BIOGRAPHICAL SKETCH

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NAME: Duke, Elizabeth

eRA COMMONS USER NAME: elizduke

POSITION TITLE: Senior Research Fellow, University of Washington, Division of Allergy and Infectious Diseases & Vaccine and Infectious Diseases Division, Fred Hutchinson Cancer Research Center

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
Marshall University, Huntington, WV	BA	05/2002	Mathematics and Latin
Marshall University, Huntington, WV	MA	05/2006	Mathematics
Marshall Univ School of Medicine, Huntington, WV	MD	05/2010	Medicine
University of Wisconsin Residency, Madison, WI		06/2013	Internal Medicine
University of Washington Fellowship, Seattle, WA		ongoing	Infectious Diseases

A. Personal Statement

Inspired by experiences caring for patients and equipped with medical, mathematical, and research training, I am well positioned to excel in the KL2 ITHS program. KL2 support will allow me to apply the basic mathematical knowledge that I learned as an undergraduate and graduate student to the important clinical problems I have encountered as an infectious diseases specialist. Specifically, I plan to optimize cytomegalovirus (CMV) prevention and treatment strategies in hematopoietic cell transplant (HCT) patients.

Dr Michael Boeckh, an expert in CMV, recently introduced me to the potential role for mathematical modeling in the prevention and treatment of CMV disease. The wealth of existing blood samples in the Fred Hutch biorepository, collected from HCT patients with untreated and treated CMV disease, provides a unique opportunity to establish a mechanistic model describing virus-host interactions; samples collected on antiviral treatment will allow me to develop *in vivo* pharmacodynamic models that approximate clinical trial conditions. This modeling will allow us to define ideal antiviral dosing of agents that are currently available and may inform clinical trials of new, safer antiviral agents, facilitating delivery to patients. Given my mathematical modeling experience in HIV in the Schiffer modeling group, I am prepared to undertake this work and look forward to translating modeling techniques to optimize CMV prevention and treatment.

B. Positions and Honors

Positions and Employment

2002-2003 Part-time Faculty, Dept of Classical Studies, Marshall University, Huntington, WV, Division Chair: Caroline Perkins, PhD

2002-2005 Graduate teaching assistant, Dept of Mathematics, Marshall University, Huntington, WV, Division Chair: Ralph Oberste-Vorth, PhD

2004-2005 Graduate research assistant, Dept of Mathematics, Marshall University, Huntington, WV, Research Mentor: Bonita A Lawrence, PhD

2005-2007 Research assistant, Dept of Anatomy and Pathology, Marshall University School of Medicine, Huntington, WV, Primary Investigator: Sasha N Zill, PhD

2010 Research assistant, Dept of Biochemistry and Microbiology, Marshall Univ SOM, Primary Investigator: Hongwei D Yu, PhD

2010-2013 Resident, Internal Medicine, Dept of Medicine, University of Wisconsin, Madison, WI, Program Director: Bennett Vogelman, MD

2013-2014 Staff Physician, Dept of Medicine, William S Middleton Memorial VA Hospital, Madison, WI,

Chief of Service: Christopher Hildebrand, MD

2014- Fellow, Division of Allergy and Infectious Diseases, University of Washington, Seattle, WA, Program Director: David Fredricks, MD

2015- Senior Research Fellow, Division of Allergy and Infectious Diseases, University of Washington; Vaccine and Infectious Disease Division, Fred Hutchinson Cancer Research Center, Seattle, WA, Division Head: Juliana McElrath, MD, PhD, Research Mentor: Joshua T Schiffer, MD, MS

2015- Investigator, Malaria Clinical Trials Center, Fred Hutchinson Cancer Research Center, Seattle, WA, Primary Investigator: James Kublin, MD

Professional Memberships

2010-2014 American College of Physicians

2014- Infectious Diseases Society of America

Honors

1998-2002 Yeager Scholarship, Marshall University

2001 William J Maier Latin Award and Scholarship, Marshall University

2002 Summa Cum Laude, BA in Latin and Mathematics, Marshall University

2006 Anagene B Heiner Memorial Basic Science Poster Presentation Award, Marshall University School of Medicine Research Day

2012 David Sundee Humanism in Medicine Award, Internal Medicine Residency, University of Wisconsin

2012 Best Oral Research Presentation and Travel Scholarship to National ACP Meeting, Wisconsin State ACP Meeting

2013 Best Poster Presentation, Research Day, Dept of Medicine, University of Wisconsin

2016 Best Poster Presentation, Conference on Cell and Gene Therapy for HIV Cure, Fred Hutchinson Cancer Research Center, Seattle, WA

