BIOGRAPHICAL SKETCH

NAME: Samuels, D. Scott

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

POSITION TITLE: Professor

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	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* (*Borreliella*) *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 routinely cycle *B. burgdorferi* between ticks and mice and are proficient with the murine model of Lyme disease. 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 two books and wrote several review articles and chapters. Lastly, I chaired the Biology of Spirochetes Gordon Research Conference.

Ongoing and recently completed projects that I am highlighting include:

U01 AI169840-01A1
Davies, Marconi, Samuels (MPI)
11/18/22-10/31/27
PlzA, cyclic-di-GMP and the enzootic cycle for Lyme disease

R01 AI130247-01A1
Samuels, Drecktrah (MPI)
06/08/18-05/31/24 (NCE)
Regulation of glycerol utilization in *Borrelia burgdorferi*

R21 AI133334-A1
Drecktrah (PI), Role: CoI
03/05/18-02/29/23 (NCE)
Metabolic regulation during the two-host lifecycle of *Borrelia*

R21 AI151597-01
Secor (PI), Role: CoI
3/10/20-2/28/22
Targeting a ubiquitous spirochete bacteriophage to prevent Lyme disease

Fairbairn Family Lyme Research Initiative at Harvard Medical School
Pier (PI), Role: Co-PI
9/1/21-8/31/22
Role of the *Borrelia* surface polysaccharide PNAG in virulence and immunity in Lyme disease

Citations:

1. **Samuels, D.S.** (2011) Gene regulation in *Borrelia burgdorferi*. *Annu. Rev. Microbiol.* **65:** 479-499.
2. Brisson, D., Drecktrah, D., Eggers, C.H., and **Samuels, D.S.** (2012) Genetics of *Borrelia burgdorferi*. *Annu. Rev. Genet.* **46:** 515-536. PMCID: PMC3856702.
3. 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. PMCID: PMC5067140.
4. **Samuels D.S.**, Lybecker M.C., Yang X.F., Ouyang Z., Bourret T.J., Boyle W.K., Stevenson B., Drecktrah D., and Caimano M.J. (2021) Gene Regulation and Transcriptomics. *Curr. Issues Mol. Biol.* **42:** 223-266. PMCID: PMC7946783.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2024 – present	Section Editor, *PLOS Pathogens*
2023	Chairperson, NIAID Investigator Initiated Program Project Applications Study Section
2023	Member, NIAID Understanding Persistent Signs and Symptoms Attributed to Post-treatment Lyme Disease Study Section
2022, 2023	Member, NIH Support for Conferences and Scientific Meetings Study Section
2022, 2023	Temporary Member, Microbiology and Infectious Diseases Research (MID) Study Section
2019, 2020, 2022, 2023	Chairperson, DOD Congressionally Directed Medical Research Programs (CDMRP), Tick Disease Research Program (TBDRP) Study Section
2019 – 2021	Guest Associate Editor, *Frontiers in Cellular and Infection Microbiology*
2018	Member, NIAID Investigator Initiated Program Project Applications (RRS-M) Study Section
2018 – 2024	Academic Editor, *PLOS Pathogens*
2018 – 2022	Chair, Biology of Spirochetes Gordon Research Conference
2017	Member, DOD CDMRP, TBDRP Study Section
2017	Member, NIH Bacteria Gene Expression (GGG-E) Study Section
2016 – 2018	Vice Chair, Biology of Spirochetes Gordon Research Conference
2014	Member, NIH Bacterial Pathogenesis (BACP-W) Study Section
2014 – Present	Editorial Advisory Board, *Infection and Immunity*
2013, 2014, 2016, 2018	Member, NIH Topics in Bacterial Pathogenesis (IDM-B) Study Section
2013 – 2018	Guest Editor, *PLOS Pathogens*
2012 – Present	Editorial Advisory Board, *Molecular Microbiology*
2012	Member, NIH Microbial Pathogens AREA Review (IDM-S) Study Section
2009	Vice Chair, NIH Topics in Microbiology (IDM-S) Study Section
2009	Member, NIH K99 Pathway to Independence (BRT-9) Study Section
2008 – Present	Professor, University of Montana, Division of Biological Sciences, Missoula, MT
2008	Member, NIH Member Conflicts in Microbiology (IDM-Q) Study Section
2006 – 2021	Chair, University of Montana, Institutional Biosafety Committee, Missoula, MT
2006, 2008, 2017, 2018, 2021	Temporary Member, NIH Bacterial Pathogenesis (BACP) 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, 2005, 2007, 2011	Member, NIH Topics in Bacterial Pathogenesis (IDM-A) Study Section
2003	Temporary Member, NIH Microbial Physiology and Genetics 2 (MBC2) Study Section
1999 – 2008	Associate Professor, University of Montana, Division of Biological Sciences, Missoula, MT
1995 – 1999	Assistant Professor, University of Montana, Division of Biological Sciences, Missoula, MT
1993 – Present	Member, American Society for Biochemistry and Molecular Biology
1993 – Present	Member, American Society for Microbiology
1991 – 1995	Intramural Research Training Award Fellow, National Institutes of Health, National Institute of Allergy and Infectious Disease, Hamilton, MT
1985 – Present	Member, American Association for the Advancement of Science
1984 – 1991	Ph.D. Candidate, University of Arizona, Department of Molecular and Cellular Biology, Tucson, AZ
1983 – 1984	Research Assistant, University of Pittsburgh, Department of Biological Sciences, Pittsburgh, PA

