BIOGRAPHICAL SKETCH

NAME: Jeffery, Constance J

eRA COMMONS USER NAME (credential, e.g., agency login): conniejeffery

POSITION TITLE: Associate Professor, Dept. Biological Sciences

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE (if applicable)	END DATE MM/YYYY	FIELD OF STUDY
Massachusetts Institute of Technology, Cambridge, Massachusetts	B.S.	06/1987	Biology
University of California at Berkeley, Berkeley, California	Ph.D.	06/1993	Biochemistry
Brandeis University, Waltham, Massachusetts	Post Doc	12/1997	Biophysics
Tufts University School of Medicine, Boston, Massachusetts	Post Doc	12/1998	Cystic Fibrosis
Brandeis University, Waltham, Massachusetts	Post Doc	09/1999	Biophysics

A. Personal Statement

My past and current research uses biochemistry, X-ray crystallography, Cryo-electron microscopy and computer-based methods to study protein structure, function and regulation. My studies of the *E. coli* aspartate receptor with Prof. Daniel Koshland, Jr., in the Dept. of Molecular and Cell Biology, Univ. of California at Berkeley, led to a Ph.D. in Biochemistry. Graduate research included mutational and biochemical studies that led to the discoveries that a single hydrophobic to hydrophobic substitution in a transmembrane helix can inhibit receptor function and that aromatic amino acids are often found at the ends of transmembrane helices in proteins with one or two transmembrane helices. I trained in X-ray crystallography as a Cystic Fibrosis Foundation postdoctoral fellow with Prof. Greg Petsko and Prof. Dagmar Ringe at Brandeis University. We determined the X-ray crystal structures of several proteins, including the moonlighting protein phosphoglucose isomerase/autocrine motility factor (PGI/AMF), which is an enzyme in glycolysis, an extracellular cytokine, and also binds to RNA. I also solved the structures of five mutant forms of *E. coli* aspartate aminotransferase to learn how those single amino acid substitutions outside of the active site pocket are able to affect catalysis. During my postdoctoral research I also developed the concept of moonlighting proteins, and the review article in which I coined the term “moonlighting proteins” has been cited over 1400 times.

I am currently an Associate Professor at the University of Illinois at Chicago (UIC). My lab studies the connections among amino acid sequences, structures and functions, with emphasis on elucidating the molecular mechanisms of protein functions in health and disease. By solving six X-ray crystal structures of PGI/AMF with different bound ligands, we developed a model of its multistep catalytic mechanism. We also solved the structures of PGI from *Trypanosoma brucei* and an *E. coli* periplasmic ligand binding protein. We constructed the MoonProt Database and advanced our understanding of moonlighting proteins through computer-based sequence and structural analyses. A current focus of our research is the structure, function , and regulation of moonlighting protiens for example enzymes in intermediary metabolism that have additional functions in binding to RNA to regulate translation, which can be important for coordinating protein expression with the metabolic state of the cell.

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 from diverse backgrounds, working with collaborators, and developing a realistic research plan, timeline, and budget. I also have significant experience in leadership and organizing or co-organizing training seminars, meetings and symposia, as well as service on faculty hiring committees, an editorial board, grant review panels, the Biophysical Society Committee for the Professional Opportunities for Women (BPS CPOW) and the UIC Department of Biological Sciences Diversity Committee. I currently serve as vice-chair of the BPS CPOW, and I am planning to serve as chair of the committee next year.

