BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Tafesse, Fikadu

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

POSITION TITLE: Assistant Professor, Molecular Microbiology and Immunology, OHSU

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
Alemaya University, Ethiopia	B.Sc. *(Summa Cum Laude)*	07/2001	Plant Sciences
Hannover University, Germany	M.S. *(Summa Cum Laude)*	09/2005	Biotechnology
Utrecht University, The Netherlands	Ph.D	12/2009	Biochemistry
Whitehead Institute, Massachusetts Institute of Technology (MIT)	Postdoctoral	06/2014	Host-Pathogen Interaction

A. Personal Statement

The overall goal of my research program is to study the intriguing phenomena of how pathogenic microbes, including emerging and re-emerging pathogens, interact with their host with the aim of understanding and treating diseases caused by these pathogens. We are especially interested in studying the role of cellular lipidome in bacterial (M. tuberculosis) and viral (SARS-CoV-2, HIV and flaviviruses) pathogenesis and their significance on innate and adaptive immunity. Since the COVID-19 pandemic started, my lab has been at the forefront of SARS-CoV-2 research working with the live virus in our BSL-3 lab. In collaboration with other labs at OHSU, my lab has made several critical findings to advance our knowledge of SARS-CoV-2 and the emerging variants (see below).

- Bates TA, McBride SK, Leier HC, Guzman G, Lyski ZL, Schoen D, Winders B, Lee JY, Lee DX, Messer WB, Curlin ME, **Tafesse FG**. Vaccination before or after SARS-CoV-2 infection leads to robust humoral response and antibodies that effectively neutralize variants. ***Sci Immunol***. 2022 Jan 25:eabn8014. doi: 10.1126/sciimmunol.abn8014. Epub ahead of print. PMID: 35076258.
- Bates TA, McBride SK, Winders B, Schoen D, Trautmann L, Curlin ME, **Tafesse FG**. Antibody Response and Variant Cross-Neutralization After SARS-CoV-2 Breakthrough Infection. ***JAMA***. 2022 Jan 11;327(2):179-181. doi: 10.1001/jama.2021.22898. PMID: 34914825; PMCID: PMC8678894.
- Bates TA, Leier HC, Lyski ZL, Goodman JR, Curlin ME, Messer WB, **Tafesse FG**. Age-Dependent Neutralization of SARS-CoV-2 and P.1 Variant by Vaccine Immune Serum Samples. ***JAMA***. 2021 Jul 21. doi: 10.1001/jama.2021.11656. PMID: 34287620.
- Leier HC, Weinstein JB, Kyle JE, Lee JY, Bramer LM, Stratton KG, Kempthorne D, Navratil AR, Tafesse EG, Hornemann T, Messer WB, Dennis EA, Metz TO, Barklis E, **Tafesse FG**. A global lipid map defines a network essential for Zika virus replication. ***Nat Commun***. 2020 Jul 21;11(1):3652. doi: 10.1038/s41467-020-17433-9. PMID: 32694525; PMCID: PMC7374707.

B. Positions, Scientific Appointments, and Honors

Positions and Employment

2016 - Assistant Professor, Molecular Microbiology & Immunology, OHSU
2014-2015 Instructor in Medicine, Assistant in Immunology, Ragon Institute of MGH, MIT and Harvard

Honors and Awards:

2022	OHSU Faculty Excellence and Innovation Award
2021	MJ Murdock Foundation- Commercialization Award
2020	Biomedical Innovation Program IDEA Award
2020	American Lung Association Innovation Award
2019	American Society for Microbiology (ASM) Peggy Cotter Award
2017	Finalist, The Beckman Young Investigator (BYI) Award
2016	Young Investigator Award, Medical Research Foundation of Oregon
2010-2012	NWO Rubicon Netherlands Organization for Scientific Research fellow (Postdoctoral fellowship)
2010	Director's fellowship allowance award, Whitehead Institute for Biomedical Research (MIT)
2009	Ceramide conference student travel award
2008	Gordon Research Conferences (Glycolipid and Sphingolipid Biology) chair's award
2003-2005	DAAD (German Academic Exchange) scholarship to study M.S. in Hannover University, Germany
2003	MASHAV (Israel's Centre for International Cooperation) scholarship for training in Bet Dagan, Israel
2001	Outstanding student award (B.S. graduating class)

