OMB No. 0925-0001 and 0925-0002 (Rev. 09/17 Approved Through 03/31/2020)

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: Broder, Christopher C.

eRA COMMONS USER NAME: (b) (6)

POSITION TITLE: Professor of Microbiology, Immunology and Emerging Infectious Diseases

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	COMPLETION DATE	FIELD OF STUDY
Florida Institute of Technology, Florida	B.S.	06/1983	Biological Science
Florida Institute of Technology, Florida	M.S.	12/1985	Molecular Biology
University of Florida, Florida	Ph.D.	05/1989	Immunology and Med-Micro

A. Personal Statement

My laboratory has been collaborating with EcoHealth Alliance and other groups for over 8 years with a major focus on serological assays for the detection of henipaviruses and filoviruses in wildlife, livestock, and human populations. I have been an active researcher in enveloped virus-host cell interactions for the past 30 years. Together with my collaborators, I have made significant contributions to the field. I developed the first oligomeric HIV-1 gp140 glycoprotein subunit vaccine, the vaccinia virus-based reporter gene assay for measuring viral glycoprotein-mediated membrane fusion, defined the fusion tropism of HIV-1 followed by the discovery of the HIV-1 coreceptors (CXCR4 and CCR5). In 1999, I established a collaborative international group of experts in Hendra and Nipah virus research, in areas from structural biochemistry, animal models and *in vivo* pathogenesis, to the development and testing of vaccines and therapeutics. My work includes the discovery of the Hendra and Nipah virus entry receptors (ephrin-B2/B3), and the development of the feline, ferret and African green monkey models of Hendra and Nipah virus pathogenesis with my collaborators. My lab's henipavirus glycoprotein work, with collaborators, have made the structural solutions and characterization of the F and the G-ephrin receptor glycoprotein interactions, and the discovery and development of antiviral human monoclonal antibodies to ABLV and Hendra and Nipah viruses; one (m102.4) having a Phase I clinical trial completed in 2016, and has been used by emergency protocol in 13 people in Australia and one in the US because of significant risk of infection. I developed the Hendra/Nipah subunit vaccine based on soluble Hendra G glycoprotein (HeV-sG); called Equivac® HeV (Zoetis, Inc.) the first commercialized vaccine to a BSL-4 agent, and being developed as a human use Nipha/Hendra vaccine supported by CEPI. Relevant to the present proposal, we have developed the first reverse genetics system for the henipavirus, Cedar virus, which will serve as a platform to assay henipavirus neutralization; and we have developed a panel 17+ different soluble envelope glycoproteins from all the known filoviruses and henipaviruses for serological surveillance studies, and have the tools to conduct the studies, and carry out capacity building and training programs.

1. Bonaparte MI, Dimitrov AS, Bossart KN, Crameri G, Mungall BA, Bishop KA, Choudhry V, Dimitrov DS, Wang L-F, Eaton BT, **Broder CC*** (2005). Ephrin-B2 Ligand is a Functional Receptor for Hendra Virus and Nipah Virus. **Proc Natl Acad Sci USA** 102(30):10652-7. (*from the cover*)
2. Middleton D, Pallister J, Klein R, Feng YR, Haining J, Arkinstall R, Frazer L, Huang JA, Edwards N, Wareing M, Elhay M, Hashmi Z, Bingham J, Yamada M, Johnson D, White J, Foord A, Heine HG, Marsh GA, **Broder CC**, Wang LF (2014). Hendra virus vaccine, a one health approach to protecting horse, human, and environmental health. **Emerg Infect Dis**. 20(3). PMCID: PMC3944873

3. Xu K, Chan YP, Bradel-Tretheway B, Akyol-Ataman Z, Zhu Y, Dutta S, Yan L, Feng Y, Wang LF, Skiniotis G, Lee B, Zhou ZH, **Broder CC**, Aguilar HC, Nikolov DB (2015). Crystal Structure of the Pre-fusion Nipah Virus Fusion Glycoprotein Reveals a Novel Hexamer-of-Trimers Assembly. **PLoS Pathog**. 8;11(12):e1005322. doi: 10.1371/journal.ppat.1005322. PMID: 26646856.
4. Mire CE, Satterfield BA, Geisbert JB, Agans KN, Borisevich V, Yan L, Chan YP, Cross RW, Fenton KA, **Broder CC**, Geisbert TW (2016). Pathogenic Differences between Nipah Virus Bangladesh and Malaysia Strains in Primates: Implications for Antibody Therapy. **Sci Rep**. 3;6:30916. doi: 10.1038/srep30916.

B. Positions and Honors

Positions and Employment

1990 -92 National Research Council, Research Associate, Laboratory of Viral Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland.
1993 -96 IRTA Fellow, LVD, NIAID, NIH, Bethesda, Maryland.
Assistant Professor, Department of Microbiology and Immunology, Joint appointment, Molecular and Cell Biology Graduate Program, Uniformed Services University, Bethesda, Maryland.
2000 -05 Associate Professor, Department of Microbiology and Immunology, Joint appointment, Emerging Infectious Diseases Graduate Program, USUHS, Bethesda, Maryland.
2005 - Professor, Department of Microbiology and Immunology, Joint appointment, Emerging Infectious Diseases Graduate Program, USUHS, Bethesda, Maryland.
2006 -18 Director, Emerging Infectious Diseases Graduate Program, USU, Bethesda, Maryland.
2018 - Chair, Department of Microbiology and Immunology, USU, Bethesda, Maryland.

Other Experience and Professional Affiliations

2009 Member, National Veterinary Stockpile Nipah virus Countermeasures Workshop; USDA. Australia
2011 Member, Discontools Nipah Virus Infection Panel Expert Group. Gap analysis. International Federation for Animal Health Europe, Brussels, Belgium
2011 Invited expert, National Academies, Washington, DC. Evaluation of site-specific risk assessment for the National Bio- and Agro-Defense Facility (NBAF) in Manhattan, Kansas

Editorial board of *J. of Virology* (2007), *Virology* (2010), *Viruses* and *Pathogens* (2011) *Virologica Sinica* (2012)

Honor and Awards

1996 The Fellows Award for Research Excellence, Office of Science Education, NIH
1996 American Association for the Advancement of Science: Breakthrough of the Year, Science Magazine; Newcomb Cleveland Prize
1996 Outstanding Instructor in Virology, USUHS, School of Medicine
2008 The Henry Wu Award for Excellence in Basic Science Research
2013 The 3rd Sidney Pestka Lecture; 22nd Annual Philadelphia Infection & Immunity Forum
2013 The 2013 Federal Laboratory Consortium (FLC) Award for Excellence in Technology Transfer
2013 Second Finalist for the Australian Infectious Diseases Research Centre Eureka Prize
2013 The CSIRO Chairman's Medal, The Commonwealth Scientific and Industrial Research Organisation (CSIRO); Australia's national science agency
2014 The Cinda Helke Award for Excellence in Graduate Student Advocacy
2016 The James J. Leonard Award for Excellence in Translational/Clinical Research
2019 The 2019 Federal Laboratory Consortium (FLC) Award for Excellence in Technology Transfer
2019 USU Outstanding Biomedical Graduate Educator Award

C. Contributions to Science

1. **My Ph.D. thesis studies centered on the discovery and characterization of a specific receptor for human plasmin on Group A Streptococci during a rotation project as a 1st year student.** My studies revealed that certain group A streptococci elaborated surface receptors that could bind selectively a key fibrinolytic enzyme, plasmin, while having no binding ability towards the zymogen precursor plasminogen or

other serine proteases. The bacterium-bound plasmin remained enzymatically active including its ability to hydrolyze a fibrin clot. Bound plasmin could not be inhibited by its physiological regulator, alpha 2-plasmin inhibitor. Since these organisms produced streptokinase, a protein that complexes with plasminogen producing an active enzyme that can convert plasminogen to plasmin, they could accelerate the destruction of the extracellular matrix environment: findings that formed a molecular-pathogenic model for the "flesh-eating streptococci".

a. Lottenberg R, **Broder CC**, Boyle MDP (1987). Identification of a Specific Receptor for Plasmin on a Group A Streptococcus. Infection and Immunity. 55(8):1914-1918.
b. **Broder CC**, Lottenberg R, Boyle MDP (1989). Mapping of the Domain of Human Plasmin Recognized by its Unique Group A Streptococcal Receptor. Infection and Immunity. 57(9): 2597-2605.
c. **Broder CC**, Lottenberg R, von Mering GO, Johnston K, Boyle MDP (1991). Isolation of a prokaryotic plasmin receptor: relationship to a plasminogen activator produced by the same microorganism. **J. Biol. Chem.** 266:4922-28.
d. Lottenberg R, **Broder CC**, Boyle MDP, Kain SJ, Schroeder BL, Curtiss R III (1992). Cloning, Sequence Analysis, and Expression in *Escherichia coli* of a Streptococcal Plasmin Receptor. **J. Bacteriology** 174:5204-5210.

