

*Curriculum Vitae*  
**David Ruchien Liu**

Born: June 12, 1973 in Riverside, CA  
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Department of Chemistry and Chemical Biology  
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## EDUCATION

- Ph.D. in Organic Chemistry, University of California at Berkeley, May 1999
- B.A. in Chemistry, *Summa Cum Laude*, Harvard College, June 1994 (1st out of 1,641)
- High School-University Program at University of California, Riverside
- Riverside Poly High School, Riverside, CA (1st out of 397)

## RESEARCH INTERESTS

Molecular evolution; chemical biology; organic chemistry; development and application of methods to evolve synthetic small molecules, synthetic polymers, proteins, and nucleic acids; reaction discovery

## EXPERIENCE

2007-present Harvard College Professor, Harvard University

2005-present Professor of Chemistry and Chemical Biology, Harvard University and Investigator, Howard Hughes Medical Institute

2003-2004 John L. Loeb Associate Professor of the Natural Sciences and Associate Professor of Chemistry and Chemical Biology, Harvard University

1999-2003 Assistant Professor of Chemistry and Chemical Biology, Harvard University

1994-1999 (Ph.D. research) Probed the mechanism of chorismate mutases using site-directed natural and unnatural amino acid mutagenesis; designed new tRNAs for unnatural amino acid mutagenesis; initiated the engineering and evolution of proteins and nucleic acids for the site-specific incorporation of unnatural amino acids into proteins in living cells. Research conducted under the guidance of Professor Peter G. Schultz at the University of California, Berkeley.

1991-1994 (B.A. research) Conducted synthetic, biochemical, and molecular biological research on 2,3-oxidosqualene cyclase (a key enzyme in steroid biosynthesis) under the guidance of Professor E. J. Corey at Harvard University.

## DISTINCTIONS

2009 Thomas T. Hoopes prize shared with Meera Atreya for her outstanding Senior Thesis

2007 Senior faculty awardee of the 2007 Joseph R. Levenson Memorial Teaching Prize for undergraduate teaching (university-wide, chosen by the undergraduate student body)

2007 Appointed as a Harvard College Professor in recognition of undergraduate teaching, graduate-student teaching, and research accomplishments

2006 American Chemical Society Pure Chemistry Award

2005 2<sup>nd</sup> Yoshimasa Hirata Memorial Lecturer (Nagoya University, Japan; lecture given in 2006)

2005 World Technology Award Fellow in Materials

- 2005 Former Liu Group graduate student Dr. Zev Gartner named one of four worldwide winners of the 2005 IUPAC Prize for Young Chemists for "best Ph.D. thesis in the chemical sciences"
- 2005 Selected to be a Howard Hughes Medical Institute Investigator
- 2004 *Small Times* Magazine Researcher of the Year (Nov./Dec. 2004 issue)
- 2004 Named to the *Popular Science* "Brilliant 10" recognizing ten scientists in the U.S. (Oct. 2004 issue)
- 2004 Named to the MIT *Technology Review* TR100 as "one of the world's top young innovators"
- 2004 Thomas T. Hoopes prize shared with Rozalina Grubina for her outstanding Senior Thesis; Rozalina's thesis also earned the 2004 Lawrence J. Henderson Prize as the "best in the Biochemical Sciences"
- 2004 Camille Dreyfus Teacher-Scholar Award
- 2004 Glaxo-Smith-Kline Chemistry Scholarship Award
- 2004 American Chemical Society Arthur C. Cope Young Scholar Award
- 2003 Roslyn Abramson Award for undergraduate teaching at Harvard (university-wide, one of two in 2003)
- 2003 Thomas T. Hoopes prize shared with Yi-Ching Ong for her outstanding Senior Thesis
- 2003 AstraZeneca Pharmaceuticals Excellence in Chemistry Award
- 2003 Merck Genome-Related Pilot Research Award
- 2003 *Synlett* and *Synthesis* Editorial Board Assistant Professor Journal Award
- 2002 Arnold and Mabel Beckman Foundation Young Investigator
- 2002 Alfred P. Sloan Foundation Research Fellow
- 2001 American Cancer Society Research Scholar
- 2001 NSF CAREER Award
- 2000 Searle Scholars Program Awardee
- 2000 Office of Naval Research Young Investigator Award
- 1999 Research Corporation Research Innovation Award
- 1998, 1999 Elected to the Harvard Society of Fellows as a Harvard Junior Fellow (declined); awarded a Life Sciences Research Foundation Postdoctoral Fellowship (declined)
- 1994-1999 National Defense Science and Engineering Graduate Fellowship (1994-1995); Howard Hughes Medical Institute Predoctoral Fellowship (1995-1999)
- 1997 Roche Award for Excellence in Organic Chemistry
- 1994 Sophia Freund Prize winner as the top ranking graduate of Harvard College, class of 1994
- 1994 One of 20 college students in the nation named to the *USA Today* All-USA 1st Academic College Team (4 Feb 1994 issue of *USA Today*)
- 1993-1994 Elected to Phi Beta Kappa as one of twelve Junior Men at Harvard; Thomas T. Hoopes Prize for outstanding senior thesis, "Studies on 2,3-Oxidosqualene Cyclase: A Synthetic and Molecular Biological Approach", shared with Professor E. J. Corey
- 1992, 1993 Pfizer Corporation Central Research Undergraduate Summer Research Fellow (two years)
- 1990 One of five students in the U.S. selected to attend the 1990 Nobel Prize Award Ceremonies in Stockholm, Sweden; Harvard Detur Prize recipient
- 1990-1994 National Merit Scholar; Barry M. Goldwater National Scholar for excellence in science
- 1990 Westinghouse National Science Talent Search, second place in the United States
- 1990 One of 20 high school students in the nation named to the *USA Today* All-USA 1st Academic High School Team (21 May 1990 issue of *USA Today*)

