

Institute of Biosciences & Technology
Texas A&M University

1993-1998 Assistant Professor of Biochemistry and Biophysics
Texas A&M University, Houston, Texas

Awards and Honors

1986-1989 Postdoctoral Fellowship
Damon Runyon-Walter Winchell Cancer Research Fund

1980-1985 NIH Predoctoral Trainee
Massachusetts Institute of Technology

1979 Phi Beta Kappa
Tufts University

Publications in Refereed Journals

Katz, S. S., Gimble, F. S. and Storici, F.* (2014) "To nick or not to nick: Comparison of I-SceI single- and double-strand break-induced recombination in yeast and human cells. *PLoS ONE* **9**:e88840.

Joshi, R., Ho, K. K., Tenney, K., Chen, J-H., Golden, B. L. and Gimble, F. S.* (2011) "Evolution of I-SceI homing endonucleases with increased DNA recognition site specificity" *J. Mol. Biol.* **405**:185-200.

Niu, Y., Tenney, K., Li, H. and Gimble, F. S. * (2008) "Engineering variants of the I-SceI homing endonuclease with strand-specific and site-specific DNA nicking activity" *J. Mol. Biol.* **382**:188-202.

Moure, C.M.*, Gimble, F. S. and Quijoch, F. A. (2008) "Crystal structures of I-SceI complexed to nicked DNA substrates: Snapshots of intermediates along the DNA cleavage reaction pathway. *Nucleic Acids Res.* **36**:3287-3296.

Posey, K., Koufopanou, V., Burt, A. and Gimble, F. S.* (2004) "Evolution of divergent DNA recognition specificities in VDE homing endonucleases from two yeast strains" *Nucleic Acids Res.* **32**:3947-3956.

Gimble, F. S.*, Moure, C. M. and Posey, K. (2003) "Assessing the plasticity of DNA target site recognition of the PI-SceI homing endonuclease using a bacterial two-hybrid selection system" *J. Mol. Biol.* **334**:993-1008.

Moure, C. M., Gimble, F. S. and Quijoch, F. A.* (2003) "The crystal structure of the gene targeting homing endonuclease I-SceI reveals the origins of its target site specificity" *J. Mol. Biol.* **334**:685-695.

Moure, C. M., Gimble, F. S., and Quijoch, F. A.* (2002) "Crystal structure of the intein homing endonuclease PI-SceI bound to its recognition sequence" *Nature Struct. Biol.* **9**:764-770.

Posey, K. and Gimble, F. S.* (2002) "Insertion of a reversible redox switch into a rare-cutting DNA endonuclease" *Biochemistry* **41**:2184-2190.

Gimble, F. S.* (2001) "Degeneration of a homing endonuclease and its target sequence in a wild yeast strain" *Nucleic Acids. Res.* **29**:4215-4223.

Hu, D. Crist, M. Duan, X., Quioco, F. A. and Gimble, F. S.* (2000) "Probing the structure of the PI-*SceI*-DNA complex by affinity cleavage and affinity photo-crosslinking" *J. Biol. Chem.* **275**:2705-2712.

Hu, D., Crist, M. Duan, X., and Gimble, F. S.* (1999) "Mapping of a DNA binding region of the PI-*SceI* homing endonuclease by affinity cleavage and alanine-scanning mutagenesis." *Biochemistry* **38**:12621-12628.

Gimble, F.S.*, Duan, X., Hu, D. and Quioco, F.A. (1998) "Identification of Lys403 in the PI-*SceI* homing endonuclease as part of a symmetric catalytic center" *J. Biol. Chem.* **273**:30524-30529.

He, Z., Crist, M., Yen, H-c., Duan, X., Quioco, F. A. and Gimble, F. S.* (1998) "Amino acid residues in both the protein splicing and endonuclease domains of the PI-*SceI* intein mediate DNA binding" *J. Biol. Chem.* **273**:4407-4615.

Duan, X., Gimble, F.S. and Quioco, F.A.* (1997) "Crystal structure of PI-*SceI*, a homing endonuclease with protein splicing activity" *Cell* **89**:555-564.

