

Marc Ostermeier

Johns Hopkins University
Department of Chemical and Biomolecular Engineering
3400 N. Charles St.
Baltimore, MD 21218 USA
Tel: 410.516.7144
Fax: 410.516.5510
oster@jhu.edu

Education

1996 Ph.D., Chemical Engineering, University of Texas at Austin
 Advisor: George Georgiou
1990 B.S., Chemical Engineering, University of Wisconsin-Madison

Positions and Employment

2011- Professor of Chemical and Biomolecular Engineering, Johns Hopkins University
2007- Faculty Member, Chemistry-Biology Interface Program, Johns Hopkins University.
2000- Faculty Member, Program in Molecular Biophysics, Johns Hopkins University.
2011-2013 Vice Chair, Chemical and Biomolecular Engineering, Johns Hopkins University
2008-2011 Director of the Graduate Program, Chemical and Biomolecular Engineering, Johns
 Hopkins University.
2007-2011 Associate Professor of Chemical and Biomolecular Engineering, Johns Hopkins
 University.
2005-2008 Director of the Undergraduate Program, Chemical and Biomolecular Engineering, Johns
 Hopkins University.
2000-2007 Assistant Professor of Chemical and Biomolecular Engineering, Johns Hopkins
 University.
1996-2000 Postdoctoral Fellow, Chemistry Department, Pennsylvania State University.
 Advisor: Stephen J. Benkovic

Honors and Awards

2011 Discover Magazine's Top 100 Science Stories of 2011
2003-2008 NSF CAREER Award
1999 Conference Fellowship, UEF Enzyme Engineering XV
1996-1999 NIH Postdoctoral Fellowship
1991 University of Texas at Austin Competitive Graduate Scholarship
1990- Member, Tau Beta Pi Engineering Honorary Society
1985-1987 New Mexico Institute of Mining and Technology Institutional Scholarship

Publications

58. Firnberg, E., J. W. Labonte, J. J. Gray, and M. Ostermeier. (submitted) "A comprehensive, high-resolution map of a gene's fitness landscape."
57. Valdes, G., R. W. Schulte, M. Ostermeier, and K. S. Iwamoto. (2013) "The high-affinity maltose switch MBP317-347 has low affinity for glucose: implications for targeting tumors with metabolically-directed enzyme prodrug therapy." *Chem. Biol. Drug Des.* DOI: 10.1111/cbdd.12249.
56. Firnberg, E. and M. Ostermeier. (2013) "The genetic code constrains yet facilitates Darwinian evolution." *Nucleic Acids Res.*, **41**, 7420-7428.
55. Choi, J. H., A. San, and M. Ostermeier. (2013) "Non-allosteric enzyme switches possess larger effector-induced changes in thermodynamic stability than their non-switch analogs." *Protein Sci.* **22**, 475-485.
54. Kanwar, M., R. C. Wright, A. Date, J. Tullman, and M. Ostermeier. (2013) "Protein switch engineering by domain insertion." *Methods in Enzymology*, **523**, 369-388.