## **PUBLICATIONS (FROM B.A. AND PH.D. RESEARCH)**

1. "The Methyl Group at C(10) of 2,3-Oxidosqualene Is Crucial to the Correct Folding of This Substrate in the Cyclization-Rearrangement Step of Sterol Biosynthesis" Corey, E. J.; Virgil, S. C.; Liu, D. R.; Sarshar, S. J. *Am. Chem. Soc.* **114**, 1524-1525 (1992).
2. "First Demonstration of a Carbocation-Olefin Cyclization Route to the Lanosterol Series" Corey, E. J.; Lee, J. M.; Liu, D. R. *Tetrahedron Lett.* **35**, 9149-9152 (1994).
3. "Molecular Cloning of the Human Gene Encoding Lanosterol Synthase From a Liver cDNA Library" Baker, C. H.; Matsuda, S. P.; Liu, D. R.; Corey, E. J. *Biochem. Biophys. Res. Comm.* **213**, 154-160 (1995).
4. "Mutagenesis Study of Active Site Residues in Chorismate Mutase from *Bacillus Subtilis*" Cload, S. T.; Liu, D. R.; Pastor, R. M.; Schultz, P. G. *J. Am. Chem. Soc.* **118**, 1787-1788 (1996).
5. "Analysis of Active Site Residues in *Escherichia coli* Chorismate Mutase by Site-Directed Mutagenesis" Liu, D. R.; Cload, S. T.; Pastor, R. M.; Schultz, P. G. *J. Am. Chem. Soc.* **118**, 1789-1790 (1996).
6. "Development of Improved tRNAs for *In Vitro* Biosynthesis of Proteins Containing Unnatural Amino Acids" Cload, S. T.; Liu, D. R.; Froland, W. A.; Schultz, P. G. *Chemistry and Biology* **3**, 1033-1038 (1996).
7. "Characterization of an 'Orthogonal' Suppressor tRNA Derived from *E. coli* tRNA<sup>Gln</sup>" Liu, D. R.; Magliery, T. J.; Schultz, P. G. *Chemistry and Biology* **4**, 685-691 (1997).
8. "Engineering a tRNA and Aminoacyl-tRNA Synthetase for the Site-Specific Incorporation of Unnatural Amino Acids into Proteins *in Vivo*" Liu, D. R.; Magliery, T. J.; Pastrnak, M.; Schultz, P. G. *Proc. Natl. Acad. Sci.* **94**, 10092-10097 (1997).
9. "Generating New Molecular Function: A Lesson from Nature" Liu, D. R. and Schultz, P. G. *Angew. Chem. Intl. Ed. Engl.* **38**, 36-54 (1999).
10. "Progress Towards the Evolution of an Organism with an Expanded Genetic Code" Liu, D. R. and Schultz, P. G. *Proc. Natl. Acad. Sci. USA*, **96**, 4780-4785 (1999).
11. "A New Functional Suppressor tRNA / Aminoacyl-tRNA Synthetase Pair for the *in Vivo* Incorporation of Unnatural Amino Acids into Proteins" Wang, L.; Magliery, T. J.; Liu, D. R.; Schultz, P. G. *J. Am. Chem. Soc.* **122**, 5010-5011 (2000).

