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: Lea Vacca Michel

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

POSITION TITLE: Associate Professor of Chemistry

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Colgate University, Hamilton, NY	B.A.	05/2002	Physics, Math
University of Rochester, Rochester, NY	MS, PhD	03/2007	Biophysics
Cornell University, Ithaca, NY	Postdoctoral	05/2009	Biophysics

A. Personal Statement

Both my graduate and postdoctoral research projects involved structural studies on site-directed mutants of recombinant proteins. My experience in preparing and analyzing mutant proteins will be particularly useful for Specific Aim 1A, for which I will prepare Pal and Lpp mutants to elucidate the role of peptidoglycan binding in their release from *E. coli*. My first job in industry as a contract scientist provided me ample experience working in the field of protein antigen/antibody detection. Specifically, I worked with human sera samples to detect protein biomarkers in cancer patients, as described in my two publications with Dr. Jon Peterson and Dr. Judah Folkman (Am J Hematology 2010; Angiogenesis 2012). These experiences will prove useful for Specific Aims 2, 3B, and 3C for which I will detect and quantify cytokines and Pal/Lpp using enzyme linked immunosorbent assays and immunoblotting. I spent my sabbatical (January 2017-August 2017) working with mice to develop an otitis media ear infection model in adult mice; through this experience, I learned multiple mouse protocols and became comfortable handling mice. I performed nasal lavages, ear washes, and bleeds to quantify bacterial loads and harvested/homogenized organs such as spleens and lungs. For the last 13 years, I have had extensive experience mentoring students both in and out of the laboratory, and plan to include undergraduate students in every aspect of this proposed project. This project will provide at least 12 undergraduate students with medically relevant and biologically important research experiences and the opportunity to learn and grow as scientists. As PI, I will ensure that the training of students remains a top priority throughout the duration of the project.

I have a strong record of training undergraduate students for future careers in science and medicine, thus aligning with one of the main goals of the NIH AREA grant program. Since the start of my faculty position at RIT, I have trained 43 undergraduate and 4 MS students in my research group. As the Chair of the Women in Science (WISe) program at RIT and Director of the Project SEED program for the Rochester Section of the American Chemical Society, I seek to recruit a diverse group of students in my research lab. My research group has included 35 female students (75%), 5 AALANA (African American, Latina/o American, Native American) students, many first generation college students, 3 McNair Scholars, 2 Louis Stokes Alliance for Minority Participation Scholars, and 9 deaf or hard-of-hearing students (including one legally blind student). I was recently nominated for RIT's Isaac L. Jordan Sr. Faculty Pluralism Award, and in June 2015, I received an INSIGHT Into Diversity's Inspiring Women in STEM national award. This past year, I received RIT's Edwina Award for my efforts towards promoting gender diversity and inclusion across campus. Undergraduate students play an integral role in my research group: designing and performing experiments, collecting and analyzing data, troubleshooting experiments, reading the scientific literature, and participating in the scientific writing process. The great majority of the my research is generated by my undergraduate students, giving them ownership of their projects, increasing their confidence and self-efficacy, and providing them strong research backgrounds so that they can succeed in graduate school and become contributing members of the scientific community. I bring my students to national meetings (39 student presentations), and several of my

students were selected to present at the National Collegiate Research Conference at Harvard University (4 student presentations) and the Annual Biomedical Research Conference for Minority Students (ABRCMS, 3 presentations). I received a travel fellowship to serve as a judge for the 2016 ABRCMS. My students have also received national awards (including research fellowships from the ASBMB), and 13 of my students are coauthors on publications (with 5 additional student coauthors on my most recent manuscript, which is in preparation).

In addition to training my students in the lab, I aim to inspire my students to pursue higher degrees and careers in science and medicine. I mentor my research students on graduate school and organize the annual Women in Science Graduate School Bootcamp program. Of my 28 research student graduates, 27 have/are pursuing higher degrees in science or medicine (96%), with 12 enrolled in PhD programs, 2 enrolled in a post baccalaureate STEM programs, 7 enrolled in or graduated from MD/DO programs, 1 enrolled in a PharmD program, 5 enrolled in/graduated from MS programs, and 1 working as a laboratory technician in academia. My students are currently enrolled in PhD programs at some of the world's leading research universities, including Duke University, Cornell University, Yale University, University of Colorado Denver, University of Rochester, SUNY Buffalo, Case Western, and Brown University. My former MS student (now a PhD graduate) was the recipient of an HHMI fellowship and was recently accepted into an NIH SPIRE postdoctoral program at UNC.

