BIOGRAPHICAL SKETCH

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NAME: Straight, Paul

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

POSITION TITLE: 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)	END DATE MM/YYYY	FIELD OF STUDY
Lewis & Clark College	BA	06/1992	Biochemistry
University of Colorado, Boulder	PHD	12/2000	Molecular/Cellular Bio.
Harvard Medical School, Boston, MA	Postdoctoral Fellow	05/2008	(PI: Roberto Kolter)

A. Personal Statement

The central focus of my research is to understand microbial mechanisms that regulate transitions in cellular physiology and metabolism in response to environmental inputs. My graduate work investigated regulatory functions in fungi (Saccharomyces cerevisiae) that coordinate starvation-induced sporulation and chromosome segregation for meiosis. From this work I have experience in eukaryotic genetics, molecular biology, and cell biology, including light and electron microscopy. As a postdoctoral researcher, I initiated my project using bacteria (Bacillus subtilis) and fungi (Aspergillus nidulans and Fusarium oxysporum) to develop a model to identify molecular mechanisms of interspecies interactions. Subsequently, I transitioned the model to B. subtilis – Streptomyces interactions due to the rich combination of bacterial development and secondary metabolism in both organisms. This project enabled me to expand my genetic expertise to bacteria and to expand my training into small molecule chemistry and enzymology. These training experiences are the foundation of my laboratory. We have developed the two-species model for bacterial competition that enables us to identify biologically active metabolites and determine their mechanisms of action in competition. In collaborative work with the Dorrestein lab, we developed an imaging mass spectrometry approach to study the spatiotemporal location of specialized metabolites in cultures of bacteria (PMID: 19915536). We used this technology for example to identify a surfactin hydrolase enzyme produced by Streptomyces sp. Mg1 (PMID: 22826229). We expanded our experimental toolset to include bacterial genomics/transcriptomics, metabolomics, and modern fluorescence (PMID: 38276359) and electron microscopy. While continuing our work on interaction mechanisms, my lab has continued to pursue a long-standing interest of mine, which is to understand how bacteria assemble biosynthetic enzyme complexes, sometimes many of them, within growing and developing cells (e.g. sporulating, branching). Key to this proposal are the discoveries that bacillaene is synthesized by a megacomplex in B. subtilis (PMID: 17190806), and that linearmycin biosynthesis by Streptomyces sp. Mg1 is intimately connected to extracellular vesicle production (PMID: 22826229). The research capabilities of the Straight laboratory and our collaborators, and the support provided at Texas A&M University, provide an excellent balance of expertise necessary to complete the microscopy, molecular, and chemical experiments included in the proposed work and to provide a high-quality training environment.

1. Fernández A, Classen A, Josyula N, Florence JT, Sokolov AV, Scully MO, Straight P, Verhoef AJ. Simultaneous Two- and Three-Photon Deep Imaging of Autofluorescence in Bacterial Communities. Sensors (Basel). 2024 Jan 20;24(2) PubMed Central PMCID: PMC10819415.
2. Liu Y, Kyle S, Straight PD. Antibiotic Stimulation of a Bacillus subtilis Migratory Response. mSphere. 2018 Jan-Feb;3(1) PubMed Central PMCID: PMC5821984.
3. Hoefler BC, Stubbendieck RM, Josyula NK, Moisan SM, Schulze EM, Straight PD. A Link between Linearmycin Biosynthesis and Extracellular Vesicle Genesis Connects Specialized Metabolism and Bacterial Membrane Physiology. Cell Chem Biol. 2017 Oct 19;24(10):1238-1249.e7. PubMed PMID: 28919037.

