

CONSTANCE JEFFERY

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CURRENT POSITION

Assistant Professor, Laboratory for Molecular Biology, Department of Biological Sciences, Univ. of Illinois, Chicago, IL 8/99 - present

Adjunct Professor, Bioengineering Department, Univ. of Illinois, Chicago, IL 5/03 - present

My lab studies the molecular mechanisms of enzyme catalysis and transmembrane signalling and transport. We employ X-ray crystallography, molecular biology, computer-based structure analysis, and biochemical characterization of our target proteins.

- Research on transmembrane proteins includes determining structures and mechanisms for multidrug resistance transmembrane transporters and a proteomics-level project for improving methods to study transmembrane proteins.
- Studies of enzyme structures and mechanisms include the moonlighting protein phosphoglucose isomerase/autocrine motility factor (PGI/AMF, the second enzyme in glycolysis and an extracellular growth factor), and enzymes from two pathogens, *Pseudomonas aeruginosa* and *Trypanosoma brucei*. By solving five structures of PGI/AMF with different ligands bound, we have developed a model of the multistep catalytic mechanism for this glycolytic enzyme.
- We are using the structures of PGI and other proteins in a computer-based study of the structural basis for single nucleotide polymorphisms (SNPs) that cause genetic disease.

EDUCATION

University of California at Berkeley (Berkeley, CA) 9/87 - 12/92
Laboratory of Prof. Daniel E. Koshland, Jr.

Ph.D. in Biochemistry, 1993. Dissertation Title: *E. coli* Chemotaxis Receptors: I. Effect of Mutations in the Aspartate Receptor Second Transmembrane Domain II. Computer-Based Homology Modeling of the Serine Receptor Ligand-Binding Domain.

Massachusetts Institute of Technology (Cambridge, MA) 9/84 - 6/87
B.S. Degree in Biology, June, 1987

Ohio State University (Columbus, OH) 9/83 - 6/84

RESEARCH EXPERIENCE

Brandeis University (Waltham, MA) 2/93 - 8/99
Cystic Fibrosis Foundation postdoctoral fellow with Prof. Greg Petsko and Prof. Dagmar Ringe at the Rosenstiel Basic Medical Sciences Research Center.

- Developed model/concept of moonlighting proteins, and wrote a review article describing examples of moonlighting proteins from the literature, their methods to switch between functions, possible methods of evolution, and potential benefits to cells
- Crystallized and solved the structure of the moonlighting protein phosphoglucose isomerase/neuroleukin/autocrine motility factor by the method of multiple isomorphous replacement. PGI is the last of the glycolytic enzymes to have its structure solved.
- Crystallized and solved the structure of *Saccharomyces cerevisiae* cytoplasmic aspartate aminotransferase by the method of molecular replacement.
- Determined the structures of five mutant forms of *E. coli* aspartate aminotransferase.
- Determined a crystal structure of porcine pancreatic elastase as part of involvement in the development of the Multiple Solvent Crystal Structures (MSCS) method of drug design.

Tufts University School of Medicine (Boston, MA)
N.I.H. postdoctoral fellow in the Physiology Department.

11/97 - 10/98

- Studied interactions of the cystic fibrosis transmembrane conductance regulator (CFTR) with a Cl⁻/HCO₃⁻ antiporter.

University of California at Berkeley

9/87 - 12/92

Graduate research with Prof. Daniel E. Koshland, Jr., Department of Molecular and Cell Biology.

- Demonstrated that a single hydrophobic to hydrophobic substitution in the transmembrane sequence can inhibit aspartate receptor function.
- Constructed over forty plasmids encoding *E. coli* aspartate receptors with mutations in the second transmembrane sequence, and expressed, purified, and characterized the mutant receptors.
- Created a three-dimensional model of the ligand binding domain of the *E. coli* serine receptor using computer-assisted homology modeling.

