BIOGRAPHICAL SKETCH

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NAME: GENGENBACHER, Martin

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POSITION TITLE: Assistant Professor (candidate)

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	10/2002	Biology
University of Heidelberg, Germany	PhD	03/2006	Infectious diseases
Novartis Institute for Tropical Diseases, Singapore	Postdoc	03/2010	Mycobacteriology

A. Personal Statement

Over the past 14 years, my research has focused on the development of new therapies against infections with pathogenic mycobacteria. This includes discovery and testing of new antibiotics aiming to cure infection, as well as development and evaluation of novel vaccines for preventing infection. I am particularly interested in developing new predictive animal models to study immune regulation of mycobacterial infections and to test new anti-mycobacterial therapies. Predictive animal models are key to facilitate successful translational research and are therefore part of my scientific priorities. In 2017, I moved from the National University of Singapore to the Public Health Research Institute (PHRI), Rutgers University, New Jersey, United States where I continue my long-standing collaboration with Dr. Véronique Dartois (expert in pharmacology and pathology of mycobacterial infection) and Dr. Thomas Dick (expert in mycobacterial drug discovery and genetics). With the strong support of Drs. Dartois and Dick, I have established existing immunocompromised *M. abscessus* mouse models at PHRI. With additional support of Dr. Christopher Sassetti (University of Massachusetts), an expert in immunology, genetics and Collaborative Cross mouse studies, I have conducted proof-of-concept experiments to develop a novel wild type mouse model of *M. abscessus* infection by leveraging on the wealth of genetically diverse CC mouse strains. Dr. Dartois, Dr. Dick and I have moved to the Center for Discovery and Innovation, Hackensack Meridian Health continuing our cross disciplinary collaboration in newly renovated state-of-the-art research facilities.

B. Positions and Honors

2010-2014 Staff Scientist and Head, BSL-3 Laboratory, Max Planck Institute for Infection Biology, Germany
2014-2017 Laboratory Head, Tuberculosis Research Laboratory, SPRINT TB Programme, National University of Singapore
2014-2017 Deputy Director BSL-3 Core Facility, National University of Singapore
2017-2019 Project Leader, Public Health Research Institute, New Jersey Medical School, Rutgers, The State University of New Jersey
2019-present Assistant Professor (candidate), Center for Discovery and Innovation, Hackensack Meridian Health, New Jersey

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

C. Contributions to Science

1. As Staff Scientist at the Max Planck Institute for Infection Biology, I have developed several new recombinant live vaccine candidates against tuberculosis, tested them in a range of preclinical models and studied their impact on host immunity (**a-d**). In a proof of concept study, we showed that overexpression of human cytokines by recombinant BCG can boost T cells in preclinical models (**a**). Another novel vaccine candidate, BCG Δ*ureC*::*hly* Δ*nuoG*, provided a 100-fold better protection than BCG in mice by enhancing host cell autophagy, which is a new mechanism of action. This work discovered a new association between the mycobacterial *nuoG* gene and host autophagy (**d**). In a collaborative project with Veronique Dartois and Thomas Dick, we first described that some antibiotics show reduced penetration into non-replicating *M. tuberculosis*. This may contribute to the notorious drug-tolerance of difficult-to-treat dormant *M. tuberculosis* subpopulations (**e**).

a. The tuberculosis vaccine candidate Bacillus Calmette-Guérin Δ*ureC::hly* coexpressing human interleukin-7 or -18 enhances antigen-specific T cell responses in mice. Rao M, Kaiser P, Schuerer S, Kaufmann SH, **Gengenbacher M**. ***PLoS One***. 2013 Nov 13;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. 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.
d. 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.
e. Reduced drug uptake in phenotypically resistant nutrient-starved nonreplicating *Mycobacterium tuberculosis*. Sarathy J, Dartois V, Dick T, **Gengenbacher M**. ***Antimicrob Agents Chemother***. 2013 Apr;57(4):1648-53.

2. As Laboratory Head and Deputy Director BSL-3 at the National University of Singapore building upon previous research we used next generation RNA sequencing to investigate the mechanisms of resting cell formation and the early events upon infection on a cellular level (**f,g**). 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 (**f**). Integrating transcriptomics and proteomics to study mycobacterial dormancy gave new clues to understand latent tuberculosis infection better, which is associated with 1/3 of the world population (**h**). More recent contributions focus on the elucidation of the mechanism of action of the TB drug pyrazinamide and discovery of new antibiotics against *M. tuberculosis* and emerging non-tuberculous pathogens, *M. abscessus* and *M. avium* (**i,j**). The discovery that rifabutin, an approved drug, is active on *M. abscessus* will offer new treatment options for patients infected with this intrinsically drug-tolerant opportunistic pathogen.

