BIOGRAPHICAL SKETCH

NAME Constance Joan Jeffery	POSITION TITLE Associate Professor

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing,*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Massachusetts Institute of Technology	B.S.	06/87	Biology
University of California at Berkeley	Ph.D.	06/93	Biochemistry
Brandeis University	Postdoctoral		X-ray crystallography
Tufts University Medical School	Postdoctoral		Cystic Fibrosis

A. Personal Statement

I have over 30 years of experience in protein biochemistry and biophysics using multiple systems and techniques. My broad background in protein structure and function includes graduate studies at the University of California at Berkeley where I focused on biochemical studies of the *E. coli* aspartate receptor in the lab of Prof. Daniel E. Koshland, Jr., in the Dept. of Molecular and Cell Biology. I learned X-ray crystallography as a Cystic Fibrosis Foundation postdoctoral fellow with Prof. Greg Petsko and Prof. Dagmar Ringe at the Rosenstiel Basic Medical Sciences Research Center.

My lab at UIC studies the connections between protein sequence, structure, and function. We use a combination of biochemical, biophysical and computer-based bioinformatics and structural analysis to study moonlighting proteins, pseudoenzymes, and metamorphic proteins. As PI or co-PI for local, regional, and national grants, I successfully administered the projects, formed successful collaborations, and produced peer-reviewed publications from each project. From this experience, I learned a great deal about lab and project management, mentoring and training students and postdoctoral fellows from diverse backgrounds, working with collaborators, and developing a realistic research plan, timeline, and budget.

B. POSITIONS, SCIENTIFIC APPOINTMENTS AND HONORS:

Positions and Employment

2021 – 2021 Director, NSF Research Experience for Undergraduates in Macromolecular Structure and Function
2015 – 2021 Member, Biophysical Society CPOW Committee
2015 – present Master Mentor for 1000 Girls/1000 Futures and Next Scholars programs, Global STEM Alliance
2005 – present Associate Professor, Department of Biological Sciences, University of Illinois, Chicago, IL
2020 – NSF Review Panel Member
2006, 2007, 2008, 2020 Mentor for UIC Summer Research Opportunities Program
2018 – 2109 President of the University of Illinois (Iota) Chapter of Phi Beta Kappa
2015 – NSF Review Panel Member
2012 – 2016 NeXXT Mentor with the New York Academy of Sciences and the U.S. State Department
2011 – 2019 Mentor for MIT GWAMIT (Graduate Women at MIT)
2011 – 2013 Mentor for Association for Women in Science (AWIS) mentoring circle
2010 – 2014 European Research Council remote referee in peer review evaluations
2009 – 2010 Visiting Associate Professor, Department of Cell Biology, Harvard Medical School, Boston, MA

2008, 2009, 2011, 2012 - Ad hoc NSF grant reviewer
2005 – present Co-Organizer of Midwest Conferences on Protein Folding, Assembly, and Molecular Motions
2005 – present Member, University of Illinois at Chicago Cancer Center
2003 – present Adjunct Professor, Department of Bioengineering, University of Illinois, Chicago, IL
2000 – present Reviewer of grant proposals for several agencies [Wellcome Trust (2010), ACS Petroleum Research Fund (2004, 2005, 2006), UIC Campus Research Board (2000), Sigma Delta Epsilon/Graduate Women in Science (GWIS) (2013, 2014, 2016), UK BBSRC (2013), UK MRC (Medical Research Council) (2013), ANR, the French National Research Agency (2015), Polish National Science Center (2015)]
1999 – present – joined several scientific societies at various times during my career - Biophysical Society, Protein Society, American Chemical Society, New York Academy of Sciences, American Association for the Advancement of Science, National Association of Biology Teachers (NABT)
1999 – 2005 Assistant Professor, Department of Biological Sciences, University of Illinois, Chicago, IL
1997 – 1998 Postdoctoral Fellow, Physiology Department, Tufts University School of Medicine, Boston, MA
1993 – 1999 Postdoctoral Fellow, Brandeis University, Waltham, MA

