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: Samuels, D. Scott

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

POSITION TITLE: 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
Colorado College, Colorado Springs, CO	B.A.	06/1983	Biology
University of Arizona, Tucson, AZ	Ph.D.	02/1991	Molecular and Cellular Biology
Rocky Mountain Laboratories, Hamilton, MT	Postdoctoral Fellow	08/1995	Bacterial Pathogenesis

A. Personal Statement

I have worked on the Lyme disease spirochete, *Borrelia burgdorferi*, since 1991. My laboratory primarily studies the molecular mechanisms by which *B. burgdorferi* persists in its tick vector, transmits to its vertebrate host and establishes an infection, with an emphasis on the regulation of gene expression. Our approach combines molecular genetics, biochemistry, transcriptomics, and the tick-mouse model. I was the first researcher to transform *B. burgdorferi* and my laboratory continues to innovatively fashion molecular tools to genetically manipulate the spirochete, including developing an inducible gene expression system that functions *in vivo*. We have made several seminal contributions toward understanding the microbiology of *B. burgdorferi* and the pathogenesis of Lyme disease: discovery of a novel architectural DNA-binding protein, discovery of a new bacteriophage and horizontal gene transfer by transduction, and discovery of the molecular mechanisms used to regulate gene expression in response to environmental signals, including a small RNA and a novel RNA chaperone. We have established the murine model of Lyme disease and we have cycled *B. burgdorferi* between ticks and mice. I have mentored many postdoctoral fellows, graduate students, undergraduate researchers, and technicians. In addition, I successfully completed several projects funded by the NIH and other granting agencies. Furthermore, I edited a book on *Borrelia* and wrote several review articles, including an *Annual Review of Microbiology*, an *Annual Review of Genetics*, and a *Cellular Microbiology* Microreview.

1. Samuels, D.S., Mach, K.E. and Garon, C.F. (1994) Genetic transformation of the Lyme disease agent *Borrelia burgdorferi* with coumarin-resistant *gyrB*. *J. Bacteriol.* **176:** 6045-6049.
2. Samuels, D.S. (2011) Gene regulation in *Borrelia burgdorferi*. *Annu. Rev. Microbiol.* **65:** 479-499.
3. Brisson, D., Drecktrah, D., Eggers, C.H., and Samuels, D.S. (2012) Genetics of *Borrelia burgdorferi*. *Annu. Rev. Genet.* **46:** 515-536.
4. Caimano, M.J., Drecktrah, D., Kung, F., and Samuels, D.S. (2016) Interaction of the Lyme disease spirochete with its tick vector. *Cell. Microbiol.* **18:** 919-927.

B. Positions and Honors

Positions and Employment

1983-1984	Research Assistant, University of Pittsburgh, Department of Biological Sciences, Pittsburgh, PA
1984-1991	Ph.D. Candidate, University of Arizona, Department of Molecular and Cellular Biology, Tucson, AZ

1991-1995	Intramural Research Training Award Fellow, National Institutes of Health, National Institute of Allergy and Infectious Disease, Hamilton, MT
1995-1999	Assistant Professor, University of Montana, Division of Biological Sciences, Missoula, MT
1999-2008	Associate Professor, University of Montana, Division of Biological Sciences, Missoula, MT
2006-	Chair, University of Montana, Institutional Biosafety Committee, Missoula, MT
2008-	Professor, University of Montana, Division of Biological Sciences, Missoula, MT

