Ben Spiller
Vanderbilt University School of Medicine
Department of Pharmacology
Department of Pathology, Microbiology, and Immunology
A-4116B MCN, 1161 21st Street South
Nashville, TN 37232
Tel: (615) 322-6766; email: benjamin.spiller@vanderbilt.edu

EDUCATION

2000-2005	Postdoctoral fellowship in Structural Biology, Harvard University/HHMI
1999-2000	Postdoctoral fellowship in Structural Biology, Yale University/HHMI
1994-1999	Ph.D. in Molecular and Cellular Biology, University of California at Berkeley
1989-1994	B.S. in Biochemistry, University of California at Davis

PROFESSIONAL EXPERIENCE

2015-present	Associate Professor of Pharmacology, Associate Professor of Pathology, Microbiology and Immunology, Vanderbilt University School of Medicine.
2006-2015	Assistant Professor of Pharmacology, Assistant Professor of Pathology, Microbiology and Immunology, Vanderbilt University School of Medicine.
2003-2006	Joint postdoctoral fellow with Stephen Harrison and David Clapham, Harvard Medical School. **Structure-function analysis of bacterial voltage-gated Na^+ channels.**
2000-2003	Joint postdoctoral fellow with Stephen Harrison and Donald Wiley, Harvard University. **Efforts toward crystallization of G-Protein Coupled Receptors.**
1999-2000	Postdoctoral fellow with Paul B. Sigler, Yale University. **Efforts toward crystallization of chemokine receptors.**
1995-1999	Graduate studies in Raymond Stevens' Laboratory, UC-Berkeley. **Crystallographic structure determination of para-Nitrobenzyl esterase: wild type, organophile, thermophile.** **Crystallographic structure determination of a Diels-Alderase antibody and its germline precursor.** **Structure determination of a Ferrochelatase catalytic antibody.**
1993-1994	Undergraduate research in the laboratory of William F. Benisek, UC-Davis. **Bronstead analysis of Keto Steroid Isomerase**.
1991-1993	Undergraduate research in the laboratory of James Murray, UC-Davis **Antisense downregulation of endogenous methyl-transferase.**

AWARDS

Helen Hay Whitney Foundation Fellowship
Agouron Foundation Fellowship
Paul Benjamin Sigler Memorial Fellow
Irvington Immunology Institute Fellowship (declined)

RESEARCH INTEREST

My research has been focused on applying structural tools to important mechanistic questions in biology. Over the years, these questions have included enzymology, antibody maturation and function, G-protein coupled receptors, and ion channels. In my independent career, I have combined these interests into a new program, broadly focused on infection and immunity. More specifically, one research effort is to understand type three secretion mechanism, focusing on how the secretion apparatus is regulated. A related effort

focuses on how bacterial effectors modulate the host's cytoskeleton. Finally, we are interested in the host's response to infection. We are contributing structural expertise to advance vaccine and antibody drug design efforts through the structural design of antibodies that neutralize viral, bacterial, and toxin-mediated disease.

PUBLICATIONS AS A VANDERBILT FACULTY MEMBER

1. Kroh HK, Chandrasekaran R, Zhang Z, Rosenthal K, Woods R, Jin X, Nyborg AC, Rainey GJ, Warrener P, Melnyk RA, **Spiller BW**, Lacy DB. A neutralizing antibody that blocks delivery of the enzymatic cargo of Clostridium difficile toxin TcdB into host cells. J Biol Chem. 2018 Jan 19;293(3):941-952. doi: 10.1074/jbc.M117.813428PMID: 29180448

2. Kroh HK, Chandrasekaran R, Rosenthal K, Woods R, Jin X, Ohi MD, Nyborg AC, Rainey GJ, Warrener P, **Spiller BW**, Lacy DB. Use of a neutralizing antibody helps identify structural features critical for binding of Clostridium difficile toxin TcdA to the host cell surface. J Biol Chem. 2017 Sep 1;292(35):14401-14412. doi: 10.1074/jbc.M117.781112. Epub 2017 Jul 13. PMID: 28705932

3. Louis M. Luttrell and Benjamin W. Spiller
Arrestin-dependent ERK activation and its disruption. Chapter in The Structural Basis of Arrestin Functions, Springer Publishing 2017.