B. Positions and Honors

Positions and Employment

Spring 2007	Adjunct Lecturer, Colgate University, Dept of Physics, Hamilton, NY
Spring 2007	Adjunct Lecturer, College at Brockport (SUNY), Dept of Chemistry, Rochester, NY
2007-2008	Postdoctoral Associate, Cornell University, Dept of Molecular Biology & Genetics, Ithaca, NY
2008-2009	Contract Research Scientist, Kelly Services, Ortho-Clinical Diagnostics, Rochester, NY
2009-2015	Assistant Professor of Chemistry, Rochester Institute of Technology, Rochester, NY
2015-present	Associate Professor of Chemistry, Rochester Institute of Technology, Rochester, NY

Other Experience and Professional Memberships

1999-2000	Phi Eta Sigma, Colgate University
2003-present	Member of the American Chemical Society (Executive committee member 2009-2010)
2006-present	Sigma Pi Sigma, National Physics Honors Society (Colgate University Chapter)
2007-2008	Member of the Cornell University Postdoc Association
2008	Organizing Committee Member of the 10th Annual Upstate NY NMR Symposium
2009-present	Member of the American Society for Biochemistry and Molecular Biology
2010-present	Member of the Women in Science Executive Committee, Rochester Institute of Technology
2011-present	Program Director for Rochester's Project SEED program (American Chemical Society)
2012-present	Chair of Women in Science Program, Rochester Institute of Technology
2015-present	Women and Gender Advisory Committee
2015-present	Advocates and Allies Advisory Committee
2017-2018	Elected to Faculty Affairs Committee

Honors

2002	Leon L. Miller Graduate Fellowship, University of Rochester, Dept Biochemistry & Biophysics
2005	ACS Women Chemists Committee Travel Award, Sponsored by Eli Lilly & Company
2005-2006	Elon Huntington Hooker Graduate Fellowship, University of Rochester
2006	William F. Neuman Award, University of Rochester, Dept of Biochemistry & Biophysics
2006	NIH National Graduate Research Festival attendee and poster presenter
2006	Alumni Induction into Sigma Pi Sigma, Colgate University
2010	Nominated for Provost Teaching Award, Rochester Institute of Technology
2011	Appointed to NIH Early Career Reviewer program (CSR)
2012	College of Science Helpful Citizen Award, Rochester Institute of Technology
2013	Featured College of Science Faculty Member, Provost's Annual Faculty Scholarship Report
2013	College of Science Leadership Award, Rochester Institute of Technology
2013	Nominated for Trustees Scholarship, Rochester Institute of Technology
2014	College of Science Outstanding Student Mentor Award, Rochester Institute of Technology
2015	Finalist for Eisenhart Provost's Award for Excellence in Teaching Award, RIT

2015 INSIGHT Into Diversity's Inspiring Women in STEM national award
2016 COS Advancing Diversity Award, Rochester Institute of Technology
2016 Nominated for Eisenhart Provost's Award for Excellence in Teaching, RIT
2016 Invited Panelist; Diplomacy Summit: Women's Empowerment, Albany, NY
2016 Travel Award, 2016 Annual Biomedical Research Conference for Minority Students
2016 Salutes to Excellence Award, Rochester Section of the American Chemical Society
2017 2017 Edwina Award for contributions to enhance gender diversity and inclusiveness, RIT
2017 Nominated for Eisenhart Provost's Award for Excellence in Teaching, RIT

C. Contributions to Science

1. Probing Protein Dynamics Using NMR Spectroscopy

The Protein Structure Initiative, launched by the National Institute of General Medical Sciences (NIGMS) in 1999, accelerated the search for new soluble and membrane-bound protein structures. However, the static structure of a protein does not relay all the necessary information that is required to fully understand the mechanism(s) of protein function. As such, protein mobility and dynamics have been accepted as key players among the structural determinants for protein function. To that end, I employed NMR spectroscopy to elucidate how the local structure and dynamics of the cytochrome *c* active site (including the heme) played an important role in modulating the protein's redox potential.