2016 Infectious Diseases Society of America IDWeek Travel Scholarship

2016 University of Washington Office of Postdoctoral Affairs Travel Award

C. Contribution to Science

1. **Intrahost mathematical modeling of HIV latency and HIV cure**
   HIV has proven incurable with antiretroviral therapy (ART) due to its ability to persist as a quiescent provirus, integrated into human DNA. Despite years of viral suppression, when people infected with HIV stop ART, viral rebound occurs due to unchecked reactivation and replication of virus. We have developed a mathematical model of HIV latency model that predicts the impacts of various cure interventions on reservoir size and have found that anti-proliferative therapy may be a promising cure strategy. Using drugs already licensed in stem cell and solid organ transplant (*e.g.* mycophenolate mofetil) given in addition to antiretroviral therapy (ART), we predicted profound reductions in the HIV reservoir. In addition, we found that due to differences in the magnitudes of natural T cell proliferation rates and viral reactivation rates, latency reversal agents (or so-called "kick-and-kill" therapy) would need to be 1,000 times more potent than anti-proliferative agents to reach the same level of reservoir reduction. I have presented these findings at the Keystone meeting on HIV Persistence: Pathogenesis and Eradication and at the Conference on Cell and Gene Therapy for HIV Cure, and the manuscript is in preparation for submission to Lancet ID. We have also explored HIV persistence in a separate model that describes HIV infected cell decay on ART. Using stochastic simulations, we showed that whereas ongoing viral replication may be occurring in anatomic drug sanctuary sites, proliferation and/or longevity of infected cells is likely the predominant mechanism sustaining the reservoir. I received a travel scholarship to present this work at IDWeek. I gave an invited lecture describing both projects at the University of Wisconsin.

   a. **Duke ER**, Reeves DB, Prilic M, Hladik F, Schiffer JT. A compound interest approach to HIV cure. Keystone HIV Persistence: Pathogenesis and Eradication (X7), Abstract 4011, Olympic Valley, CA, 2016.
   b. Reeves DB**, Duke ER**, Spivak AM, Schiffer JT. Latent Cell Proliferation Sustains the HIV Reservoir on Long-term ART—A Mathematical Modeling Study with Implications for Cure. IDWeek, Abstract 58639, New Orleans, LA, 2016.

2. **Drug development of anti-malarials and clinical trials experience**
As a fellow, I have also had the opportunity to serve as a clinical investigator in human malaria challenge trials. As study physician, I have screened participants for the trials, injected them with *P. falciparum* sporozoites, observed the administration of infectious bites from mosquitoes, treated participants for malaria, and monitored their labs and clinical status throughout the study. These experiences informed my desire to continue working in clinical trials and developing these important skills for translational medicine.

    a. Murphy SC, **Duke ER**, Jensen R, Fong Y, Fritzen E, VonGoedert T, Duparc S, Chalon S, Kerr N, Rueckle T, Kublin JG. A proof-of-concept, randomized study in non-immune healthy adult volunteers to investigate the safety, tolerability, pharmacokinetic profile and prophylactic activity of a single dose of DSM265 in a controlled human malarial infection challenge either by direct venous inoculation of *Plasmodium falciparum* sporozoites of a single episode of bites by mosquitoes carrying *P. falciparum*. American Society of Tropical Medicine & Hygiene, Abstract 1534, Atlanta, GA, 2016.

3. **Time Scales Calculus**
Time Scales Calculus seeks to integrate discrete and continuous-time mathematical systems under a single calculus. Continuous differential equation systems are thought to describe most accurately natural phenomena such as weather patterns, bacterial growth, fluid dynamics, etc. However, we are unable to solve all but the simplest systems with traditional analytical methods. Rather, differential equations are solved numerically (with computers) using difference equations (discrete calculus). Further, when addressing small quantities or infrequent events (when one or zero viral particles are present or when there are long periods of inactivity in a system), difference equations are needed. Thus, a unifying calculus that would allow the same system to contain mixtures of discrete and continuous parts, could be extremely useful. While it had previously been shown that time scales calculus could be used to linearize first-order mixed time scale systems, in my master's thesis, I showed that second order systems on any time scale, can be linearized and solved numerically. However, in higher-order systems, time scales that mix continuous and discrete points cannot be solved in this way. I created a graphical user interface (GUI) software called tsSolver that solves dynamic equations on time scales. My thesis has been downloaded 107 times in 26 countries as of October 2016. The experience I gained in mathematics and in solving dynamic systems has proved invaluable in my current work as mathematical modeler.