Honors

2012	The Paul Lauren Undergraduate Research Faculty Mentor Award, University of Montana
2002, 2021	Sabbatical, University of Montana
1998, 2001, 2003, 2005, 2011, 2014, 2019, 2023	Merit Award, University of Montana
1994	Fellow Travel Grant, American Society for Microbiology
1987 – 1991	National Research Service Award, National Cancer Institute
1984 – 1986	Graduate Academic Scholarship, University of Arizona
1983	Phi Beta Kappa, Colorado College
1979 – 1981	Regent's Scholarship, New York State

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 genetic manipulation methodologies. We have freely distributed all of the genetic and biochemical tools along with providing experimental support when necessary. These include selectable markers, shuttle vectors, 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. 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.
   c. 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.
   d. Boyle W.K., Hall L.S., Armstrong A.A., Dulebohn D.P., **Samuels D.S.**, Gherardini F.C., and Bourret T.J. (2020) Establishment of an *in vitro* RNA polymerase transcription system: a new tool to study transcriptional activation in *Borrelia burgdorferi*. *Sci. Rep.* **10:** 8246. PMCID: PMC7237435.

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, nucleoid-associated proteins, RNA chaperones, and ribonucleases. 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 characterized an intermediary metabolic enzyme that controls redox balance and is required for infectivity.
   a. 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.
   b. 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.
   c. Drecktrah, D., Hall, L.S., Crouse, B., Schwarz, B., Richards, C., Bohrnsen, E., Wulf, M., Long, B., Bailey, J., Gherardini, F., Bosio, C.M., Lybecker, M.C., and **Samuels, D.S.** (2022) The glycerol-3-phosphate dehydrogenases GpsA and GlpD constitute the oxidoreductive metabolic linchpin for Lyme

disease spirochete host infectivity and persistence in the tick. *PLOS Pathog.* **18:** e1010385. PMCID: PMC8929704.

d. Van Gundy, T., Patel, D., Bowler, B.E., Rothfuss, M.T., Hall, A.J., Davies, C., Hall, L.S., Drecktrah, D., Marconi, R.T., **Samuels, D.S.**, and Lybecker, M.C. (2023) c-di-GMP regulates activity of the PlzA RNA chaperone from the Lyme disease spirochete. *Mol. Microbiol.* **119:** 711-727.

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, the demonstration that the stringent response is required for spirochete persistence in the tick vector, and the characterization of an RNA regulator of RNA polymerase.
   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., 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.
   d. Drecktrah, D., Hall, L.S., Brinkworth, A., Comstock, J.R., Wassarman, K., and **Samuels, D.S.** (2020) Characterization of 6S RNA in the Lyme disease spirochete. *Mol. Microbiol.* **113:** 399-417. PMCID: PMC7047579

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. More 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.
   d. Faith, D.R., Kinnersley, M., Brooks, D.M., Drecktrah, D., Hall, L.S., Luo, E., Santiago-Frangos, A., Wachter, J., **Samuels, D.S.**, and Secor, P.R. (2024) Characterization and genomic analysis of the Lyme disease spirochete bacteriophage ϕBB-1. *PLoS Pathog.* **20:** e1012122. PMID: 38558079.

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 MyBibliography:
https://www.ncbi.nlm.nih.gov/myncbi/d..samuels.1/bibliography/40498653/public/