1. Michel LV, Ye T, Bowman, SEJ, Levin BD, Hahn MA, Russell BS, Elliott SJ, Bren KL (2007) Heme attachment motif mobility tunes cytochrome *c* redox potential, *Biochemistry* 46: 11753-11760. PMID: 17900177
2. Ye T, Kaur R, Senguin FT, Michel LV, Bren KL, Elliott SJ (2008) Methionine ligand lability of type I cytochromes *c*: Detection of ligand loss using protein film voltammetry, *J Am Chem Soc* 130: 6682-6683. PMID: 18454519
3. Michel LV, Bren KL (2008) Submolecular unfolding units of *Pseudomonas aeruginosa* cytochrome *c*551, *J Biol Inorg Chem* 13: 837-845. PMID: 18392863

2. Detection of angiogenesis regulatory proteins in human platelets

Angiogenesis regulatory proteins are important diagnostic biomarkers, which can identify patients who may be entering different stages of tumor growth. However, efforts to use these important proteins as biomarkers have been hindered by their low concentrations in human sera. It was proposed that in the microenvironment of the tumor, angiogenesis regulatory proteins are scavenged by platelets early in tumor growth and released by platelets locally. At Ortho-Clinical Diagnostics, I worked on a team that developed methods to detect these low level biomarkers to determine the biovariability of these proteins in the platelets of healthy and sick patients.

1. Peterson JE, Zurakowski D, Italiano JE, Michel LV, Fox L, Klement GL, Folkman J (2010) Normal ranges of angiogenesis regulatory proteins in human platelets, *Am J Hematology* 85: 487-493. PMID: 20575035
2. Peterson JE, Zurakowski D, Italiano JE, Michel LV, Connors S, Oenick M, D'Amato RJ, Klement GL, Folkman MJ (2012) VEGF, PF4 and PDGF are elevated in platelets of colorectal cancer patients, *Angiogenesis*, 15: 265-273. PMID: 22402885

3. Dual orientation of two Peptidoglycan-Associated Lipoproteins

Nontypeable *Haemophilus influenzae* (NTHi) are Gram-negative bacteria and the cause of several respiratory illnesses, including acute otitis media and sinusitis. Lipoprotein and leading vaccine candidate P6 has been well studied for its immunological properties, but not much was known about its structural orientation or localization in NTHi. For years it was assumed that P6 was a transmembrane protein, allowing it to interact with both intracellular and extracellular molecules by physically spanning the membrane. Using nuclear magnetic resonance (NMR) spectroscopy and protein modeling, our group demonstrated that P6 could not span the membrane. Further studies showed that P6 was inserted into the outer membrane on NTHi in two distinct orientations- a biological phenomenon seen in only one other bacterial lipoprotein. More recently, we

discovered that P6's homologue in *Escherichia coli*, Pal, was also dual oriented. Currently, we are working on understanding the biological significance of lipoprotein dual orientation and the role Pal plays in the clinical condition of sepsis.

1. Chang A, Kaur R, Michel LV, Casey JR, Pichichero ME (2011) *Haemophilus influenzae* vaccine candidate outer membrane protein P6 is not conserved in all strains*, Hum Vaccines* 7: 102-105. PMID: 21285530
2. Michel LV, *Kalmeta B, #McCreary M, *Snyder J, Craig P, Pichichero ME (2011) Vaccine candidate P6 of nontypable *Haemophilus influenzae* is not a transmembrane protein based on protein structural analysis, *Vaccine* 29: 1624-1627. PMID: 21215345
3. Michel LV, *Snyder J, *Schmidt R, *Milillo J, *Grimaldi K, *Kalmeta B, Khan N, Sharma S, Wright LK, Pichichero ME (2013) Dual orientation of the outer membrane lipoprotein P6 of nontypeable Haemophilus influenzae, *J Bacteriology* 195: 3252-3259. PMID: 23687267
4. Michel LV, *Shaw J, *MacPherson V, *Barnard D, *Bettinger J, *D'Arcy B, Surendran N, Hellman J, Pichichero ME (2015) Dual orientation of the outer membrane lipoprotein Pal in *Escherichia coli*, *Microbiology* 161: 1251-1259. PMID 25808171

