

Shuang-yong Xu
Senior Scientist, Restriction Enzyme Division

Education:

1978-1982 B.S. in Microbiology, Nankai University, Tianjin, China
1983-1989 Ph.D. in Microbiology, University of Iowa, Iowa City, IA
1989-1991 Postdoctoral Associate, New England Biolabs (NEB), Inc. Beverly, MA
1996-2000 Certificate of Special Studies in Administration and Management
Harvard University

Research Interests:

My research interests include structure and function studies of restriction enzymes and catalytic mechanism. I'm also interested in engineering strand-specific nicking enzymes and artificial endonucleases. The new research direction in my group will be using genetic screening system for methylation-dependent endonucleases, DNA demethylase and 5mC-specific DNA glycosylases based on the "endo-blue" method.

Selected Publications:

1. Xu, S.-y. and Feiss, M. (1991) Structure of the bacteriophage cohesive end site: genetic analysis of the site (cosN) at which nicks are introduced by terminase. *J. Mol. Biol.* 220: 281-292.
2. Xu, S.-y. and Feiss, M. (1991) The last duplex base-pair of the phage chromosome: involvement in packaging, ejection and routing of DNA. *J. Mol. Biol.* 220: 293-306.
3. Xu, S.-y. and Schildkraut, I. (1991) Isolation of *Bam*HI variants with reduced cleavage activities. *J. Biol. Chemistry* 266: 4425-4429.
4. Xu, S.-y. and Schildkraut, I. (1991) Cofactor requirement of *Bam*HI mutant endonuclease E77K and its suppressor mutants. *J. Bacteriology* 173: 5030-5035.
5. Xu, S.-y. and Schildkraut, I. (1993) Protecting recognition sequences on DNA by a cleavage-deficient restriction endonuclease. *Biotechniques* 15: 310-315.
6. Fomenkov, A., Xiao, J.-P., Dila, D., Raleigh, E. and Xu, S.-y. (1994) The "endo-blue method" for direct cloning of restriction endonuclease genes in *E. coli*. *Nucl. Acids Res.* 22: 2399-2403.
7. Fomenkov, A. and Xu, S.-y. (1995) Isolation of temperature-sensitive mutants of the *Bam*HI restriction endonuclease. *Gene* 157: 303-310.
8. Fomenkov, A. and Xu, S.-y. (1995) Nucleotide sequence of a small plasmid isolated from *Acetobacter pasteurianus*. *Gene* 158: 143-144.
9. Fomenkov, A. and Xu, S.-y. (1995) Cloning of a gene from *Thermus filiformis* and characterization of the thermostable nuclease. *Gene* 163: 109-113.
10. Ruan, H., Lunnen, K., Wilson, G., and Xu, S.-y. (1996) Cloning and sequence comparison of *Ava*I and *Bso*BI restriction-modification systems. *Mol. Gen. Genetics* 252: 695-699.
11. Morgan, R., R. Camp, Wilson, G., and Xu, S.-y. (1996) Molecular cloning and expression of *Nla*III restriction-modification system in *E. coli*. *Gene* 183: 215-218.