2. **My independent postdoctoral fellowship focused on the early stages of HIV-1 envelope glycoprotein mediated membrane fusion as a surrogate model of HIV-1 entry.** I established a vaccinia virus-based reporter gene assay for measuring viral (HIV-1) glycoprotein-mediated membrane fusion and generated the first panel of T-cell tropic and Macrophage-tropic HIV-1 envelope glycoprotein (Env) encoding recombinant vaccinia virus vectors and I used these tools to be the first to hypothesize that the cellular tropism of HIV-1 could be explained by specific membrane fusion factors required for the different classes of HIV-1 Envs. I also developed the first soluble and secreted full-length oligomeric HIV-1 gp140 glycoprotein and explored the importance of its native oligomeric structure in terms of its presentation of conformational and virus-neutralizing epitopes through the development and characterization of more than 100 murine monoclonal antibodies.
   a. **Broder CC,** Dimitrov DS, Blumenthal R, Berger EA (1993). The block to HIV-1 envelope glycoprotein-mediated membrane fusion in animal cells expressing human CD4 can be overcome by a human cell component(s). **Virology** 193:483-491.
   b. Nussbaum O, **Broder CC,** Berger EA (1994). HIV-1 Envelope Glycoprotein/CD4 Mediated Cell Fusion: A Novel Recombinant Vaccinia Virus-Based Assay Measuring Activation of a Reporter Gene by Bacterio-phage T7 RNA Polymerase Selectively In Fused Cells. **J.Virol.** 68:5411-5422.
   c. **Broder CC,** Earl PL, Long D, Moss B, Doms RW (1994). Antigenic implications of HIV-1 envelope glycoprotein quaternary structure: oligomer-specific and -sensitive mAbs. **PNAS** 91:11699-11703.
   d. **Broder CC**, Berger EA (1995). Fusogenic Selectivity of the Envelope Glycoprotein is a Major Determinant of HIV-1 Tropism for CD4+ T-Cell Lines vs. Macrophages. **PNAS** USA. 92:9004-08.

3. **My early studies on the cellular and viral membrane fusion tropism of HIV-1 and the development of a sensitive and specific reporter gene assay of cell-cell membrane fusion facilitated the discovery of the first membrane fusion accessory factor** (fusin, now known as CXCR4) that we earlier hypothesized existed, and this rapidly led to the discovery by us and others of the second factor for macrophage-tropic Envs (CCR5); the HIV-1 coreceptors. These findings were a significant breakthrough in HIV research leading to numerous new directions in understanding HIV-1 pathogenesis as well as new therapeutic strategies.
   a. Feng Y, **Broder CC**, Kennedy PE, Berger EA (1996). HIV-1 Entry Cofactor: Functional cDNA Cloning of a Seven-Transmembrane, G Protein-Coupled Receptor. **Science** 272:872-877.
   b. Alkhatib* G*, Combadiere C*, **Broder CC***, Feng Y*, Kennedy PE*, Murphy PM, Berger EA (1996). CC CKR5: a RANTES, MIP-1α , MIP-1β Receptor as a Fusion Cofactor for Macrophage-Tropic HIV-1. **Science** 272:1955-1958. (*equal contribution).

c. Rucker J, Samson M, Doranz BJ, Libert F, Berson JF, Yi Y, Collman RG, **Broder CC**, Vassart G, Doms RW, Parmentier M (1996). Regions in β-chemokine Receptors CCR-5 and CCR-2b that Determine HIV-1 Cofactor Specificity. **Cell** 87:1-10.
d. Edinger AL, Amedee A, Miller K, Doranz BJ, Endres M, Sharron M, Samson M, Lu Z-h, Clements JE, Murphey-Corb M, Peiper SC, Parmentier M, **Broder CC**, Doms RW (1997). Differential utilization of CCR5 by macrophage and T cell tropic simian immunodeficiency virus strains. **PNAS** USA. 94:4005-4010.

4. **My initial work on HIV-1 entry led to further independent studies which focused on follow-up investigations characterizing the roles of the HIV-1 coreceptors in the virus entry process.** These studies revealed the interplay between the HIV-1 entry receptors, mapped important domains of the coreceptors involved in HIV-1 Env interaction, and also revealed possible avenues of how an HIV-1 Env might engage and differently utilize the CXCR4 and CCR5 coreceptors for infection. In addition, I also engaged in collaborative follow-up studies exploring the utility of soluble oligomeric HIV-1 envelope glycoproteins as subunit vaccine immunogens (gp140) which I initiated at NIH while a postdoctoral fellow, with the unusual R2 HIV-1 Env isolate and led to the first NIAID program project grant funded at USU.
   a. Chabot DJ, Zhang PF, Quinnan GV, **Broder CC** (1999). Mutagenesis of CXCR4 Identifies Important Domains for HIV-1 X4 Isolate Envelope-Mediated Membrane Fusion and Virus Entry and Reveals Cryptic Coreceptor Activity for R5 Isolates. **J. Virol**. 73:6598-6609.
   b. Xiao X, Wu L, Stantchev TS, Feng Y-R, Ugolini S, Chen H, Shen Z, **Broder CC**, Sattentau QJ, Dimitrov DS (1999). Constitutive cell surface association between CD4 and CCR5. **PNAS** 96:7496-7501.
   c. Chabot DJ, Chen H, Dimitrov DS, **Broder CC** (2000). N-linked Glycosylation in CXCR4 Masks Coreceptor Function for CCR5-Dependent HIV-1 Isolates. **J. Virol.** 74:4404-4413.
   d. Zhang PF, Cham F, Dong M, Choudhary A, Bouma P, Zhang Z, Shao Y, Feng YR, Wang L, Mathy N, Voss G, **Broder CC**, Quinnan GV Jr (2007). Extensively cross-reactive anti-HIV-1 neutralizing antibodies induced by gp140 immunization. **PNAS** USA. 104(24):10193-8.

5. **My most recent research has been on emerging viruses that impact human and domestic livestock populations; including Australian bat lyssavirus (rabies-like virus), filoviruses (Ebola and Marburg) and the henipaviruses (Hendra and Nipah).** My lab was the first to publish on Hendra virus outside of Australia. I obtained the first NIAID funded project providing monetary support on select agent research to an overseas laboratory (2003). Henipavirus research has been the major focus of my lab for the past 20 years, covering areas from structural biochemistry, *in vivo* pathogenesis and animal model development to the development and testing of vaccines and therapeutics. My lab developed the first peptide henipavirus fusion inhibitors, subunit vaccine and neutralizing human monoclonal antibodies (mAb), and supported the development of the feline and ferret models of Hendra and Nipah infection and pathogenesis in Australia and the development of the first nonhuman primate model (USAMRIID). We and our collaborators tested the *in vivo* efficacy of the Hendra/Nipah vaccine (HeV-sG) and an anti-HeV/NiV G-specific neutralizing human mAb. One human mAb (m102.4) has been used by compassionate emergency protocol in 13 people in Australia and one individual in the United States; a Phase I clinical trial was completed in May, 2016. The henipavirus subunit vaccine, HeV-sG, was launched; called Equivac® HeV (Zoetis, Inc.) and is the first commercialized and deployed vaccine to a BSL-4 agent. Additional findings include the discovery of the henipavirus entry receptors (ephrin-B2/B3) and produced soluble versions of the G and F proteins facilitating their structural solutions.
   a. Bossart KN, Zhu Z, Middleton D, Klippel J, Crameri G, Bingham J, McEachern JA, Green D, Hancock TJ, Chan YP, Hickey AC, Dimitrov DS, Wang L-F, **Broder CC*** (2009). A neutralizing human monoclonal antibody protects against lethal disease in a new ferret model of acute Nipah virus infection. **Plos Pathogens** 5(10). PMCID: PMC2765826.
   b. Bossart KN, Geisbert TW, Feldmann H, Zhu Z, Feldmann F, Geisbert JB, Yan L, Feng Y-R, Brining D, Scott D, Wang Y, Dimitrov AS, Callison J, Chan Y-P, Hickey AC, Dimitrov DS, **Broder CC***,

Rockx B (2011). A neutralizing human monoclonal antibody protects African Green monkeys from Hendra virus challenge. **Sci. Transl. Med.** 3, 105ra103. *corresponding author (***from the cover***). PMCID: PMC3313625.

c. Bossart KN, Rockx B, Feldmann F, Brining D, Scott D, Lacasse R, Geisbert JB, Feng YR, Chan YP, Hickey AC, **Broder CC***, Feldmann H, Geisbert TW (2012). A Hendra virus G glycoprotein subunit vaccine protects African green monkeys from Nipah virus challenge. **Sci Transl Med**. 4(146):146ra107. *corresponding (***from the cover***) PMCID: PMC3516289.

d. Geisbert TW*, Mire CE, Geisbert JB, Chan YP, Agans KN, Feldmann F, Fenton KA, Zhu Z, Dimitrov DS, Scott DP, Bossart KN, Feldmann H, **Broder CC*** (2014). Therapeutic treatment of Nipah virus infection in nonhuman primates with a neutralizing human monoclonal antibody. **Sci Transl Med.** *corresponding author 6(242):242ra82. PMCID: PMC4467163.