Grant Reviews, Editorial and Other Professional Activities:

2021	*Ad hoc* Reviewer DFG German Research Foundation
2020	*Ad hoc* NIH Study Section Topics in Bacterial Pathogenesis (ZRG1 IDM-B 80, ZRG1 IDM-B 81)
2019	Co-Organizer, Pacific North TB Pathogenesis (PacTB) Symposium, March 21-22, 2019.
2019	*Ad hoc* NIH Early Career Reviewer for CSR Anonymization Study
2019	*Ad hoc* NIH Early Career Reviewer for Topics in Bacterial Pathogenesis
2016	*Ad hoc* NIH Early Career Reviewer for The Membrane Biology and Protein Processing (MBPP) study section
2016-	Editorial Board, Frontiers in Microbiology
2016-	*Ad hoc* Reviewer for several Journals (JAMA, Nature Communications, Science Immunology, JCI Insight, eLife, iScience, Cell Reports, Front Immunology, J. Lipid Research, etc.)

Invited talks/Seminars (selected, in the last three years)

1. Harvard School of Public Health, 2021 (Virtual)
2. American Society for Biochemistry and Molecular Biology (ASBMB) Lipid Signaling Seminar Series, 2020 (Virtual)
3. Series on Sphingolipid Biology, 2020 (Virtual)
4. Annual Meeting of the Society for Leukocyte Biology, 2020 (Virtual)
5. Global Infectious Disease Seminar Series at Seattle Children's Research Institute in Seattle, 2020
6. UCSF Integrative Microbiology (I-Micro) program, San Francisco, 2020
7. International Ceramide and Glycosphingolipid Conference, Lisbon, Portugal, May 2019.
8. Department of Biology & Center for Cellular Nanoanalytics, University of Osnabrueck, Germany, February 2019.
9. Institute of Immunology, Essen University, Germany, February 2019.
10. Boston Tuberculosis-HIV Co-Infection Symposium, November 1-2, 2018.
11. American Society for Microbiology Northwest Branch Meeting, Portland, OR, October 2018
12. 4th International Conference on the Molecular Medicine of Sphingolipids, Rehovot, Israel, October 2018
13. Oregon State University Spring Symposium, Corvallis, OR, March 2018
14. Gordon Research Conference, Galveston, TX, February 2018

Professional Memberships

- Member, The American Society for Biochemistry and Molecular Biology (ASBMB)
- Member, The American Society for Microbiology (ASM)
- Member, The American Association for the Advancement of Science (AAAS)