53. Firnberg, E. and M. Ostermeier. (2012) "PFunkel: efficient, expansive, user-defined mutagenesis." *PLoS One* **7(12)**: e52031.
52. Chaikind, B., K. P. Kilambi, J. J. Gray, and M. Ostermeier. (2012) "Targeted DNA methylation using an artificially bisected M.HhaI fused to zinc fingers." *PLoS One* **7(9)**: e44852.
51. Ke, W., A. H. Laurent, M. D. Armstrong, Y. Chen, W. E. Smith, J. Liang, C. M. Wright, M. Ostermeier, and F. van den Akker. (2012) "Structure of an engineered β -lactamase maltose binding protein fusion protein: insights into heterotropic allosteric regulation" *PLoS One*, **7(6)**: e39168.
50. Guntas, G., M. Kanwar, and M. Ostermeier. (2012) "Circular permutation in the Ω -loop of TEM1 β -lactamase results in improved activity and altered substrate specificity." *PLoS One* **7(4)**: e35998.
49. Cheung, L. S.-L., M. Kanwar, M. Ostermeier, and K. Konstantopoulos. (2012) "A hot-spot motif characterizes the interface between a designed ankyrin-repeat protein and its target ligand" *Biophys. J.* **102**, 407-416.
48. Heins, R. A., J. H. Choi, T. Sohka, and M. Ostermeier. (2011) "In vitro recombination of non-homologous genes can result in gene fusions that confer a switching phenotype to cells." *PLoS One* **6(11)**: e27302.
47. Wright, C. M., R. C. Wright, J. R. Eshleman, and M. Ostermeier. (2011) "A protein therapeutic modality founded on molecular regulation." *Proc. Nat. Acad. Sci. USA*, **108**, 16206-16211.
46. Zayats, M., M. Kanwar, M. Ostermeier, and P. C. Searson. (2011) "Tuning protein recognition at the molecular level." *Macromolecules* **44**, 3966–3972.
45. Tullman, J., G. Guntas, M. Dumont, and M. Ostermeier. (2011) "Protein switches identified from diverse insertion libraries created using S1 nuclease digestion of supercoiled-form plasmid DNA." *Biotechnol. Bioeng.*, **108**, 2535-2543.
44. Zayats, M., M. Kanwar, M. Ostermeier, and P. C. Searson. (2011) "Surface-tethered protein switches." *Chem. Commun.* **47**, 3398–3400.
43. Hida, K., S. Y. Won, G. Di Pasquale, J. Hanes, J. A. Chiorini, and M. Ostermeier (2010) Sites in the AAV5 capsid tolerant to deletions and tandem duplications. *Arch. Biochem. Biophys.* **496**, 1-8.
42. Meister, G. E., S. Chandrasegaran, and M. Ostermeier. (2010) Heterodimeric DNA methyltransferases as a platform for creating designer zinc finger methyltransferases for targeted DNA methylation in cells. *Nucleic Acids Res.* **38**, 1749–1759.
41. Wright, C. M., A. Majumdar, J. R. Tolman, and M. Ostermeier. (2010) NMR characterization of an engineered domain fusion between maltose binding protein and TEM1 β -lactamase provides insight into its structure and allosteric mechanism. *Proteins.* **78**, 1423–1430.
40. Sohka, T., R. A. Heins, and M. Ostermeier. (2009) Morphogen-defined patterning of *Escherichia coli* enabled by an externally tunable band-pass filter. *J. Biol. Eng.* **3**, 10.
39. Kim, C., B. Pierre, M. Ostermeier, L. L. Looger, and J. R. Kim. (2009) Enzyme stabilization by domain insertion into a thermophilic protein. *Protein Eng. Des. Sel.* **22**, 615-623.
38. Ostermeier, M. (2009) Designing switchable enzymes. *Curr. Opin. Struct. Biol.* **19**, 442-448.
37. Sohka, T., R. A. Heins, R. M. Phelan, J. M. Greisler, C. A. Townsend and M. Ostermeier. (2009) An externally-tunable bacterial band-pass filter. *Proc. Nat. Acad. Sci. USA* **106**, 10135-10140.
36. Phelan, R. M., M. Ostermeier, and C. A. Townsend. (2009) Design and synthesis of a β -lactamase activated 5-fluorouracil prodrug. *Bioorg. Med. Chem. Let.* **19**, 1261-1263.
35. Meister, G.E., M. Kanwar, M. Ostermeier (2009) Circular permutation of proteins. In: S. Lutz, and U. Bornscheuer (eds) *Protein Engineering Handbook*, Wiley-VCH.
34. Meister, G. E., S. Chandrasegaran, and M. Ostermeier. (2008) An engineered split M.HhaI-zinc finger fusion lacks the intended methyltransferase specificity. *Biochem. Biophys. Res. Commun.* **377**, 226-230.
33. Berrondo, M., M. Ostermeier, and J.J. Gray (2008) Structure prediction of domain insertion proteins from structures of the individual domains. *Structure* **16**, 513-527.
32. Hida, K., J. Hanes, M. Ostermeier (2007) Directed evolution for drug and nucleic acid delivery. *Adv. Drug Deliv. Rev.* **59**, 1562-1578.