(166 publications; total citations: >19,800). more complete list of published work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/christopher.broder.1/bibliography/41141103/public/?sort=date&direction=ascending

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

Ongoing Research Support

HDTRA1-17-10037 Epstein (PI) 05/01/17 - 04/30/20
Serological Biosurveillance for Spillover of Henipaviruses and Filoviruses at Agricultural and Hunting Human-Animal Interfaces in Peninsular Malaysia.
To characterize the distribution and detect the spillover of henipaviruses and filoviruses among indigenous farming and hunting communities in Peninsular Malaysia.
Role: Co-PI)

R21 AI137813-01 Broder (PI) 04/01/18 - 03/31/20
A Recombinant Cedar Virus-based Henipavirus Replication Platform for High-throughput Inhibitor Screening.
Develop, characterize and adapt a rCedPV reporter virus for use in HTS; Optimize the HTS parameters; and pilot an HTS assay using a small molecule library.

CRADA Broder (PI) 07/01/12 - 09/30/40
Collaborative development and evaluation of an equine vaccine against Hendra virus

(b) (4) Eldridge (PI) 05/24/18 - 05/23/23
A Subunit Vaccine (HeV-sG) to Protect Against Nipah and Hendra Diseases

CRADA from (b) (4) Broder (PI)
Development of a Cedar virus-based Henipavirus neutralization assay
Develop, characterize and test chimeric, luciferase/GFP encoding henipaviruses using CedPV.

NIAID/NIH (CETR) U19AI142764 Broder (PI) 03/01/19 - 02/28/24
Advancement of Vaccines and Therapies for Henipaviruses
The Center focus on developing strategies effective against all pathogenic henipaviruses. The primary objective of the Center is to perform pivotal studies that will facilitate the development of products used for the prevention and treatment of Nipah and Hendra infections. RPs, and Center Cores: Administrative; human monoclonal antibody; and BSL-4; work together to provide broadly effective countermeasures.

Administrative Core (A) Broder (PI) 03/01/19 - 02/28/24
Description: Core A: organize, schedule, coordinate meetings between the RPs, Cores B and C, and the Scientific Advisory Committee; oversee and manage the submission of progress reports; serve as a liaison and facilitate communication between the RPs, Core staff, Scientific Advisory Committee, and the NIAID/NIH.

Recombinant CedPV-based vaccine development Broder (PI) 03/01/19 - 02/28/24
Objective of RP3 will be to use recombinant Cedar virus (rCedPV) as an authentic, non-pathogenic, live attenuated henipavirus system. RP3 will examine its potential as a live-attenuated universal henipavirus vaccine platform that can induce a long-lasting and balanced protective immune response.

OMB No. 0925-0001 and 0925-0002 (Rev. 09/17 Approved Through 03/31/2020)

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: Laing, Eric D.

eRA COMMONS USER NAME (credential, e.g., agency login): (b) (6)

POSITION TITLE: Research Assistant Professor

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 Maryland, College Park, MD	B.S. (hons)	05/2008	Biology
Uniformed Services University, Bethesda, MD	Ph.D.	10/2016	Emerging Infectious Diseases

A. Personal Statement

Bats are increasingly identified as animal reservoirs of medically-relevant emerging RNA viruses (e.g. Nipah virus, Ebola virus and SARS-coronavirus). However, the environmental, behavioral and host dynamics that contribute to spill over into human populations remains largely unknown; this is especially true for ebolaviruses. In the past year, two novel filoviruses with unknown pathogenicity have been discovered: Bombali virus and Mengla virus. We anticipate that a diversity of related-filoviruses exists undetected in bat reservoir hosts, and identifying these unknown viruses and understanding known filovirus-host interactions will improve our knowledge of bat species that are hosts for ebolaviruses. Collectively, these results will be used to understand transmission dynamics in wildlife hosts and generate risk-models for Ebola virus disease outbreaks. I have had a collaborative research relationship with the EcoHealth Alliance (EHA) for 5+ years, and this Emerging Infectious Diseases Research Centers Coordination Center (EIDRC CC) for the Emerging Infectious Diseases Research Centers (EIDRC) proposal will allow for an important extension of our collaboration and mutual research interests on emerging viruses, infectious disease surveillance and building threat reduction networks. Additionally, I have expertise in virology, biosurveillance and capacity training in international settings to successfully contribute to the aims of this proposal. In collaboration with EHA, we have developed a multiplex serologically immunoassay that can detect antibodies specific to or cross-reactive with all presently described filoviruses. This immunoassay tool will be key for detecting the serological footprint of known and unknown filoviruses in bat hosts. This assay is presently being used for biosurveillance by collaborators in Southeast Asia and South Asia. Assay validation is being undertaken between our laboratory (USU) and collaborators at the Dr. Vincent Munster's group at the NIH Rocky Mountain Laboratory and United States Army Medical Institute of Infectious Diseases.

1. **Laing ED***, Mendenhall IH*, Chen Y, Yan L, Wen DLH, Lynn JLS, Sterling SL, Skiles M, Lee BPY-H, Linster M, Wang L-F, Broder CC, Smith GJD (2018). Serologic evidence of fruit bat exposure to filoviruses, Singapore, 2011–2016. **Emerg Infect Dis**. 24(1):122-126.

B. Positions and Honors

Positions and Employment

2003 -04 Howard Hughes Medical Institute student intern, Cellular and Developmental Neurobiology Section, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, MD.
2005 -06 Undergraduate research assistant, Department of Animal and Avian Sciences, University of Maryland, College Park, MD.
2007 -08 Undergraduate research assistant, Biology Departmental Honors research, Department of Biology, University of Maryland, College Park, MD.
2008 -09 Research assistant, Department of Pharmacology, Uniformed Services University, Bethesda, MD.
2010 Research assistant, Department of Microbiology, Uniformed Services University, Bethesda, MD.
2010 -16 Graduate research student, Department of Microbiology, Uniformed Services University, Bethesda, MD.
2016 -17 Postdoctoral fellow, Henry M. Jackson Foundation, Department of Microbiology, Uniformed Services University, Bethesda, MD.
2017 -18 Scientist, Henry M. Jackson Foundation, Department of Microbiology, Uniformed Services University, Bethesda, MD.
2019 - Research Assistant Professor, Uniformed Services University, Department of Microbiology and Immunology, Uniformed Services University, Bethesda, MD.

Other Experience and Professional Membership

2009 Mentor, At-Risk Student Mentoring, Bethesda Chevy Chase High School, Bethesda, MD.
2009- 10 Mentor, EnvironMentors, Washington, D.C.
2013 Mentor, high school, undergraduate, and graduate students, Uniformed Services University, Bethesda MD.
2014 Participant, American Society of Microbiology Kadner Institute
2014 -15 Volunteer, AAAS/Senior Scientists and Engineers STEM Volunteer Program
2014 -17 Member, American Society of Tropical Medicine and Hygiene
2014 -19 Member, American Society of Microbiology
2015 -16 Member, USU Global Health Interest Group

Honors

2004 -07 Maryland House of Delegates Scholarship
2005 -07 Semester Academic Honors
2006 College Park Life Sciences Scholars Program Citation
2008 High Honors, Biology Departmental Honors Program
2015 USU Research Days Graduate Student Poster Presentation Finalist (Won)
2015 NSF East Asia and Pacific Summer Institutes (EAPSI) Fellowship
2015 -16 Val G. Hemming Fellowship, Henry M. Jackson Foundation

C. Contributions to Science

1. **Virus-host interactions.** My Ph.D. thesis research was focused on virus-host interactions: understanding bats as hosts of zoonotic viruses and Australian bat lyssavirus (ABLV) cellular entry. This work entailed exploring the antiviral mechanisms that enable cellular persistence of viruses in bats, particularly, authophagy. Findings revealed that the autophagy pathway is induced upon infection with Australian bat lyssavirus (ABLV), a Rabies-virus related virus carried by Australian *Pteropus* bats. The combined pharmacological and genetic studies of the autophagy pathway in the context of this virus-host interaction indicated that autophagy functions as an antiviral defense. The study also demonstrated that bat-derived cell lines have elevated levels of basal autophagy, which might help to explain the cellular mechanism that contribute to the ability of bats to act as host to these viruses. An additional finding from these studies was that activation of autophagy may have therapeutic benefits during neurotropic virus infection.

a. Weir DL, **Laing ED**, Smith IL, Wang L-F, Broder CC (2013). Host cell entry mediated by Australian bat lyssavirus G envelope glycoprotein occurs through a clathrin-mediated endocytic pathway that requires actin and Rab5. **Virology Journal** 11:40.
b. **Laing ED**, Sterling SL, Weir DL, Beauregard CR, Smith IL, Larsen SE, Wang L-F, Snow AL, Schaefer BC, Broder CC (2019). Enhanced autophagy contributes to reduced viral infection in black flying fox cells. **Viruses** 11:260.