Massachusetts Institute of Technology

6/85 - 7/87

Undergraduate research:

- Assisted in research on the T cell receptor in the lab of Prof. David Raulet (Biology Dept.)
- Studied the *Klebsiella pneumoniae* nitrogenase protein in the lab of Prof. W. Orme-Johnson (Chemistry Dept.).

AWARDS AND FELLOWSHIPS

American Heart Association Scientist Development Grant, 2003-6

American Cancer Society Research Grant, 2002-3

University of Illinois Cancer Center/American Cancer Society Institutional Research Grant, 2001

UIC Campus Research Board Grant, 2001

UIC Award for Significant Impact on Undergraduates, 2000

NIH Postdoctoral Fellowship 1997-1998

Cystic Fibrosis Foundation Postdoctoral Fellowship, 1993-96

Honor Students Society, U. C. Berkeley, 1992

Regents Graduate Student Fellowship, 1988-89

Fankhauser Graduate Student Fellowship, 1987-88

Phi Beta Kappa, 1987

INVITED SEMINARS (1999 - present)

11/03 Northern Illinois University, DeKalb, IL

10/03 Notre Dame University, Notre Dame, IN

8/03 American Crystallographic Summer Course, Chicago, IL

3/03 Undergraduate Colloquium, Illinois Institute of Technology, Chicago, IL

7/02 Symposium at Brandeis University, Waltham, MA

5/02 Massachusetts Institute of Technology (MIT) Chemistry Department, Cambridge, MA

4/02 UIC/UIUC Bioinformatics Symposium

2/02 University of California, Berkeley, Department of Molecular and Cell Biology

10/01 Midwest Enzyme Conference, Chicago, IL

10/00 UIC Chemistry Department Seminar, Chicago, IL

10/99 Illinois Institute of Technology, Dept. of Biological, Chemical, and Physical Sciences, Chicago, IL

PUBLICATIONS

20. Jeffery, C. J. Moonlighting Proteins and Proteomics: Discovering, Predicting, and Annotating proteins with multiple functions. Invited review for *Targets*. *Submitted*.
19. Roux, C., J. H. Lee, C. J. Jeffery, and L. Salmon. Potent inhibition of type I yeast and type II *Pseudomonas aeruginosa* phosphomannose isomerases by the reaction intermediate analogue 5-phospho-D-arabinonohydroxamic acid. *Biochemistry*. *In press*.
18. Jeffery, C. J. (2003) Moonlighting Proteins: Old Proteins Learning New Tricks. *Trends in Genetics*. 19:415-417.
17. Jeffery, C. J. (2003) Multifunctional Proteins: Examples of gene sharing. *Annals of Medicine*. 35:28-35.
16. Arsenieva, D. and C. J. Jeffery. (2002) Conformational Changes in Phosphoglucose Isomerase Induced by Ligand Binding. *Journal of Molecular Biology* 323:77-84
15. Arsenieva, D., R. Hardré, L. Salmon, and C. J. Jeffery. (2002) The 1.9 Å Resolution Crystal Structure of Rabbit Phosphoglucose Isomerase Complexed with 5-phospho D-arabinonhydroxamate. *Proc. Nat. Acad. Sci., USA*. 9:5872-5877.
14. Lee, J. H., K. Z. Chang, V. Patel, and C. J. Jeffery. (2001) The Crystal Structure of Rabbit Phosphoglucose Isomerase Complexed with its Substrate, D-Fructose-6-Phosphate. *Biochemistry*, 40(26): 7799-7805.
13. Pasternak, A., A. White, C. J. Jeffery, N. Medina, M. Cahoon, D. Ringe, and L. Hedstrom. (2001) Crystal structures of Trypsinogen Mutants with Enhanced Activity and Inhibitor Binding. *Protein Science*, 10:1331-1342.
12. Jeffery, C. J., R. Hardré, and L. Salmon. (2001) The Crystal Structure of Rabbit Phosphoglucose Isomerase Complexed with 5-Phospho-D-Arabinonate Identifies the Role of Glu357 in Catalysis. *Biochemistry*, 40(6): 1560-1566.
11. Jeffery, C. J., B. Bahnson, W. Chien, D. Ringe, and G. A. Petsko. (2000) Crystal Structure of Rabbit Phosphoglucose Isomerase, a Glycolytic Enzyme that Moonlights as Neuroleukin, Autocrine Motility Factor, and Differentiation Mediator. *Biochemistry*. 39(5): 955-964.
10. Jeffery, C. J., L.M. Gloss, G. A. Petsko, and D. Ringe. (2000) The Role of Residues Outside of the Active Site in Catalysis: Structural basis for function of C191 mutants of *E. coli* Aspartate Aminotransferase. *Protein Engineering*. 13(2): 101-108.
9. Jeffery, C. J. Moonlighting Proteins. (1999) *Trends in Biochemical Sciences*. 24: 8-11.
8. Jeffery, C. J., T. Barry, S. Doonan, G. A. Petsko, and D. Ringe. (1998) Crystal Structure of *Saccharomyces cerevisiae* Cytosolic Aspartate Aminotransferase. *Protein Science* 7: 1218-1288.