#### **PUBLICATIONS (AS A PRINCIPAL INVESTIGATOR)**

12. "Enzyme Mechanisms for Polycyclic Triterpene Formation" Wendt, K. U.; Schulz, G. E.; Corey, E. J.; Liu, D. R. *Angew. Chem. Intl. Ed. Engl.* **39**, 2813-2833 (2000).
13. "The Generality of DNA-Templated Synthesis as a Basis for Evolving Non-Natural Small Molecules" Gartner, Z. J. and Liu, D. R. *J. Am. Chem. Soc.* **123**, 6961-6963 (2001). A Highlight describing this work appears in *Angew. Chem. Intl. Ed.* **41**, 89-90 (2002).
14. "An *In Vivo* Selection System for Homing Endonuclease Activity" Gruen, M.; Chang, K.; Serbanescu, I.; Liu, D. R. *Nucleic Acids Research* **30**, e29 (2002).
15. "Recent Advances in the *In Vitro* Evolution of Nucleic Acids" Bittker, J. A.; Phillips, K. J.; Liu, D. R. *Curr. Opin. Chem. Biol.*, **6**, 367-374 (2002).
16. "Expanding the Reaction Scope of DNA-Templated Synthesis" Gartner, Z. J.; Kanan, M. W.; Liu, D. R. *Angew. Chem. Intl. Ed.*, **41**, 1796-1800 (2002). This work is featured in an online *Nature Science Update* ([http://www.nature.com/nsu/nsu\\_pf/020527/020527-1.html](http://www.nature.com/nsu/nsu_pf/020527/020527-1.html)).
17. "Nucleic Acid Evolution and Minimization by Nonhomologous Random Recombination" Bittker, J. A.; Le, B. V.; Liu, D. R. *Nature Biotechnology* **20**, 1024-1029 (2002).