12. Nwankwo, D.O., Maunus, R.E., Xu, S.-y. (1997) Cloning and expression of *AatII* restriction-modification system in *E. coli*. *Gene* 185: 105-109.
13. Ruan, H., Lunnen, K.D., Pelletier, J.J., Xu, S.-y. (1997) Overexpression of *BsoBI* restriction endonuclease in *E. coli*, purification of the recombinant *BsoBI*, and identification of catalytic residues of *BsoBI* by random mutagenesis. *Gene* 188: 35-39.
14. Wayne, J. and Xu, S.-y. (1997) Identification of a thermophilic plasmid origin and its cloning within a new *Thermus-E. coli* shuttle vector. *Gene* 195: 321-328.
15. Xu, S.-y., Xiao, J.-p., Posfai, J., Maunus, R., and Benner, J. (1997) Cloning of the *BssHII* restriction-modification system in *E. coli*: *BssHII* methyltransferase contains circularly permuted cytosine-5 methyltransferase motifs. *Nucl. Acids Res.* 25: 3991-3994.
16. Wayne, J., Holden, M., and Xu, S.-y. (1997) The *Tsp45I* restriction-modification system is plasmid-borne within its thermophilic host. *Gene* 202: 83-88.
17. Morgan R., Xiao, J.-p., and Xu, S.-y. (1998) Characterization of an extreme thermostable restriction enzyme *PspGI* from *Pyrococcus sp.* and cloning of the *PspGI* restriction-modification system in *E. coli*. *Applied and Environmental Microbiology* 64: 3669-3673.
18. Xu, S.-y. et al. (1998) Cloning and expression of the *ApaLI*, *NspI*, *NspHI*, *SacI*, *Scal*, and *SapI* restriction-modification systems in *E. coli*. *Mol. Gen. Genetics* 260: 226-231.
19. Hsieh P.C., Xiao, J.-p., O'Loane, D. and Xu, S.-y. (2000) Cloning, expression, and purification of a thermostable non-homodimeric restriction enzyme *BsII*. *J. Bacteriology* 182: 949-955.
20. Vander Woerd, M., Pelletier, J., Xu, S.-y., and Friedman, A. (2001) Restriction enzyme *BsoBI*-DNA complex: a tunnel for recognition of degenerate DNA sequences and potential histidine catalysis. *Structure* 9: 133-144.
21. Xu, Q, Morgan, R.D., Roberts, R.J., Xu, S.-y., van Doorn, L.J., J.P. Donahue, Miller, G.G., Blaser, M.J. (2002) Functional analysis of *iceA1*, a CATG-recognizing restriction endonuclease gene in *Helicobacter pylori*. *Nucl. Acids Res.* 30: 3839-3847.
22. Samuleson, J.C. and Xu, S.-y. (2002) Directed Evolution of Restriction Endonuclease *BstYI* to Achieve Increased Substrate Specificity. *J. Mol. Biol.* 319: 673-683.
23. Wei, A., Yuan, A., Fawcett, G., Butler, A. Davis, T. Xu, S.-y. and Salkoff, L. (2002) Efficient isolation of targeted *Caenorhabditis elegans* deletion strains using highly thermostable restriction endonucleases and PCR. *Nucl. Acids Res.* 30: e110.
24. Zhu, Z., Zhou, J. Friedman, A., and Xu, S.-y. (2003) Isolation of *BsoBI* variants with altered specificity. *J. Mol. Biol.* 330: 359-372.
25. Pingoud, V., Conzelmann, C., Kinzibach, S., Valeri, A., Kubareva, E., Bujnicki, J.M., Xu, S.-y. and Pingoud, A. (2003) *PspGI*, a Type II Restriction Endonuclease from the Extreme Thermophile *Pyrococcus sp.*: Structural and Functional Studies to Investigate an Evolutionary Relationship with Several Mesophilic Restriction Enzymes. *J. Mol. Biol.* 329: 913-929.