**Undergraduate student coauthors, #MS student coauthors*

4. Quiet Chemistry: Working with Deaf Students in a Chemistry Research Lab

Rochester Institute of Technology (RIT) is home to the National Technical Institute for the Deaf (NTID), the world's first and largest technological colleges for deaf and hard-of-hearing (DHH) students. RIT takes pride in providing deaf and HOH students with a quality education focused on technical training for future employment. As a faculty member in Chemistry at RIT, I educate both hearing and DHH students in the classroom and in my research lab. In this project, I proposed to use a multifaceted approach to address the problem of inflated unemployment for DHH people by educating them about the paths to graduate school and the improved career possibilities graduate study affords. Specifically, I proposed the following initiatives to progress toward achieving that goal: 1) Mentor DHH students in my research group on independent research projects; 2) Evaluate various mentoring techniques (ex. working directly with the students, having the students mentored by other DHH students, having the students mentored by hearing students, having the students work independently in the lab); 3) Evaluate communication devices as effective means of communication with DHH students in the lab; 4) Design and hold a Graduate School 101 Workshop to educate DHH students on the benefits of graduate education; 5) Prepare how-to lab videos, caption them, and make them available on a website; 6) Develop the "Quiet Chemistry" website, which will describe my assessments of mentoring techniques and communication devices, as well as house the how-to lab videos; and 7) Dissemination: presentations and publications.

1. Gehret AU, Trussell JW, Michel LV (2017) Approaching Undergraduate Research with Students who are Deaf and Hard-of-Hearing, *Journal of Science Education for Students with Disabilities* 20: Article 4.

5. *Probing the interactions between gamma crystallin proteins*

The eye lens contains a very high concentration of proteins, most of which are called crystallins. The crystallin proteins (α, β, and γ) are a diverse family of structural proteins whose main biological function is to control the refractive/reflective properties of the lens. *In vivo*, the α, β, and γ crystallins can interact with themselves and each other and can also aggregate into large clusters/chains. These intermolecular interactions are thought to help control the amount of light scattered by the lens itself. As a person (or animal) ages, crystallins lose function and the proteins aggregate to form an opaque "cloud" in the lens (cataract), thus reducing the amount of light able to enter the eye and severely decreasing vision. The interactions between crystallin proteins have proven quite complex. For example, γ crystallins interact with each other and also play an important role in how the α crystallins interact with each other. Even small structural changes (mutations) can have a significant effect on the "cloud" point of the γ crystallins, thus increasing ones susceptibility to cataracts. One of the major goals of our study is to elucidate the specific interactions between bovine γ-B (homolgous to human γ-D) crystallin proteins. We are currently working on mapping the specific interaction sites using NMR spectroscopy to understand changes in those interactions with changes in pH, protein concentration, and temperature (several manuscripts currently in preparation).

D. Research Support (past 3 years)

ONGOING/APPROVED

NIH R15
6/1/13-8/31/17
Source: NIH
Title: Phase Boundaries and Liquid Structure of Concentrated Eye Lens Protein Mixtures
Overall Goal: To use biophysical theoretical and experimental approaches, including nuclear magnetic resonance (NMR) spectroscopy, to understand the detailed molecular interactions between gamma crystallin proteins.
PI: George Thurston
Role: Co-Investigator

HHMI Undergraduate Science Education – Inclusive Excellence Grant
9/1/17-8/31/22
Source: HHMI
Overall Goal: To create a more inclusive climate at RIT for underrepresented students including minorities, first generation college students, and deaf and hard-of-hearing students.
PI: Scott Franklin
Role: Co-Investigator

COMPLETED
Special Grant Program in the Chemical Sciences
9/1/13-12/31/16
Source: Camille and Henry Dreyfus Foundation
Title: Quiet Chemistry: Working with Deaf Students in a Chemistry Research Laboratory
Overall Goal: To gain a better understanding of how deaf and hard-of-hearing students work and learn best in a research environment.
PI: Lea Vacca Michel
Role: Principal Investigator

Faculty development grant
7/1/15-1/31/16
Source: Rochester Institute of Technology
Title: Implicating Dual oriented Pal in Gram-negative sepsis
Overall Goal: To develop methods for detecting released Pal from *Escherichia coli* in human sera/urine.
PI: Lea Vacca Michel
Role: Principal Investigator