18. "Multistep Small-Molecule Synthesis Programmed by DNA Templates" Gartner, Z. J.; Kanan, M. W.; Liu, D. R. *J. Am. Chem. Soc.*, **124**, 10304-10306 (2002). News stories describing this work appear in *Chem. & Eng. News* **80** [34] 12 (2002), and in *Science*, **300**, 242 (2003).
19. "Directing Otherwise Incompatible Reactions in a Single Solution Using DNA-Templated Organic Synthesis" Calderone, C. T.; Puckett, J. W.; Gartner, Z. J.; Liu, D. R. *Angew. Chem. Int. Ed.* **41**, 4104-4108 (2002). This work is featured as an Editor's Choice in *Science* **298** [5598], 1517 (2002).
20. "Two Enabling Architectures for DNA-Templated Organic Synthesis" Gartner, Z. J.; Grubina, R.; Calderone, C. T.; Liu, D. R. *Angew. Chem. Int. Ed.* **42**, 1370-1375 (2003). A Science and Technology Concentrate describing this work appears in *Chem. & Eng. News* **81** [13] 24 (2003).
21. "In Vivo Evolution of an RNA Transcriptional Activator" Buskirk, A. R.; Kehayova, P. D.; Landrigan, A.; Liu, D. R. *Chem. Biol.* **10**, 533-540 (2003). This paper is noted as an article of interest in *Cell* **113** (7) and previewed in a separate article in *Chem. Biol.* **10**, 584-585 (2003).
22. "Stereoselectivity in DNA-Templated Organic Synthesis and Its Origins" Li, X. and Liu, D. R. *J. Am. Chem. Soc.* **125**, 10188-10189 (2003).
23. "Highly Sensitive In Vitro Selections for DNA-Linked Synthetic Small Molecules with Protein Binding Affinity and Specificity" Doyon, J. B.; Snyder, T. M.; Liu, D. R. *J. Am. Chem. Soc.* **125**, 12372-12373 (2003).
24. "Efficient and Sequence-Specific DNA-Templated Polymerization of PNA Aldehydes" Rosenbaum, D. M. and Liu, D. R. *J. Am. Chem. Soc.* **125**, 13924-13925 (2003). This work is highlighted in a Science and Technology story in *Chem. & Eng. News* **82** [3] 64 (2004).
25. "Expanding the Genetic Code In Vitro and In Vivo" Magliery, T. J.; Liu, D. R. in *The Genetic Code and the Origin of Life* Ed. Ribas de Pouplana, L. Landes Bioscience and Springer, (2004).
26. "Translation of DNA into Synthetic N-Acyloxazolidines" Li, X.; Gartner, Z. J.; Tse, B. N.; Liu, D. R. *J. Am. Chem. Soc.* **126**, 5090-5092 (2004).
27. "DNA-Templated Organic Synthesis: Nature's Strategy for Controlling Chemical Reactivity Applied to Synthetic Molecules" Li, X.; Liu, D. R. *Angew. Chem. Int. Ed.* **43**, 4848-4870 (2004). This paper was selected by the *Angewandte Chemie* Editorial Board as one of the 12 best *Angewandte Chemie* review articles in 2004.
28. "Directed Evolution of Protein Enzymes Using Nonhomologous Random Recombination" Bittker, J. A.; Le, B. V.; Liu, J. M.; Liu, D. R. *Proc. Natl. Acad. Sci. USA* **101**, 7011-7016 (2004).
29. "Engineering a Ligand-Dependent RNA Transcriptional Activator" Buskirk, A. R.; Landrigan, A.; Liu, D. R. *Chem. Biol.* **11**, 1157-1163 (2004). This work is featured in a Research Highlight in *Nature Methods* **1**, 6-7 (2004).
30. "Directed Evolution of Ligand Dependence: Small Molecule-Dependent Protein Splicing" Buskirk, A. R.; Ong, Y.-C.; Gartner, Z. J.; Liu, D. R. *Proc. Natl. Acad. Sci. USA* **101**, 10505-10510 (2004).
31. "DNA-Templated Organic Synthesis and Selection of a Library of Macrocycles" Gartner, Z. J.; Tse, B. N.; Grubina, R.; Doyon, J. B.; Snyder, T. M.; Liu, D. R. *Science* **305**, 1601-1605 (2004). Featured as a Research Highlight in *Nature Biotechnology* **22**, 1247 (2004).
32. "Reaction Discovery Enabled by DNA-Templated Synthesis and In Vitro Selection" Kanan, M. W.; Rozenman, M. M.; Sakurai, K.; Snyder, T. M.; Liu, D. R. *Nature* **431**, 545-549 (2004). This work is featured in a news focus article in *Science* **305**, 1558 (2004), in a Science and Technology Concentrate in *Chem. & Eng. News* **82** [40], 31 (2004), and in a News and Views commentary in *Nature Biotechnology* **22**, 1378-1379 (2004).
33. "Nucleic Acid-Templated Synthesis as a Model System for Ancient Translation" Calderone, C. T. and Liu, D. R. *Curr. Opin. Chem. Biol.* **8**, 645-653 (2004).
34. "In Vitro Characterization of IroB, a Pathogen-Associated C-Glycosyltransferase" Fischbach, M. A.; Lin, H.; Liu, D. R.; Walsh, C. T. *Proc. Natl. Acad. Sci. USA* **102**, 571-576 (2005).