- Member, Society for Leukocyte Biology

C. Contributions to Science

1. **The role of sphingolipids in *Mycobacterium tuberculosis (Mtb)* infection.** In addition to viruses, I have been interested in understanding how Mtb, the causative agent of tuberculosis, uses the host lipid and protein factors during infection. In a collaborative work, we recently reported critical roles for sphingomyelin biosynthesis in an early step of Mtb uptake by phagocytes. Disrupting sphingolipid production affects the segregation of the regulatory phosphatases from the nascent phagosome, a critical step in the progression of phagocytosis. We also show that blocking sphingolipid biosynthesis impairs activation of small GTPases and phosphoinositide turnover at the host-pathogen contact sites. Moreover, production of sphingomyelin, not glycosphingolipids, is critical for the phagocytic uptake of Mtb. Currently, we are working towards understanding the roles of other cellular lipids in Mtb infection and immunity.
   - Niekamp P, Guzman G, Leier H, Rashidfarrokhi A, Richina V, Pott F, Holthuis JCM*, **Tafesse FG***. Sphingomyelin biosynthesis is essential for phagocytic signaling during *Mycobacterium tuberculosis* host cell entry. ***mBio***. 2021.
   - Guzman G, **Tafesse FG**. Visualization and Quantification of Phagocytosis by Neutrophils. ***Methods Mol Biol***. 2020;2087:141-148. doi: 10.1007/978-1-0716-0154-9_11. PubMed PMID: 31728989.
   - Bryson BD, Rosebrock TR, **Tafesse FG**, Itoh CY, Nibasumba A, Babunovic GH, Corleis B, Martin C, Keegan C, Andrade P, Realegeno S, Kwon D, Modlin RL, Fortune SM. Heterogeneous GM-CSF signaling in macrophages is associated with control of Mycobacterium tuberculosis. ***Nat Commun***. 2019 May 27;10(1):2329. doi: 10.1038/s41467-019-10065-8. PubMed PMID: 31133636; PubMed Central PMCID: PMC6536549.
   - Rashidfarrokhi, A, Richina, V, **Tafesse, FG.** Visualizing the early stages of phagocytosis. ***J Vis Exp***. 2017 Feb 3;(120). doi: 10.3791/54646.
2. **The roles of host lipids in viral infection.** I have a long-standing interest in host lipid-virus interactions, especially the emerging and re-emerging viral pathogens, including Zika and influenza viruses. Using a lipidomic approach, we recently reported a detailed map of the host lipid profiling during Zika virus infection and showed that the sphingolipid metabolic pathways are essential for viral replication. Previously, I reported that the influenza virus requires sphingomyelin to transport its glycoproteins- hemagglutinin and neuraminidase- from the Golgi to the cell surface and for efficient production of viral particles. We recently showed that deletion of CerS2, the enzyme that makes long acyl chain ceramide, doesn't affect HIV-1 virus production. However, the virions are less infectious. We further show that this is due to a defect in the cell fusion step (a function that is mediated via HIV-Envelope protein).
   - Barklis E, Alfadhli A, Kyle JE, Bramer LM, Bloodsworth KJ, Barklis RB, Leier HC, Petty RM, Zelnik ID, Metz TO, Futerman AH, **Tafesse FG**. Effects of ceramide synthase 2 deletion on the infectivity of HIV-1. ***Journal of Biological Chemistry***. 2021.
   - Leier HC, Weinstein JB, Kyle JE, Lee JY, Bramer LM, Stratton KG, Kempthorne D, Navratil AR, Tafesse EG, Hornemann T, Messer WB, Dennis EA, Metz TO, Barklis E, **Tafesse FG.** A global lipid map defines a network essential for Zika virus replication. ***Nature Communications, 2020.***
   - Leier HC, Messer W, **Tafesse FG**. Lipids and pathogenic flaviviruses: An intimate union. ***PLoS Pathog***. May 2018.
   - **Tafesse FG**, Sanyal S, Ashour J, Guimaraes PC, Hermansson M, Somerharju P, and Ploegh H. Intact sphingomyelin biosynthetic pathway is essential for intracellular transport of influenza virus glycoproteins. ***Proc. Natl. Acad. Sci. USA***. 2013. PMCID: PMC3631694.
3. **Efficacy of convalescent and vaccine-elicited antibodies against the emerging SARS-CoV-2 variants.** In collaboration with clinicians within OHSU, we recently showed that SARS-CoV-2 variants such as B.1.1.7 (Alpha), B.1.351 (Beta), P.1 (Gamma) and B.1.617.2 (Delta) escape antibody neutralization elicited by the Pfizer vaccine or natural infection. We also show that previously infected and vaccinated individuals have superior protection against these variants. These studies were done using live strains of viruses in our BSL-3 lab, and we are currently actively performing similar studies with the Omicron SARS-CoV-2 variant.
   - Bates TA, McBride SK, Winders B, Schoen D, Trautmann, L Curlin ME, **Tafesse FG**. Antibody Response and Variant Cross-Neutralization After SARS-CoV-2 Breakthrough Infection. ***JAMA***. 2021 December 16, 2021. doi:10.1001/jama.2021.22898

