THERESA KOEHLER

CANDIDACY STATEMENT

I have honed my administrative skills as chair of a medical school microbiology department and as a leader in multiple professional groups at national and international levels. As President-elect, I will apply my leadership experience and passion for microbiology to promote the microbial sciences across a large arena. I am enthused by strategies of the current ASM leadership to support the diverse activities of the society. I will work to (1) strengthen public confidence in our ability to improve the human condition through the advancement of scientific knowledge, (2) employ creative approaches to enhance and embrace membership of diverse backgrounds, and (3) capitalize on increased interest in infectious disease to engage scientists who are not formally trained in microbiology to join in our efforts to respond to emerging threats. My goal is to continue our trajectory toward making the ASM the most impactful professional organization for scientists in the country.

ASM-RELATED ACTIVITIES

- Annual Biomedical Research Conference for Minoritized Students (ABRCMS), Student Travel Award Review Task Group, Reviewer, 2017
- American Academy of Microbiology Fellow, elected 2008
- ASM Biodefense and Emerging Infectious Diseases Research Meeting, Co-Chair, 2008 – 2010
- ASM Biodefense and Emerging Infectious Diseases Research Meeting, Program Committee, 2006 – 2007
- Reviewer, Book Proposals for American Society for Microbiology Press

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: Theresa M. Koehler

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

POSITION TITLE: Professor and Chair, Microbiology and Molecular Genetics

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
Virginia Tech, Blacksburg, VA	BS	05/1981	Biology
University of Massachusetts, Amherst, MA	MS	07/1984	Microbiology
University of Massachusetts, Amherst, MA	PhD	08/1987	Microbiology
Harvard Medical School, Boston, MA	Postdoc	12/1990	Microbiology & Molecular Genetics

A. Personal Statement

I have been actively and continuously engaged in investigations of the physiology and genetics of Gram-positive pathogens since 1981. My major focus has been bacteria of the *Bacillus cereus* group. Research in my laboratory is at the forefront *B. anthracis* genetics and regulation of gene expression and our findings have been reported in multiple peer-reviewed publications. In recent years, the knowledge base and technical repertoire of my laboratory have expanded to include host - *B. anthracis* interactions using murine infection models. We have also developed expertise in genomic analysis to discern similarities and differences in closely-related species, including use of quantitative PCR and RNASeq to assess the presence and expression of critical virulence genes and their regulators. I have established collaborations with experts in protein structure, immunology, biochemistry, and cell biology, and I have co-authored publications resulting from the combined expertise of multiple laboratories. In addition, I have authored widely-referenced texts on *B. anthracis* and anthrax. Our work using virulent and attenuated *B. anthracis* strains to explore the molecular basis for virulence gene expression, in combination with animal studies assessing significance of key virulence genes and their regulators for anthrax disease, is progressing to reveal candidate genes/proteins/pathways that represent targets for therapeutic intervention, while furthering our understanding of host-pathogen interactions.

I contribute to the training and mentoring of postdoctoral fellows, graduate students, medical students, and undergraduates in summer research programs. As Chair of the Department of Microbiology & Molecular Genetics, I play a key administrative and support role in the Microbiology & Infectious Diseases Graduate Training Program. I serve as PI on a T32 Training Grant. My laboratory provides a supportive environment for students from a variety of backgrounds. My trainees report their findings in peer-reviewed publications and at national and international conferences. My students and postdocs have also served as my co-authors on widely referenced reviews and book chapters. Former trainees hold positions in academia, government, and industry. As mentor, my goals are to: (1) teach trainees how to develop and test hypotheses with an emphasis on scientific rigor, (2) foster trainees' development of academic excellence and technical skills in a specific research area, (3) encourage trainees to maintain a broad knowledge base of microbiology, with some focus on host-pathogen interactions, and (4) facilitate trainees' interactions with leading researchers in related fields.

B. Positions, Scientific Appointments, and Honors

Positions

1978-1980 Clinical Laboratory Technician, Virginia Tech Cooperative Education Program, Sibley Memorial Hospital, Washington, D.C.

