BIOGRAPHICAL SKETCH

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NAME: Gengenbacher, Martin

eRA COMMONS USER NAME (credential, e.g., agency login): GENGENM1435

POSITION TITLE: Associate Member, Center for Discovery and Innovation, Hackensack Meridian Health; Assistant Professor, Hackensack Meridian School of Medicine

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
University of Heidelberg, Germany	MSc	2002	Biology
University of Heidelberg, Germany	PhD	2006	Infectious diseases
Novartis Institute for Tropical Diseases, Singapore	Postdoc	2006-2010	Mycobacteriology

A. Personal Statement

Over the past 16 years, my research has focused on the development of new therapies against infections of pathogenic mycobacteria. This includes discovery and testing of new antibiotics aiming to cure infection, as well as the design, development, and evaluation of novel recombinant vaccines. Predictive animal models are key to facilitating successful translational research and are therefore part of my scientific priorities. In 2017, I moved from the National University of Singapore to the United States where I continue my research in translational infection biology. At the Hackensack Meridian Health Center for Discovery and Innovation, I established a cutting-edge immunolopathology research platform including high parameter flow cytometry and analyte multiplexing to study the dynamics of immune cell phenotypes in response to mycobacterial infections. I assembled a team with in-depth expertise in immunology and a spectrum of animal models. My particular interest is the development of novel and more predictive animal models that can overcome the disconnect between preclinical assessment of novel therapies and clinical outcomes. We combine traditional microbiological and pathological readouts with an advanced immunology approach to validate our models and gain new insights into the immunopathology of mycobacterial pathogens. I have published 60 peer-reviewed manuscripts and book chapters in the fields of infection biology, novel therapy approaches and preclinical development with a major focus on mycobacterial infections (h-index: 31, Google Scholar, Sep. 2023).

Ongoing and completed projects that I would like to highlight include:

R21 AI145396
Gengenbacher (PI)
05/2019-04/2022 (NCE)
Using Collaborative Cross mice to develop a novel model of *Mycobacterium abscesses* lung infection

R01 AI145436
Gengenbacher (PI), Wilkinson (MPI)
03/2020-02/2025
Harnessing B cells for TB vaccine development to improve therapy of TB and TB-HIV coinfection

R01 AI161013
Gengenbacher (PI), Wilkinson (MPI), Lai (MPI)
07/2021-06/2026
Harnessing B cells for TB vaccine development to improve therapy of TB and TB-HIV coinfection

U19 AI162568
Ehrt/Glickman (PIs), Gengenbacher (Core leader)
04/2021-06/2026
Determinants of TB control, relapse and reinfection

P01 AI159402
Rhee/Nathan (PIs), Gengenbacher (Core leader)
04/2021-04/2026
Transmission Aerobiology of *M. tuberculosis*: Genes and Metabolic Pathways that sustain Mtb across an evolutionary Bottle Neck

Citations:

1. Rifabutin is active against *Mycobacterium abscessus* in mice. **Dick T**, Shin SJ, Koh WJ, Dartois V, **Gengenbacher M**. Antimicrob Agents Chemother. 2020 Jan 27;64(2).
2. Novel acetamide indirectly targets mycobacterial transporter MmpL3 by proton motive force disruption. Shetty A, Xu Z, Lakshmanan U, Hill J, Choong ML, Chng SS, Yamada Y, Poulsen A, **Dick T**, **Gengenbacher M**. Front Microbiol. 2018 Dec 4;9:2960
3. Cyclohexyl-griselimycin Is active against *Mycobacterium abscessus* in mice. Aragaw WW, Roubert C, Fontaine E, Lagrange S, Zimmerman MD, Dartois V, **Gengenbacher M**, **Dick T**. Antimicrob Agents Chemother. 2022 Jan 18;66(1):e0140021
4. NOS2-deficient mice with hypoxic necrotizing lung lesions predict outcomes of tuberculosis chemotherapy in humans. **Gengenbacher M**, Duque-Correa MA, Kaiser P, Schuerer S, Lazar D, Zedler U, Reece ST, Nayyar A, Cole ST, Makarov V, Barry III CE, Dartois V, Kaufmann SHE. Sci Rep. 2017 Aug 18;7(1):8853.