4. Stubbendieck RM, Straight PD. Linearmycins Activate a Two-Component Signaling System Involved in Bacterial Competition and Biofilm Morphology. J Bacteriol. 2017 Sep 15;199(18) PubMed Central PMCID: PMC5573067.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2014 -	Associate Professor, Texas A&M University, Biochemistry & Biophysics, College Station, TX
2008 - 2014	Assistant Professor, Texas A&M University, Biochemistry & Biophysics, College Station, TX
2007 - 2008	Instructor, Harvard Medical School/M.I.T./Broad Institute, Cambridge, MA
2000 - 2001	Postdoctoral Researcher, University of Colorado, Boulder, CO
1994 - 1995	Research Assistant, University of Virginia, Charlottesville, VA
1992 - 1994	Research Assistant, University of California, San Francisco, CA

Honors

2013 - 2018	CAREER AWARD, National Science Foundation
2003 - 2005	Postdoctoral Fellowship in Microbial Biology, National Science Foundation
2012	Faculty Recognition Award, Biochemistry Graduate Association, Texas A&M University
2006	US/EU Task Force Fellowship for Biotechnology, European Commission

C. Contribution to Science

(https://www.ncbi.nlm.nih.gov/myncbi/paul.straight.2/bibliography/public/)

1. I have made contributions in different fields of biological research throughout the duration of my training and professional career. As a research assistant for Dr. Judith M. White, I co-authored a paper describing the ADAM family of proteins. The ADAM protein family is extensive and highly conserved, being recognized as a predominant motif mediating cell-cell interactions and regulating membrane function.

    a. Wolfsberg TG, Straight PD, Gerena RL, Huovila AP, Primakoff P, Myles DG, White JM. ADAM, a widely distributed and developmentally regulated gene family encoding membrane proteins with a disintegrin and metalloprotease domain. Dev Biol. 1995 May;169(1):378-83. PubMed PMID: 7750654.

2. During my doctoral work, I studied the function in Mps1p kinase during sporulation in budding yeast. The work shed light on how a regulatory function that controls mitosis is re-purposed for the different requirements of meiosis. This work demonstrated that Mps1p is required to duplicate spindle poles during meiosis, and is also required for proper spore development. Furthermore, a mutant allele of mps1 revealed an essential function in chromosome segregation during meiosis. This latter finding contributed to a recent (2013) publication in Science Magazine.

    a. Meyer RE, Kim S, Obeso D, Straight PD, Winey M, Dawson DS. Mps1 and Ipl1/Aurora B act sequentially to correctly orient chromosomes on the meiotic spindle of budding yeast. Science. 2013 Mar 1;339(6123):1071-4. PubMed Central PMCID: PMC3604795.
    b. Winey M, Morgan GP, Straight PD, Giddings TH Jr, Mastronarde DN. Three-dimensional ultrastructure of Saccharomyces cerevisiae meiotic spindles. Mol Biol Cell. 2005 Mar;16(3):1178-88. PubMed Central PMCID: PMC551483.
    c. Straight PD, Giddings TH Jr, Winey M. Mps1p regulates meiotic spindle pole body duplication in addition to having novel roles during sporulation. Mol Biol Cell. 2000 Oct;11(10):3525-37. PubMed Central PMCID: PMC15011.

3. As a postdoctoral researcher, I established the co-culture system for analyses of B. subtilis-S. coelicolor interactions. The mechanisms of competition used between species of bacteria in the environment are not well understood outside the antibiotic paradigm. I chose to focus on B. subtilis-S. coelicolor interactions as the empirically-determined best model at that time for co-culture studies of diffusible metabolites. This work has demonstrated that specialized metabolites may have competitive functions that are distinguishable from growth inhibitory or environmental activities. For example, our work showed that surfactin, a

lipopeptide produced by B. subtilis, is not simply a surface-active agent for motility. In addition, surfactin inhibits spore development by competing S. coelicolor. The co-culture model was instrumental in identifying bacillaene, an antibiotic produced by B. subtilis that had eluded detection in earlier studies. Intriguingly, our work on bacillaene led to the discovery that the biosynthetic enzymes arrange themselves in the B. subtilis cytoplasm as an unprecedented, organelle-like megacomplex. This work was a significant part of building a NIH-funded collaborative project between the Kolter, Clardy, and Walsh laboratories at Harvard Medical School. During my postdoctoral research, I also collaborated on a project to develop a phage display method of mining genomes for natural product gene clusters. This work was high impact in the protein-tagging field as evident by the number of publications citing our original work.