35. "Creating Small Molecule-Dependent Switches to Modulate Biological Functions" Buskirk, A. R. and Liu, D. R. *Chem. Biol.* **12**, 151-161 (2005).
36. "DNA-Templated Functional Group Transformations Enable Sequence-Programmed Synthesis Using Small-Molecule Reagents" Sakurai, K.; Snyder, T. M.; Liu, D. R. *J. Am. Chem. Soc.* **127**, 1660-1661 (2005).
37. "Functional Dissection of sRNA Translational Regulators Using Nonhomologous Random Recombination and In Vivo Selection" Liu, J. M.; Bittker, J. A.; Lonshteyn, M.; Liu, D. R. *Chem. Biol.* **12**, 757-767 (2005).
38. "In Vitro Characterization of Salmochelin and Enterobactin Trilactone Hydrolases IroD, IroE, and Fes" Lin, H.; Fischbach, M. A.; Liu, D. R.; Walsh, C. T. *J. Am. Chem. Soc.* **127**, 11075-11084 (2005).
39. "Ordered Multistep Synthesis in a Single Solution Directed by DNA Templates" Snyder, T. M. and Liu, D. R. *Angew. Chem. Int. Ed.* **44**, 7379-7382 (2005).
40. "Small-Molecule Diversification From Iterated Branching Reaction Pathways Enabled by DNA-Templated Synthesis" Calderone, C. T. and Liu, D. R. *Angew. Chem. Int. Ed.* **44**, 7383-7386 (2005).
41. "DNA-Templated Synthesis in Organic Solvents" Rozenman, M.; Liu, D. R. *ChemBioChem* **7**, 253-256 (2006).
42. "Enzymatic Tailoring of Enterobactin Alters Membrane Partitioning and Iron Acquisition" Luo, M.; Lin, H.; Fischbach, M. A.; Liu, D. R.; Walsh, C. T.; Groves, J. T. *ACS Chemical Biology* **1**, 29-32 (2006).
43. "Directed Evolution and Substrate Specificity Profile of Homing Endonuclease I-SceI" Doyon, J.; Pattanayak, V.; Meyer, C. B.; Liu, D. R. *J. Am. Chem. Soc.* **128**, 2477-2484 (2006).
44. "How Pathogenic Bacteria Evade Mammalian Sabotage in the Battle for Iron" Fischbach, M. A.; Lin, H.; Liu, D. R.; Walsh, C. T. *Nature Chemical Biology* **2**, 132-138 (2006).
45. "A Protein Interaction Surface in Nonribosomal Peptide Synthesis Mapped by Combinatorial Mutagenesis and Selection" Lai, J. R.; Fischbach, M. A.; Liu, D. R.; Walsh, C. T. *Proc. Natl. Acad. Sci. USA* **103**, 5314-5319 (2006).
46. "Control of Transcription Factor Activity and Osteoblast Differentiation in Mammalian Cells Using an Evolved Small-Molecule-Dependent Intein" Yuen, C. M.; Rodda, S. J.; Vokes, S. A.; McMahon, A. P.; Liu, D. R. *J. Am. Chem. Soc.* **128**, 8939-8946 (2006). This work is featured in a Science and Technology Concentrate in *Chem & Eng. News* **84** [26], 34 (2006), as a Spotlight in *ACS Chemical Biology* **1**, 328 (2006), and as a News and Views article in *Nature* **442**, 517-518 (2006).
47. "Bromoenterobactins as Potent Inhibitors of a Pathogen-Associated, Siderophore-Modifying C-Glycosyltransferase" Lin, H.; Fischbach, M. A.; Gatto Jr., G. J.; Liu, D. R.; Walsh, C. T. *J. Am. Chem. Soc.* **128**, 9324-9325 (2006).
48. "Localized Protein Interaction Surfaces on the EntB Carrier Protein Revealed by Combinatorial Mutagenesis and Selection" Lai, J. R.; Fischbach, M. A.; Liu, D. R.; Walsh, C. T. *J. Am. Chem. Soc.* **128**, 11002-11003 (2006).
49. "Binding and Stability Determinants of the PPAR $\gamma$  Nuclear Receptor/Coactivator Interface as Revealed by Shotgun Alanine Scanning and In Vivo Selection" Phillips, K. J.; Rosenbaum, D. M.; Liu, D. R. *J. Am. Chem. Soc.* **128**, 11298-11306 (2006).
50. "The Pathogen-Associated *iroA* Gene Cluster Mediates Bacterial Evasion of Lipocalin 2" Fischbach, M.A.; Lin, H.; Zhou, L.; Yu, Y.; Abergel, R. J.; Liu, D. R.; Raymond, K. N.; Wanner, B. L.; Strong, R. K.; Walsh, C. T.; Aderem, A.; Smith, K. D. *Proc. Natl. Acad. Sci. USA* **103**, 16502-16507 (2006).
51. "In Vivo Evolution of an RNA-Based Transcriptional Silencing Domain in *S. cerevisiae*" Kehayova, P. D. and Liu, D. R. *Chem. Biol.* **14**, 65-74 (2007). This work is featured in a Research Highlight in *Nature Methods* **4**, 297 (2007).
52. "Synthesis of Acyclic  $\alpha,\beta$ -Unsaturated Ketones via Pd(II)-Catalyzed Intermolecular Reaction of Alkynamides and Alkenes" Momiyama, N.; Kanan, M. W.; Liu, D. R. *J. Am. Chem. Soc.* **129**, 2230-2231 (2007).