Other Experience and Professional Memberships

1985-	Member, American Association for the Advancement of Science
1993-	Member, American Society for Biochemistry and Molecular Biology
1993-	Member, American Society for Microbiology
2003	Temporary Member, NIH Microbial Physiology and Genetics 2 (MBC2) Study Section
2004	Temporary Member, NIH Bacteriology and Mycology 1 (BM1) Study Section
2004	Member, CDC Research on the Laboratory Diagnosis, Immunology, and Pathogenesis of Lyme Disease Study Section
2004-2011	Member, NIH Topics in Bacterial Pathogenesis (IDM-A) Study Section
2006, 2008	Temporary Member, NIH Bacterial Pathogenesis (BACP) Study Section
2008	Member, NIH Member Conflicts in Microbiology (IDM-Q) Study Section
2009	Vice Chair, NIH Topics in Microbiology (IDM-S) Study Section
2009	Member, NIH K99 Pathway to Independence (BRT-9) Study Section
2011	Member, NIH Bacterial Pathogenesis Review (IDM-A) Study Section
2012-	Editorial Advisory Board, *Molecular Microbiology*
2012	Member, NIH Microbial Pathogens AREA Review (IDM-S) Study Section
2013	Member, NIH Topics in Bacterial Pathogenesis (IDM-B and IDM L) Study Section
2013-2018	Guest Editor, *PLOS Pathogens*
2014	Member, NIH Topics in Bacterial Pathogenesis (IDM-B) Study Section
2014	Member, NIH Bacterial Pathogenesis (BACP-W) Study Section
2014-	Editorial Advisory Board, *Infection and Immunity*
2016	Member, NIH Topics in Bacterial Pathogenesis (IDM-B) Study Section
2016-2018	Vice Chair, Biology of Spirochetes Gordon Research Conference
2017	Member, DOD Congressionally Directed Medical Research Programs (CDMRP), Tick Borne Disease Research Program (TBDRP), Treatment and Prevention (TP) Study Section
2017	Temporary Member, NIH Bacterial Pathogenesis (BACP) Study Section
2017	Member, NIH Bacteria Gene Expression (GGG-E) Study Section
2018	Member, NIAID Investigator Initiated Program Project Applications (RRS-M) Study Section
2018-	Associate Editor, *PLOS Pathogens*
2018	Member, NIH Topics in Bacterial Pathogenesis (IDM-B) Study Section
2018	Temporary Member, NIH Bacterial Pathogenesis (BACP) Study Section
2018-2020	Chair, Biology of Spirochetes Gordon Research Conference

Honors

1979-1981	Regent's Scholarship, New York State
1983	Phi Beta Kappa, Colorado College
1984-1986	Graduate Academic Scholarship, University of Arizona
1987-1991	National Research Service Award, National Cancer Institute
1994	Fellow Travel Grant, American Society for Microbiology
1998, 2001, 03, 05, 11, 14	Merit Award, University of Montana
2002	Sabbatical, University of Montana
2012	The Paul Lauren Undergraduate Research Faculty Mentor Award, University of Montana

C. Contributions to Science

1. As a postdoctoral fellow, I was the first researcher to transform *B. burgdorferi*. My laboratory continues to develop and utilize state-of-the-art mutagenesis techniques. We have freely distributed all of the genetic tools and provided support when necessary. These include selectable markers, shuttle vectors, counterselectable markers, and an inducible gene system that functions *in vivo* in the tick-mouse model. The molecular genetics has proved to be a powerful approach toward understanding the microbiology of *B. burgdorferi* and the pathogenesis of Lyme disease.
   a. Samuels, D.S., Mach, K.E. and Garon, C.F. (1994) Genetic transformation of the Lyme disease agent *Borrelia burgdorferi* with coumarin-resistant *gyrB*. *J. Bacteriol.* **176:** 6045-6049. PMCID: PMC196823.
   b. Eggers, C.H., Caimano, M.J., Clawson, M.L., Miller, W.G., Samuels, D.S., and Radolf, J.D. (2002) Identification of loci critical for replication and compatibility of a *Borrelia burgdorferi* cp32 plasmid and use of a cp32-based shuttle vector for expression of fluorescent reporters in the Lyme disease spirochaete. *Mol. Microbiol.* **43:** 281-296. PMID: 11985709.
   c. Gilbert, M.A., Morton, E.A., Bundle, S.F., and Samuels, D.S. (2007) Artificial regulation of *ospC* expression in *Borrelia burgdorferi*. *Mol. Microbiol*. **63:** 1259-1273. PMID: 17257307.
   d. Drecktrah, D., Douglas, J.M., and Samuels, D.S. (2010) Use of *rpsL* as a counterselectable marker in *Borrelia burgdorferi*. *Appl. Environ. Microbiol.* **76:** 985-987. PMCID: PMC2813015.

