

**BIOGRAPHICAL SKETCH**

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.  
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME David S. Lawrence	POSITION TITLE Fred Eshelman Distinguished Professor		
eRA COMMONS USER NAME dlawrenc			
EDUCATION/TRAINING ( <i>Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.</i> )			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
University of California at Irvine	B. S.	1976	Biological Sciences
University of California at Los Angeles	Ph.D.	1982	Chemistry
University of Chicago/Rockefeller University	Postdoc	1983-85	Chemical Biology

**A. Positions and Honors:**

1976 - 1982 Graduate Student, UCLA with R. V. Stevens  
 1982 - 1985 Postdoctoral Fellow, University of Chicago and Rockefeller University with E. T. Kaiser  
 1985 - 1991 Assistant Professor of Chemistry, SUNY at Buffalo  
 1991 - 1994 Associate Professor of Chemistry/Medicinal Chemistry, SUNY at Buffalo  
 1995 Professor of Chemistry, SUNY at Buffalo  
 1996- Professor of Biochemistry, Albert Einstein College of Medicine; Albert Einstein Comprehensive Cancer Center  
 2007- Fred Eshelman Distinguished Professor, University of North Carolina; Professor of Medicinal Chemistry (Pharmacy), Chemistry (Arts & Sciences), and Pharmacology (Medicine); Member, Lineberger Comprehensive Cancer Center

Scientific Advisory Committee on Biochemistry and Endocrinology, American Cancer Society (1991-96); Scientific Advisory Committee on Cancer Drug Development, American Cancer Society (1996-97); Chemical and Related Sciences Special Emphasis Study Section, National Institutes of Health (1994); Clinical and Experimental Therapeutics Study Section, The USAMRMC Breast Cancer Research Program (1997); Chemical and Related Sciences Special Emphasis Study Section, National Institutes of Health (1997); International Advisory Board, The International Conference on Inhibitors of Protein Kinases, Warsaw, Poland (1998); Organizer of the symposium on "Biosensors: Visualizing the Chemistry of Living Cells", American Chemical Society Western Regional Meeting (1999); Biochemistry Study Section, National Institutes of Health (1999); Bio-Organic and Natural Products Chemistry Study Section, National Institutes of Health (2000-04); Samuel M. Rosen Award (2000); Leo M. Davidoff Society (2000); Olympia Dukakis Award/Grant in A-T Research (2000); Scientific Advisory Board, Keryx Biopharmaceuticals (2000-), International Advisory Board, The 2<sup>nd</sup> International Conference on Inhibitors of Protein Kinases, Warsaw, Poland (2001); Guest Editor, Accounts of Chemical Research Special Issue on Signal Transduction (2003); International Advisory Board, The 3<sup>rd</sup> International Conference on Inhibitors of Protein Kinases, Warsaw, Poland (2003); Scientific Advisory Board, Panomics (2003-); Editorial Advisory Board, *Current Organic Synthesis* (2003-); Editorial Advisory Board, *Accounts Chemical Research* (2004-); Scientific Co-founder, OnSetThera Pharmaceuticals (2004); Member, The Harvey Society (2005-); AAAS Fellow (2005); Member, American Society for Cell Biology (2006-); Consultant, Sigma-Aldrich (2006-).

**B. Selected Recent Publications:**

A. A. Profit, T. R. Lee, J. Niu, & D. S. Lawrence "Molecular Rulers: An Assessment of Distance and Spatial Relationships of Src Tyrosine Kinase SH2 and Active Site Regions", *J. Biol. Chem.*, 2001, 276, 9446-51.

Principal Investigator/Program Director (Last, First, Middle):

R. Yeh, T. R. Lee, & D. S. Lawrence "From Consensus Sequence Peptide to High Affinity Ligand: A "Library-Scan" Strategy", *J. Biol. Chem.*, 2001, 276, 12235-40.

K. Shen, Y.-F. Keng., Li Wu, X.-L. Guo, D. S. Lawrence, & Z.-Y. Zhang "Acquisition of A Specific and Potent PTP1B Inhibitor from a Novel Combinatorial Library and Screening Procedure" *J. Biol. Chem.*, 2001, 276, 47311-19.

R.-H. Yeh, X. Yan, M. Cammer, A. R. Bresnick, & D. S. Lawrence "Real Time Visualization of Protein Kinase Activity in Living Cells" *J. Biol. Chem.*, 2002, 277, 11527-32.

M. Ghosh, I. Ichetovkin, I. Song, J. S. Condeelis, & D. S. Lawrence "A New Strategy for Caging Proteins Regulated by Kinases" *J. Amer. Chem. Soc.*, 2002, 121, 2440-1.