a. Butcher RA, Schroeder FC, Fischbach MA, Straight PD, Kolter R, Walsh CT, Clardy J. The identification of bacillaene, the product of the PksX megacomplex in Bacillus subtilis. Proc Natl Acad Sci U S A. 2007 Jan 30;104(5):1506-9. PubMed Central PMCID: PMC1785240.
b. Straight PD, Fischbach MA, Walsh CT, Rudner DZ, Kolter R. A singular enzymatic megacomplex from Bacillus subtilis. Proc Natl Acad Sci U S A. 2007 Jan 2;104(1):305-10. PubMed Central PMCID: PMC1765455.
c. Straight PD, Willey JM, Kolter R. Interactions between Streptomyces coelicolor and Bacillus subtilis: Role of surfactants in raising aerial structures. J Bacteriol. 2006 Jul;188(13):4918-25. PubMed Central PMCID: PMC1483000.
d. Yin J, Straight PD, McLoughlin SM, Zhou Z, Lin AJ, Golan DE, Kelleher NL, Kolter R, Walsh CT. Genetically encoded short peptide tag for versatile protein labeling by Sfp phosphopantetheinyl transferase. Proc Natl Acad Sci U S A. 2005 Nov 1;102(44):15815-20. PubMed Central PMCID: PMC1276090.

4. The co-culture studies have been continuously productive into my independent research at Texas A&M University. In collaborative work with Dr. Dorrestein's group at UCSD, my lab demonstrated the use of MALDI- Imaging Mass Spectrometry (IMS) to analyze metabolites secreted by competing microbes on an agar surface. Subsequently, my lab identified a secreted enzyme, surfactin hydrolase, by analyzing spatial patterns of the surfactin metabolite using IMS during competition studies of B. subtilis and Streptomyces sp. Mg1 (a). This model interaction of B. subtilis and Streptomyces spp. is an ongoing, developing system for understanding the complex mechanisms of competition between bacteria. We have also identified both a lytic metabolite and a mechanism of resistance (c). This study highlights the capacity of our competition model system to uncover new mechanisms that contribute to bacterial fitness. Recently, we have collaborated with the group of John Kirby and others to extend the two-species competition model to myxobacteria (b). Importantly, the first study emerging from this work highlights our purification and stabilization of bacillaene, which is typically highly unstable when purified. This work enables us to probe bacillaene function using the purified compound. In collaboration with the Winkler laboratory, we discovered LoaP, a protein that functions in processive antitermination to support expression of long operons, such as those associated with antibiotic biosynthesis (d). This paper highlights considerations of bacterial metabolism important for improving antibiotic production, focusing on antibiotic regulation in B. amyloliquefaciens.

a. Goodson JR, Klupt S, Zhang C, Straight P, Winkler WC. LoaP is a broadly conserved antiterminator protein that regulates antibiotic gene clusters in Bacillus amyloliquefaciens. Nat Microbiol. 2017 Feb 13;2:17003. PubMed Central PMCID: PMC5913657.
b. Stubbendieck RM, Straight PD. Escape from Lethal Bacterial Competition through Coupled Activation of Antibiotic Resistance and a Mobilized Subpopulation. PLoS Genet. 2015 Dec;11(12):e1005722. PubMed Central PMCID: PMC4672918.
c. Müller S, Strack SN, Hoefler BC, Straight PD, Kearns DB, Kirby JR. Bacillaene and sporulation protect Bacillus subtilis from predation by Myxococcus xanthus. Appl Environ Microbiol. 2014 Sep;80(18):5603-10. PubMed Central PMCID: PMC4178607.
d. Hoefler BC, Gorzelnik KV, Yang JY, Hendricks N, Dorrestein PC, Straight PD. Enzymatic resistance to the lipopeptide surfactin as identified through imaging mass spectrometry of bacterial competition. Proc Natl Acad Sci U S A. 2012 Aug 7;109(32):13082-7. PubMed Central PMCID: PMC3420176.