4. Benjamin W. Spiller, Xuanzhi Zhan, Vsevolod V. Gurevich. Arrestin-3: the structural basis of lower receptor selectivity. Chapter in The Structural Basis of Arrestin Functions, Springer Publishing 2017.

5. Gonzalez-Rivera C, Barke T, Pyburn T, Ohi M, **Spiller BW**, Cover TL, and Lacy DB. A structural analysis of the monomeric p88 vacuolating toxin from *Helicobacter pylori*. Infection and Immunity. 2016 Aug 19;84(9):2662-70. doi: 10.1128/IAI.00254-16. Print 2016 Sep.

6. LeNoue-Newton ML, Wadzinski BE, Spiller BW. The three Type 2A protein phosphatases, PP2Ac, PP4c and PP6c, are differentially regulated by Alpha4. Biochem Biophys Res Commun. 2016 May 8. pii: S0006-291X(16)30728-8. doi: 10.1016/j.bbrc.2016.05.036. [Epub ahead of print] PubMed PMID: 27169767.

7. Chumbler NM, Rutherford SA, Zhang Z, Farrow MA, Lisher JP, Farquhar E, Giedroc DP, Spiller BW, Melnyk RA, and Lacy DB. Crystal structure of Clostridium difficile toxin A. Crystal structure of Clostridium difficile toxin A. Nature Microbiology 1, Article number: 15002 (2016). http://doi.org/10.1038/nmicrobiol.2015.2

8. Winarski KL, Thornburg NJ, Yu Y, Sapparapu G, Crowe JE Jr, **Spiller BW**. Vaccine-elicited antibody that neutralizes H5N1 influenza and variants binds the receptor site and polymorphic sites. Proc Natl Acad Sci U S A. 2015 Jul 28;112(30):9346-51. doi: 10.1073/pnas.1502762112. Epub 2015 Jul 13. PMID: 26517043.

9. Archuleta TL, **Spiller BW**. A gatekeeper chaperone complex directs translocator secretion during type three secretion. PLoS Pathog. 2014 Nov 6;10(11. PMID: 25375170

10. Markadieu N, Rios K, Spiller BW, McDonald WH, Welling PA, Delpire E. Short forms of Ste20-related proline/alanine-rich kinase (SPAK) in the kidney are created by aspartyl aminopeptidase (Dnpep)-mediated proteolytic cleavage. J Biol Chem. 2014 Oct 17;289(42):29273-84. PMID: 25164821.

11. Aiyegbo MS, Eli IM, **Spiller BW**, Williams DR, Kim R, Lee DE, Liu T, Li S, Stewart PL, Crowe JE Jr. Differential Accessibility of a Rotavirus VP6 Epitope in Trimers Comprising Type I, II, or III Channels as Revealed by Binding of a Human Rotavirus VP6-Specific Antibody. J Virol. 2013 Oct 23. PMID: 24155406.

12. Thornburg NJ, Nannemann DP, Blum DL, Belser JA, Tumpey TM, Deshpande S, Fritz GA, Sapparapu G, Krause JC, Lee JH, Ward AB, Lee DE, Li S, Winarski KL, **Spiller BW**, Meiler J, Crowe JE Jr. Human antibodies that neutralize respiratory droplet transmissible H5N1 influenza viruses. J Clin Invest. 2013 Sep 3. PMID: 23999429

13. Aiyegbo MS, Sapparapu G, **Spiller BW**, Eli IM, Williams DR, Kim R, Lee DE, Liu T, Li S, Woods VL Jr, Nannemann DP, Meiler J, Stewart PL, Crowe JE Jr. Human rotavirus VP6-specific antibodies mediate intracellular neutralization by binding to a quaternary structure in the transcriptional pore. PLoS One. 2013 May 9;8(5):e61101. PMID 23671563

14. Mchaourab HS, Lin YL, **Spiller BW**. Crystal structure of an activated variant of small heat shock protein Hsp16.5 Biochemistry. 2012 Jun 26;51(25):5105-12. PMID: 22670769

15. Watkins GR, Wang N, Mazalouskas MD, Gomez RJ, Guthrie CR, Kraemer BC, Schweiger S, **Spiller BW**, Wadzinski BE. Monoubiquitination promotes calpain cleavage of the protein phosphatase 2A (PP2A) regulatory subunit cleavage of the protein phosphatase 2A (PP2A) regulatory subunit ubunit y subunJ Biol Chem. 2012 Jul 13;287(29):24207-15. PMID: 22613722.