Throughout my career I have also strived for diversity, equity, and inclusion in STEM. Examples of my efforts within the university and in the community include serving as an inaugural member of the Biology Department Diversity, Equity, and Inclusion Committee and serving as a volunteer mentor for women and young people interested in STEM through the New York Academy of Science's NeXXT, 1000Girls/1000Futures and Junior Academy programs. I created and served as the director of the Macromolecular Structure and Function NSF Research Experiences for Undergraduates (REU) in the Summer of 2021, and I am currently the director of and American Heart Association undergraduate research and mentoring program. I received a UIC "Award for Significant Impact on Undergraduates" for mentoring undergraduates in my lab. Student researchers include UIC students as well as students from other schools through the UIC Summer Research Opportunities Program (SROP) who are members of groups that are under-represented in science careers. For my efforts for DEI both in the university and in the community, I also received a Diversity and Inclusion Award from Women in Bio and a Making a Difference Award from Women in the Enterprise of Science & Technology (WEST).

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2024 -	Visiting Faculty, Northeastern University, Boston, MA
2009 - 2010	Visiting Associate Professor, Harvard Medical School, Boston, MA
2005 -	Member, Center for Cancer Research, University of Illinois at Chicago, Chicago, IL
2005 -	Associate Professor, Dept. Biological Sciences, University of Illinois at Chicago, Chicago, IL
2003 -	Adjunct Professor, Dept. Bioengineering, University of Illinois at Chicago, Chicago, IL
1999 - 2005	Assistance Professor, Dept. Biological Sciences, University of Illinois at Chicago, Chicago, IL
1998 - 1999	Postdoctoral Fellow, Brandeis University, Waltham, MA
1997 - 1998	NIH Postdoctoral Fellow, Tufts University School of Medicine, Boston, MA
1993 - 1997	Cystic Fibrosis Foundation Postdoctoral Fellow, Brandeis University, Waltham, MA

Other Experience and Professional Memberships

2024–present	Vice-chair, Biophysical Society National Committee, Committee for Professional Opportunities for Women (CPOW)
2024	NIH Reviewer - Study Section
2024–present	Director, American Heart Association Institutional Award for Undergraduate Student Training
2023	NSF Reviewer – Study Section
2023–present	Biophysical Society National Committee, Committee for Professional Opportunities for Women (CPOW)
2021	Director and Mentor, NSF REU on Macromolecular Structure and Function
2021–present	Member, UIC chapter of Phi Beta Kappa Advisory Board
2017–2018	President, UIC chapter of Phi Beta Kappa
2014	Co-organizer of Chicago Symposium in Honor of the International Year of Crystallography
2011–2013	Mentor for Association for Women in Science (AWIS) mentoring circle
2011–2019	Mentor for MIT GWAMIT (Graduate Women at MIT)
2012–2015	Mentor for NeXXt Scholars Program with the New York Academy of Sciences and the U.S. State Department
2015–present	Mentor, STEMU, 1000 Girls/1000 Futures, and Junior Academy programs organized by the New York Academy of Sciences
2015–2021	Biophysical Society National Committee, Committee for Professional Opportunities for Women (CPOW)
2020	Ad hoc Grant Reviewer for Keck Foundation
2019	Ad hoc Grant Reviewer for Human Frontiers Science Program (HFSP)
2019	ESF College of Expert Reviewers, European Science Foundation
2019	Ad hoc Grant Reviewer for Natural Sciences and Engineering Research Council of Canada Herzberg Prize application
2018	Ad hoc Grant Reviewer for Poland National Science Centre
2018	Ad hoc Grant Reviewer (pre-proposals) for NAR, the French National Research Agency
2018	Ad hoc Grant Reviewer for Natural Sciences and Engineering Research Council of Canada Discovery Grant