Gimble, F.S.* and Wang, J. (1996) "Substrate recognition and induced DNA distortion by the PI-*SceI* endonuclease, an enzyme generated by protein splicing" *J. Mol. Biol.* **263**:163-180.

Brenneman, M., Gimble, F.S. and Wilson, J. H.* (1996) "Stimulation of intrachromosomal homologous recombination in human cells by electroporation with site-specific endonucleases." *Proc. Natl. Acad. Sci. USA*, **93**:3608-3612.

Gimble, F.S.* and Stephens, B.W. (1995) "Substitutions in conserved dodecapeptide motifs that uncouple the DNA binding and DNA cleavage activities of PI-*SceI* endonuclease" *J. Biol. Chem.* **270**: 5849-5856.

Perler, F.B.* , Davis, E.O., Dean, G.E., Gimble, F.S., Jack, W.E., Noren, C.J., Thorner, J., and Belfort, M. (1994) "Protein splicing elements: inteins and exteins - a definition of terms and recommended nomenclature" *Nucleic Acids Res.* **22**: 1125-1127.

Gimble, F.S. and Thorner, J.* (1993) "Purification and characterization of VDE, a site-specific endonuclease from the yeast *Saccharomyces cerevisiae*" *J. Biol. Chem.* **268**:21844-21853.

Bremer, M., Gimble, F.S., Thorner, J. and Smith, C.* (1992) "VDE endonuclease cleaves *Saccharomyces cerevisiae* genomic DNA at a single site: Physical mapping of the *VMA1* gene"

Gimble, F.S. and Thorner, J.* (1992) "Homing of a DNA endonuclease gene by meiotic gene conversion in *Saccharomyces cerevisiae*" *Nature* **357**:301-306.

Gimble, F.S. and Sauer, R.T.* (1989) "Lambda repressor mutants that are better substrates for RecA-mediated cleavage" *J. Mol. Biol.* **206**:29-39.

Gimble, F.S. and Sauer, R.T.* (1986) "Lambda repressor inactivation: Properties of purified *ind⁺* proteins in the autodigestion and RecA-mediated cleavage reactions" *J. Mol. Biol.* **192**:39-47.

Gimble, F.S. and Sauer, R.T.* (1985) "Mutations in bacteriophage lambda repressor that prevent RecA-mediated cleavage" *J. Bacteriol.* **162**:147-154.

Sauer, R.T.*, Nelson, H.C.M., Hehir, K., Hecht, M.H., Gimble, F.S., DeAnda, J., and Poteete, A.R. (1983) "The Lambda and P22 Repressors" *J. Biomole. Str. Dyns.* **1**:1011-1022.

Invited Reviews

Gimble, F. S.* (2007) "Engineering homing endonucleases to modify complex genomes" *Gene Therapy & Regulation.* **3**:33-50.

Gimble, F. S.* (2006) "Broken symmetry in homing endonucleases." *Structure* **14**:804-806.

Gimble, F. S.* (2000) "Invasion of a multitude of genetic niches by mobile endonuclease genes" *FEMS Microbiol. Lett.* **185**:99-107.

Gimble, F. S.* (1998) "Putting protein splicing to work." *Chem. & Biol.* **5**:251-256.

Book Chapters:

Joshi, R. and Gimble, F. S.* (2014) "A bacterial one-hybrid system to isolate homing endonuclease variants with altered DNA target specificities" *Methods Mol. Biol.* **1114**:221-236.

Gimble, F. S.* (2005) "Engineering homing endonucleases for genomic applications" in *Inteins and Homing Endonucleases* (M. Belfort, V. Derbyshire, B. Stoddard and D. Wood, eds.) Springer-Verlag. Berlin Heidelberg, pp 175-190.