16. Pruitt RN, Chumbler, NM, Rutherford SA, Farrow MA, Friedman DB, **Spiller B**, Lacy DB. Structural determinants of the Clostridium difficile toxin A glucoslytransferase activity. J Biol Chem 2012 Mar 9;287(11):8013-20.

17. Archuleta TL, Du Y, English CA, Lory S, Lesser C, Ohi MD, Ohi R, **Spiller BW**. The Chlamydia effector chlamydial outer protein N (CopN) sequesters tubulin and prevents microtubule assembly. J Biol Chem. 2011 Sep 30;286(39):33992-8.

18. Coffa S, Breitman M, **Spiller BW**, Gurevich VV. A single mutation in arrestin-2 prevents ERK1/2 activation by reducing c-Raf1 binding. Biochemistry. 2011 Aug 16;50(32):6951-8.

19. LeNoue-Newton M., Watkins GR, Zou P, Germane KL, McCorvey LR, Wadzinski BE, **Spiller BW**. The Mid1 and PP2Ac binding domains of Alpha4 are both required for Alpha4 to inhibit PP2Ac degradation. 2011 May 20;286(20):17665-71.

20. Germane KL, **Spiller BW**. Structural and functional studies indicate that the EPEC effector, EspG, directly binds p21 activated kinase. Biochemistry 2011 Feb 15;50(6):917-9.

21. Zhan X, Gimenez LE, Gurevich VV, **Spiller BW**. Crystal structure of arrestin-3 reveals the basis of the difference in receptor binding between two non-visual subtypes. J Mol Biol. 2011 406(3):467-78.

22. Schmitt J, Karalewitz A, Benefield DA, Mushrush DJ, Pruitt RN, **Spiller BW**, Barbieri JT, Lacy DB. Structural analysis of botulinum neurotoxin type G receptor binding. Biochemistry. 2010 Jun 29;49(25):5200-5.

23. McConnell JL, Watkins GR, Soss SE, Franz HS, McCorvey LR, **Spiller BW**, Chazin WJ, Wadzinski BE. Alpha4 is a Ubiquitin-Binding protein that regulates PP2A ubiquitination. Biochemistry. 2010. 49(8):1713-8.

24. Pruitt RN, Chagot B, Cover M, Chazin WJ, **Spiller B**, Lacy DB. Structure-function analysis of inositol hexakisphosphate-induced autoprocessing in *Clostridium difficile* toxin A. J Biol Chem. 2009 Aug 14;284(33):21934-40.

25. Germane KL, Ohi R, Goldberg MB, **Spiller BW**. Structural and functional studies indicate that Shigella VirA is not a protease and does not directly destabilize microtubules. Biochemistry. 2008 Sep 30;47(39):10241-3.

26. Gangwer KA, Mushrush DJ, Stauff DL, **Spiller B**, McClain MS, Cover TL, Lacy DB. Crystal structure of the *Helicobacter pylori* vacuolating toxin p55 domain. Proc Natl Acad Sci U S A. 2007 Oct 9;104(41):16293-8.

PUBLICATIONS PRIOR TO EMPLOYMENT AT VANDERBILT

17 Fujinami S, Sato T, Trimmer JS, **Spiller BW**, Clapham DE, Krulwich TA, Kawagishi I, and Ito M (2007) The Voltage-Gated Na+ Channel 1 NaVBP Co-localizes with Methyl-Accepting Chemotaxis Protein at Cell Poles of Alkaliphilic *Bacillus pseudofirmus* OF4. *Microbiology* Dec;153(Pt 12):4027-38.