B. Positions, Scientific Appointments, and Honors

2022	Ad hoc Member of NIH study section 'Host Interactions with Bacterial Pathogens'
2021-Present	Associate Member of the Center for Discovery and Innovation
2021	Member of NIH study section 'Special Emphasis Panel ZAI1 KJK-I (C1)
2019-Present	Assistant Professor, Hackensack Meridian School of Medicine
2019-2021	Assistant Member of the Center for Discovery and Innovation
2017-2019	Project Leader, Public Health Research Institute, New Jersey Medical School, Rutgers, The State University of New Jersey
2014-2017	Senior Research Fellow, Department of Microbiology and Immunology, National University of Singapore
2014-2017	Laboratory Supervisor, Tuberculosis Research Laboratory, SPRINT TB Programme, National University of Singapore
2010-2014	Staff Scientist, Max Planck Institute for Infection Biology, Germany

2015-Present	Scientific Consultant at the European Developing Countries Clinical Trials Partnership
2013-Present	Member of the American Society for Microbiology
2011-Present	Member of the European Federation of Microbiology Societies

C. Contributions to Science

1. As a Staff Scientist at the Max Planck Institute for Infection Biology, I have developed several new recombinant BCG vaccine candidates against tuberculosis and tested them in a range of preclinical mouse models that I have developed as well. Two of the novel BCG candidates expressed human cytokines (**a**), the efficacy of one BCG candidate having a deletion in the biosynthetic pathway for vitamin B6 could be controlled by exogenous vitamin B6 (**b**) and another candidate, BCG Δ*ureC*::*hly* Δ*nuoG*, provided a 100-fold better protection than parental BCG in mice by enhancing host cell autophagy, which is a new mechanism of action. This work resulted in the

discovery of a new association between the mycobacterial *nuoG* gene and host autophagy (**c**). Our work revealed that recombinant BCG vaccine can induce autophagy in the host cell by inflammasome activation (**d**).

a. Rao M, Vogelzang A, Kaiser P, Schuerer S, Kaufmann SH, **Gengenbacher M**. The tuberculosis vaccine candidate Bacillus Calmette-Guérin ΔureC::hly coexpressing human interleukin-7 or -18 enhances antigen-specific T cell responses in mice. ***PLoS One***. 2013;8(11):e78966.
b. Dietary pyridoxine controls efficacy of vitamin B6-auxotrophic tuberculosis vaccine bacillus Calmette-Guérin Δ*ureC*::*hly* Δ*pdx1* in mice. **Gengenbacher M**, Vogelzang A, Schuerer S, Lazar D, Kaiser P, Kaufmann SH. ***mBio***. 2014 Jun 3;5(3):e01262-14.
c. Deletion of *nuoG* from the vaccine candidate BCG Δ*ureC*::*hly* improves protection against tuberculosis. **Gengenbacher M**, Nieuwenhuizen N, Vogelzang A, Liu H, Kaiser P, Schuerer S, Lazar D, Wagner I, Mollenkopf HJ, Kaufmann SH. ***mBio***. 2016 May 24;7(3):e00679-16.
d. The Recombinant BCG Δ*ureC*::*hly* Vaccine Targets the AIM2 Inflammasome to Induce Autophagy and Inflammation. Saiga H, Nieuwenhuizen N, **Gengenbacher M**, Koehler AB, Schuerer S, Moura-Alves P, Wagner I, Mollenkopf HJ, Dorhoi A, Kaufmann SH. ***J Infect Dis.*** 2015 Jun 1;211(11):1831-41.

2. As a Senior Research Fellow at the National University of Singapore we used next generation RNA sequencing to investigate the early events upon infection on a cellular level. We discovered that infected host cells up-regulate cholesterol biosynthesis while *M. tuberculosis* up-regulates cholesterol degradation, indicating that cholesterol is a major carbon source for the intracellular pathogen (**e**). We developed a novel mouse model to test the therapeutic efficacy of vaccines after drug treatment (**f**). By screening a library of FDA-approved drugs, we discovered that the antitubercular drug, rifabutin, is active against *M. abscessus* (**g**). In a highly collaborative project, we elucidated a novel mechanism of action of the TB drug pyrazinamide, the key sterilizing component of current TB first line regimens (**h**).