2. **Molecular virology technologies.** My research experience as a postdoctoral fellow furthered my training in molecular virology techniques. I constructed a recombinant Cedar virus cDNA plasmid and optimized a reverse genetics approach to rescue a recombinant Cedar virus reporter virus, a non-pathogenic *Henipavirus* species. This virus will be used as a model *Henipavirus* to explore host cell-pathogen interactions, cellular tropism, and test novel therapeutics against henipaviruses.
   a. **Laing ED***, Amaya M*, Navaratnarajah CK, Cattaneo R, Wang L-F, Broder CC (2019). Rescue and characterization of recombinant Cedar virus, a non-pathogenic *Henipavirus* species. **Virology Journal** 15(1):56.

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

Ongoing Research Support

(b) (4) Hertz (PI) 10/01/18 – 09/30/19
Sero-survey of Nipah virus and other pathogenic bat borne paramyxoviruses in Cambodia
The goal of this study is to retrospectively investigate potential human exposure to Nipah virus and related paramyxoviruses in geographies with and without *Pteropus* colonies to inform risk assessments of Nipah virus spillover.
Role: Co-Investigator

(b) (4) Epstein (PI) 05/01/17 – 04/30/20
Serological Biosurveillance for Spillover of Henipaviruses and Filoviruses at Agricultural and Hunting Human-Animal Interfaces in Peninsular Malaysia
The overarching goal is to characterize the distribution and detect the spillover of henipaviruses and filoviruses among indigenous farming and hunting communities in Peninsular Malaysia. As part of this process, we will build capacity at key government labs in human and animal health sectors to enhance serological surveillance in animals and human populations for these high consequence pathogens.
Role: Scientist

Completed Research Support

(b) (4) Broder (PI) 12/01/18 – 04/30/19
Chulalongkorn Luminex Training and Research Preparedness
The goal of this study was to transfer a multiplex serological assay to collaborators at the Thai Red Cross Emerging Infectious Diseases (TRC-EID) Research Center and provide in-country assay training and collaborative support. This serological assay has been designed to detect antibodies reactive with antigens from all presently described filoviruses and henipaviruses, and complement Nipah virus biosurveillance work at the TRC-EID.
Role: Co-Principal Investigator

OMB No. 0925-0001 and 0925-0002 (Rev. 09/17 Approved Through 03/31/2020)

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: Keusch, Gerald T.

eRA COMMONS USER NAME (credential, e.g., agency login): (b) (6)

POSITION TITLE: Professor of Medicine, Associate Director, NEIDL. BU 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
Columbia College, New York, NY	AB	06/1958	Pre-Medicine
Harvard University, Boston MA	M.D.	06/1963	Medicine
State University of NY, Buffalo NY		06/1995	Intern and Resident in Medicine
National Institutes of Health, Bethesda MD		06/1997	Research Associate
Tufts University School of Medicine/New England Medical Center, Boston MA		06/1970	Fellow in Infectious Diseases

A. Personal Statement

I have considerable experience in collaborative international research and training programs. I have held major academic leadership positions over my career. I was the Founding Chief of the Division of Geographic Medicine and Infectious Diseases at Tufts Medical School and oversaw its participation in the Rockefeller Foundation's "Great Neglected Diseases Biomedical Research Network" from 1979-1988. For the next decade I was responsible for a Rockefeller Foundation funded research and training partnership with Christian Medical College, Vellore, India. From 1998 through 2003 I was Associate Director for International Research and Director of the Fogarty International Center at the NIH. I returned to Boston in 2004 as Associate Provost for Global Health at Boston University. Since 2009 I have been the Associate Director of the National Emerging Infectious Diseases Laboratory at BU, responsible for international collaborations. I am an internist with specialty training in infectious diseases and I practiced clinical medicine in academic medical centers from 1970-1998, first at Mt. Sinai in New York and then as Division Chief at Tufts in Boston. I have been a bench and field researcher in infectious diseases from the time I was a research associate at NIAID from 1965-1967, assigned to the SEATO Medical Research Laboratory in Bangkok, Thailand, until I closed my lab in 2000. My publication record is evidence of the productivity of my laboratory. I have personally led research projects in Asia, Africa, and Latin America with NIH and other sources of support, including a major NIAID International Collaboration for AIDS Research grant in the Democratic Republic of the Congo. I have been the PI of multiple NIH training grants and have mentored and overseen the training of dozens of fellows from the U.S. and other countries. I have also personally supervised capacity building programs in low and middle income countries, and as Director of the Fogarty International Center I conceptualized and implemented programs in global health, including both communicable and non-communicable diseases. I am committed to developing sustainable, fair, equitable, and quality partnerships and supporting mutually beneficial research between research institutions in developed countries with collaborating institutions in the developing world.

B. Positions and Honors

Positions and employment

1960 -61 Research Assistant, Department of Experimental Medicine, Hebrew University, Jerusalem, Israel
1965 -67 Research Associate, National Institute of Allergy and Infectious Diseases, NIH, Bethesda MD
1967 -70 Research Fellow in Infectious Diseases (NIAID T-32 training grant) and Chief Resident in Medicine (Infectious Diseases), Tufts-New England Medical Center, Boston MA
1970 -72 Assistant Professor of Medicine, Department of Medicine, Mount Sinai School of Medicine, NY NY
1972 -77 Associate Professor of Medicine, Department of Medicine, Mount Sinai School of Medicine, NY NY
1977 -78 Professor of Medicine, Department of Medicine, Mount Sinai School of Medicine, NY NY
1977 -78 Visiting Professor of Microbiology, Columbia University College of Physicians & Surgeons, NY NY
1979 -98 Professor of Medicine and Chief, Division of Geographic Medicine and Infectious Diseases, Tufts University School of Medicine and New England Medical Center, Boston MA
1998 -03 Director Fogarty International Center and Associate Director for International Research, Office of the Director, National Institutes of Health, Bethesda MD
2004 - Professor of Medicine and International Health, Boston University, Boston MA
2004 -09 Associate Provost for Global Health, Boston University Medical Center, Boston MA
2009 - Associate Director, National Emerging Infectious Diseases Laboratory at Boston University, and Director, Collaborative Core, Boston MA

Other Experience and Professional Memberships

National Research Council/National Academy of Sciences: Committee on International Relations, World Food and Nutrition Study, Member Study Team #9; Food and Nutrition Board; Committee on International Nutrition Programs, Member and Chair, Subcommittee on Interactions of Nutrition and Infection, Member Subcommittee on Nutrition and Diarrheal Diseases Control; Roundtable on Science and Technology for Sustainability, Member; Taskforce on Linking Knowledge to Action for Sustainable Development, Member; Institute of Medicine: Committee on Health, Biomedical Research and Development, Member; Committee on Issues and Priorities for New Vaccine Development, Member; Board on Global Health, Member and Co-Chair; Forum on Microbial Threats, Member;

National Academy of Medicine: Committee on Global Surveillance Systems for Emerging Infectious Diseases of Zoonotic Origin, Co-Chair; Committee on Integrating Clinical Research Into Epidemic Response: The Ebola Experience, Co-Chair; Committee on Enhancing Global Health Security Through International Biosecurity and Health Engagement Programs, Co-Chair

National Institutes of Health: NIDDK: US-Japan Cooperative Medical Sciences Program, Nutrition and Metabolism Panel, Member and Chairman; NIAID: Bacteriology and Mycology Study Section 1; Special Emphasis Panel, “Research for the Development of Vaccines, Adjuvants, Therapeutics, Immunotherapeutics, and Diagnostics for Biodefense and SARS; Indo-U.S. Vaccine Action Program, Chair US Delegation, NICHD, Global Network for Women’s and Infant Research; Multilateral Initiative on Malaria, Chair Secretariat

World Health Organization: Advisory Committee on Tobacco and Health; Advisory Committee on Health Research; TDR, Expert Advisory Panel on Health Science and Technology; Advisory Committee on Tropical Medicine (TropIKA), Chair; Strategy Advisory Committee on Stewardship for Infectious Diseases of Poverty; Global Report for Research on Infectious Diseases of Poverty, Member, Disease Reference Group 6

United States Agency for International Development: Nutrition Collaborative Research Support Program, External Evaluation Panel; Consultative Group on Vaccine Development, Member and Chair

Accreditation Council for Graduate Medical Education: Pre-review Committee for Internal Medicine Subspecialty Residency Programs (Infectious Diseases)