18. Koishi R, Xu HX, Ren DJ, Navarro B, **Spiller BW**, Shi Q, Clapham DE (2004). A superfamily of voltage-gated sodium channels in bacteria. J Biol Chem. **279** 9532-9538.

19. **Spiller B**, Gershenson A, Arnold FH, and Stevens RC (1999). A Structural view of Evolutionary Divergence. *Proc Natl Acad Sci U S A*., **96,** 12305-12310.

20. Romesberg FE, Santarsiero BD, **Spiller B**, Yin J, Barnes D, Schultz PG, Stevens RC (1998) Structural Evidence for Strain in Biological Catalysis. *Biochemistry* **37**, 14404-14409.

21. Romesberg FE,* **Spiller B**,* Schultz PG, Stevens RC (1997) Immunological Origins of Binding and Catalysis in a Diels-Alderase Antibody. *Science* **279**, 1929-1933. ***(authors contributed equally)**

22. Stevens RC, Hsieh-Wilson LC, Santarsiero BD, Wedemayer GJ, **Spiller B**, Wang LH, Barnes D, Ulrich HD, Patten PA, Romesberg FE, and Schultz PG (1996) Structural Studies of Catalytic Antibodies *Israel Journal of Chemistry*, **36** 121-132

GRANTS and CONTRACTS

ACTIVE

Medimmune Contract (Spiller, B. PI) 01/03/2018- 01/3022020
Epitope determination for SAN481 and SAN177.
Total Award Amount: $280,934.00

1R01AI108778-01 (Spiller, B. PI) 07/01/2014-06/30/2019
NIH/NIAID $250,000 per year direct
CopN mechanism as a key to understanding Type Three Secretion in bacteria

Discovery Grant: Vanderbilt University (Spiller, B PI) 6/1/2016-6/30/2017
Vanderbilt $50,000 per year direct
Structural studies of human IgE antibodies bound to natural allergens.
We have begun a collaboration with Scott Smith in the Dept. of Medicine to determine the first structures of IgE antibodies in complex with allergens.

Center For Aids Research Core Award (Spiller, B PI) 6/1/2016-6/30/2018
NIH/NIAID $50,000 per year direct
Structural studies of human IgE antibodies bound to natural allergens.
We have begun a collaboration with Scott Smith in the Dept. of Medicine to determine the first structures of IgE antibodies in complex with allergens.

COMPLETED

R21 AI092268-01A1 (Spiller, B.) 08/15/2011-07/31/2014
Epitope shifting and antibody maturation during rotavirus infection

We will determine the mechanism of a newly identified aspect of affinity maturation, epitope shift, and provide new molecular immunology paradigms that may influence the choice of antigens and the use of surrogate markers

HHSN272200900047C (Crowe, J. PI) 09/30/2009 – 09/29/2014
Genetic and Structural basis for virus neutralization

2R01 EY012018-11 (Mchaourab, H.) 02/01/2008-01/31/2013
Mechanisms of chaperone functions in the lens
To determine the structure of mutant forms of the small heat shock protein from *Methanococcus jannaschii*, with the overall goal of determining how changes in oligomeric state are functionally important.

R01 AI072453-05 (Lacy, Dana B.) 05/1/2011-04/30/2012
Directed evolution of inhibitors of anthrax toxin
The goal here was to develop drug candidates for disseminated anthrax, a disease incurable with antibiotics. With anthrax toxin as the target, peptide ligands were produced by ribosomal display.

R01 AI075259-04 (Lacy, Dana B.) 01/01/2011-12/21/2013
Structural Mechanisms of Botulinum Neurotoxin Pathogenesis
This project was focused on understanding the pore-forming and receptor binding mechanisms of different serotypes of botulinum neurotoxin.

DDRC Pilot Grant. 3p30 DK058404-08S1 06/1/09-05/31/11
Structural & Functional Study of VirA in Shigellosis

5R01 GM 081778-02 (B.W. Spiller PI) 09/15/2007-07/31/2011
Structural Studies of Voltage Gating in Voltage-Gated Sodium Channels
The major goals of this grant were to develop methods to stabilize flexible structures, and to complete the structure of a bacterial sodium channel.