    a. **Duke ER**. Solving Higher Order Dynamic Equations on Time Scales as First Order Systems. Theses, Dissertations and Capstones, Marshall University Digital Commons. 2006, Paper 577. http://mds.marshall.edu/etd/577
    b. **Duke ER**, Hall KJ, Oberste-Vorth RW. Changing time scales I: The continuous case as a limit. Proceedings of the Sixth WSEAS Intl Conf on Applied Mathematics, 2004.
    c. Hall KJ, **Duke ER**, Oberste-Vorth RW. Changing time scales II: Bifurcations in second degree equations. Proceedings of the Sixth WSEAS Intl Conf on Applied Mathematics, 2004.

4. **MRSA colonization at multiple body sites**
I became interested in MRSA and particularly its role in community-acquired furunculosis in medical school in West Virginia when I witnessed the high burden of these infections in the community. The patients who repeatedly came to ER with painful abscesses requiring drainage wanted to avoid future episodes, which led to my interest in colonization and decolonization. During residency, I gave two formal lectures to the Department of Medicine (Advances in Medicine Lecture Series) addressing MRSA decolonization and colonization of multiple body sites, respectively. I worked with Christopher Crnich, MD who had collected serial MRSA swabs from 5 body sites of nursing home residents at local skilled nursing facilities and analyzed the data according to body site. We found that not only do nursing home residents have much greater rates of MRSA colonization (33% in our study) than ICU patients (around 10%), but also that screening for MRSA in the nose alone detects only about 2/3 of those colonized with MRSA. I presented these findings at the Wisconsin state ACP meeting and won the oral presentation competition. I also received a travel scholarship to present these findings at the national ACP meeting.

a. **Duke ER**. Decolonizing carriers of community-Acquired-MRSA skin and soft tissue infections, Advances in Medicine, Dept of Medicine, University of Wisconsin, 2011.
b. **Duke ER**. How to wield an MRSA screening swab: screening at multiple body sites and contact precautions, Advances in Medicine, Dept of Medicine, University of Washington, 2012.
c. **Duke ER**, Hess TM, Crnich C. Screening for MRSA at Multiple Body Sites in Nursing Home Residents, ACP National Meeting, San Francisco, CA, 2013.

5. **Neurophysiology of standing and walking**
Regulation of posture and walking in humans is complex and occurs at multiple levels of the nervous system. Studying the neurophysiology of cockroaches yields important information about neuromuscular control of walking because cockroaches walk extremely quickly and on uneven terrain and because their neurons are relatively large such that neurophysiologic recordings can be measured directly from single neurons. Further, there are characteristics of the control mechanisms of standing and walking that are remarkably similar in humans and invertebrates. In addition, collaborating engineers use the insights gained in these studies to improve the locomotion of robots. In the following manuscripts, we showed via direct recordings taken from sensory organs near the cockroaches' "knees" (similar to Golgi tendon organs in humans) that their neurons fire when weight is applied and removed (Keller et al. 2007) and in response to the placement of their other legs (Zill et al. 2009), allowing coordinated walking. In recordings from neurons in their "feet," we demonstrated firing in response to engagement with surfaces that may be important in preventing falls (Zill et al. 2010).

a. Keller BR, **Duke ER**, Amer AS, Zill SN. Tuning posture to body load: decreases in load produce discrete sensory signals in the legs of freely standing cockroaches. J Comp Physiol A 2007, 93:881-891. PMID: 17541783.
b. Zill SN, Keller BR, **Duke ER**. Sensory signals of unloading in one leg follow stance onset in another leg: Transfer of load and emergent coordination in cockroach walking. J Neurophysiol 2009, 101:2297-2304. PMID: 19261716.
c. Zill SN, Keller BR, Chaudry S, **Duke ER**, Neff D, Quinn R, Flannigan C. Detecting substrate engagement: responses of tarsal campaniform sensilla in cockroaches. J Comp Physiol A Neuroethol Sens Neural Behav Physiol. 2010, 196:407-420. PMID: 20396892.

Complete List of Publications in MyBibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/elizabeth.duke.1/bibliography/41375452/public

D. Research Support

Ongoing Research Support

T32 AI 0070-44 **Van Voorhis (PI)** 07/01/15-present
University of Washington
Title: Host Defense Training in Allergy and Infectious Disease
Goal: Salary support for training of academicians in Infectious Diseases, Allergy, and Geographic Medicine, with emphasis on research training
Role: Fellow/Trainee