Technology Transfer

1992 License agreements between UC-Berkeley and New England Biolabs, Inc. and Boehringer-Mannheim GmbH
"A site-specific endonuclease for the cleavage of very large DNA molecules"

1995 Licensing agreement between UC-Berkeley and Somatix Therapy Corporation
"A site-specific endonuclease for the cleavage of very large DNA molecules"

2002 U. S. Provisional Patent Application
"Endonuclease containing a molecular switch and method for controlling the activity of an endonuclease"
Inventors: Frederick S. Gimble and Karen L. Posey

Reference number: TAMUS 1798
Status: abandoned

- 2004 Interinstitutional Licensing agreement with Collectis, S. A. through Baylor College of Medicine
“Crystal structure of the gene targeting homing endonuclease with bound DNA”

Conference Presentations (Oral and Poster)

Gimble, F.S. and Sauer, R.T. (1984) Lambda repressor mutants having a non-inducible (*ind⁻*) phenotype. Program, Cold Spring Harbor Laboratory Bacteriophage Meeting, Cold Spring Harbor, NY, Abstract #189.

Gimble, F.S. and Thorner, J (1989) Detection of a factor from *Saccharomyces cerevisiae* that binds to the pheromone response element, ATGAAACA. Joint meeting of The American Society for Biochemistry and Molecular Biology and The American Society for Cell Biology. San Francisco, CA. *J. Cell Biol.* 107:332a.

Gimble, F.S. Lo, E.C-M. and Thorner, J. (1989) Purification of a factor that recognizes the pheromone response element (ATGAAACA) of *Saccharomyces cerevisiae*. UCLA Symposium on Molecular and Cellular Biology of Yeasts and Filamentous Fungi. Steamboat Springs, Colorado. *Jour. Cell. Biochem. Suppl.* 13E: 40.

Gimble, F.S., Davis, J.L., Hasson, M.S., Barfod, E.T., and Thorner, J (1990) Trans-acting factors required for peptide hormone-induced gene expression in yeast. UCLA Symposium on Receptor-mediated second messenger pathways. Keystone, Colorado. *Jour. Cell. Biochem. Suppl.* 14B: 251.

Gimble, F.S., Davis, J.L., Hasson, M.S., Barfod, E. T. and Thorner, J. (1990). Trans-acting factors required for peptide hormone-induced gene expression in yeast. West Coast Regional Conference of the Society for Developmental Biology. Fallen Leaf Lake, California.

Gimble, F.S. and Thorner, J. (1991) Characterization of PBF, a novel site-specific DNA endonuclease that is encoded by the *TFPI* gene. Cold Spring Harbor Laboratory Yeast Cell Biology Meeting, Cold Spring Harbor, NY. Abstract #243.

Gimble, F.S. and Thorner, J. (1993) Purification and characterization of VDE, a site-specific endonuclease from the yeast *Saccharomyces cerevisiae*. Texas Protein Folders Meeting. Abstract #3B.

Gimble, F.S. and Thorner, J. (1993) Purification and characterization of VDE, a site-specific endonuclease from *Saccharomyces cerevisiae*. FASEB Summer Research Conference on Restriction endonucleases and modification methyltransferases: Structures and mechanisms. Abstract #69.

Gimble, F.S. and Stephens, B.W. (1994) The yeast *VMA1* gene product involved in protein intron homing and protein splicing. Keystone Symposia on Transposition and site -specific recombination: Mechanism & Biology. *Jour. Cell. Biochem. Suppl.* 18B: 10.

Gimble F.S. and Stephens, B.W. (1994) Substitution of two conserved acidic amino acids in the PI-*SceI* endonuclease uncouples the DNA binding and DNA cleavage activities. Lost Pines Molecular Biology Conference. Abstract #102.

Gimble F.S. and Wang, J. (1996) Substrate recognition and induced DNA distortion by the PI-*SceI* endonuclease, an enzyme generated by protein splicing. FASEB Summer Research Conference on Enzymes that Act on Nucleic Acids. Saxtons River, VT.

Gimble F.S. and Wang, J. (1996) Substrate recognition and induced DNA distortion by the PI-*SceI* endonuclease, an enzyme generated by protein splicing. Lost Pines Molecular Biology Conference.

Gimble, F.S., Yen, H-c., He, Z., Duan, X. and Quioco, F.A. (1997) The role of Lys301 in DNA cleavage by the PI-*SceI* homing endonuclease. 11th symposium of The Protein Society, July, 1997 *Protein Science*, vol. 6, suppl. 2, p. 125.