2. We have had extensive experience in the biochemical and genetic analyses of protein function, particularly proteins that bind nucleic acids. These include DNA topoisomerases, architectural DNA-binding proteins, and RNA chaperones. We discovered Gac, a novel HU-like DNA-binding protein in *B. burgdorferi* that is identical to the C-terminal domain of DNA gyrase A, but translated in a unique fashion from a transcript distinct from the canonical *gyrBA* polycistronic message. We also identified and characterized an atypical Hfq required for gene regulation and infectivity.
   a. Tilly, K., Fuhrman, J., Campbell, J. and Samuels, D.S. (1996) Isolation of *Borrelia burgdorferi* genes encoding homologues of DNA-binding protein HU and ribosomal protein S20. *Microbiology* **142:** 2471-2479. PMID: 8828214.
   b. Knight, S.W. and Samuels, D.S. (1999) Natural synthesis of a DNA-binding protein from the C-terminal domain of DNA gyrase A in *Borrelia burgdorferi*. *EMBO J*. **18:** 4875-4881. PMCID: PMC1171559.
   c. Lybecker, M.C., Abel, C.A., Feig, A.L., and Samuels, D.S. (2010) Identification and function of the RNA chaperone Hfq in the Lyme disease spirochete *Borrelia burgdorferi*. *Mol. Microbiol.* **78:** 622-635. PMCID: PMC2963666.
   d. Anacker, M.L., Drecktrah, D., LeCoultre, R.D., Lybecker, M., and Samuels, D.S. (2018) RNase III processing of rRNA in the Lyme disease spirochete *Borrelia burgdorferi*. *J. Bacteriol.* **200:** e00035-18. PMCID: PMC5996687.

3. We have contributed seminal studies regarding both the fundamental molecular biology of *B. burgdorferi* and the regulation of gene expression during infection of both the tick vector and vertebrate host. These include defining the regulatory sequences required for the expression of a major virulence factor expressed during transmission, the discovery of a novel non-coding RNA that functions in activating the regulon required for mammalian infection, and the demonstration that the stringent response is required for spirochete persistence in the tick vector.
   a. Alverson, J., Bundle S.F., Sohaskey, C.D., Lybecker, M.C., and Samuels, D.S. (2003) Transcriptional regulation of the *ospAB* and *ospC* promoters from *Borrelia burgdorferi*. *Mol. Microbiol.* **48:** 1665-1677. PMID: 12791146.
   b. Lybecker, M.C. and Samuels, D.S. (2007) Temperature-induced regulation of RpoS by a small RNA in *Borrelia burgdorferi*. *Mol. Microbiol*. **64:** 1075–1089. PMID: 17501929.
   c. Drecktrah, D., Hall, L.S., Hoon-Hanks, L.L., and Samuels, D.S. (2013) An inverted repeat in the *ospC* operator is required for induction in *Borrelia burgdorferi*. *PLOS One* **8:** e68799. PMCID: PMC3700930.
   d. Drecktrah, D., Lybecker, M., Popitsch, N., Rescheneder, P., Hall, L.S., and Samuels, D.S. (2015) The *Borrelia burgdorferi* RelA/SpoT homolog and stringent response regulate survival in the tick vector and global gene expression during starvation. *PLOS Pathog.* **11:** e1005160. PMCID: PMC4570706.