26. Roberts, R.J. et al. Xu, S.-y. (2003) A nomenclature for restriction enzymes, DNA methyltransferases, homing endonucleases and their genes. *Nucl. Acids Res.* 31: 1805-1812.
27. Vanamee ES, Hsieh P, Zhu Z, Yates D, Garman E, Xu S.-y., and Aggarwal AK (2003) Glucocorticoid receptor-like Zn(Cys)₄ motifs in *BsI* restriction endonuclease. *J. Mol. Biol.* 334: 595-603.
28. Zhu Z, Samuelson JC, Zhou J., Dore A., and Xu S.-y. (2004) Engineering Strand-specific DNA Nicking Enzymes from the Type IIS Restriction Endonucleases *BsaI*, *BsmBI*, and *BsmAI*. *J. Mol. Biol.* 337: 573-583.
29. Samuelson J.C., Zhu Z., and Xu, S.-y. (2004) The Isolation of Strand-specific Nicking Endonucleases from a Randomized *SapI* Expression Library. *Nucl. Acids Res.* 32: 3661-3671.
30. Chan, S.-h. Zhu, Z., Van Etten, J., and Xu, S.-y. (2004) Nt.CviPII from *Chlorella* virus: cloning of the three-base nicking endonuclease and its application in random DNA amplification. *Nucl. Acids Res.* 32: 6187-99.
31. Townson S.A., Samuelson J.C., Vanamee E.S., Edwards, T.A., Escalante C.R., Xu S.-y., and Aggarwal A.K. (2004) Crystal structure of *BstYI* at 1.85 Å resolution: a thermophilic restriction endonuclease with overlapping specificities to *BamHI* and *BglII*. *J. Mol. Biol.* 338: 725-733.
32. Townson S.A., Samuelson J.C., Xu S.-y., and Aggarwal A.K. (2005). Crystal structure of *BstYI* in complex with DNA. *Structure* 13: 791-801.
33. Sawaya MR., Zhu Z., Mersha F., Chan S-H., Dabur R., Xu S.-y., Balendiran GK (2005) Crystal structure of the restriction-modification system control element C.*BclI* and mapping of its binding site. *Structure* 13: 1837-1847.
34. Samuelson J.C., Morgan R. and Xu, S.-y. (2005) Engineer *NotI* variants with relaxed specificity. *Nucl. Acids Res.* 34: 796-805.
35. Chan S.-H., Zhu, Z., Van Etten J., and Xu, S.-y. (2006) Expression of *CviQII* nicking-modification system in a heterologous host: M.*CviQII* displays relaxed specificity towards AG sequence. *Protein Expression and Purification* 49: 138-50.
36. Parashar V., Capalash N., Xu, S.-y., Sako Y., Sharma, P. (2006) *TspMI*, a thermostable isoschizomer of *XmaI* (5'C/CCGGG3'): characterization and single molecule imaging with DNA. *Appl. Microbiol. Biotechnol.* 72: 917-23.
37. Townson, S.A., Samuelson, J.C., Bao, Y.M., Xu, S.-y. and Aggarwal, A.K. (2007) *BstYI* bound to noncognate DNA reveals a "hemispecific" complex: implications for DNA scanning. *Structure* 15: 449-459.
38. Zhang, P.H., Bao, Y.M., Sears, L., Lunnen, K. and Xu, S.-y. (2007) Rational design of a chimeric endonuclease targeted to *NotI* recognition site. *Protein engineering, Design, & Selection* 20: 497-504.
39. Chan, S.H., Bao, Y.M., Laget, S., and Xu, S.-y. (2007) *BmrI* nuclease domain as a cleavage module for combinatorial endonuclease with novel substrate specificity. *Nucl. Acids Res.* 35: 6238-48.

40. Xu, S.-y., Zhu, Z., Zhang, P.H., Samuelson, J.C., Chan, S.H., and Wilson, G. (2007) Discovery of Nb.*Bsr*DI and Nb.*Bts*I, and engineering of top strand nicking variants from *Bsr*DI and *Bts*I. *Nucl. Acids Res.* 35: 4608-4618.
41. Bao, Y.M., Higgins, L., Xu, S.-y. (2007) Cloning and expression of *Bmr*I restriction-modification system and construction of *Bmr*I nuclease variants with a single Cystein. *Protein Exp. & Purification* 58: 42-52.
42. Lambert, A., Shen, B., Samuelson, J., Maunus, R., Xu, S.-y., and Stoddard, B. (2008) Structures of the rare-cutting restriction endonuclease *Not*I reveal a novel metal binding fold in DNA recognition. *Structure* 16: 558-569.
43. Fomenkov, A., Too, P., Chan, S.-H., Vaisvila, R., Cantin, B.A., Tam, V., Xu, S.-y. (2008) Targeting DNA 5mCpG sites with chimeric endonucleases. *Anal. Biochemistry* 381: 135-141. doi:10.1016/j.ab.2008.06.035.

Patent Awards:

I am the inventor or co-inventor of 36 patent awards in the United States. I am also the co-inventor of 6 patent applications filed in the past 5 years.

NIH Grants:

I have received three phase I grants and one phase II grant from the National Institutes of Health.