- Bates TA, Leier HC, Lyski ZL, Goodman JR, Curlin ME, Messer WB, **Tafesse FG**. Age-Dependent Neutralization of SARS-CoV-2 and P.1 Variant by Vaccine Immune Serum Samples. ***JAMA***. 2021 Jul 21. doi: 10.1001/jama.2021.11656. Epub ahead of print. PMID: 34287620.
- Bates TA, Leier HC, Lyski ZL, McBride SK, Coulter FJ, Weinstein JB, Goodman JR, Lu Z, Siegel SAR, Sullivan P, Strnad M, Brunton AE, Lee DX, Curlin ME*, Messer WB*, **Tafesse FG***. Neutralization of SARS-CoV-2 variants by convalescent and BNT162b2 vaccinated serum. ***Nature Commun.*** 12, 5135 (2021). https://doi.org/10.1038/s41467-021-25479-6.
- Bates TA, Weinstein JB, Farley S, Leier HC, Messer WB, **Tafesse FG**. Cross-reactivity of SARS-CoV structural protein antibodies against SARS-CoV-2. ***Cell Reports***. 2021 Feb 16;34(7):108737. doi: 10.1016/j.celrep.2021.108737. PMID: 33545052; PMCID: PMC7835103.
- Lyski ZL, Brunton AE, Strnad MI, Sullivan PE, Siegel SAR, **Tafesse FG**, Slifka MK, Messer WB. SARS-CoV-2 specific memory B-cells from individuals with diverse disease severities recognize SARS-CoV-2 variants of concern. ***J Infect Dis***. 2021 Dec 1:jiab585. doi: 10.1093/infdis/jiab585. Epub ahead of print. PMID: 34865053.

4. **The role of antibodies in tuberculosis control:** I have been interested in understanding how antibodies plays a role during Mtb infection. In collaboration with the laboratory of Sarah Fortune and Galit Alter (Ragon Institute/Harvard), we found that antibodies from latently infected patients control TB disease more efficiently than antibodies from actively infected individuals. Interestingly, we also found that these antibodies from latently infected patients have enhanced ability to induce the antimicrobial processes such as the inflammasome pathway that is known to effectively control Mtb infection.
    - Lu LL, Chung AW, Rosebrock TR, Ghebremichael M, Yu WH, Grace PS, Schoen MK, **Tafesse F**, Martin C, Leung V, Mahan AE, Sips M, Kumar MP, Tedesco J, Robinson H, Tkachenko E, Draghi M, Freedberg KJ, Streeck H, Suscovich TJ, Lauffenburger DA, Restrepo BI, Day C, Fortune SM, Alter G. A Functional Role for Antibodies in Tuberculosis. ***Cell***. 2016. PMID: 27667685.

      Comment in: Casadevall A To Be or Not Be a (Functional) Antibody Against TB. ***Cell***. 2016 Oct 6;167(2):306-307. doi: 10.1016/j.cell.2016.09.041.
5. **The use of nanobodies to modulate viral infections.** In collaboration with the lab of Eric Barklis in our Department, we show that nanobodies that bind the HIV-1 Capsid protein block viral assembly and infectivity. Our findings demonstrate the feasibility of targeting HIV proteins, including the Gag/Capsid protein, with nanobodies to inhibit HIV-1 infection. In a related study, we employed a sortase-mediated coupling method to fuse different nanobodies that target immune receptors with the bacterial Exotoxin A from *Pseudomonas aeruginosa*. When introduced into mice, these nanobody-toxin conjugates were able to specifically kill immune cells that express the receptors. These studies demonstrate our abilities to produce and analyze high-affinity nanobodies with therapeutic and diagnostic potential.
    - Alfadhli A, Romanaggi C, Barklis RL, Merutka I, Bates TA, **Tafesse FG***, Barklis E*. Capsid-specific nanobody effects on HIV-1 assembly and infectivity. ***Virology***. 2021 Jul 5;562:19-28. doi: 10.1016/j.virol.2021.07.001. PMID: 34246112. *Co-corresponding authors
    - Bachran C, Schröder M, Conrad L, Cragnolini JJ, **Tafesse FG**, Helming L, Ploegh HL, Swee LK. The activity of myeloid cell-specific VHH immunotoxins is target-, epitope-, subset- and organ dependent. ***Sci Rep.*** 2017 Dec 20;7(1):17916. doi: 10.1038/s41598-017-17948-0.

Complete List of Published Work: https://pubmed.ncbi.nlm.nih.gov/?term=fikadu+tafesse&sort=date