Infectious Diseases Society of America: Fellow; Council member; Society Awards Committee, Member

Wellcome Trust: Tropical Medicine Interest Group, Member; Joint Global Health Clinical Trials Committee, Member
Gates Foundation: Founding Board, Global Alliance to Improve Nutrition; Grand Challenges in Global Health, Scientific Advisory Board; MAL-ED Advisory Committee, Member; EED Consultation Committee, Chair
One Health Commission: Council of Advisors
Consortium of Universities for Global Health: Founding Board Member
National Center for Genetic Engineering and Biotechnology, National Science and Technology Development Agency, Government of Thailand: International Scientific Advisory Committee, Member
Institute for Healthcare Improvement: Scientific Advisory Committee, Member
Council on Health Research for Development (COHRED): Board of Directors, Chair
Nevin Scrimshaw International Nutrition Foundation: Board of Directors, Member, Vice-Chair
American Federation for Clinical Research: Member
American Society for Microbiology: Member and Fellow,
American Association for the Advancement of Science: Member
American Society for Clinical Investigation: Member
Association of American Physicians: Member
New York Academy of Sciences: Member

Honors

1972 -	American Board of Internal Medicine, Diplomate, Internal Medicine and Infectious Disease
1973 -76	Career Scientist Award, Health Research Council of the City of New York
1974 -79	Research Career Development Award, NIAID
1981	Oswald Avery Award, Infectious Diseases Society of America
1991	Heath-Clark Visiting Professor, University of London, School of Hygiene and Tropical Medicine
1997	Maxwell Finland Lectureship, Infectious Diseases Society of America
2000	Edward K. Barsky Award, Physicians Forum/Physicians for Social Responsibility
2002	Alexander Fleming Award, Infectious Diseases Society of America
2002	National Academy of Medicine, Elected Member
2009	Rama-Robbins Award, Indo-U.S. Vaccine Action Program, NIAID
2013	Distinguished Leadership Award, Consortium of Universities for Global Health

C. Contributions to Science

1. **I rediscovered Shiga toxin during my fellowship, while participating in a training program at the Institute of Nutrition for Central America and Panama in 1969.** A significant part of my research career has focused on Shiga toxin and its role in pathogenesis. The major recognized virulence factor of *Shigella* was its ability to invade gut epithelial cells; the previously described Shiga 'neurotoxin' was long forgotten until I showed that a protein produced by *Shigella dysenteriae* type 1 (Sd) caused inflammatory mucosal damage of the bowel and bloody inflammatory exudates similar to dysentery in a rabbit model. I later proved the two toxin activities were due to the same protein. My work resulted in purification of Shiga toxin (Stx), sequenced the binding subunit, identified its mammalian cell receptor, described its translocation to the cell cytoplasm via receptor mediated endocytosis, and identified its effects on vascular endothelium. This work paved the way to understand the pathogenesis of *E. coli* O157 and other serotypes associated with hemorrhagic colitis and hemolytic-uremic syndrome (HUS). My lab developed monoclonal antibodies essential for a rapid commercial diagnostic test for all Stx producing bacteria. I was principal investigator in all of these studies.

   a. **Keusch GT**, Grady GF, Mata LJ, McIver JM (1972). The pathogenesis of Shigella diarrhea. 1. Enterotoxin production by Shigella dysenteriae I. **J. Clin. Invest.** 51:1212-1218.

b. Donohue-Rolfe A, **Keusch GT**, Edson C, Thorley Lawson D, Jacewicz M (1984). Pathogenesis of Shigella diarrhea. IX. Simplified high yield purification of Shigella toxin and characterization of subunit composition and function by the use of subunit specific monoclonal and polyclonal antibodies. **J. Exp. Med.** 160:1767-1781.
c. Jacewicz M, Clausen H, Nudelman E, Donohue-Rolfe A, **Keusch GT** (1986). Pathogenesis of shigella diarrhea. XI. Isolation of a shigella toxin binding glycolipid from rabbit jejunum and HeLa cells and its identification as globotriaosylceramide. **J. Exp. Med.** 163:1391-1404.
d. Kandel G, Donohue-Rolfe A, Donowitz M, Keusch GT (1989). Pathogenesis of Shigella diarrhea. XVI. Selective targetting of Shiga toxin to villus cells of rabbit jejunum explains the effect of the toxin on intestinal transport. **J. Clin. Invest.** 84:1509-1517.

2. **In the 1980's I began work on the molecular pathogenesis of giardiasis and cryptosporidiosis.** We first developed a method to grow Giardia trophozoites in bulk using roller bottle culture, and used these parasites to Identify a trypsin-activated mannose-6-P lectin mediating binding to mammalian cell surfaces. These properties were consistent with activation in upper small bowel precisely where Giardia colonizes. We also discovered a Cryptosporidium parvum lectin which mediated binding to mammalian cells, and showed it is a member of a family of mucin-like glycoproteins containing α-N-acetylgalactosamine. Together these pioneering studies documented the role and relevance of carbohydrate binding ligands in the pathogenesis of intestinal protozoal infections. I was primary or co-investigator in all of these studies.
   a. Lev B, Ward H, **Keusch GT**, Pereira MEA (1986). Lectin activation in Giardia lamblia by host protease: A novel host parasite interaction. **Science** 232:71-73
   b. Ward HD, Alroy J, Lev BI, **Keusch GT**, Pereira MEA (1988). Analysis of surface carbohydrates of Giardia lamblia: Detection of N acetyl D glucosamine as the only saccharide moiety and identification of two distinct subsets of trophozoites by lectin binding. **J. Exp. Med.** 167:73 88.
   c. Hamer DH, Ward H, Tzipori S, Pereira MEA, Alroy JP, **Keusch GT** (1994). Attachment of Cryptosporidium parvum sporozoites to MDCK cells in vitro. **Infect Immun** 62:2208 13.
   d. Ortega-Barria E, Ward HD, **Keusch GT**, Pereira MEA (1994). Growth inhibition of the intestinal parasite Giardia lamblia by a dietary lectin is associated with arrest of the cell cycle. **J. Clin. Invest.** 94:2283-2288.

3. **I have made multiple contributions to the understanding of nutrition-infection interactions in laboratory and field research.** I developed a rat model of protein energy malnutrition and demonstrated macrophage functional abnormalities, including chemotaxis, phagocytosis, and intracellular bactericidal activity. Together with colleagues in Guatemala we documented multiple host defense defects in malnourished children including impaired neutrophil function, decreased serum opsonic activity, complement deficiency, and T-cell deficits, and their reversal with nutritional interventions. Subsequent studies in Zaire (now DRC) in AIDS patients on the pathogenesis of wasting syndrome revealed markedly elevated pro-inflammatory cytokine levels that could drive metabolic shifts underlying cachexia. HIV-infected but clinically stable non-wasted subjects also had high pro-inflammatory cytokine levels, however this was countered by elevated levels of the antagonist cytokines IL-1RA and TNFα-soluble receptor p55 at a molar ratio known to block inflammatory effects of IL-1β and TNFα in vitro. This was the first biologically plausible mechanism to explain the preservation of weight and body composition in long term clinical non-progressors.
   a. **Keusch GT**, Douglas SD, Hammer G, Braden K (1978). Macrophage antibacterial functions in experimental protein calorie malnutrition. II. Cellular and humoral factors for chemotaxis, phagocytosis, and intracellular bactericidal activity. **J. Infect. Dis.** 138:134

b. Cruz JR, Chew F, Fernandez RA, Torun B, Goldstein AL, **Keusch GT** (1987). Effects of nutritional recuperation on E rosetting lymphocytes and in vitro response to thymosin in malnourished children. **J. Ped. Gastro. Nutr.** 6:350-358.
c. Thea DM, Porat R, Khondi N, Matela B, St. Louis ME, Kaplan G, Dinarello CA, **Keusch GT** (1996). Relationship of cytokine and cytokine antagonist plasma levels to disease progression in African women with HIV-1 infection. **Ann Int Med** 124:757-762.
d. Kotler DP, Thea DM, Heo M, Allison DB, Engelson ES, Wang J, Pierson RN Jr, St Louis M, **Keusch GT** (1999). Relative influence of sex, race, environment, and HIV infection on body composition in adults. **Am J Clin Nutr** 69:432-439.