1981-1985 Teaching Assistant, Microbiology, University of Massachusetts, Amherst, MA

1985-1987	Graduate Research Assistant, Microbiology, University of Massachusetts
1987-1990	Postdoctoral Fellow, Microbiology & Molecular Genetics, Harvard Medical School, Boston, MA
1991-2000	Assistant Professor, Microbiology & Molecular Genetics, McGovern Medical School, Graduate School of Biomedical Sciences, The Univ. of Texas Health Science Center, Houston, TX
2000-2005	Associate Professor, Microbiology and Molecular Genetics, McGovern Medical School, Graduate School of Biomedical Sciences, The University of Texas Health Science Center
2005-Present	Professor, Microbiology and Molecular Genetics, McGovern Medical School, Graduate School of Biomedical Sciences, The University of Texas Health Science Center
2011-Present	Chair, Microbiology and Molecular Genetics, McGovern Medical School, Graduate School of Biomedical Sciences, The University of Texas Health Science Center

Scientific Appointments (since 2001)

2001	Member, Review Panel, US Army Medical Research and Material Command Therapeutics Program, American Institute of Biological Sciences
2001-2002	Ad-Hoc Member, Bacteriology and Mycology Review Group 2 (BM-2 Study Section), CSR, NIH
2002	Member, P01 Grant Review Panel, CSR, NIH
2002-2008	Member, Scientific Advisory Board, Region VI Center of Excellence for Biodefense and Emerging Infectious Diseases Research
2002-2010	Member, Special Emphasis and Small Mechanisms Scientific Review Groups, CSR, NIH
2003	Chair, P01 Grant Review Panel, CSR, NIH
2003-2009	Organizer, Cold Spring Harbor Microbial Pathogenesis Meeting, Cold Spring Harbor, New York
2003-2012	Member, Board of Directors, International Conference on *Bacillus anthracis, cereus, and thuringiensis*
2005	Organizer, International Conference on Bacillus Anthracis, Cereus, and Thuringiensis
2006-2007	Member, Program Committee, American Society for Microbiology Biodefense Meeting
2006-2014	Member, Editorial Board, Journal of Bacteriology
2007-Present	Associate Editor, PLoS Pathogens
2007	Ad-Hoc Member, Scientific Counselors Review Panel, NIAID
2008-2009	Co-Chair, American Society for Microbiology Biodefense Meeting
2009	Member, Review Committee for Dissertation Research Award, National Center on Minority Health and Health Disparities
2009-2015	Member, External Advisory Committee, Idaho IDeA Network of Biomedical Research Excellence Program
2011	Ad-Hoc Member, Bacterial Pathogenesis Scientific Review Group (BACP), CSR, NIH
2011-2013	Regular Member, BACP Study Section, CSR, NIH
2011-present	Association of Medical School Microbiology and Immunology Chairs (Vice President 2020)
2013-2015	Chair, BACP Study Section, CSR, NIH
2014-2018	Member, National Science Advisory Board for Biosecurity
2015-Present	Chair, External Advisory Committee, Idaho IDeA Network of Biomedical Research Excellence
2020	Chair, Special Emphasis Scientific Review Group, CSR, NIH

Honors

1994, and 1996-2001	Dean's Excellence Award, MD Anderson UTHealth Graduate School of Biomedical Sciences, (awarded annually)
2001	Invited Participant, Balancing National Security and Open Scientific Communications: Implications of September 11th for the Research Community, The National Academies
2004	Dean's Teaching Excellence Award, McGovern Medical School, The University of Texas Health Science Center
2006-present	Herbert L. & Margaret W. DuPont Professorship, Biomedical Science, The University of Texas Health Science Center
2008-present	Fellow, American Academy of Microbiology
2009	Paul E. Darlington Mentor Award, Graduate School of Biomedical Sciences, The University of Texas Health Science Center
2014-present	Member, Hall of Distinction, Virginia Tech College of Science, Blacksburg, VA
2020-2022	Elected President-elect/President of the Association of Medical School Microbiology and Immunology Chairs