C.-A. Chen, R.-H. Yeh, & D. S. Lawrence "Design and Synthesis of a Fluorescent Reporter of Protein Kinase Activity" *J. Amer. Chem. Soc.*, 2002, 121, 3840-1.

W. Lin & D. S. Lawrence "A Strategy for the Construction of Caged Diols Using a Photolabile Protecting Group" *J. Org. Chem.*, 2002, 67, 2723-26.

R. Yeh, T. R. Lee, & D. S. Lawrence "From consensus sequence to high-affinity ligands: acquisition of signaling protein modulators" *Pharmacology & Therapeutics*, 2002, 93, 179-91.

X.-L. Guo, K. Shen, F. Wang, D. S. Lawrence, & Z. Y. Zhang "Probing the Molecular Basis for Potent and Selective PTP1B Inhibition" *J. Biol. Chem.*, 2002, 277, 41014-41022.

W. Lin, C. Albanese, R. G. Pestell, & D. S. Lawrence "Spatially-Discrete Protein Expression via A Light-Activated Ecdysone-Inducible Construct", *Chem. & Biol.*, 2002, 9, 1347-53.

L. Shang, Y.-G. Kwon, S. K. Nandy, D. S. Lawrence, & A. M. Edelman, "Catalytic and Regulatory Domains of Doublecortin Kinase-1", *Biochemistry*, 2003, 42, 2185-2194.

J.-P. Sun, A. A. Federov, S.-Y. Lee, X.-L. Guo, K. Shen, D. S. Lawrence, S. C. Almo, & Z.-Y. Zhang "Crystal Structure of PTP1B Complexed with a Potent and Selective Bidentate Inhibitor", *J. Biol. Chem.*, 2003, 278, 12406-14.

D. S. Lawrence "Chemical Biology of Signal Transduction", *Accts. Chem Res.*, 2003, 39, 353-354.

D. S. Lawrence "New Chemical Tools for Signal Transducing Enzymes", *Accts. Chem. Res.*, 2003, 39, 401-409.

F. Liang, Z. Huang, S.-Y. Lee, J. Liang, M. I. Ivanov, A. Alonso, J. B. Bliska, D. S. Lawrence, T. Mustelin, & Z.-Y. Zhang "Aurintricarboxylic Acid Blocks *in vitro* and *in vivo* Activity of YopH, an Essential Virulent Factor of *Yersinia pestis*, the Agent of Plague" *J. Biol. Chem.*, 2003, 278, 41734-41741.

L. Xie, S.-Y. Lee, J. N. Andersen, S. Waters, K. Shen, X.-L. Guo, N. P. H. Moller, J. M. Olefsky, D. S. Lawrence, & Z.-Y. Zhang "Cellular Effects of Small Molecule PTP1B Inhibitors on Insulin Signaling" *Biochemistry*, 2003, 42, 12792-12804.

W. F. Veldhuyzen, Q. Nguyen, G. McMaster, & D. S. Lawrence "A Light-Activated Probe of Intracellular Protein Kinase Activity" *J. Amer. Chem. Soc.*, 2003, 125, 13358-13359.

R.-H. Yeh, C.-A. Chen, & D. S. Lawrence "Biosensors of Protein Kinase Action: From *In Vitro* Assays to Living Cells" *Biochim Biophys. Acta*, 2004, 1697, 39-51.

J. H. Lee, S. K. Nandy, & D. S. Lawrence "A Highly Potent and Selective PKCa Inhibitor Generated Via Combinatorial Modification of A Peptide Scaffold", *J. Amer. Chem. Soc.*, 2004, 126, 3394-3395.

Principal Investigator/Program Director (Last, First, Middle):

B. Xi, F. Guan, & D. S. Lawrence "Enhanced Production of Functional Proteins From Defective Genes", *J. Amer. Chem. Soc.*, 2004, 126, 5660-5661.

M. Ghosh, X. Song, G. Mouneimne, M. Sidani, D. S. Lawrence, & J. S Condeelis "Cofilin Generates Barbed Ends for Actin Polymerization and Defines the Direction of Protrusion and Locomotion *in vivo*", *Science*, 2004, 303, 743-746.

S. Kumar, F. Lianga, D. S. Lawrence, & Z.-Y. Zhang "Small Molecule Approach to Studying Protein Tyrosine Phosphatase" *Methods* 2005, 35, 9-21.

S.-Y. Lee, F. Liang, X.-L. Guo, L. Xie, S. M. Cahill, M. Blumenstein, H. Y. Yang, D. S. Lawrence, & Z.-Y. Zhang "Design, Construction, and Cellular Effects of A Signal Transduction Inhibitor Based on the AB Protein Toxin Motif" *Angew. Chem.* 2005, 44, 4242-4244.