4. **I have helped the development of global health as a field of inquiry.** At the NIH I shaped the agenda for a systematic exploration of the importance of micronutrients on susceptibility to and outcome of infectious diseases, and led changes in the management of intellectual property to improve outcomes for low and middle income countries. I have promoted the inclusion of low and middle income countries in the setting of priorities and governance for research, and called for a new investment and partnerships for a global health system. I initiated research and training in diverse topics such as ethics, stigma, macroeconomics and health, and environment and health and economic development. I played a lead role in the creation of the Consortium of Universities for Global Health.
   a. **Keusch GT** (2000). The National Institutes of Health agenda for international research in micronutrient nutrition and infection interactions. **J. Infect. Dis.** 182 (Suppl 1):S139-S142.
   b. **Keusch GT** (2004). Intellectual Property and Licensing Impacts on Global Public Goods for Health: Options for public sector and academic leadership. **IP Strategy Today** 10:1-22.
   c. **Keusch GT**, Medlin CA (2003). Tapping the power of small institutions. **Nature** 422: 561-562.
   d. **Keusch GT**, Kilama WL, Moon S, Szlezák NA, Michaud CM (2010). The Global Health System: Linking Knowledge with Action - Learning from malaria. **PLoS Medicine** 7:e1000179.

Complete List of Published Work in MyBibliography
https://www.ncbi.nlm.nih.gov/pubmed/?term=keusch+gt

D. Research Support

Ongoing Research Support

5UC7 AI09532-03 R. Corley (PI) 06/01/16 – 05/31/20
National Emerging Infectious Diseases Laboratories Operations
The award provides core support for this NBL and its mission to study pathogenesis of emerging and re-emerging infectious diseases and develop diagnostics, drugs, vaccines, and treatments against them, and to support NIAID's strategic plan for biodefense research.
Role: Associate Director and Director, Collaborative Research Core

Completed Research Support (last 3 years only)

1UC7 AI0953215 R. Corley (PI) 06/01/14 – 05/31/16
National Emerging Infectious Diseases Laboratories Operations
This award provided core support for this NBL and its mission to study pathogenesis of emerging and re-emerging infectious diseases and develop diagnostics, drugs, vaccines, and treatments against them, and to support NIAID's strategic plan for biodefense research.
Role: Associate Director and Director, Collaborative Research Group Core

OMB No. 0925-0001 and 0925-0002 (Rev. 09/17 Approved Through 03/31/2020)

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: Corley, Ronald B.

eRA COMMONS USER NAME (credential, e.g., agency login): (b) (6)

POSITION TITLE: Director, National Emerging Infectious Diseases Laboratories at Boston University
Professor and Chair, Department of Microbiology, Boston University 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
Duke University, Durham, NC	B.S.	05/1970	Zoology
Duke University, Durham, NC	Ph.D.	05/1975	Microbiology & Immunology

A. Personal Statement

My role in the current application is as Contact Co-Principal Investigator. My responsibilities will include the overall administration of the Center, including monitoring of scientific progress and ensuring effective communication between EIDRC components, ensuring that budgeted funds are appropriately used, and to manage any changes that occur as the result of interactions with the EIDRC CC and with NIAID staff. I have over 4 decades of research and management experience to bring to the administration of complex applications, including the EIDRC. I have extensive experience in research in immunology and in the interactions between immune cells and viruses in experimental systems. I came to Boston University in 1994 as Chair of Microbiology, and built a research-intensive department focusing on RNA viral biology and pathogenesis. Building in these areas have continued as Director of the NEIDL. My experience in recruiting and team building will help foster a sense of shared commitment throughout the organization. I have experience in building multidisciplinary teams of faculty for innovative projects, and also foster a sense of shared commitment in team building. Because of my experience in working with faculty in diverse research fields, I was appointed Associate Provost for Research for the Boston University Medical Campus, a position in which I gained experience in working in complex organizations and dealing with diverse constituencies to achieve common goals. Since becoming director of the NEIDL, I have continued to work toward building the NEIDL from an institute that not only carries out emerging infectious diseases research at all biosafety levels, but also engages internationally for the global public health.

B. Positions and Honors

Positions and Employment

1975 -77 Member, Basel Institute for Immunology, Basel, Switzerland
1977 -79 Assistant Medical Research Professor, Department of Microbiology and Immunology, Duke University Medical Center, Durham, NC 27710
1977, Visiting Scientist, Basel Institute for Immunology, Basel, Switzerland
1979 Visiting Scientist, Basel Institute for Immunology, Basel, Switzerland
1980 Visiting Scientist, Basel Institute for Immunology, Basel, Switzerland
1978 -94 Member, Comprehensive Cancer Center, Duke University, Durham, NC
1980 -82 Assistant Professor of Immunology, Duke University School of Medicine

1982 -94 Associate Professor of Immunology, Duke University School of Medicine
1994 - Professor and Chair, Department of Microbiology, Boston University School of Medicine
2007 -14 Associate Director, National Emerging Infectious Diseases Laboratories Institute, Boston University
2009 -14 Associate Provost for Research, Boston University Medical Campus
2014 - Director, National Emerging Infectious Diseases Laboratories Institute, Boston University

Other Experience and Professional Membership

1988 -92 Immunobiology Study Section, NIH
1996 -00 Immunobiology Study Section, NIH
2004 Immunobiology Study Section, NIH
1978 - American Association of Immunologists; AAI program committee, 1991-1994
1991 - American Society for Microbiology
1992 -93 Special Reviewer, NIH SBIR Study Section
1997 -98 Chair, Cell Biology and Immunology Predoctoral Committee, HHMI/NRC
2000 Chair, Cell Biology and Immunology Predoctoral Committee, HHMI/NRC
2001 -03 Member, Research Training Fellowships for Medical Students Committee, HHMI
2005 Member, Research Training Fellowships for Medical Students Committee, HHMI
2002 Advisory Panel, Alliance for Lupus Research, NY
2005 -06 Chair, "Med into Grad Initiative" Review Committee, HHMI
2007 Member, NIH Review Panels on "B Cell Immunology and Protective HIV-1 Vaccines"
2009, 10 Member, NIH Review Panels on "Basic HIV Discovery Research"
2011 -13 Member, *ad hoc* Review Panel, "Immune Mechanisms of Virus Control" Program, NIH/NIAID
2011 -14 SmithGroup JJR Science & Technology Advisory Board
2016, 17 Reviewer, National Research Foundation, Competitive Research Program, Singapore
Ongoing: Security Risk Assessment (SRA) cleared by the FBI/CJIS through CDC for access to Biological Select Agents and Toxins (BSAT)
Ongoing: BSL-4 suit-trained and certified, Boston University

Honors

1979 -84 Leukemia Society of America Scholar
2015 Fellow of the American Association for the Advancement of Science

C. Contributions to Science

1. **Innate role of B lymphocytes in antigen capture and transport.** A body of work had shown that secreted IgM antibodies had unique functions in concentrating pathogens and antigen into secondary lymphoid organs, and prevented dissemination into vital organs. We sought to understand how IgM was responsible for these activities, and to understand the consequences for the immune system. We demonstrated that IgM immune complexes became concentrated onto marginal zone B cells, which then transported these complexes to follicular dendritic cells for deposition. This suggested an unappreciated innate role for this subset of B lymphocytes in the early steps of initiation of primary immune responses. A role for orchestrated transport of antigen and immune complexes in secondary lymphoid organs is now widely accepted as early events in immune responses.

   a. Ferguson AR, **Corley RB** (2005). Accumulation of marginal zone B cells and accelerated loss of follicular dendritic cells in NF-κB p50-deficient mice. **BMC Immunology** 6:8.
   b. Ferguson AR, Youd ME, **Corley RB** (2004). Marginal zone B cells transport and deposit IgM-containing immune complexes onto follicular dendritic cells. **Int. Immunol**. 16: 1411-1422 ("featured article of the month").
   c. Youd ME, Ferguson AR, **Corley RB** (2002). Synergistic roles of IgM and complement in antigen trapping and follicular localization. **Eur. J. Immunol.** 32: 2328-2337.

2. **The function of alternative forms of IgM antibodies in immune responses.** Data from our laboratory and others had indicated that IgM antibodies were not always secreted as pentameric molecules with J chain, but little evidence existed to indicate if these antibodies shared functions with pentameric IgM, or if they had unique functions. We demonstrated that two alternative forms of IgM, IgM hexamers and IgM monomers, had discrete activities. Hexamers active complement far more efficiently than pentamers and could be deleterious in certain autoimmune diseases, while monomers did not fix complement, lacked the ability to function in antigen trapping, and could also accelerate disease manifestations in autoimmune prone mice. These data supported the important role for strict quality control standards in the assembly and secretion of IgM antibodies for maintenance of proper homeostasis in the immune system.
   a. Youd ME, Luus L, **Corley RB** (2004). IgM monomers accelerate disease manifestations in autoimmune-prone *fas*-deficient mice. **J. Autoimmunity** 23:333-343.
   b. Hughey CT, Brewer JW, Colosia AD, Rosse WF, **Corley RB** (1998). Production of IgM hexamers by normal and autoimmune B cells: Implications for the physiologic role of hexameric IgM. **J. Immunol.** 161: 4091-4097.
   c. Brewer JW, **Corley RB** (1997). Late events in assembly regulate the polymeric structure and biological activity of secretory IgM. **Mol. Immunol.** 34: 323-331.
   d. Brewer JW, Randall TD, Parkhouse RME, **Corley RB** (1994). IgM hexamers? **Immunol. Today** 15: 165-168.