2022-present Fellow, American Association for the Advancement of Science

C. Contributions to Science

1. *Bacillus anthracis* Virulence Gene Control

My laboratory has been at the forefront of mechanistic studies of *B. anthracis* virulence gene expression for over 25 years, beginning with our independent discovery of the master virulence regulator AtxA in 1994. Our work includes signaling and transcriptional control of the *atxA* gene, *in vivo* and *in vitro* function of AtxA, discernment of the AtxA regulon, function of AtxA-controlled small RNAs, and relevance of AtxA during infection. We have developed detailed models for complex pathways controlling synthesis of the critical virulence factors, toxin and capsule, and expression of additional factors that affect host-pathogen interactions. We developed tools for manipulation of this previously understudied bacterium, now widely employed in laboratories worldwide. We determined the crystal structure of AtxA and established the protein as the archetype of a newly discerned class of virulence regulators with ties to the phosphoenolpyruvate: carbohydrate phosphotransferase system, a highly conserved system for uptake and metabolism of sugars.

a. Hammerstrom TG, Horton LB, Swick MC, Joachimiak A, Osipiuk J, **Koehler TM**: Crystal structure of *Bacillus anthracis* virulence regulator AtxA and effects of phosphorylated histidines on multimerization and activity. Mol Microbiol. 2015 Feb;95(3):426-41. doi: 10.1111/mmi.12867. Epub 2014 Dec 30. PubMed PMID: 25402841; PubMed Central PMCID: PMC4352578.
b. Raynor MJ, Roh JH, Widen SG, Wood TG, **Koehler TM**: Regulons and protein-protein interactions of PRD-containing *Bacillus anthracis* virulence regulators reveal overlapping but distinct functions. Mol Microbiol. 2018 Mar;109(1):1-22. doi.org/10.1111/mmi.13961; PMID: 29603836.
c. Bier, N, Hammerstrom, TG, **Koehler, TM**: Influence of the Phosphoenolpyruvate:Carbohydrate Phosphotransferase System on Toxin Gene Expression and Virulence in *Bacillus anthracis*. Mol Microbiol. 2020 Jan;113(1):237-252. Doi: 10.111/mmi.14413. PMID: 31667937.
d. Corsi, ID, Dutta S, van Hoof A, **Koehler TM**.: AtxA-controlled Small RNAs of *Bacillus anthracis* Virulence Plasmid pXO1 Regulate Gene Expression *in trans.* Front Microbiol. 2021 Jan 15;11:610036. doi: 10.3389/fmicb.2020.610036. eCollection 2020. PMID: 33519762

2. *Bacillus anthracis* Protease Expression and Function

The *B. anthracis* capsule and anthrax toxin have garnered much attention as important virulence factors, but the *B. anthracis* arsenal includes many other secreted proteins with known or suspected roles in infection. The secreted metalloprotease InhA1 degrades many host-associated proteins and has been implicated in anthrax-associated hemorrhaging and disruption of the blood brain barrier. We determined that in addition to mammalian proteins, InhA1 degrades other secreted bacterial proteins including, paradoxically, the anthrax toxin proteins and other proteases. We demonstrated that deletion of the *inhA1* gene, together with its paralog, inhA2, attenuates *B. anthracis* virulence in a murine model for inhalation anthrax. We determined that InhA1-mediated cleavage of serum proteins during *B. anthracis* culture facilitates acquisition of essential amino acids. We have also shown that *inhA1* gene expression is controlled in part by a regulatory system that controls *B. anthracis* development. Together, these data suggest that InhA1 activity is of significance in multiple stages of disease and highlight the importance of non-toxin factors in *B. anthracis* pathogenesis.

a. Pflughoeft KJ, Sumby P, **Koehler TM**. *Bacillus anthracis sin* locus and regulation of secreted proteases. J Bacteriol. 2011 Feb;193(3):631-9. doi: 10.1128/JB.01083-10. Epub 2010 Dec 3. PubMed PMID: 21131488; PubMed Central PMCID: PMC3021211.
b. Pflughoeft KJ, Swick MC, Engler DA, Yeo, HJ, **Koehler, TM**. Modulation of the *Bacillus anthracis* secretome by the immune inhibitor A1 protease. J Bacteriol. 2014 Jan;196(2):424-35. doi: 10.1128/JB.00690-13. Epub 2013 Nov 8. PubMed PMID: 24214942; PubMed Central PMCID: PMC3911237.
c. Terwilliger A, Swick MC, Pflughoeft KJ, Pomerantsev A, Lyons CR, **Koehler TM**, Maresso A. *Bacillus anthracis* overcomes an amino acid auxotrophy by cleaving host serum proteins. J Bacteriol. 2015 Jul;197(14):2400-11. doi: 10.1128/JB.00073-15. Epub 2015 May 11. PubMed PMID: 25962917; PubMed Central PMCID: PMC4524190.