7. Jeffery, C. J., T. Barry, S. Doonan, G. A. Petsko, and D. Ringe. (1998) Crystallization and Preliminary X-ray Diffraction Analysis of *S. cerevisiae* Aspartate Aminotransferase. *Acta Cryst D54*: 659-661.
6. Allen, K., C. Bellamacina, X. Ding, C. J. Jeffery, G. Petsko, and D. Ringe. (1996) An Experimental Approach to Mapping the Binding Surface of Crystalline Proteins. *The Journal of Physical Chemistry*. 100: 2605-2611.
5. Jeffery, C. J. and D. E. Koshland, Jr. (1999) The *E. coli* Aspartate Receptor: Sequence Specificity of a Transmembrane Helix Studied by Hydrophobic-Biased Random Mutagenesis. *Protein Engineering*. 12: 863-872.
4. Jeffery, C. J. and D. E. Koshland, Jr. (1994) A Single Hydrophobic to Hydrophobic Substitution in the Transmembrane Domain Impairs Aspartate Receptor Function. *Biochemistry* 33: 3457-3463.
3. Jeffery, C. J. and D. E. Koshland, Jr. (1993) *Vibrio cholerae* hlyB is a Member of the Chemotaxis Receptor Gene Family. *Protein Science*. 2: 1532-1535.
2. Jeffery, C. J. and D. E. Koshland, Jr. (1993) Three-dimensional Structural Model of the Serine Receptor Ligand-Binding Domain. *Protein Science* 2: 559-566.
1. Lynch, B. A., C. J. Jeffery, H.-P. Biemann, and D. E. Koshland, Jr. (1992) Transmembrane Signaling in the Bacterial Aspartate Receptor. *Proceedings of the Robert A. Welch Foundation Conference on Chemical Research*. XXXVI.

OTHER PROFESSIONAL ACTIVITIES

Manuscript Reviews (in the last four years):

Science, FEBS Letters, Nucleic Acids Reviews, Biochemistry, Protein Science, Proceedings of the National Academy of Sciences, Bioinformatics, Biochimica et Biophysica Acta, Acta Crystallographica, Archives of Microbiology, Trends in Plant Science, Journal of Bacteriology

Professional Societies

Member of the Protein Society

Member of the Biophysical Society

Member of the American Chemical Society

Member of the American Association for the Advancement of Science

Advanced Photon Source (synchrotron) User

TEACHING

Formal recognition of teaching ability:

Award for Significant Impact on Undergraduate Students at UIC, Spring 2000

Supervision of Postdoctoral Researcher:

Dr. Joseph Orgel

12/00 - 6/02

Dr. Orgel is now a Research Assistant Professor at Finch University Chicago Medical School

Supervision of Graduate Students in my laboratory:

