

Witold A. Witkowski

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Objective

To work as a scientist in a fast paced and challenging research environment developing novel applications from biologically inspired systems.

Education and Background

Ph.D. Chemistry, May, 2011 University of Massachusetts, Amherst, MA
Dissertation Title: Caspase-7 Loop Conformations as a Means of Allosteric Control
B.S. Chemistry and B.S. Biochemistry, 2005 College of Charleston, Charleston, SC
U.S. Citizen. Fluent English and Polish speaker.

Summary of Research

My doctoral research focuses on allosteric and direct control by small drug-like molecules of the apoptotic protein caspase-7 through a multidiscipline approach which spans biochemistry, molecular biology, and computer science. The goal of this research is to develop new methods for controlling caspase-7 that can be directly applied to clinical and pharmaceutical research. Techniques employed range from cloning and protein expression, DNA manipulation, PCR amplification and computational protein redesign, to analytical methods such as x-ray crystallography, analytical ultracentrifugation, mass spectrometry and fluorescence spectroscopy.

Previous research work as an undergraduate was with silane and germane small molecule vacuum manifold synthesis and characterization by spectroscopic (IR and Raman) and *ab initio* computational methods.

Research Experience and Technical Expertise

- Cloning, expression, and purification of recombinant proteins
 - Rational design of protein mutants, and corresponding DNA oligomers
 - DNA isolation, PCR amplification and characterization by gel electrophoresis
 - Bacterial culture and sterile procedure
 - Protein concentration and filtration for x-ray crystallography
- Multi-factor protein characterization
 - Enzyme kinetics monitored by fluorescence
 - Immunoblot detection
 - Affinity, Ion Exchange and Gel Filtration chromatography
 - UV/Vis & Fluorescence spectroscopy
 - Fluorescence Anisotropy
 - Tryptophan fluorescence
 - Circular Dichroism
 - Mass spectrometry
 - LC/MS, Direct Inject
 - Analytical Ultracentrifugation

- Protein x-ray crystallography
 - Crystal growth, screening, and stereo microscope crystal manipulation
 - Solved multiple novel protein crystal structures with and without inhibitor bound
 - Assisted in teaching graduate level protein x-ray crystallography course
- Taught PyMOL figure and motion figure generation class as part of a graduate course
- Mentor of incoming graduate students for 4 years and undergraduate researchers
- IR/Raman spectroscopy

Technical Skills and Expertise

- Molecular and protein visualization software
 - PyMOL
 - Avogadro
 - ChemDraw
 - Chem3D
 - jMol
- Data analysis software
 - GraphPad Prism 5
 - QuantumSoft ProFit 6.2
 - OmniGraphSketcher
 - OriginLabs Origin Pro
- Image manipulation software
 - ImageJ
 - Photoshop CS 4,5
 - Acorn
- Protein Crystallography suites and hardware
 - HKL2000
 - CCP4i
 - COOT
 - O
 - Crystalclear
 - Rigaku hardware
 - Beamline X25, Brookhaven National Lab
- Molecular Devices hardware and SpectraMAX software
- Molecular dynamics and quantum chemistry software
 - gromacs
 - GAMESS
 - Gaussian
 - EGAD
 - Developed integrated scripting system for in-house data analysis
- Expert knowledge in Windows, Mac OS X, and experienced in Linux/Unix systems.

Publications

- Witkowski, W. A. and Hardy, J.A. "L2' loop is critical for caspase-7 active-site formation." **Protein Science**, 2009, 18, 1459-1468.
- Klaeboe P, Nielsen C. J., Horn A, Guirgis G. A., Witkowski W. "Vibrational Spectra, conformational equilibrium, *ab initio* calculations and spectral assignments of ethylmethylgermane." **Vibrational Spectroscopy**, 2010, 54, 56-64.
- Klaeboe P., Guirgis G.A., Witkowski W.A., Horn A., Nielsen C. J. "Vibrational spectroscopic studies, conformations and quantum chemical calculations of 3,3,3-trifluoropropyl-silane and 3,3,3-trifluoropropylsilane-d₃" **Journal of Raman Spectroscopy**, 2006, 37, 29-51.

Horn A, Klæboe P., Nielsen C. J., Samdal, S., Guirgis G. A., Witkowski W. A. "Conformational equilibrium of ethoxytrichlorosilane investigated by infrared and Raman spectroscopy and by *ab initio* calculations." **Bulgarian Chemical Communications**, 2005, 37, 332-343.

Manuscripts in Press or Preparation

Witkowski, W. A. and Hardy, J.A., "A designed redox controlled caspase." In Press, Protein Science.

Witkowski, W. A. and Hardy, J.A., "Caspase-7 active site geometry, non-covalently bound to un-cleavable substrate mimic." In Preparation.

Selected Presentations

Witold A. Witkowski and Jeanne A. Hardy, "Studies of motion in the caspase-7 L2' loop." **Protein Society 23rd Annual Symposium**, Boston MA, 7/26/2009. Poster Presentation.

Witold A. Witkowski and Jeanne A. Hardy. "Investigation of L2' Loop in caspase-7 by Alanine Scanning Mutagenesis" **Pacific Coast Protease Symposium**, Warner Springs Ranch, CA. 4/18/2009.

Dipankar Basa, Nagamani Chikkannagari, Shilpi Sanghi, Michael Thorn, Witold A. Witkowski. "Developing a Blueprint for Innovations in Charge Transport Materials" **NSF Research2Innovation Workshop**, Cambridge, MA. 4/3/2009

Witold A. Witkowski and Jeanne A. Hardy. "Role of Caspase-7 L2' Loop in Active Site Formation and Allosteric Inhibition." **Protein Society 22nd Annual Symposium**, San Diego, CA. 7/27/2008 Poster Presentation.

Awards

Award of Distinction, Chemistry-Biology Interface Training Program, University of Massachusetts, Amherst. April 2011.

Richard and Meryl Brown Graduate Fellowship for Outstanding Research in Chemistry (2010) \$5000 cash award, one student per year.

References

Dr. Jeanne A. Hardy
Doctoral Research Advisor 2006-present
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Dr. Scott C. Garman
Dissertation Committee Member 2006-present
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