Honors
2022 Fellow of the American Association for the Advancement of Science
2020 Women in Bio Diversity and Inclusion Award
2020 Paper included in Special Virtual Issue of Protein Science featuring Outstanding Research Articles authored by Women in Honor of International Women's Day 2020
2017 Women in the Enterprise of Science & Technology (WEST) Making a Difference Award
2006 Society for Biomolecular Screening Award
2000 Citation for Significant Impact on Students, University of Illinois at Chicago, Chicago, IL
1997 NIH Postdoctoral Fellow
1993 – 1996 Cystic Fibrosis Foundation Postdoctoral Fellow
1992 Honor Students Society, U. C. Berkeley
1988 Regents Graduate Student Fellowship
1987 Fankhauser Graduate Student Fellowship
1987 Phi Beta Kappa

C. Contributions to Science

1. Moonlighting Proteins

In recent years, hundreds of proteins have been found to be moonlighting proteins, where a single protein performs multiple physiologically relevant biochemical or biophysical functions that are not due to gene fusions, multiple RNA splice variants, or pleiotropic effects. I have been a major contributor to our understanding about moonlighting proteins through seventeen published review articles, five book chapters, an internet database, and nine additional research papers. During my postdoctoral studies, I wrote a review article in which I coined the term "moonlighting proteins", developed the idea/concept of moonlighting proteins and discussed their methods to switch between functions, possible methods of evolution, and potential benefits to cells. The 1999 *Trends in Biochemistry* article has been cited over 1000 times. More recently my lab created the MoonProt Database, a manually curated, searchable, internet-based database with information about the over 500 proteins that have been experimentally verified to be moonlighting proteins. The availability of this organized information provides a more complete picture of what is currently known about moonlighting proteins. The database will also aid researchers in other fields, including determining the functions of genes identified in genome sequencing projects, interpreting data from proteomics projects and annotating protein sequence and structural databases. In addition, information about the structures and functions of moonlighting proteins can be helpful in understanding how novel protein functional sites evolved on an ancient protein scaffold, which can help in the design of proteins with novel functions.

a) Chen, C., H. Liu, S. Zabad, N. Rivera, E. Rowin, M. Hassan, S.M. Gomez De Jesus, P. S. Llinás Santos, K. Kravchenko, M. Mikhova, S. Ketterer, A. Shen, S. Shen, E. Navas, B. Horan, J. Raudsepp, C.J. Jeffery (2021) MoonProt 3.0: an update of the moonlighting proteins database, *Nucleic Acids Research*, gkaa1101,
b) Jeffery, C. J. (2020) Enzymes, pseudoenzymes, and moonlighting proteins: diversity of function in protein superfamilies. *FEBS J.* 287(19):4141-4149. doi: 10.1111/febs.15446. PMID: 32534477.
c) Wang, W. and C. J. Jeffery. (2016) An Analysis of Surface Proteomics Results Reveals Novel Candidates for Intracellular/Surface Moonlighting Proteins in Bacteria. *Mol Biosyst.* 12(5):1420-31.
d) Jeffery, C. J. Moonlighting Proteins. (1999) *Trends in Biochemical Sciences*. 24: 8-11.

2. X-ray crystal structure and molecular mechanism of the Moonlighting Protein PGI/AMF

During my postdoctoral research, I determined the X-ray crystal structure of a glycolytic enzyme that moonlights as a tumor cell motility factor in breast cancer cells: phosphoglucose isomerase/autocrine motility factor (PGI/AMF). PGI was the last of the glycolytic enzymes to have its structure solved. In my own lab in the Department of Biological Sciences at the University of Illinois at Chicago, we elucidated the multistep catalytic reaction mechanism by solving six structures of PGI/AMF with different ligands bound. I was the PI on grants from my university and the American Cancer Society that supported the additional structure and catalytic mechanism studies of PGI/AMF and phosphomannose isomerases (PMI). Our work on PMI included a fruitful collaboration in which enzyme inhibition studies using small molecule ligands were combined with other methods in the development of a model of the catalytic mechanism for PMI.