Hu, D., He, Z., Crist, M., Yen, H-c., Duan, X., Quioco, F. A. and Gimble, F.S. (1998) Structural and genetic characterization of the DNA binding and cleavage properties of the PI-*SceI* intein. Texas Protein Folders Meeting, Camp Allen, Texas.

Gimble, F.S., He, Z., Hu, D., Crist, M., Yen, H-c., Duan, X., and Quioco, F.A. (1998) The endonuclease and protein splicing domains of the PI-*SceI* intein are both required for DNA binding. 12th symposium of The Protein Society, *Protein Science*, vol. 7, suppl. 1, p. 183.

Hu, D., Crist, M., Duan, X., Quioco, F. A., and Gimble, F.S. (1999) Structure of the PI-*SceI*-DNA complex probed by affinity cleavage and affinity photo-crosslinking. Lost Pines Molecular Biology Conference.

Hu, D., Crist, M., Duan, X., Quioco, F. A., and Gimble, F. S. (2000) Probing the structure of the PI-*SceI*/DNA complex by affinity cleavage and affinity photocross-linking. Fifth Annual Structural Biology Symposium. Galveston, Texas

Posey, K. and Gimble, F. S. (2000) Localization of amino acids in PI-*SceI* that contact the phosphate backbone of the recognition sequence. Lost Pines Molecular Biology Conference.

Posey, K. and Gimble, F. S. (2001) Identification of a DNA binding loop in PI-*SceI* and the effect of divalent metal ions on DNA binding. Sixth Annual Structural Biology Symposium. Galveston, Texas.

Gimble, F. S. Structural insights into the function and evolution of inteins. ASBMB Graduate/Postdoctoral Travel Award Program, ASBMB Meeting, Orlando, Florida. (2001)

Gimble, F. S. (2001) Degeneration of a homing endonuclease and its target recognition sequence in a wild yeast strain. 15th Symposium of The Protein Society, *Protein Science*, vol. 10, suppl. 2, p. 175.

Moure, C.M., Gimble, F.S., and Quioco, F.A. (2002) Crystal structure of the intein homing endonuclease PI-*SceI* bound to its recognition sequence. FASEB Summer Research Conference on Nucleic Acid Enzymes: Structures, Mechanisms & Novel Applications. Saxtons River, VT.

Moure, C.M. Gimble, F. S. and Quioco, F. A. (2002) Structural basis of DNA recognition by the intein-encoded homing endonuclease PI-*SceI*. The 16th Symposium of The Protein Society, *Protein Science*, vol. 11, suppl. 2.

Gimble, F. S., Moure, C. M. and Posey, K. (2003) Selection of DNA endonucleases with shifted specificities using a bacterial two-hybrid strategy. The 17th Symposium of the Protein Society. *Protein Science*, vol 12. suppl. 2.

Li, H. and Gimble, F. S. (2004) Partial uncoupling of the two active sites of the I-*SceI* homing endonuclease through mutation. Lost Pines Molecular Biology Conference.

Li, H. and Gimble, F. S. (2005) DNA strand scission by two active sites in the yeast I-*SceI* homing endonuclease. 25th Midwest Enzyme Chemistry Conference, Chicago, Illinois.

Li, H. and Gimble, F. S. (2006) DNA strand scission by two active sites in the yeast I-*SceI* homing endonuclease. FASEB Summer Research Conference on Nucleic Acid Enzymes, Saxtons River, VT.

Uncoupling the active sites of the I-*SceI* homing endonuclease to create DNA nicking enzymes with high specificity. ACS Central Regional Meeting: Protein and Peptide Engineering, Columbus, OH (2008)

Joshi, R., Tenney, K., Ho, K. K., Chen, J-H., Golden, B. L. and Gimble, F. S. (2009) Biochemical and crystallographic analysis of I-*SceI* derivatives displaying a shift in substrate specificity, 2nd Northwest Genome Engineering Consortium Workshop on Genome Engineering, Seattle, WA.

