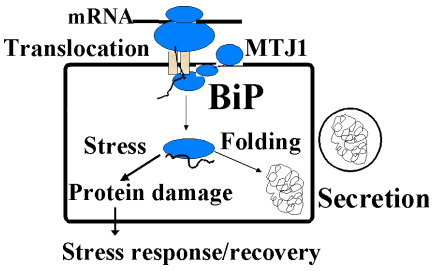
# Center for Pharmaceutical Biotechnology

College of Pharmacy
The University of Illinois at Chicago
http://www.uic.edu/pharmacy/research/cphb/

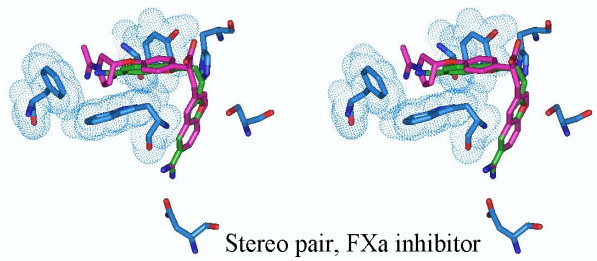
***Current Faculty Research Interests***

- **Dr. Sylvie Y. Blond**, Assistant Professor: Stress protection, recovery from drug-induced protein damage and assisted protein folding mediated by Heat Shock Proteins and Molecular Chaperones. The three-dimensional structure of a protein determines its biological activity. Protein misfolding result in the production of defective proteins, that may lead to dramatic symptoms such as those observed in certain genetic diseases and several types of cancers. Protein misfolding can also be induced by certain drugs that react specifically with reactive groups in proteins. BiP, a molecular chaperone localized in the endoplasmic reticulum, plays an essential role in protein translocation, folding, assembly and quality control of secreted and membrane proteins and participates in complex pathways involved in stress protection and recovery. Our goal is to isolate and characterize the partners that regulate BiP functions by using a combination of biochemical, genetic, spectroscopic, structural and mutational approaches.



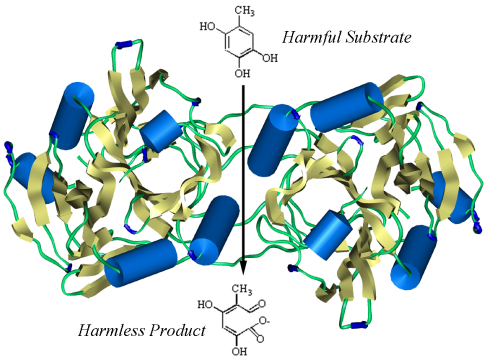

- **Dr. Scott G. Franzblau**, Professor: Discovery and development of new therapeutics for tuberculosis and other mycobacterioses. Development of high throughput screening assays using gene reporters and redox reagents for *in vitro* evaluation of drug candidates. Reporter assay development for anti-TB activity assessment in macrophages, mice and in non-growing, "dormant" *M. tuberculosis* cultures through identification of appropriate promotors. Development of TB drug susceptibility assays for use in developing countries. Structure-activity relationships of a variety of novel synthetic and natural products. Evaluation of role of efflux transporters in resistance of *M. tuberculosis* to established classes of anti-TB agents and assessment of the potential of efflux pump inhibitors as therapeutic agents. Drug-delivery systems for use in TB. Protein expression profiles of *M. tuberculosis* in response to established and new agents. Clinical evaluation of new agents.

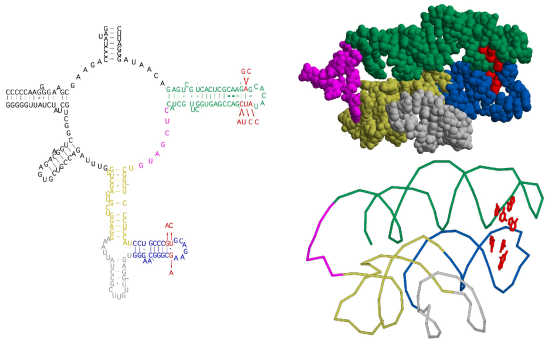
- **Dr. Michael E. Johnson**, Professor and Director of the Center: Nuclear magnetic resonance (NMR) studies of protein and peptide 3D structure, macromolecule-ligand interactions, computer-aided design and structural bioinformatics. Applications to sickle hemoglobin, the coagulation proteases, structural studies of the cytosckeletal protein, spectrin, and mechanisms of antibiotic resistance. Computer-aided molecular design of potential therapeutic agents. Current projects include NMR structure determination of spectrin domains, QSAR analysis of bacterial antibiotic potentiators, design of inhibitors for the coagulation cascade enzymes thrombin and factor Xa, and design of antisickling agents.