3. *Bacillus anthracis* Virulence Factors and Host-Pathogen Interactions

Despite the plethora of information regarding structure and function of well-studied *B. anthacis* virulence factors, contributions of these factors to pathogenesis and host response are not clear, and in many cases appear to be model host-specific. We have collaborated with many other investigators to discern the roles of

toxin, capsule, and regulatory proteins in anthrax disease in different model systems. Our data contribute to understanding of niche- and animal-specific host responses and distinct stages of anthrax disease.

a. McGillivray SM, Ebrahimi CM, Fisher N, Sabet M, Zhang DX, Chen Y, Haste NM, Aroian RV, Gallo RL, Guiney DG, Friedlander AM, **Koehler TM**, Nizet V: ClpX contributes to innate defense peptide resistance and virulence phenotypes of *Bacillus anthracis*. J Innate Immun. 2009;1(5):494-506. doi: 10.1159/000225955. Epub 2009 Jun 18. PubMed PMID: 20375606; PMCID: PMC2920483.
b. Lovchik JA, Drysdale M, **Koehler TM**, Hutt JA, Lyons CR: Expression of either lethal toxin or edema toxin by Bacillus anthracis is sufficient for virulence in a rabbit model of inhalational anthrax. Infect Immun. 2012 Jul;80(7):2414-25. doi: 10.1128/IAI.06340-11. Epub 2012 Apr 23. PubMed PMID: 22526673; PubMed Central PMCID: PMC3416453.
c. Scarff JM, Raynor MJ, Seldina YI, Ventura, CL, **Koehler, TM**, O'Brien, AD: The roles of AtxA orthologs in virulence of anthrax-like *Bacillus cereus* G9241. Mol Microbiol. 2016 Nov;102(4):545-561. doi: 10.1111/mmi.13478. Epub 2016 Sep 4. PubMed PMID: 27490458; PubMed Central PMCID: PMC5118089.
d. Dutta, S, Corsi, ID, Bier, N, **Koehler, TM**: BrnQ-Type Branched Chain Amino Acid Transporters Influence *Bacillus anthracis* Growth and Virulence. mBio. 2022 Jan 25;13(1):e0364021. doi: 10.1128/mbio.03640-21. PMID: 35073743.

4. *B. anthracis* Signaling and Development

As a member of the "*B. cereus* group" species, *B. anthracis* transitions between lifestyles in the soil and in a mammalian host. The B. anthracis cell cycle, which includes metabolically active vegetative cells and dormant spores, is directed by distinct environmental signals. Our work, examining germination, vegetative growth, and sporulation in diverse settings, has revealed niche-specific signals and responses, and most has demonstrated a mechanistic link between virulence gene expression and bacterial development.

a. Saile E, **Koehler TM**: *Bacillus anthracis* multiplication, persistence, and genetic exchange in the rhizosphere of grass plants. Appl Environ Microbiol. 2006 May;72(5):3168-74. PubMed PMID: 16672454; PubMed Central PMCID: PMC1472387.
b. Barua S, McKevitt M, DeGiusti K, et al: The mechanism of *Bacillus anthracis* intracellular germination requires multiple and highly diverse genetic loci. Infect Immun. 2009 Jan;77(1):23-31. doi: 10.1128/IAI.00801-08. Epub 2008 Oct 20. PubMed PMID: 18936179; PMCID: PMC2612280.
c. Ross CL, Thomason KS, **Koehler TM**: An extracytoplasmic function sigma factor controls beta-lactamase gene expression in *Bacillus anthracis* and other *Bacillus cereus* group species. J Bacteriol. 2009 Nov;191(21):6683-93. doi: 10.1128/JB.00691-09. Epub 2009 Aug 28. PubMed PMID: 19717606; PubMed Central PMCID: PMC2795285.
d. Dale, JL, Raynor, MJ, Ty MC, Hadjifrangiskou, M, **Koehler TM**: A Dual role for the *Bacillus anthracis* master virulence regulator AtxA: Control of sporulation and anthrax toxin production. Front Microbiol. 2018 Mar 15;9:482. Doi: 10.3389/fmicr.2018.00482. eCollection 2018. PMID: 29599764.

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/pubmed/?term=Koehler+tm