ACS-IRG-58-009-49 (Spiller, B.) 07/01/2007-06/30/2008
ACS
Crystal structure determination of alpha4, a novel phosphatase subunit
To determine the structure of alpha4 and characterize the phosphatase binding surface.

Helen Hay Whitney Post-doctoral Fellowship 05/01-05/04
Structural Studies of Chemokine Receptors
The goal of this project was post-doctoral training and structure determination of a chemokine receptor.
Role: Investigator

INVITED PRESENTATIONS

2017 Tennessee Technical University
2016 Baylor College of Medicine
2015 *Chlamydia* Basic Sciences Meeting
2014 Purdue University
2014 University of Illinois, Chicago
2014 Notre Dame University
2014 University of North Carolina, Chapel Hill
2013 Midwestern Microbial Pathogenesis Meeting, The Ohio State University
2013 Middle Tennessee State University
2012 Oklahoma Health Sciences, Dept of Microbiology.
2012 University of Massachusetts Amherst, Dept of Chemistry.
2011 Advanced Photon Source LS-CAT users meeting

2010 Vanderbilt University Center for Structural Biology
2009 NIH Roadmap to High Resolution Membrane Protein Structures
2008 Rinat Pharmaceuticals, South San Francisco
2007 NIH Roadmap to High Resolution Membrane Protein Structures
2003 Agouron Institute
2003 Helen Hay Whitney Foundation
1999 West Coast Crystallography Meeting. Asilomar, CA

ACADEMIC SERVICE

Teaching

2015 (1) Graduate Seminar in Molecular Biophysics, BCHM349, ~15 students, 1 hour
(2) Pharmacology, Targets, PHARM320, 3 hours, ~10 students
(3) Foundations of Microbiology and Immunology, M&IM 332 10 students, 4 hours.
(4) Advanced topics in virology, M&IM ~10 students, 1 hour.
(5) Chemical and Physical Biology, CPB306, ~15 students 10 hours
(6) Advanced Membrane Protein Biology: from Molecule to Disease. IGP MM1 21 students, 16 hours
(7) Protein interfaces. IGP MM2. 22 students, 2 hours.

2014 (1) Graduate Seminar in Molecular Biophysics, BCHM349, ~15 students, 1 hour
(2) Pharmacology, Targets, PHARM320, 3 hours, ~10 students
(3) Foundations of Microbiology and Immunology, M&IM 332 10 students, 4 hours.
(4) Advanced topics in virology, M&IM ~10 students, 1 hour.
(5) Chemical and Physical Biology, CPB306, ~15 students 10 hours
(6) Advanced Membrane Protein Biology: from Molecule to Disease. IGP MM1 10 students, 16 hours

2013 (1) Graduate Seminar in Molecular Biophysics, BCHM349, ~15 students, 1 hour
(2) Pharmacology, Targets, PHARM320, 3 hours, ~10 students
(3) Foundations of Microbiology and Immunology, M&IM 332 12 students, 4 hours.
(4) Advanced topics in virology, M&IM ~10 students, 1 hour.
(5) Chemical and Physical Biology, CPB306, ~15 students 10 hours
(6) Advanced Membrane Protein Biology: from Molecule to Disease. IGP MM1 ~15 students, 16 hours

2012 (1) Graduate Seminar in Molecular Biophysics, BCHM349, ~15 students, 1 hour
(2) Pharmacology, Targets, PHARM320, 6 hours, ~15 students
(3) Foundations of Microbiology and Immunology, M&IM 332 12 students, 4 hours.
(4) Advanced topics in virology, M&IM ~10 students, 3 hours.
(5) Chemical and Physical Biology, CPB306, ~20 students 6 hours

2011 (1) Graduate Seminar in Molecular Biophysics, BCHM349, ~15 students, 1 hour
(2) Pharmacology, Targets, PHARM320, 6 hours, ~15 students
(3) Foundations of Microbiology and Immunology, M&IM 332 12 students, 4 hours.
(4) Advanced topics in virology, M&IM ~10 students, 3 hours.
(5) Chemical and Physical Biology, CPB306, ~20 students 6 hours