2016	Ad hoc Grant Reviewer for Sigma Delta Epsilon/Graduate Women in Science (GWIS)
2015–2021	Reviewer of Travel Awards for the Biophysical Society
2015	Ad hoc Grant Reviewer for pre-proposals, NAR, the French National Research Agency
2015	NSF Reviewer - Study Section
2015	Ad hoc Grant Reviewer for Poland National Science Centre (Narodowe Centrum Nauki–NCN)
2014	Reviewer of Grant Applications for Sigma Delta Epsilon/Graduate Women in Science
2013	Ad hoc Grant Reviewer for UK Biotechnology and Biological Sciences Research Council
2013	Ad hoc Grant Reviewer for UK MRC (Medical Research Council)
2013	Reviewer of Grant Applications for Sigma Delta Epsilon/Graduate Women in Science
2012	Ad hoc NSF grant reviewer
2011	Ad hoc NSF grant reviewer
2010–2013	European Research Council remote referee in peer review evaluations
2010	Reviewer of Wellcome Trust grant proposal
2009	Ad hoc NSF grant reviewer
2008	Ad hoc NSF grant reviewer
2006	Reviewer of ACS Petroleum Research Fund grant proposals
2005–present	Co-Organizer of Midwest Conferences on Protein Folding, Assembly, and Molecular Motions (MWFold), Notre Dame University, Notre Dame, IN
2005	Reviewer of ACS Petroleum Research Fund grant proposals
2004	Reviewer of ACS Petroleum Research Fund grant proposals

Honors

2022	Fellow, American Association for the Advancement of Science
2020	Diversity and Inclusion Award, Women in Bio
2017	Making a Difference Award, Women in the Enterprise of Science & Technology (WEST)
2000	Citation for Significant Impact on Students, University of Illinois at Chicago
1997	Postdoctoral Fellow, NIH
1993 - 1996	Postdoctoral Fellow, Cystic Fibrosis Foundation
1992	Honor Students Society, University of California at Berkeley
1988	Regents Graduate Student Fellowship, University of California at Berkeley
1987	Elected Member, Phi Beta Kappa
1987	Fankhauser Graduate Student Fellowship, University of California at Berkeley

C. Contribution 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 1400 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, Liu H, Zabad S, Rivera N, Rowin E, Hassan M, Gomez De Jesus SM, Llinás Santos PS, Kravchenko K, Mikhova M, Ketterer S, Shen A, Shen S, Navas E, Horan B, Raudsepp J, Jeffery C.

MoonProt 3.0: an update of the moonlighting proteins database. Nucleic Acids Res. 2021 Jan 8;49(D1):D368-D372. PubMed Central PMCID: PMC7778978.

b. Wang W, Jeffery CJ. An analysis of surface proteomics results reveals novel candidates for intracellular/surface moonlighting proteins in bacteria. Mol Biosyst. 2016 Apr 26;12(5):1420-31. PubMed PMID: 26938107.

c. Amblee V, Jeffery CJ. Physical Features of Intracellular Proteins that Moonlight on the Cell Surface. PLoS One. 2015;10(6):e0130575. PubMed Central PMCID: PMC4481411.

d. Jeffery CJ. Moonlighting proteins. Trends Biochem Sci. 1999 Jan;24(1):8-11. PubMed PMID: 10087914.

2. **X-ray Crystal Structures 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. Arsenieva D, Jeffery CJ. Conformational changes in phosphoglucose isomerase induced by ligand binding. J Mol Biol. 2002 Oct 11;323(1):77-84. PubMed PMID: 12368100.

   b. Arsenieva D, Hardre R, Salmon L, Jeffery CJ. The crystal structure of rabbit phosphoglucose isomerase complexed with 5-phospho-D-arabinonohydroxamic acid. Proc Natl Acad Sci U S A. 2002 Apr 30;99(9):5872-7. PubMed Central PMCID: PMC122869.

   c. Lee JH, Chang KZ, Patel V, Jeffery CJ. Crystal structure of rabbit phosphoglucose isomerase complexed with its substrate D-fructose 6-phosphate. Biochemistry. 2001 Jul 3;40(26):7799-805. PubMed PMID: 11425306.

   d. Jeffery CJ, Bahnson BJ, Chien W, Ringe D, Petsko GA. Crystal structure of rabbit phosphoglucose isomerase, a glycolytic enzyme that moonlights as neuroleukin, autocrine motility factor, and differentiation mediator. Biochemistry. 2000 Feb 8;39(5):955-64. PubMed PMID: 10653639.