Q. Wang & D. S. Lawrence "Phosphorylation-Driven Protein-Protein Interactions: A New Protein Kinase Sensing System", *J. Amer. Chem. Soc.*, 2005, 127, 7684-7685.

F. Liang, S.-Y. Lee, Jiao Liang, D. S. Lawrence, & Z.-Y. Zhang "The Role of Protein Tyrosine Phosphatase 1B in Integrin Signaling", *J. Biol. Chem.*, 2005, 280, 24857-63.

H. Li & D. S. Lawrence "Acquisition of Fyn-Selective SH3 Domain Ligands via A Combinatorial Library Strategy", *Chemistry & Biology*, 2005, 12, 905-12.

R. H. Singer, D. Lawrence, B. Ovrnyn, & J. Condeelis "Light-Activated Imaging of Gene Expression in Living Cells", *J. Biomed. Optics* 2005, 10, 051406-1 – 051406-9.

D. S. Lawrence "In vivo Applications of Caged Proteins and Peptides", *Cur. Opin. Chem. Biol.*, 2005, 9, 570-575.

D. S. Lawrence "Signaling Protein Inhibitors Via The Combinatorial Modification Of Peptide Scaffolds", *Biochim. Biophys. Acta*, 2005, 1754, 50-57.

H. Lee, L. Xie, Y. Luo, S. Y. Lee, D. S. Lawrence, X. B. Wang, F. Sotgia, M. P. Lisanti, & Z. Y. Zhang. "Identification of Phosphocaveolin-1 as a Novel Protein Tyrosine Phosphatase 1B Substrate", *Biochemistry* 2006, 45, 234-240.

Q. Wang, S. M. Cahill, M. Blumenstein, & D. S. Lawrence "Self-Reporting Fluorescent Substrates of Protein Tyrosine Kinases", *J. Amer. Chem. Soc.*, 2006, 128, 1808-9.

J.-M. Hah, V. Sharma, H. Li, & D. S. Lawrence "Acquisition of a "Group A"-Selective Tyrosine Kinase Inhibitor via a Global Targeting Strategy", *J. Amer. Chem. Soc.* 2006, 128, 5996-7.

Q. Wang, S. M. Cahill, M. Blumenstein, & D. S. Lawrence "Light-Regulated Sampling of Protein Tyrosine Kinase Activity", *J. Amer. Chem. Soc.*, 2006, 128, 14016-7.

C. D. Morrison, C. White, Z. Wang, S.-Y. Lee, D. S. Lawrence, W. T. Cefalu, Z.-Y. Zhang, & T. W. Gettys "Increased Hypothalamic PTP1B Contributes to Leptin Resistance with Age", *Endocrinology*, 2007, 148, 433-40.

Q. Wang & D. S. Lawrence "Seeing is Believing: Peptide-Based Fluorescent Sensors of Protein Tyrosine Kinase Activity", *ChemBiochem*, 2007, 8, 373-8.

V. Sharma, R. S. Agnes, & D. S. Lawrence "Deep Quench: Extending the Dynamic Range of Protein Kinase Sensors", *J. Amer. Chem. Soc.*, 2007, 129, 2742-3.

S. K. Nandy, R. A. Agnes, & D. S. Lawrence "Photochemically-Activated Probes of Protein-Protein Interactions", *Organic Lett.*, 2007, 9, 2249-52.

## **C. Research Support.**

### **Ongoing Projects:**

**Intracellular Probes for Studying PKG Activity** NIH; The cGMP-dependent protein kinase is the key downstream participant of NO-mediated signaling pathways that regulate a range of cell-based processes, from smooth muscle relaxation to neuronal synaptic plasticity. The overall goal of this research program is to develop molecular tools to establish the intracellular spatiotemporal dynamics of PKG during long-term potentiation and long-term depression.

**Synthetic Regulators of Tyrosine Protein Kinases** NIH; This research program seeks to expand upon our development of low nM affinity agents that target the SH1, SH2, and SH3 domains of tyrosine kinases, as well as sensors that allow us to fluorescently follow kinase activity in the context of Fyn and Lck in T cell activation.

**Light-Activated Gene Expression In Single Cells** NIH; Specific Aims are: 1. Constructing a stable cell line with a photoactivatable gene and an mRNA reporter. 2. Photoactivating the gene and then detecting RNA transcription in real time and imaging the single RNA molecules released from the transcription site in single cells. 3. Intravital imaging of this expression in a single cell within tumor tissue.

**Deep Quench: Sensors of Serine/Threonine Protein Kinases** Panomics, Inc. Development of a cell-based protein kinase sensor technology.