53. "Solving Chemical Problems Through the Application of Evolutionary Principles" Rozenman, M. M.; McNaughton, B. R.; Liu, D. R. *Curr. Opin. Chem. Biol.* **11**, 259-268 (2007).
54. "Directed Evolution Can Rapidly Improve the Activity of Chimeric Assembly-Line Enzymes" Fischbach, M. A.; Lai, J. R.; Roche, E. D.; Walsh, C. T.; Liu, D. R. *Proc. Natl. Acad. Sci. USA* **104**, 11951-11956 (2007).
55. "Supercharging Proteins Can Impart Extraordinary Resilience" Lawrence, M. S.; Phillips, K. J.; Liu, D. R. *J. Am. Chem. Soc.* **129**, 10110-10112 (2007). This work is featured in a Research Highlight in *Nature* **448**, 973 (2007) and in a News & Views article in *Nature* **449**, 555 (2007).
56. "Identification of Eukaryotic Promoter Regulatory Elements Using Nonhomologous Random Recombination" Doyon, J. B.; Liu, D. R. *Nucleic Acids Res.* **35**, 5851-5860 (2007).
57. "Directed Evolution Approaches to the Study of Proteins" Yuen, C. M.; Liu, D. R. *Nature Methods* **4**, 995-997 (2007).
58. "Discovery of a mRNA Mitochondrial Localization Element in *Saccharomyces cerevisiae* by Nonhomologous Random Recombination and *In Vivo* Selection" Liu, J. M.; Liu, D. R. *Nucleic Acids Res.* **35**, 6750-6761 (2007).
59. "Development and Initial Application of a Hybridization-Independent, DNA-Encoded Reaction Discovery System Compatible with Organic Solvents" Rozenman, M. M.; Kanan, M. W.; Liu, D. R. *J. Am. Chem. Soc.* **129**, 14933-14938 (2007). This work is featured in a Science and Technology Concentrate in *Chem. & Eng. News* **85** (47), 43.
60. "Effects of Template Sequence and Secondary Structure on DNA-Templated Reactivity" Snyder, T. M.; Tse, B. N.; Liu, D. R. *J. Am. Chem. Soc.* **130**, 1392-1401 (2008).
61. "DNA-Templated Polymerization of Side-Chain-Functionalized Peptide Nucleic Acid Aldehydes" Kleiner, R. E.; Brudno, Y.; Birnbaum, M. E.; Liu, D. R. *J. Am. Chem. Soc.* **130**, 4646-4659 (2008).
62. "Translation of DNA into a Library of 13,000 Synthetic Small-Molecule Macrocycles Suitable for In Vitro Selection" Tse, B. N.; Snyder, T. M.; Shen, Y.; Liu, D. R. *J. Am. Chem. Soc.* **130**, 15611-15626 (2008).
63. "Recent Progress Towards the Templated Synthesis and Directed Evolution of Sequence-Defined Synthetic Polymers" Brudno, Y. and Liu, D. R. *Chem. Biol.* **16**, 265-276 (2009).
64. "Mammalian Cell Penetration, siRNA Transfection, and DNA Transfection by Supercharged Proteins" McNaughton, B. R.; Cronican, J. J.; Liu, D. R. *Proc. Natl. Acad. Sci. USA* **106**, 6111-6116 (2009). This work was featured as a Research Highlight in *Nature Methods*.
65. "Wnt Signaling Promotes Pluripotency in Murine Embryonic Stem Cells by Activating Nanog Expression" Yuen, C. M. and Liu, D. R. **submitted** (2009).
66. "A Chemical Screen for Biological Small Molecule-RNA Conjugates Reveals Coenzyme A-Linked RNA" Kowtoniuk, W. E.; Shen, Y.; Heemstra, J. M.; Agarwal, I.; Liu, D. R. *Proc. Natl. Acad. Sci. USA* **106**, 7768-7773 (2009). This work was featured in a news story in *Chemistry World* (April 20, 2009), in a news story in *C&E News* **87** [17], 9 (2009), and in a Research Highlight in *Nature Chemical Biology* **5**, 380 (2009).
67. "Conversion of 5-Methylcytosine to 5-Hydroxymethylcytosine in Mammalian DNA by the MLL Fusion Partner, TET1" Tahiliani, M.; Koh, K. P.; Shen, Y.; Pastor, W. A.; Bandukwala, H.; Brudno, Y.; Agarwal, S.; Iyer, L. M.; Liu, D. R.; Aravind, L.; Rao, A. *Science* **324**, 930-935 (2009). This work was featured in a Spotlight in *ACS Chemical Biology* **4**, 315 (2009) and in a Research Highlight in *Nature* **458**, 1080 (2009).
68. "Reactivity-Dependent PCR: Direct, Solution-Phase In Vitro Selection for Bond Formation" Gorin, D. J.; Kamlet, A. S.; Liu, D. R. *J. Am. Chem. Soc.* **in press** (2009). This work was featured in a news story in *Chemistry World* (June 18, 2009).
69. "NAD-Linked RNA Discovered Using a Highly General Screen for Biological Small Molecule-RNA Conjugates" Chen, Y. G.<sup>‡</sup>; Kowtoniuk, W. E.<sup>‡</sup>; Agarwal, I.; Shen, Y.; Liu, D. R. **submitted** (2009).