3. **X-ray Crystal Structures of Several Proteins**. 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 and 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. Open Conformation of the Escherichia coli Periplasmic Murein Tripeptide Binding Protein, MppA, at High Resolution. Biology (Basel). 2018 May 19;7(2) PubMed Central PMCID: PMC6022919.

   b. Arsenieva D, Appavu BL, Mazock GH, Jeffery CJ. Crystal structure of phosphoglucose isomerase from Trypanosoma brucei complexed with glucose-6-phosphate at 1.6 A resolution. Proteins. 2009 Jan;74(1):72-80. PubMed PMID: 18561188.

   c. Jeffery CJ, Barry T, Doonan S, Petsko GA, Ringe D. Crystal structure of Saccharomyces cerevisiae cytosolic aspartate aminotransferase. Protein Sci. 1998 Jun;7(6):1380-7. PubMed Central PMCID: PMC2144045.

   d. Allen KN, Bellamacina CL, Ding X, Jeffery CJ, Mattos C, Petsko GA, Ringe D. Experimental Approach to Mapping the Binding Surfaces of Crystalline Proteins. J Phys Chem. 1996; 100(7):2605. DOI: 10.1021/jp952516o

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. 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 CJ. Expression, Solubilization, and Purification of Bacterial Membrane Proteins. Curr Protoc Protein Sci. 2016 Feb 2;83:29.15.1-29.15.15. PubMed PMID: 26836409.
    b. Bhatt FH, Jeffery CJ. Expression, detergent solubilization, and purification of a membrane transporter, the MexB multidrug resistance protein. J Vis Exp. 2010 Dec 3; PubMed Central PMCID: PMC3159675.
    c. Madhavan V, Bhatt F, Jeffery CJ. Recombinant expression screening of P. aeruginosa bacterial inner membrane proteins. BMC Biotechnol. 2010 Nov 29;10:83. PubMed Central PMCID: PMC3009615.
    d. Jeffery CJ, Koshland DE Jr. A single hydrophobic to hydrophobic substitution in the transmembrane domain impairs aspartate receptor function. Biochemistry. 1994 Mar 29;33(12):3457-63. PubMed PMID: 8142342.

5. **Development of Research Projects to Include Undergraduates from Under-represented Groups in Research and Mentoring Opportunities**. I have mentored over 40 undergraduates in my lab at UIC, a minority-serving institution, and I have used my experience to develop opportunities combining research, mentoring and professional development activities. This experience became especially important during the first summer of the COVID-19 pandemic (2020), when students were unable to do research in labs and receive the training and mentoring that accompanies that experience. I created a remote, collaborative project for undergraduates and high school students in updating and expanding our MoonProt Database, an online resource used by labs around the world. The project resulted in adding over 200 proteins to the database and a publication that included high school students, high school teachers, and undergraduates as authors. I then created and served as the director of the Macromolecular Structure and Function NSF Research Experiences for Undergraduates (REU) in the Summer of 2021. I am currently the director of an American Heart Association funded program, UICHeart: University of Illinois Undergraduate Mentoring and Experience in Heart Research.

    a. Jeffery, CJ, MSFP: Undergraduate “Collaborate from Home” Research in Macromolecular Structure and Function, *Bioinformatics Advances*, 2023;, vbad074, DOI: 10.1093/bioadv/vbad074
    b. Jeffery CJ. Updating MoonProt From Home: An Online Student Research Project During the COVID-19 Pandemic *The Biophysicist* 2021 2 (2): 23–27. DOI: 10.35459/tbp.2021.000190.
    c. Jeffery CJ. “Developing an inter-institutional student research opportunity in biophysics during the COVID era: Updating MoonProt From Home: An Online Student Research Project During the COVID-19 Pandemic” Webinar Sponsored by the Biophysicist and the Biophysical Society Education Committee, March 2021

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/myncbi/constance.jeffery.1/bibliography/public/