a) Roux, C., F. Bhatt, J. Foret, B. de Courcy, N. Gresh, J.-P. Piquemal, C. J. Jeffery, and L. Salmon. (2011) Inhibition and Polarizable Molecular Mechanics Studies of Type I Phosphomannose Isomerases Reveal Information about the Reaction Mechanism*. Proteins: Structure, Function, and Bioinformatics* 79: 203-220*.*
b) Arsenieva, D., R. Hardré, L. Salmon, and C. J. Jeffery. (2002) The Crystal Structure of Rabbit Phosphoglucose Isomerase Complexed with 5-phospho-D-arabinonhydroxamate. *Proc. Nat. Acad. Sci., USA*. 99: 5872-7.
c) Arsenieva, D. and C. J. Jeffery. (2002) Conformational Changes in Phosphoglucose Isomerase Induced by Ligand Binding. *Journal of Molecular Biology.* 323: 77-84
d) 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: 955-64.

3. Determined Additional X-ray Crystal Structures

In addition to the structure and mechanism of PGI/AMF I determined the X-ray crystal structures of several other proteins, including a crystal structure of porcine pancreatic elastase for the development of the Multiple Solvent Crystal Structures (MSCS) method of drug design. I also crystallized and solved the structure of *Saccharomyces cerevisiae* cytoplasmic aspartate aminotransferase by the method of molecular replacement, and determined the structures of five mutant forms of *E. coli* aspartate aminotransferase. In my lab at UIC, I've been training graduate and undergraduate students in X-ray crystallography, and we have solved the structure of a trypanosomal PGI and the *E. coli* periplasmic murein tripeptide binding protein, MppA, in addition to the six structures of mammalian PGI mentioned above.

a) Bhatt F, Patel V, Jeffery CJ. (2018) Open Conformation of the *Escherichia coli* Periplasmic Murein Tripeptide Binding Protein, MppA, at High Resolution. *Biology (Basel)*. 7(2). pii: E30. doi: 10.3390/biology7020030. PMID: 29783769
b) Arsenieva, D., B. L. Appavu, G. Mazock, and C. J. Jeffery. (2009) X-ray Crystal Structure of *Trypanosoma brucei* Phosphoglucose Isomerase Complexed with Glucose-6-phosphate at 1.6 Å Resolution*. Proteins: Structure, Function, and Bioinformatics* 74:72-80

c) 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: 1380-7.
d) 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: 2605-11.

4. Transmembrane Proteins

During my graduate studies at the University of California at Berkeley I focused on biochemical studies of a transmembrane protein, the *E. coli* aspartate receptor. I constructed over forty plasmids encoding *E. coli* aspartate receptors with mutations in the second transmembrane sequence, and expressed, purified, and characterized the mutant receptors. Through these studies, I demonstrated that a single hydrophobic to hydrophobic substitution in a transmembrane helix can inhibit aspartate receptor function. I also discovered that aromatic amino acids are more often found at the ends than in the middle of transmembrane helices in proteins with one or two transmembrane helices, and I created a three-dimensional model of the ligand binding domain of the *E. coli* serine receptor using computer-assisted homology modeling. At UIC, I was PI on two national grants for developing improved methods to improve the expression and purification of membrane proteins. Each of these projects led to multiple peer-reviewed publications.

a) Jeffery, C. J. (2016) Expression, Solubilization and Purification of Bacterial Membrane Proteins. *Current Protocols in Protein Science.* 3:29.15.1-29.15.15. doi: 10.1002/0471140864.ps2915s83. PMID: 26836409.
b) Bhatt, F. and C. J. Jeffery. (2010) Expression, Detergent Solubilization, and Purification of a Membrane Transporter, the MexB Multidrug Resistance Protein. *J Vis Exp.* Dec 3;(46). pii: 2134. doi: 10.3791/2134.
c) Madhavan, V, F. Bhatt, and C. J. Jeffery. (2010) Recombinant expression screening of *P. aeruginosa* bacterial inner membrane proteins. *BMC Biotechnol.* 10:83.
d) 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: 3457-63.

Complete List of Published Work in MyBibliography:

http://www.ncbi.nlm.nih.gov/sites/myncbi/constance.jeffery.1/bibliography/47708816/public/?sort=date&direction=ascending.