f. 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.
g. Developmental transcriptome of resting cell formation in *Mycobacterium smegmatis*. Wu ML, **Gengenbacher M**, Chung JC, Chen SL, Mollenkopf HJ, Kaufmann SH, Dick T. ***BMC Genomics***. 2016 Oct 26;17(1):837.
h. Absolute Proteome Composition and Dynamics during Dormancy and Resuscitation of *Mycobacterium tuberculosis*. Schubert OT, Ludwig C, Kogadeeva M, Zimmermann M, Rosenberger G, **Gengenbacher M**, Gillet LC, Collins BC, Röst HL, Kaufmann SH, Sauer U, Aebersold R. ***Cell Host Microbe***. 2015 Jul 8;18(1):96-108.
i. 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.
j. 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). Pii: e00155-17.

3. As Project Leader at the Public Health Research Institute, Rutgers University and leveraging on previous work, a collaborative systems biology approach revealed that *M. tuberculosis* relies on a complex diet during early infection (**k**). Moreover, we have developed a new mouse model for tuberculosis drug testing that is characterized by consistent human-like pathology and thus may better predict clinical outcomes (**m**). We found the gut microbiome metabolite indolepropionic acid active on *M. tuberculosis* providing the first molecular link between the gut microbiota and TB (**n**). The most recent contributions discovered a new class of potent inhibitors targeting the mycobacterial membrane (**o**) and the impact of the TB first line drug pyrazinamide on immunopathology (**p**).

k. Integration of Metabolomics and Transcriptomics Reveals a Complex Diet of *Mycobacterium tuberculosis* during Early Macrophage Infection. Zimmermann M, Kogadeeva M, **Gengenbacher M**, McEwen G, Mollenkopf HJ, Zamboni N, Kaufmann SHE, Sauer U. ***mSystems***. 2017 Aug 22;2(4). pii: e00057-17.
m. 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.
n. Whole-Cell Screen of Fragment Library Identifies Gut Microbiota Metabolite Indole Propionic Acid as Antitubercular. Negatu DA, Liu JJJ, Zimmerman M, Kaya F, Dartois V, Aldrich CC, **Gengenbacher M**, Dick T. ***Antimicrob Agents Chemother***. 2018 Feb 23;62(3). pii: e01571-17.
o. Indolyl Azaspiroketal Mannich Bases Are Potent Antimycobacterial Agents with Selective Membrane Permeabilizing Effects and *in Vivo* Activity. Nyantakyi SA, Li M, Gopal P, Zimmerman M, Dartois V, **Gengenbacher M**, Dick T, Go ML. ***J Med Chem.*** 2018 Jul 12;61(13):5733-5750.
p. Impact of immunopathology on the antituberculous activity of pyrazinamide. Blanc LP, Sarathy JP, Alvarez-Cabrera N, O'Brien P, Diaz-Freedman I, Mina M, Sacchettini JC, Savic R, **Gengenbacher M**, Podell B, Prideaux B, Ioerger T, Dr. Dick T, Dartois V. ***J Exp Med.*** 2018 Aug 6;215(8):1975-1986.

D. Additional Information: Research Support and/or Scholastic Performance

Active research support:

1R21AI145396-01; M Gengenbacher (PI): 2019-2021; NIH/NIAID; Hackensack Meridian Health; 'Using Collaborative Cross mice to develop a novel model of *Mycobacterium abscessus* lung infection'. Goal: Utilize the genetic diversity of Collaborative Cross mouse strains and *M. abscessus* clinical isolates to identify mouse/pathogen pairs that develop and sustain infection.

Completed research support:

NMRC/OFYIRG/001/2016; M Gengenbacher (PI); 2016-2018; NMRC; National University of Singapore; 'Novel approaches for better BCG vaccines against tuberculosis' Goal: Develop novel vaccine candidates with new mechanism of action against tuberculosis and test them in innovative animal models.

NMRC/OFIRG/0026/2016; R. Ee (PI) M Gengenbacher (Co-Investigator); 2016-2019; NMRC; National University of Singapore; 'Towards Stable Peptide-Based Therapeutics for Adjunctive Treatment of Tuberculosis'. Goal: Develop peptide-based antimycobacterials and test efficacy *in vivo*.

NMRC/TA/0042/2015; C. Ong (PI) M Gengenbacher (Co-Investigator), 2015-2018; NMRC; National University of Singapore; 'Host inflammatory responses driving immunopathology in human central nervous system tuberculosis'. Goal: Testing of MMP inhibitors in animal models and study immunopathology and efficacy.