4. We discovered a novel bacteriophage of *B. burgdorferi* and identified the cp32 family of 32-kb circular plasmids as prophage. We also demonstrated transduction via the cp32 prophage, which may be an

important mechanism of horizontal gene exchange and antigenic variation. Most recently, we have shown that the stringent response regulates transcription of the cp32 late operon.

a. Eggers, C.H. and Samuels, D.S. (1999) Molecular evidence for a new bacteriophage of *Borrelia burgdorferi*. *J. Bacteriol.* **181:** 7308-7313. PMCID: PMC103694.
b. Damman, C.J., Eggers, C.H., Samuels, D.S., and Oliver, D.B. (2000) Characterization of *Borrelia burgdorferi* BlyA and BlyB proteins: a prophage-encoded holin-like system. *J. Bacteriol.* **182:** 6791-6797. PMCID: PMC111423.
c. Eggers, C.H., Kimmel, B.J., Bono, J.L., Elias, A., Rosa, P., and Samuels, D.S. (2001) Transduction by ϕBB-1, a bacteriophage of *Borrelia burgdorferi*. *J. Bacteriol.* **183:** 4771-4778. PMCID: PMC99531.

5. We have isolated and characterized the only antibiotic-resistant mutants of *B. burgdorferi*. Although antibiotic resistance has not yet been a clinical problem in the treatment of Lyme disease, the mutant alleles have been utilized to construct selectable and counterselectable markers that have served as the foundation for molecular genetic methodologies.
   a. Samuels, D.S., Marconi, R.T., Huang, W.M. and Garon, C.F. (1994) *gyrB* mutations in coumermycin A_1-resistant *Borrelia burgdorferi*. *J. Bacteriol.* **176:** 3072-3075. PMCID: PMC205466.
   b. Frank, K.L., Bundle, S.F., Kresge, M.E., Eggers, C.H., and Samuels, D.S. (2003) *aadA* confers streptomycin resistance in *Borrelia burgdorferi*. *J. Bacteriol.* **185:** 6723-6727. PMCID: PMC262111.
   c. Galbraith, K.M., Ng, A.C., Eggers, B.J., Kuchel, C.R., Eggers, C.H., and Samuels, D.S. (2005) *parC* mutations in fluoroquinolone-resistant *Borrelia burgdorferi*. *Antimicrob. Agents Chemother.* **49:** 4354-4357. PMCID: PMC1251557.
   d. Criswell, D., Tobiason, V.L., Lodmell, J.S., and Samuels, D.S. (2006) Mutations conferring aminoglycoside and spectinomycin resistance in *Borrelia burgdorferi*. *Antimicrob. Agents Chemother.* **50:** 445-452. PMCID: PMC1366916.

Complete List of Published Work in My Bibliography:
http://www.ncbi.nlm.nih.gov/myncbi/d..samuels.1/bibliography/40498653/public/?sort=date&direction=ascending

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

Ongoing Research Support

R01 AI051486-11A1 Samuels (PI) 04/01/2002-11/30/2019 (NCE)
Regulation of gene expression in *Borrelia burgdorferi*
The goal of this project is to dissect, using molecular, genetic, biochemical, and transcriptomic techniques, the regulation of gene expression during transmission from the tick vector to the vertebrate host.
Role: PI

R21 AI133334-A1 Drecktrah (PI) 03/05/18-02/29/20
Metabolic regulation during the two-host lifecycle of *Borrelia*.
The goal of this project is to examine the role of carbonyl stress and methylglyoxal in *B. burgdorferi* murine infectivity and tick persistence.
Role: CoI

R01 AI130247-01A1 Samuels, Drecktrah, Lybecker (MPI) 06/8/18-05/31/23
Regulation of glycerol utilization in *Borrelia burgdorferi*
The goal of this project is to elucidate the biochemical and genetic basis of glycerol metabolism and its regulation, as well as its role in regulating spirochete survival in the tick vector.
Role: PI (contact)