Dmitry Suchkov (Joint student with Prof. David Stone) 3/00 - 3/01

Diana Arsenieva 3/00 - present

Ji Hyun Lee 3/00 - present

Forum Bhatt 3/01 - present

Ryo Kawamura 6/03 - present

Honors/Awards won by Graduate Students:

- Two of my students each won a Biology Department Graduate Student award for their research in my laboratory: Ji (2002) and Diana (2003).
- Ji won a US National Committee for Crystallography/NASA travel award for the International Union of Crystallography (IUCr) Congress in Geneva, Switzerland, Aug., 2002.
- Diana was awarded travel expenses to attend the Institut des Hautes Etuds Scientifiques meeting "Folding and Self-assembly of Macromolecules" in France Nov., 2001.

Supervision of Undergraduate Students in my laboratory:

Kathy Chang Fall 1999 - Summer 2002

Vishal Patel Fall 1999 - Summer 2003

Bong Bae Fall 2002 - Summer 2003

Brian Appavu Fall 2003 - present

Adita Gulabani Fall 2003 - present

Honors/Awards, Publications, and Presentations by Undergraduate Students:

- Undergraduate poster award Protein Society National Symposium, Boston, MA (2003).
- Kathy and Vishal each won a Sarah Madonna Kabbes Scholarship for Undergraduate Research from the Honors College for their research in my lab (2000).
- Vishal and Kathy won an award for their poster in the UIC Undergraduate Research Symposium (2002).
- Two undergraduates were authors on a publication: Lee, J. H., K. Z. Chang, V. Patel, and C. J. Jeffery. (2001) The Crystal Structure of Rabbit Phosphoglucose Isomerase Complexed with its Substrate, D-Fructose-6-Phosphate. *Biochemistry*, 40(26): 7799-7805. Vishal and I are currently writing another manuscript.
- Vishal and Kathy presented a poster at the American Chemical Society National Meeting, Chicago, IL (2001)
- Due in large part to his research experience in my lab, Vishal was selected to participate in summer programs for undergraduates at the Argonne National Laboratory synchrotron (2000), the National Institutes of Health (2001), and at Cold Spring Harbor Laboratories (2002).

Rotation students in my laboratory: 19

Qualifying Exam Committees and Ph. D. Thesis Committees: 14

Courses taught:

LAS100 Introduction to Liberal Arts	Fall 2000, 2001
Bios399 Independent Research	Fall 2000, 2001, 2002, 2003, Spring 2001, 2002, 2003
Bios454 Biochemistry II	Spring 2001, 2002, 2003
Bche513 Structure of Biopolymers	Spring 2001
Bios524 Molecular Biology I	Fall 2000, 2001, 2002, 2003
Bios594 Special Topics in Biological Sciences	Spring 2002

Course Development:

- Developed new part of Bche513 (Structure of Biopolymers) - 6 lectures about structures and molecular mechanisms of membrane proteins, enzymes, and proteins in signal transduction pathways
- Developed new part of Bios524 (Molecular Biology I) - my section (4 weeks) of this graduate student course covers protein structure, macromolecular X-ray crystallography, examples of protein structures and molecular mechanisms, and protein homology, design and proteomics.
- Designed new LAS100 section (Introduction to Liberal Arts) - "Determining the Three-dimensional Structure of Proteins" - Semester-long course to introduce information about protein structure and function, the technique of macromolecular x-ray crystallography, and genetic diseases at a level suitable for freshmen

Previous teaching experience:

Brandeis University: Trained and supervised undergraduate students in experiments involving protein crystallization and molecular biology.

University of California at Berkeley: Teaching assistant for Biochemistry 100, the Senior Biochemistry lecture course and for Biochemistry 101, the Junior/Senior Biochemistry lab.

UIC SERVICE

Member of Biology Department Graduate Admissions Committee

Honors College Fellow (Advisor to 8 - 10 honors students each semester) 9/99 - 7/02

REFERENCES

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