BIOGRAPHICAL SKETCH

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NAME	POSITION TITLE
Lees, Watson James	Associate Professor of Chemistry
eRA COMMONS USER NAME (credential, e.g., agency login) LEESWATSON	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
McGill University, Montreal, PQ	B.Sc.	05/85	Chemistry
Harvard University, Cambridge, MA	Ph.D.	06/93	Chemistry
Harvard Medical School, Boston, MA	Postdoctoral	06/96	Enzymology

A. Personal Statement

I have the expertise and experience necessary to carry out the proposed research and to supervise undergraduate and graduate students. As the number of protein-based drugs, most of which contain disulfide bonds, increases, so does the need for the efficient production of proteins via in vitro protein folding. I have published numerous papers in the field of in vitro protein folding, including two in JACS, and I have written three review articles. My prior work on protein folding focused on the in vitro oxidative folding of disulfide containing proteins with aromatic thiols. We demonstrated that aromatic thiols could significantly improve the in vitro folding rate and yield of lysozyme and RNase A even at high protein concentration. However, to improve the in vitro protein folding further we needed to better understand the origins of the enhancements by investigating how these reagents affected the folding pathway. The folding pathway of bovine pancreatic trypsin inhibitor (BPTI) is arguably the best characterized of any system but prior work had focused on the pathway and not on the overall folding rate. Initially, we optimized the in vitro folding of reduced BPTI using the standard reagents glutathione disulfide (GSSG) and glutathione (GSH) and to our surprise found that previously disregarded pathways were likely important for efficient folding. Herein, we propose to confirm the importance of these pathways and then demonstrate strategies that further improve the folding rate of BPTI with GSSG and GSH, days to hours. Aromatic disulfides will then be used to develop strategies that minimize folding times even further. Strategies that improve in vitro protein folding have the potential to improve the production of an ever-expanding number of protein-based drugs and to address protein misfolding diseases.

I have a long and successful history of educating underrepresented students, including women, Hispanic and African American students. This commitment is represented in the composition of the undergraduate students in the research group. From 2004-2012, 24 undergraduate students were exposed to research in the Lees' group of which 54% were women, 58% were Hispanic and 8% were African American. These students have been coauthors on nine publications and gone on to pursue graduate degrees at Boston University, Duke, Michigan State, University of Mississippi etc., as well as pursuing professional degrees. In addition, during this time frame I have graduated 4 Masters students and 3 Ph.D. students and currently have 3 Ph.D. students in the laboratory. After graduation one of the graduate students obtained a job in academics (Univ. of Long Island) while the rest now work in the chemical/pharmaceutical industry. In summary, I have demonstrated the ability to perform productive research with graduate and undergraduate students and would like the opportunity to continue to do so.

B. Positions and Honors

Positions and Employment

1996-2003 Assistant Professor, Department of Chemistry, Syracuse University, Syracuse, NY
2003- Associate Professor, Department of Chemistry and Biochemistry, Florida International University, Miami, FL

Other Experience and Professional Memberships
1989- Member, American Chemical Society

C. Selected Peer-reviewed Publications (Selected from 57 peer-reviewed publications) (graduate students underlined, **undergraduate students** bolded)

Most relevant to the current application

1. Gough, J.D., **Williams, R.H.,** Donofrio, A.E. & Lees W.J. (2002). Folding Disulfide Containing Proteins Faster with an Aromatic Thiol. Journal of the American Chemical Society, 124 (15), 3885-3892. PMID: 11942825.

2. Gurbhele-Tupkar, M.C., **Perez, L.R., Silva, Y**. & Lees, W.J. (2008). Rate enhancement of the oxidative folding of lysozyme by the use of aromatic thiol containing redox buffers. Bioorganic and Medicinal Chemistry, 16(5), 2579-2590. PMID: 18065232

3. Kibria, F.M. & Lees, W.J. (2008). Balancing conformational and oxidative kinetic traps during the folding of bovine pancreatic trypsin inhibitor (BPTI) with glutathione and glutathione disulfide. Journal of the American Chemical Society, 130(3), 796-797. PMID: 18166059.

4. Lees W.J. (2008). Small-molecule catalysts of oxidative protein folding. Current Opinion in Chemical Biology, 2(6), 740-745. PMID: 18824127

5. Madar, D.J., Patel, A.S. & Lees, W.J. (2009) Comparison of the oxidative folding of lysozyme at a high protein concentration using aromatic thiols versus glutathione. Journal of Biotechnology, 142(3-4), 214-219. PMID: 19477205

6. Patel, A.S. & Lees, W.J. (2012) Oxidative Folding of Lysozyme with Aromatic Dithiols, and Aliphatic and Aromatic Monothiols. Bioorganic and Medicinal Chemistry, 20(2), 1020-1028. PMID: 22197395

7. Lothrop, A., Snider, G., Ruggles, E., Patel, A.S., Lees, W.J. & Hondal R. (2014) Selenium as an Electron Acceptor During the Catalytic Mechanism of Thioredoxin Reductase. Biochemistry, 53(4), 654-663. PMCID: PMC3957198

Additional recent publications of importance (in chronological order)

1. Islamova, N.I., Chen, X., **Digirolamo, J.A., Silva, Y.** & Lees W.J. (2008) Thermal stability and photochromic properties of a fluorinated indolylfulgimide in a protic and aprotic solvent. Journal of Photochemistry and Photobiology A: Chemistry, 199(1), 85-91. PMCID: PMC2654622

2. Cordes, T., Herzog, T.T., Malkmus, S., Draxler, S., Brust, T., **Digirolamo, J.A.**, Lees, W.J. & Braun, M. (2009) Wavelength and solvent independent photochemistry: the electrocyclic ring-closure of indolylfulgides. Photochemical & Photobiological Sciences, 8(4), 528-534. PMCID: PMC2845542

3. Draxler, S., Brust, T., Malkmus, S., **DiGirolamo, J.A.**, Lees, W.J., Zinth, W. & Braun, M. (2009). Ring-opening reaction of a trifluorinated indolylfulgide: mode-specific photochemistry after pre-excitation. Physical Chemistry Chemical Physics, 11(25), 5019-5027. PMCID: PMC2872927

4. Chen, X., Islamova, N.I., Garcia, S.P., **DiGirolamo, J.A.** & Lees, W.J. (2009) Synthesis and optical properties of aqueous soluble indolylfulgimides. Journal of Organic Chemistry 74(17), 6777-6783. PMCID: PMC2738845

5. Chen, X., Islamova, N.I., **Robles, R.V.** & Lees W.J. (2011). Photochromic properties of awater-soluble methyl carboxylic acid indolylfulgimide. Photochemical & Photobiological Sciences, 10(6), 1023-1029. PMCID: PMC3131137

6. Islamova, N.I., Chen, X., Fan, C., **Andino, R.** & Lees W.J. (2013). Photochromic copolymers containing 3-indolylfulgides/indolylfulgimides: synthesis and photochemical properties in toluene and as films. Polymer Degradation and Stability, 98(9), 1662-1670. PMCID: PMC3735237.

D. Research Support

Completed Research Support

1SC3GM084752-04 Lees (PI) 08/29/08-06/30/13
Using visible light to modulate biological systems
The goal of this study was to prepare photochromic compounds that would regulate the activity of biological systems
Role: PI