e. Comprehensive insights into transcriptional adaptation of intracellular mycobacteria by microbe-enriched dual RNA sequencing. Rienksma RA, Suarez-Diez M, Mollenkopf HJ, Dolganov GM, Dorhoi A, Schoolnik GK, Martins Dos Santos VA, Kaufmann SH, Schaap PJ, **Gengenbacher M**. ***BMC Genomics***. 2015 Feb 5;16:34.
f. Post exposure vaccination with the vaccine candidate Bacillus Calmette-Guérin Δ*ureC*::*hly* induces superior protection in a mouse model of subclinical tuberculosis. **Gengenbacher M**, Kaiser P, Schuerer S, Lazar D, Kaufmann SH. ***Microbes Infect***. 2016 May;18(5):364-8.
g. Rifabutin Is Active against Mycobacterium abscessus Complex. Aziz DB, Low JL, Wu ML, **Gengenbacher M**, Teo JWP, Dartois V, Dick T. ***Antimicrob Agents Chemother.*** 2017 May 24;61(6):e00155-17.
h. Pyrazinamide resistance is caused by two distinct mechanisms: prevention of coenzyme A depletion and loss of virulence factor synthesis. Gopal P, Yee M, Sarathy J, Low JL, Sarathy JP, Kaya F, Dartois V, **Gengenbacher M**, Dick T. ***ACS Infect Dis***. 2016 Sep 9;2(9):616-626.

3. As a Project Leader at the Public Health Research Institute, Rutgers University, we developed a new mouse model for tuberculosis for drug testing characterized by consistent human-like pathology, which may thus better predict clinical outcomes than routine models (**i**). I contributed to the development of another new model implementing humanized mice into TB therapy development (**j**). In a collaborative project, we correlated the activity of the key sterilizing anti-TB drug, pyrazinamide, with immunopathology (**k**).

i. NOS2-deficient mice with hypoxic necrotizing lung lesions predict outcomes of tuberculosis chemotherapy in humans. **Gengenbacher M**, Duque-Correa MA, Kaiser P, Schuerer S, Lazar D, Zedler U, Reece ST, Nayyar A, Cole ST, Makarov V, Barry III CE, Dartois V, Kaufmann SHE. ***Sci Rep***. 2017 Aug 18;7(1):8853.
j. Humanized mouse model mimicking pathology of human tuberculosis for *in vivo* evaluation of drug regimens. Arrey F, Löwe D, Kuhlmann S, Kaiser P, Moura-Alves P, Krishnamoorthy G, Lozza L, Maertzdorf J, Skrahina T, Skrahina A, **Gengenbacher M**, Nouailles G, Kaufmann SHE. ***Front Immunol.*** 2019 Jan 31.
k. Impact of immunopathology on the antituberculous activity of pyrazinamide. Blanc L, Sarathy JP, Alvarez Cabrera N, O'Brien P, Dias-Freedman I, Mina M, Sacchettini J, Savic RM, **Gengenbacher M**, Podell BK, Prideaux B, Ioerger T, Dick T, Dartois V. ***J Exp Med.*** 2018 Aug 6;215(8):1975-1986.

4. As an Assistant Member and Associate Member at the Center for Discovery and Innovation, I have focused on refining existing animal models and development of novel animal models of mycobacterial infection. I discovered a new acetamide that inhibits the mycobacterial transporter MmpL3 (**m**) and demonstrated that the

antitubercular drug, rifabutin, kills *M. abscessus* in a mouse model of infection, which may facilitate fast-track development of this drug (**n**). In collaboration with Dr. Dick I contributed to the discovery and preclinical evaluation of many new drug candidates against *M. abscessus*. Two examples include **o**,**p**.

m. Novel acetamide indirectly targets mycobacterial transporter MmpL3 by proton motive force disruption. Shetty A, Xu Z, Lakshmanan U, Hill J, Choong ML, Chng SS, Yamada Y, Poulsen A, Dick T, **Gengenbacher M**. ***Front Microbiol.*** 2018 Dec 4;9:2960.
n. Rifabutin is active against *Mycobacterium abscessus* in mice. Dick T, Shin SJ, Koh WJ, Dartois V, **Gengenbacher M**. ***Antimicrob Agents Chemother***. 2020 Jan 27;64(2).
o. A Leucyl-tRNA Synthetase Inhibitor with Broad-Spectrum Anti-Mycobacterial Activity. Ganapathy US, Del Rio RG, Cacho-Izquierdo M, Ortega F, Lelièvre J, Barros-Aguirre D, Lindman M, Dartois V, **Gengenbacher M**, Dick T. ***Antimicrob Agents Chemother.*** 2021 Feb 8;65(5):e02420-20
p. Activity of Tricyclic Pyrrolopyrimidine Gyrase B Inhibitor against *Mycobacterium abscessus*. Madani A, Negatu DA, El Marrouni A, Miller RR, Boyce CW, Murgolo N, Bungard CJ, Zimmerman MD, Dartois V, **Gengenbacher M**, Olsen DB, Dick T. ***Antimicrob Agents Chemother***. 2022 Sep 20;66(9):e0066922

Complete publication record can be found on PubMed.