2010 (1) Graduate Seminar in Molecular Biophysics, BCHM349, ~15 students, 1 hour
(2) X-ray crystallography, BCHM303, ~10 students, 9 hours
(3) Foundations of Microbiology and Immunology, M&IM 332 12 students, 4 hours.
(4) Advanced topics in virology, M&IM ~10 students, 3 hours.
(5) Chemical and Physical Biology, CPB306, ~20 students 9 hours

2009 (1) Graduate Seminar in Molecular Biophysics, BCHM349, 7 students, 1 hour
(2) X-ray crystallography, BCHM303 (course organizer 2009), ~10 students, 9 hours
(3) Introduction to X-ray crystallography, IGP, 25 students, 4 hours.
(4) Foundations of Microbiology and Immunology, M&IM 332 12 students, 4 hours.

2008 (1) Graduate Seminar in Molecular Biophysics, BCHM349, 7 students, 1 hour discussion
(2) X-ray crystallography, BCHM303, 2 students 6 hours.
(3) Foundations of Microbiology and Immunology, M&IM 332 12 students, 4 hours.
(4) Advanced Topics in Neurobiology: Excitable Membranes, NURO 324, 12 students 4 hours
(5) Bridges to Success: Excitable Membranes, IGP, 15 students 6 hours

2007 (1) Graduate Seminar in Molecular Biophysics, BCHM349, 7 students, 1 hour discussion
(2) Introduction to X-ray crystallography, IGP, 25 students, 4 hours.

2006 (1) Graduate Seminar in Molecular Biophysics, BCHM349, 7 students, 1 hour discussion
(2) Introduction to X-ray crystallography, IGP, 25 students, 4 hours.

Training of Graduate Students

Katherine Germane, 2007-2011, B.S. from University of Pittsburg, Pennsylvania, 2006. Funded by the Molecular Biophysics Training Grant. Currently employed at the SEDD Biotechnology Office, Army Research Lab.

Mohammed Aiyegbo, 2007- 2013. Joint with J. Crowe. Funded by R21.

Michele LeNoue, 2008-present, B.S. from University of Louisville, 2000. Funded by the Pharmacology Training Grant, followed by NIH NRSA.

Tara Archuleta, 2009-present, B.S. from University of Arizona, 2009. Funded by Integrative Training in Therapeutic Discovery, followed by AHA Fellowship

Katherine Winarski, 2010-present, B.S. from University of Pittsburg, Pennsylvania, 2007. Funded by the Molecular Biophysics Training Grant, followed by R21

Thesis Committees (Advisor)
Aiyegbo. Mohammed (Crowe)
Archuleta, Tara (Spiller)
Bokiej, Magda (Dermody)
LeNoue, Michele (Spiller)
Gibson, Elisabeth (Osheroff)
Jagessar, Kevin (Mchaourab)
Perry, Nicole (Gurevich)
Wan, William (Stubbs)
Wandishin, Clayton (Crowe)
Watkins, Guy (Wadzinski)
Winarski, Katherine (Spiller)
Willis, Jordan (Crowe)
Yufenyuy, Ernest (Aiken)

University Service

2006-present	Member of Vanderbilt Center for Structural Biology
2006-present	Member of Vanderbilt X-Ray Crystallography Users' Group
2007-2010	Member of minority recruitment committee, Molecular Biophysics Training Grant
2010-present	Member of Chemical and Physical Biology curriculum committee

2014-present Chair of Chemical and Physical Biology curriculum committee

Ad hoc Manuscript Review
Acta Crystallography
Biochemistry
Cell Reports
Journal of Biological Chemistry
Journal of Molecular Biology
Molecular Pharmacology
Protein Science
Proceedings of the National Academy of Sciences
Science
Cellular Microbiology
Journal of Lipid Research

Ad hoc Grant Review Committees
North Carolina Biotechnology Center
NIH RFA-RM-09-012
NIH Neurotransporters, Receptors, Channels, and Calcium Signaling study section
Advanced Photon Source Beamtime Allocation Proposals.
Medical Research Council, UK