Gimble, F. S., Tenney, K., Ho, K. K., Chen, J-H., Golden, B. L., Joshi, R. (2010) Evolution of I-*SceI* derivatives with increased specificity. FASEB Summer Research Conference on Nucleic Acid Enzymes. Saxtons River, VT.

Joshi, R., Tenney, K., Ho, K. K., Chen, J-H., Golden, B. L. and Gimble, F. S. (2010) Evolution of I-*SceI* derivatives exhibiting narrowed specificity. 24th Annual Symposium of The Protein Society, San Diego, CA.

Invited Lectures

Internal:

Engineering and evolution of homing endonucleases. Purdue University iGEM group, Purdue University, West Lafayette, IN (2017)

Protein engineering of homing endonuclease target specificity. Department of Chemistry, Purdue University, West Lafayette, IN (2010)

Adding new value to old enzymes: Directed evolution of homing endonucleases to create novel enzymes. Department of Biochemistry, Purdue University. West Lafayette, IN (2007)

Adding new value to old enzymes: Engineering novel homing endonucleases through studies of structure, function and evolution. Department of Biochemistry, Purdue University. West Lafayette, IN (2005)

Evolution and engineering of DNA recognition specificities in homing endonucleases. Department of Biochemistry, Purdue University. West Lafayette, IN (2011)

External:

Evolution and engineering of DNA recognition specificities in homing endonucleases. Department of Chemistry and Biochemistry, Tucson, AZ (2011).

Evolution and engineering of DNA recognition specificities in homing endonucleases. New England Biolabs, Ipswich, MA (2011)

Adding new value to old enzymes: Engineering novel homing endonucleases through studies of structure, function and evolution. Department of Biochemistry, University of Western Ontario, London, Ontario (2007)

Adding new value to old enzymes: Engineering novel homing endonucleases through studies of structure, function and evolution. Department of Biology, Rensselaer Polytechnic University. Troy, NY (2005)

Adding new value to old enzymes: Engineering novel homing endonucleases through studies of structure, function and evolution. Wadsworth Center, New York State Department of Health. Albany, New York. (2005)

Homing on the range: The structure, function, evolution and engineering of a DNA endonuclease. Department of Physics, Sam Houston State University, Huntsville, Texas. (2003)

Homing on the range: The structure, function, evolution and engineering of a DNA endonuclease. Department of Genetics, University of Wisconsin, Madison, Wisconsin. (2003)

Structural insights into the function and evolution of inteins. ASBMB Graduate/Postdoctoral Travel Award Program, Orlando, Florida. (2001)

Structure, function and evolution of the PI-*SceI* intein from *Saccharomyces cerevisiae*. Department of Medical Biochemistry and Genetics, Texas A&M University Health Science Center, College Station, Texas (1999)

Structure, function and evolution of a homing endonuclease from yeast. Department of Microbiology, Arizona State University, Tempe, Arizona. (1999)

Structure, function and evolution of a homing endonuclease from yeast. Department of Microbiology and Immunology, Baylor College of Medicine, Houston, Texas. (1998)

Structure, function and evolution of a homing endonuclease from yeast. Department of Biochemistry, University of Massachusetts Medical School, Worcester, Massachusetts. (1998)

Structure, function and evolution of a homing endonuclease from yeast. Department of Microbiology and Molecular Genetics, University of Texas Health Science Center, Houston, Texas. (1998)

Characterization of the PI-*SceI* endonuclease from yeast: Evolutionary Implications for a Family of Mobile Elements. New England Biolabs, Beverly, Massachusetts. (1997)

Structure, function and evolution of a homing endonuclease from yeast. Department of Biochemistry and Molecular Biology, The University of Texas, Houston, Texas. (1997)

The curious case of the PI-*SceI* intein from yeast: Insights into the function and evolution of a homing endonuclease. Departments of Physics and Chemistry, Sam Houston State University, Huntsville, Texas. (1997)

Characterization of a Rare-cutting DNA Endonuclease from Yeast: Evolutionary Implications for a Family of Mobile Elements. Department of Biochemistry and Molecular Biology, The University of Texas, Houston, Texas. (1995)