31. Wright, C. M., R. A. Heins, and M. Ostermeier. (2007) As easy as flipping a switch? *Curr. Opin. Chem. Biol.* **11**, 342-346.
30. Liang, J., J. R. Kim, J. T. Boock, T. J. Mansell and M. Ostermeier. (2007) Ligand binding and allostery can emerge simultaneously. *Protein Sci.* **16**, 929-937.
29. Ostermeier, M. (2007) Beyond cataloging the Library of Babel. *Chem. Biol.* **14**, 237-238.
28. Durai, S., A. D. Bosley, A. B. Abulencia, S. Chandrasegaran, and M. Ostermeier, (2006) A bacterial one-hybrid selection system for interrogating zinc finger-DNA interactions. *Comb. Chem. High Throughput Screen.* **9**, 301-311.
27. Kim, J.R. and M. Ostermeier, (2006) Modulation of effector affinity by hinge region mutations also modulates switching activity in an engineered allosteric TEM1 β -lactamase. *Arch. Biochem. Biophys.* **446**, 44-51.
26. Paschon, D. E., Patel, Z. S. and Ostermeier, M. (2005) Enhanced catalytic efficiency of aminoglycoside phosphotransferase (3')-IIa achieved through protein fragmentation and reassembly. *J. Mol. Biol.* **353**, 26-37.
25. Ostermeier, M. (2005) Engineering allosteric protein switches by domain insertion. *Protein Eng. Des. Sel.* **18**, 359-364.
24. Guntas, G., Mansell, T. J., Kim, J. R., and Ostermeier, M. (2005) Directed evolution of protein switches and their application to the creation of ligand-binding proteins. *Proc. Nat. Acad. Sci. USA* **102**, 11224-11229.
23. Choe, W., S. Chandrasegaran, and M. Ostermeier, (2005) Protein fragment complementation in M.HhaI DNA methyltransferase. *Biochem. Biophys. Res. Commun.* **334**, 1233-1240.
22. Bosley, A. D. and Ostermeier, M. (2005) Mathematical expressions useful in the construction, description and evaluation of protein libraries. *Biomolecular Engineering* **22**, 57-61.
21. Guntas, G., Mitchell, S.F. and Ostermeier, M. (2004) A molecular switch created by *in vitro* recombination of non-homologous genes. *Chem. Biol.* **11**, 1483-1487.
20. Paschon, D.E. and Ostermeier, M. (2004) Construction of protein fragment complementation libraries using incremental truncation. *Methods Enzymol.* **388**, 103-116.
19. Guntas, G. and Ostermeier, M. (2004) Creation of an allosteric enzyme by domain insertion. *J. Mol. Biol.* **336**, 263-273.
18. Ostermeier, M. (2003) Synthetic gene libraries: in search of the optimal diversity. *Trends Biotechnol.* **21**, 244-247.
17. Ostermeier, M. (2003) Theoretical distribution of truncation lengths in incremental truncation libraries. *Biotechnol. Bioeng.* **82**, 564-577.
16. Ostermeier, M. and Lutz, S. (2003) The creation of ITCHY hybrid protein libraries. *Methods Mol. Biol.* **231**, 129-142.
15. Lutz, S. and Ostermeier, M. (2003) Preparation of SCRATCHY hybrid protein libraries: size- and in-frame selection of nucleic acid sequences. *Methods Mol. Biol.* **231**, 143-152.
14. Ostermeier, M., Lutz, S. and Benkovic, S.J. (2002) Generation of protein fragment libraries by incremental truncation. In: Golemis, E.A. (ed) *Protein-Protein Interactions: A Molecular Cloning Manual*, Cold Spring Harbor Laboratory Press (Cold Spring Harbor, NY).
13. Lutz, S., Ostermeier, M., Moore, G., Maranas, C., and Benkovic, S.J. (2001) Creating multiple-crossover DNA libraries independent of sequence identity. *Proc. Nat. Acad. Sci. USA* **98**, 11248-11253.
12. Lutz, S., Ostermeier, M. and Benkovic, S. J. (2001) Rapid generation of incremental truncation libraries for protein engineering using α -phosphothioate nucleotides. *Nucleic Acids Res.* **29**, e16.
11. Ostermeier, M. and Benkovic, S. J. (2001) Construction of hybrid gene libraries involving the circular permutation of DNA. *Biotechnology Letters* **23**, 303-310.
10. Ostermeier, M. and Benkovic, S. J. (2000) Evolution of protein function by domain swapping. *Advances in Protein Chemistry* **55**, 29-77.