3. **Quality control in modulating the assembly and secretion of IgM.** Prior to these studies there was controversy in the field as to how J chain was added to assembling IgM, and whether the addition of J chain was responsible for catalyzing assembly of IgM into polymers. Where assembly occurred was also controversial. We demonstrated, however, that IgM assembly is regulated in the endoplasmic reticulum by a process involving thiol regulation. Further, J chain plays no role in mediated IgM assembly, and its addition is a terminally late step in the production of polymeric IgM. To complete these studies, we made use of various biochemical assays including pulse chase experiments. We also cloned and expressed J chain to demonstrate its role in modulating polymer assembly, and this work remains the definitive description of IgM assembly.
   a. Reddy PS, **Corley RB** (1999). The contribution of ER quality control to the biologic functions of secretory IgM. **Immunol. Today** 20: 582-588.
   b. Brewer JW, **Corley RB** (1996). Quality control in protein biogenesis: thiol-mediated retention monitors the redox state of proteins in the endoplasmic reticulum. **J. Cell Sci.** 109:2383-2392.
   c. Brewer JW, Randall TD, Parkhouse RME, **Corley RB** (1994). Mechanism and subcellular localization of secretory IgM polymer assembly. **J. BIol. Chem.** 269: 17338-17348.
   d. Randall TD, Brewer JW, **Corley RB** (1992). Direct evidence that J chain regulates the polymeric structure of IgM in antibody secreting B cells. **J. Biol. Chem.** 267: 18002-18007.

4. **Defining mouse mammary tumor virus as an endogenous superantigen, and demonstrating the role of B lymphocytes in the MMTV life cycle.** Prior to these studies there was evidence for the existence of that endogenous superantigens which played important roles in shaping the T cell repertoire in mice, but the identity and nature of these superantigens were unknown. During a differential subtraction cloning process, we identified a mouse mammary tumor virus, Mtv-9, as a differentially expressed gene during activation of B cells, and later linked this to superantigens and suggested a role for B cells in the MMTV life cycle.
   a. Sharma S, King LB, **Corley RB** (1988). Molecular events during B lymphocyte differentiation. Induction of endogenous mouse mammary tumor proviral *env* transcripts following B cell stimulation. **J. Immunol.** 141: 2510-2518.

b. King LB, Lund FE, White DA, Sharma S, **Corley RB** (1990). Molecular events in B lymphocyte differentiation. Inducible expression of the endogenous mouse mammary tumor proviral gene, *Mtv-9*. **J. Immunol.** 144: 3218-3227.
c. King LB, **Corley RB** (1990). Lipopolysaccharide and dexamethasone induce mouse mammary tumor proviral gene expression and differentiation in B lymphocytes through distinct regulatory pathways. **Mol. Cell. Biol**. 10: 4211-4220.
d. **Corley RB**, Lund FE (1991). Endogenous superantigens and retroviruses: "who's zooming who?". **Current Biol.** 1: 278-280.

5. **Studies on emerging viruses.** Emerging viruses present a number of interesting and important problems in understanding how they are transmitted, how they disseminate through the body, and in determining interruption strategies that could be used to combat these pathogens. Collaborative work in the NEIDL represents some aspects addressed at these concerns.
   a. Olejnik J, Ryabchikova E, **Corley RB**, Mühlberger E (2011). Intracellular events and cell fate in filovirus infection. **Viruses** 3: 1501-1531.
   b. Schultz MJ, Isern S, Michael SF, **Corley RB**, Connor JH, Frydmann HM (2017). Variable inhibition of Zika virus replication by different *Wolbachia* strains in mosquito cell cultures. **J. Virol.** 91(14). pii: e00339-17. doi: 10.1128/JVI.00339-17.

Published Work in My Bibliography:

http://www.ncbi.nlm.nih.gov/pubmed/?term=Corley+RB

D. Research Support

Ongoing Research Support

5UC7 AI095321-06 R.B. Corley (PI) 06/01/14 – 05/31/2021
National Emerging Infectious Diseases Laboratories Operations
The award provides core support for this NBL, the mission of which is to study and develop diagnostics, drugs, vaccines, and treatments against emerging and re-emerging infectious diseases and to support NIAID's strategic plan for biodefense research.
Role: NEIDL Director and Director, Immunology Core

OMB No. 0925-0001 and 0925-0002 (Rev. 09/17 Approved Through 03/31/2020)

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: Sims, Amy Catherine

eRA COMMONS USER NAME (credential, e.g., agency login): (b) (6)

POSITION TITLE: Research Associate Professor

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 Alabama at Birmingham, AL	B.S.	05/1995	Molecular Biology
Vanderbilt University, TN	Ph.D.	05/2001	Microbiology & Immuno.
Duke University, NC	Postdoctoral	08/2002	RNA/Protein Interaction
University of North Carolina at Chapel Hill, NC	Postdoctoral	10/2005	Virology

A. Personal Statement

The identification of highly pathogenic human coronaviruses (SARS-CoV and MERS-CoV) underscored the importance of understanding how viruses emerge from zoonotic reservoirs and how these emergent viruses replicate and cause pathogenesis in the new host. My research has focused on several key aspects of these questions by working to understand the cellular tropism of SARS-CoV and MERS-CoV in primary human lung cells, how host genetic pathways and gene networks affect virus replication and pathogenesis and how manipulating the coronavirus genome changes the host innate immune response to virus infection. I have more than 15 years' experience working with highly pathogenic human coronaviruses primarily as part of large multi-institutional projects that require constant lines of communication and data sharing to be successful. I have worked closely with Dr. Baric to lead and manage at least 4 large multi-institutional projects/awards and am familiar with all of the day to day and long term requirements for a successful collaboration. This project will extend an existing collaboration with Dr. Daszak and team at EcoHealth and world-wide and the required lines of communication have already been established to make this application a success.

Relevant publications: My most relevant work to date focuses on using primary human lung cells as culture models for human coronavirus strains, which can be used to characterize the virus strains we propose to study in the current proposal.

1. **Sims A***, Sheahan TP*, Graham RL, Menachery VD, Gralinski LE, Case JB, Leist SR, Pyrc K, Feng JY, Trantcheva I, Bannister R, Park Y, Babusis D, Clarke MO, Mackman RL, Siegel D, Ray AS, Cihlar T, Jordan R, Denison MR, Baric RS (2017). Broad-spectrum antiviral GS-5734 inhibits both epidemic and zoonotic coronaviruses. **Sci Transl Med** 28;9(396). * co-first authors

2. Becker MM, Graham RL, Donaldson EF, Rockx B, **Sims A**, Sheahan T, Pickles R, Corti D, Johnston RE, Baric RS, Denison MR (2008). Platforms for the Synthetic Reconstitution of Noncultivable Zoonotic Viruses. **PNAS** 105(50): 19944-49.

3. Scobey T, Yount BL, **Sims A**, Donaldson EF, Agnihothram SS, Menachery VD, Graham RL, Swanstrom J, Bove PF, Kim JD, Grego S, Randell SH, Baric RS (2013). Reverse genetics with a full-

length infectious cDNA of the Middle East respiratory syndrome coronavirus. **PNAS** 1;110(40):16157-62.

4. Menachery VD, Yount BL, **Sims A**, Agnihothram S, Gralinski LE, Plante JA, Graham RL, Scobey T, Royal S, Pickles RJ, Randell SH, Lanzavecchia A, Marasco WA, Shi Z-L, Baric RS. (2016). SARS-like WIV1-CoV poised for human emergence. **PNAS** 15:113(11):3048-53.

B. Positions and Honors

Positions and Employment

1993 American Society of Microbiology Undergraduate Research Award
1994 Albert Einstein College of Medicine Summer Student Award
1996 -01 Graduate Student, Laboratory of Mark Denison, Vanderbilt University, Nashville, TN
1999 Dissertation Enhancement Award, Vanderbilt University
2001 -02 Postdoctoral Fellow, Duke University, Durham, NC
2002 -04 Infectious Disease Pathogenesis Training Grant Fellow (NIH/NIAID 5T32AI07151-27)
2002 -05 Postdoctoral Fellow, University of North Carolina at Chapel Hill
2005 -17 Research Assistant Professor, Department of Epidemiology, University of North Carolina
2017- Research Associate Professor, Department of Epidemiology, University of North Carolina Hons.