70. "Templated Synthesis of Peptide Nucleic Acids via Sequence-Selective Base-Filling Reactions" Heemstra, J. M.; Liu, D. R. **submitted** (2009).
71. "An *In Vitro* Selection System for Peptide Nucleic Acid" Brudno, Y.; Birnbaum, M. E.; Kleiner, R. E.; Liu, D. R. **submitted** (2009).

## U. S. AND INTERNATIONAL PATENT APPLICATIONS AND ISSUED PATENTS

1. "Directed Evolution of Protein Enzymes Using Nonhomologous Random Recombination" Liu, D. R.; Bittker, J. USSN 60/562,761.
2. "Ligand-Dependent Protein Splicing" Liu, D. R.; Buskirk, A. R. USSN 60/557,865; U. S. Patent #7192739 issued March 20, 2007 and U.S. Patent #7,476,500 issued January 13, 2009.
3. "*In Vivo* Evolution of an RNA-Based Transcriptional Activator" Liu, D. R. ; Buskirk, A. R.; Kehayova, P. D. USSN 60/472,876.
4. "Discovering New Chemical Reactions by DNA-Templated Synthesis and *In Vitro* Selection" Liu, D. R.; Kanan, M. W. USSN 03/25,984.
5. "An *In Vivo* Selection System for Homing Endonuclease Activity" Liu, D. R. ; Gruen, M.; Doyon, J. B. USSN 10/102,056; U.S. Patent #7,476,500 issued January 13, 2009.
6. "Methods in Directed Evolution" Liu, D. R. USSN 60/277,094 and 60/306,691.
7. "Non-Homologous Random Recombination of Nucleic Acids" Liu, D. R.; Bittker, J. A. USSN 10/101,461.
8. "Evolving New Molecular Function" (DNA-Templated Chemistry) Liu, D. R.; Gartner, Z.; Kanan, M. W. USSN 10/101,030; U. S. Patent #7070928 issued July 4, 2006.
9. "*In Vivo* Incorporation of Unnatural Amino Acids" Schultz, P.; Wang, L.; Anderson, J.C.; Chin, J.; Liu, D. R.; Magliery, T. J.; Meggers, E. L.; Mehl, R. A.; Pastrnak, M.; Santoro, S. W.; Zhang, Z. USSN 10/126,927; U. S. Patent #7,368,275 issued May 6, 2008.
10. "Methods and Composition for the Production of Orthogonal tRNA-tRNA Synthetase Pairs" Schultz, P.; Wang, L.; Anderson, J.C.; Chin, J.; Liu, D. R.; Magliery, T. J.; Meggers, E. L.; Mehl, R. A.; Pastrnak, M.; Santoro, S. W.; Zhang, Z. USSN 10/126,931.
11. "Evolving New Molecular Function" Liu, D. R.; Gartner, Z.; Kanan, M. W.; U. S. Patent #7,442,160 issued October 28, 2008.
12. "Nucleotide Analogs" (for single-molecule DNA sequencing) Liu, D. R. USSN 11/295,155; U. S. Patent #7,476,734 issued January 13, 2009.
13. "Evolving New Molecular Function" Liu, D. R.; Gartner, Z. J.; Calderone, C. T. USSN 10/643,752; U. S. Patent #7,491,494 issued February 17, 2009.