9. Ostermeier, M. and Benkovic, S. J. (2000) A two-phagemid system for the creation of non-phage displayed antibody libraries approaching one trillion members. *J. Immunol. Methods* **237**, 175-186.
8. Ostermeier, M., Shim, J. H. and Benkovic, S. J. (1999) A combinatorial approach to hybrid enzymes independent of DNA homology. *Nature Biotechnol.* **17**, 1205-1209.
7. Ostermeier, M., Nixon, A. E. and Benkovic, S. J. (1999) Incremental truncation as a strategy in the engineering of novel catalysts. *Bioorg. Med. Chem.* **7**, 2139-2144.
6. Ostermeier, M. and Benkovic, S. J. (1999) Finding Cinderella's slipper—proteins that fit. *Nature Biotechnol.* **17**, 639-640.
5. Ostermeier, M., Nixon, A. E., Shim, J. H. and Benkovic, S. J. (1999) Combinatorial protein engineering by incremental truncation. *Proc. Nat. Acad. Sci. USA* **96**, 3562-3567.
4. Nixon, A. E., Ostermeier, M. and Benkovic, S. J. (1998) Hybrid enzymes: manipulating enzyme design. *Trends Biotechnol.* **16**, 258-264.
3. Ostermeier, M., De Sutter, K. and Georgiou, G. (1996) Eukaryotic protein disulfide isomerase complements *Escherichia coli dsbA* mutants and increases the yield of a heterologously secreted protein with disulfide bonds. *J. Biol. Chem.* **271**, 10616-10622.
2. Georgiou, G., Valax, P., Ostermeier, M. and Horowitz, P. M. (1994) Folding and aggregation of TEM β -lactamase: analogies with the formation of inclusion bodies in *Escherichia coli*. *Prot. Sci.* **3**, 1953-1960.
1. Ostermeier, M. and Georgiou, G. (1994) The folding of bovine pancreatic trypsin inhibitor in the *Escherichia coli* periplasm. *J. Biol. Chem.* **269**, 21072-21077.

Patents

6. M. Ostermeier and E. Firnberg "Efficient, expansive, user-defined DNA mutagenesis", U.S. patent pending.
5. M. Ostermeier and C. M. Wright "Prodrug activation in cancer cells using molecular switches" U.S. patent pending.
4. M. Ostermeier, "Molecular switches and methods for making and using the same." U.S. patent 8,492,122.
3. M. Ostermeier and G. Guntas, "Methods for making and using molecular switches involving circular permutation" U.S. patent 8,338,138.
2. S. J. Benkovic, M. Ostermeier, A. E. Nixon, and S. Lutz, "Incrementally truncated nucleic acids and methods of making same" U.S. patent 7,332,308.
1. G. Georgiou and M. Ostermeier, "Methods for producing soluble, biologically-active disulfide-bond containing eukaryotic proteins in bacterial cells" U.S. patent 6,027,888.