison, UCSF, and the University of Utah on topics ranging from scientific questions, career advice, and grant writing feedback.

Community Outreach:

- Anatomy of a chalk talk for IRACDA/ASRET fellows 2023
- UCSF ImmunoSpectrum Virtual Mentorship. 2021-2023
I meet virtually with aspiring scientists from under-represented groups who are interested in learning more about a career in science.
- Guest Lecturer. San Francisco, CA, San Francisco AIDS Foundation. 2018
Talk and discussion on HIV and the microbiota with HIV+ members of the community.
- Volunteer Teacher. Salt Lake City, UT, Genetic Science Learning Center. 2016
Designed and taught interactive lessons on evolution and gene regulation in Salt Lake City public schools.

Invited Speaker Presentations:*Local*

- *Mechanisms of Diet-Microbiota-Immune Interactions in IBD.* IBD Conference UW-Madison. 2024
- *A diet-dependent host metabolite shapes the gut microbiota to protect from autoimmunity.* Kenneth B. Raper Symposium, UW-Madison 2024
- *A diet-dependent host metabolite shapes the gut microbiota to protect from autoimmunity.* UW-Madison MMI departmental retreat 2024
- *A diet-dependent host metabolite shapes the gut microbiota to protect from autoimmunity.* Allergy-Immunology Research Conference, UW-Madison 2024
- *Microbiota-dependent protective effect of a ketogenic diet in a mouse model of multiple sclerosis.* 5th Annual IgEquity Women in Immunology Symposium, UCSF. 2022

- *A diet-dependent enzyme from the human gut microbiome promotes Th17 accumulation and colitis.* UCSF Biomedical Science Program retreat. Tahoe, CA. 2019
- *Immune cell intercellular communication via exosomal microRNAs.* Molecular Biology Program recruiting talk. University of Utah. 2016
- *Exosome-delivered microRNAs modulate the inflammatory response to endotoxin.* Immunology, Inflammation and Infectious Diseases (III) Summer Symposium and Membrane Trafficking Mini-Symposium. Utah. 2015

Regional

- *A ketogenic diet-dependent host metabolite shapes the gut microbiota to protect from autoimmunity.* ASM NCB meeting. Mankato, MN 2024
- *Investigating a diet-dependent mechanism of Th17 and colitis induction by Eggerthella lenta.* Bay Area Microbial Pathogenesis Symposium. San Francisco, CA. 2019
- *Small talk: exosomally transferred miRNAs in immune cell communication.* Exofest. San Francisco, CA. 2019

National

- *A diet-dependent host metabolite shapes the gut microbiota to protect from autoimmunity.* Impact of Diet on Mucosal Immunity and Immune-mediated Digestive Diseases NIH Workshop. NIH, Rockville, MD. 2024
- *Microbiome Influence on Metabolism and Immunity.* Gordon Conference Immunometabolism in Health and Disease discussion leader. Rhode Island. 2024
- *A diet-dependent host metabolite shapes the gut microbiota to protect from autoimmunity.* Selected abstract short talk. Keystone Symposium. Snowbird, UT. 2023
- *Microbiota-dependent protective effect of a ketogenic diet in a mouse model of multiple sclerosis.* Selected abstract short talk. Keystone Symposium. Breckenridge, CO. 2022
- *Immune miRNAs are functionally transferred between immune cells altering response to endotoxin.* Gordon Conference on Extracellular Vesicles. Sunday River, ME. 2016

International

- *Evidence for the effect of short-term and long-term diet on the human gut microbiome.* ISAPP. Invited expert. Sitges, Spain. 2022
- *Examining interactions between diet, microbiome, and immunity to gain mechanistic insight into health and disease.* Benefiq2021, Diet and Immunity, Quebec/hybrid. 2021

Selected Poster Presentations:

1. *Dietary arginine-responsive human gut bacterial metabolism drives Th17 activation and colitis.* Reshaping the Microbiome through Nutrition Conference. Virtual. 2021
2. *Investigating a diet-dependent mechanism of Th17 and colitis induction by Eggerthella lenta.* Keystone Symposium. Montreal, Canada. 2019
3. *Exosomal miRNAs regulate inflammatory responses.* Poster presentation. AAI Conference. New Orleans, LA. 2015 and immunology, infection, and inflammation Summer Symposium. Zermat, UT. 2015
4. *Endogenous microRNAs are functionally transferred between immune cells via exosomes.* Poster presentation. MB/BC symposium and student retreat, III Summer Symposium, and Microbial Pathogenesis Retreat. Utah. 2014

5. *miR-155 transfer between dendritic cells via exosomes leads to increases of miR-155 in recipient cells and decreases of miR-155 target, SHIP1.* Poster presentation. MB/BC symposium and student retreat. Zermatt, UT. 2013

Awards and Achievements:

Kenneth Rainin Foundation Innovations Symposium Travel Award Recipient	2024
Keystone Future of Science Fund scholarship recipient	2023
Berkelhammer Postdoc Travel Award recipient	2019
Keystone Future of Science Fund scholarship recipient	2019
Finalist for A.P. Giannini Foundation postdoctoral fellowship	2018
Winner of research as art competition at University of Utah	2017
Poster prize winner University of Utah Immunology and student retreats	2014 and 2015

Patents:

Ryan O'Connell and Margaret Alexander . Exosome delivery of microRNAs. International patent WO 2016179417.	2016
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Service:

University

CMB graduate program faculty advisor	2024
MDTP graduate program admissions committee	2024-2027
Member of the UCSF Benioff Center for Microbiome Medicine	2020-2023
Reviewer for UCSF microbiome research center grants	2019

Professional

Ad hoc peer reviewer for the following scientific journals: <i>Science</i> ; <i>Cell Host and Microbe</i> ; <i>Nature Reviews Immunology</i> , <i>Arthritis & Rheumatology</i> ; <i>The Pharmaceutical Journal</i> ; <i>PLOS Pathogens</i>	2018-Present
Reviewer for Multiple Sclerosis Research Program; Department of Defense; Congressionally Directed Medical Research Programs	2024