C. Contributions to Science

1. **In vitro models for emerging human respiratory viruses.** Finding suitable in vitro models for studying newly identified or emerged human respiratory viruses can be a challenge. Primary cells isolated from the human conducting airway can be cultured at an air liquid interface and following maturation recapitulate the morphology of the airway epithelium. These cultures provide a unique in vitro model and for one human coronavirus, HKU1, provide the only in vitro model for studying this virus.

   a. **Sims A**, Pyrc K, Dijkman R, Jebbink M, Long C, Deming D, Donaldson E, Vabret A, Baric R, van der Hoek L, Pickles R (2010). Culturing the unculturable: human coronavirus HKU1 infects, replicates, and produces progeny virions in human ciliated airway epithelial cell cultures. **J.Virol**. 84(21):11255-63.

   b. **Sims A**, Baric RS, Yount B, Burkett SE, Jeffers L, Pickles RJ (2005). SARS-CoV infection of human ciliated airway epithelium: the role of the ciliated cell in viral spread in the conducting airways of the lung. **J Virol**. 79(24):15511-15524.

   c. Huang X, Dong W, Milewska A, Golda A, Qi Y, Zhu Q, Marasco W, Baric R, **Sims A***, Pyrc K*, Li W, Sui J* (2015). HCoV-HKU1 Spike protein uses O-acetylated sialic acid as an attachment receptor determinant and employs HE protein as a receptor-destroying enzyme. **J Virol**. 89(14):7202-13. *indicates co-senior authorship

2. **Development of coronavirus infectious clones**. The isolation of coronavirus infectious clones has drastically increased the understanding of how specific genes or open reading frames affect replication and pathogenesis as well as identifying sets of mutations that can make coronavirus genomes recombination proof live vaccine vector candidates.

   a. Thornbrough JM, Jha BK, Yount B, Goldstein SA, Li Y, Elliott R, **Sims A**, Baric RS, Silverman RH, Weiss SR (2016). Middle East Respiratory Syndrome Coronavirus NS4b Protein Inhibits Host RNase L Activation. **MBio** 29;7(2).

   b. Menachery VD, Gralinski LE, Mitchell HD, Dinnon KH 3rd, Leist SR, Yount BL, Graham RL, McAnarney ET, Stratton KG, Cockrell AS, Debbink K, **Sims A**, Waters KM, Baric RS (2017). Middle East Respiratory Syndrome Coronavirus Nonstructural Protein 16 is Necessary for Interferon Resistance and Viral Pathogenesis. **mSphere** 2(6). e00346-17.

3. **Research to determine the genes that regulate the host virus interaction in primary human lung cells following highly pathogenic human coronavirus infection**. In collaboration with researchers at the University of Wisconsin Madison and Pacific Northwest National Laboratories, I have been working to identify specific host gene networks and pathways that regulate lethal human respiratory virus replication and pathogenesis. Specifically, I was interested in determining genes that regulate SARS-CoV and MERS-CoV replication in human cell lines, models of the human conducting airway and mouse models.

   a. **Sims A***, Tilton SC, Menachery VD, Gralinski LE, Schäfer A, Matzke MM, Webb-Robertson BM, Chang J, Luna ML, Long CE, Shukla AK, Bankhead III AR, Burkett SE, Zornetzer G, Tseng CK, Metz TO, Pickles R, McWeeney S, Smith RD, Katze MG, Waters KM, Baric RS (2013). Release of SARS-CoV Nuclear Import Block Enhances Host Transcription in Human Lung Cells. **J Virol**. 87(7):3885-902.

   b. Menachery VD*, Eisfeld AJ, Josset L, **Sims A**, Schaefer A, Proll S, Fan S, Li C, Neumann G, Tilton SC, Chang J, Gralinski LE, Long C, Green R, Matzke MM, Webb-Robertson BJ, Shukula AK, Burkett S, Metz TO, Pickles R, Smith RD, Waters KM, Katze M, Kawaoka Y, Baric RS (2014). Pathogenic influenza and coronaviruses utilize similar and contrasting approaches to control global ISG responses. **MBio** 5(3): e01174-14.

   c. Aevermann BD*, Pickett BE, Kumar S, **Sims A**, Sova P, Tam VC, Tchitchek N, Thomas PG, Tilton SC, Totura A, Wang J, Webb-Robertson BJ, Wen J, Weiss J, Yang F, Yount B, Zhang Q, McWeeney S, Smith RD, Waters KM, Kawaoka Y, Baric R, Katze AA, Scheuermann R (2014). A Comprehensive Collection of Systems Biology Data Characterizing the Host Response to Viral Infection. **Nature's Scientific Data** 1:140033.

   d. Menachery VD*, Schäfer A*, Burnum-Johnson KE, Mitchell HD, Eisfeld AJ, Walters KB, Nicora CD, Purvine SO, Casey CP, Monroe ME, Weitz KK, Stratton KG, M. Webb-Robertson BJ, Gralinski LE, Metz TO, Smith RD, Waters KM, Kawaoka Y^, Baric RS^, **Sims A**^ (2018). MERS-CoV and H5N1 influenza virus antagonize antigen presentation by altering the epigenetic landscape.**PNAS** 115(5):E1012-E1021. * co-first authors and ^ co-senior authors

Complete List of Published Work in NCBI MyBibliography:
http://www.ncbi.nlm.nih.gov/myncbi/collections/bibliography/49189460/

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

Ongoing Research Support

U19 AI142759 CETR — Whitley (PI) — 03/07/19 - 02/29/24
Antiviral Drug Discovery and Development Center
The specific aims of the proposal will identify small molecule inhibitors of CoV fidelity and RNA capping, define their mechanism of action, and determine their efficacy against SARS-CoV and across CoV families using in vivo mouse models of acute and persistent CoV disease.
Role: Investigator

U19 AI109761 CETR — Lipkin (PI) — 03/01/14 - 02/28/20
Diagnostic and Prognostic Biomarkers for Viral Severe Lung Disease
The overall goal of this program is to develop new platform technologies that use functional genomics as diagnostic and prognostic indicators of severe end stage lung disease following virus infection of the lung.
Role: Investigator

R01 AI110700 — Baric (PI) — 04/01/15 - 03/31/20
Mechanisms of MERS-CoV Entry, Cross-species Transmission and Pathogenesis

The overall goal is to build a comprehensive understanding of the molecular mechanisms guiding group 2c CoV receptor recognition, entry and pathogenesis.
Role: Investigator

1R01 AI132178-01 Sheahan/Baric (MPI) 08/06/17 - 07/31/22
Broad-spectrum antiviral GS-5734 to treat MERS-CoV and related emerging CoV
In partnership with Gilead Sciences, we aim to accelerate the preclinical development of GS-5734 and promote IND licensure. We define the pharmacokinetics, pharmacodynamics, resistance profile, efficacy breadth and mechanism of action of GS-5734 against MERS-CoV and related emerging CoV.
Role: Investigator

Completed Research Support (last 3 years only)

(b) (4) Kawaoka (PI) 06/01/14 - 05/31/16
Epigenetic Regulation of Interferon-Stimulated Genes Following MERS-CoV Infection
The overriding hypothesis of this supplemental application is that MERS-CoV and H5N1 manipulate host epigenetic programs to specifically down-regulate certain classes of ISGs, which likely antagonize virus replication efficiency in vitro. The goal is to develop systems biology datasets and unbiased modeling algorithms to deconvolute the complex pathogen-host interactions that regulate severe disease outcomes following infection and identify common host pathways/genes that can be exploited for therapeutic control.
Role: Project PI

U19-AI100625 Baric (PI) 08/05/12 - 07/31/17
Systems Immunogenetics of Biodefense Pathogens in the Collaborative Cross
Specific Aims: In this proposal, we are utilizing the Collaborative Cross (CC), a novel panel of reproducible, recombinant inbred (RI) mouse lines to identify genes and gene interactions, which regulate the induction, kinetics, and magnitude of the innate, inflammatory and adaptive arms of the immune response following virus infection. Specifically, we will develop novel modeling algorithms to predict and validate the causal relationships between natural genetic variation and host signaling networks, immune cell recruitment, and immune function.
Role: Investigator and Co-Education Director

(b) (4) Kawaoka (PI) 06/01/16 - 05/31/17
Systems Virology for MERS-CoV in vivo
The goal is to develop systems biology datasets and unbiased modeling algorithms to deconvolute the complex pathogen-host interactions that regulate severe disease outcomes following infection and identify common host pathways/genes that can be exploited for therapeutic control. These studies will build on our current data set by collecting data sets for MERS-CoV in vivo.
Role: Project PI

(b) (4) Sims (PI) 06/07/17 - 06/06/18
(b) (4)
The overall goal of this project is to test (b) (4) protease inhibitor/interferon cocktails in comparison to and with nucleoside analog compounds to determine the best course of treatment for patients infected with highly pathogenic human coronaviruses.

U19-AI106772-01 Kawaoka (PI) 06/01/13 - 05/31/19
MERS-CoV Supplement for (b) (4)
The proposed studies will provide a more detailed look at the intracellular environment by taking "snapshots" of the lipids, metabolytes, and proteins present during viral infection time courses. These assays will allow us to

determine the innate immune response occurring immediately following virus infection and to determine how the virus and cell interact over a 72-hour window.
Role: Project PI