## TEACHING EXPERIENCE

*Fall 1999-2000, Fall 2000-2001, Fall 2002-2003, Fall 2003-2004: Chemistry 170 (Chemical Biology).* I constructed this graduate-level course from hundreds of papers in the primary chemical and biological literature. Topics included: physical properties of nucleic acids and proteins, non-natural nucleotides, novel biosyntheses of proteins, mechanistic enzymology, *de novo* protein design, protein engineering, nucleic acid catalysis, emerging roles of RNA (including RNAi), molecular evolution, DNA damage and repair, novel natural proteins (GFP, inteins, catalytic antibodies, and prions), metabolic engineering, molecular mechanisms of drug resistance, rational design of macromolecular ligands, combinatorial approaches to small molecule discovery, chemical genetics, introduction to genomics, introduction to proteomics. Enrollment is

approximately 60 students (two-thirds undergraduates). Committee for Undergraduate Education (CUE) instructor ratings by students (out of 5.0): 4.5 ('99-'00); 4.6 ('00-'01); 4.6 ('02-'03); 4.6 ('03-'04).

*Spring 2001-2002: Chemistry 27 (Organic Chemistry of Life).* This course presents the organic chemistry behind many fundamental biological processes and was first developed by colleagues including Professor Stuart Schreiber and Professor Matthew Shair. Topics include protein structure, peptide sequencing, polypeptide synthesis, proteases, enzyme mechanisms, cofactors, signal transduction, nucleic acid structure and synthesis, DNA-damaging reagents, nonribosomal peptide biosynthesis, polyketide biosynthesis, and terpene biosynthesis. Enrollment is approximately 230 undergraduates. Committee for Undergraduate Education (CUE) instructor ratings by students (out of 5.0): 4.1 ('01-'02).

*Fall 2005-2006, Spring 2005-2006, Fall 2006-2007: Life Sciences 1a (An Integrated Introduction to the Life Sciences).* I co-created this new course—the largest natural science course offered at Harvard—to combine key components of general chemistry, organic chemistry, molecular biology, and cell biology into an integrated introduction to the life sciences. What are the fundamental features of living systems? What are the molecules that impart these features, and how do their chemical properties explain their biological roles? The answers to these questions form the basis for an understanding of the molecules of life, the cell, diseases, and medicines. In contrast with a traditional presentation of relevant scientific disciplines in separate courses, the above concepts are examined through an integrated presentation of concepts framed within central problems such as HIV and cancer. Fall 2006 enrollment is approximately 620 undergraduates (predominantly first-year undergraduates). Committee for Undergraduate Education (CUE) instructor ratings by students (out of 5.0): 4.6 (fall '05-'06); 4.8 (spring '05-'06); 4.2 (fall '06-'07).

*Fall 2008-2009: Science of Living Systems 11 (Molecules of Life).* This course, co-taught with Professor Jon Clardy, is one of the first General Education courses offered at Harvard. It evolved from an earlier Core Curriculum class (Science B-47) co-taught by Professor Jon Clardy and Professor Stuart Schreiber. SLS11 explores the relationships between large molecules and small molecules in living systems. Illustrative examples come from sexual development, metabolism, behavior, nerve transmission, infectious disease, cancer, diabetes, and stem cells. The course also emphasizes the increasing importance of genetic studies in identifying the molecular alterations underlying differences in human behavior, susceptibility to disease, and methods of drug discovery. As a General Education course, SLS11 relates these scientific concepts to problems of wide concern, and presents their historical, social, economic, or ethical context. Weekly hands-on activities, including simple experiments and roleplaying exercises, are integrated with lecture concepts. This course seeks to prepare students for civic engagement by equipping them with a basic understanding of the scientific principles underlying genes, proteins, and medicines, and also by identifying specific social issues at the crossroads of science and society such as privacy in the era of the inexpensive genome, the ways genes and small molecules combine to govern human behavior, and the extraordinary challenges associated with fighting disease and developing new drugs. Fall 2008 enrollment is approximately 80 undergraduates. Committee for Undergraduate Education (CUE) instructor ratings by students (out of 5.0): 4.7 ('08-'09).

## SERVICE AND ACTIVITIES OUTSIDE HARVARD UNIVERSITY

- Editorial Board, *Current Opinion in Chemical Biology* (Elsevier)
- Editorial Advisory Board, *Chemical Reviews* (American Chemical Society)
- Editorial Advisory Board, *ChemBioChem* (Wiley-VCH)
- Ad hoc member, NIH study section on Bioorganic Chemistry and Natural Products (BNP)
- Scientific Founder, Ensemble Discovery Corporation. (Cambridge, MA)
- Scientific Advisory Board Member, Helicos Biosciences Corporation (Cambridge, MA)
- Scientific Advisory Board Member, Codon Devices (Cambridge, MA)