Stereo pair, FXa inhibitor

- **Dr. Andrew D. Mesecar**, Assistant Professor: We are studying the structure and function of enzymes and receptors involved in genetically inherited diseases, biological detoxification and cancerchemoprevention. Our lab utilizes a rangeof experimental methodologies in our research, including, but not limited to: x-ray crystallography, enzyme kinetics, fluorescence and CD spectroscopy, molecular biology, genetic engineering, DNA arrays, molecular modeling, 3-D visualization and bioinformatics. We are studying the catalytic, molecular recognition, and dynamic processes of biological systems at the molecular level by constructing atomic level

molecular movies from out experimental data and theoretical models. Our long term goals are to: 1) design novel therapeutic agents for chemotherapeutic, anti-parasitic and anti-bacterial applications, as well as for activating protein and enzymes subject to genetic mutations; 2) re-engineer and *de novo* design enzymes involved in bioremediation of environmentally hazardous compounds in order to expand their biodegradative repertoire to include currently non-biodegradable pollutants; 3) elucidate the mechanisms of and identify new chemopreventative compounds isolated from botanicals and foods.

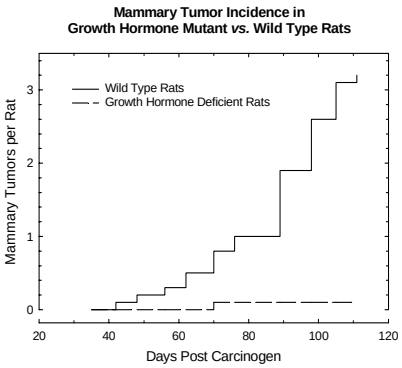


- **Dr. Alexander S. Mankin**, Associate Professor: All proteins in the cell are synthesized by the ribosome. The main interests of this laboratory are: 1) mechanisms of action of ribosome-targeted antibiotics and 2) functions of ribosomal RNA in protein synthesis. We investigate how antibiotics interact with the ribosome, and in particular, ribosomal RNA. We explore mechanisms of drug resistance and ways to overcome it. In another set of projects, we use a combination of genetic and biochemical techniques trying to understand how ribosomal RNA participates in catalysis of peptide bond formation and how the ribosome evolved.

- **Dr. Alexander A. Neyfakh**, Associate Professor: Mechanisms of bacterial resistance to antibiotics. A novel functional genomics approach is used to identify genes involved in the intrinsic resistance of bacteria to antimicrobial agents. The approach is based on a newly developed original method, which allows for previously unattainable selection and characterization of bacterial mutants hypersensitive to antibacterial compounds. The expected benefits of this strategy include identification of novel protein targets for antibiotics and antibiotic potentiators, as well as the discovery of previously obscure functional interactions of seemingly unrelated biochemical pathways within the bacterial cell. The same method is employed for studying the processes of molecular macroevolution under laboratory conditions.

- **Dr. Steven M. Swanson**, Assistant Professor: My laboratory is interested in mechanisms by which hormones can modulate susceptibility of target cells to cancer causing agents. We are using a wide range of techniques to address this problem. We study the response to carcinogens of mutant and transgenic animals with disruptions in genes for specific hormones or growth factors. We also use molecular and cellular techniques to evaluate the impact of hormone or growth factor treatments on specific cell signaling pathways both in whole animals and cells in culture. In one of our current projects, we are following up on a new observation that rats lacking growth hormone are nearly completely refractory to a powerful mammary carcinogen (*N*-methyl-*N*-nitrosourea).




- **Dr. Cele Abad-Zapatero**, Adjunct Professor (Abbott Laboratories, primary affiliation): Structure-based drug design for several targets, including aspartic proteinases, protein tyrosine phosphatases, RNA-methyl transferases and protein kinases. Protein Engineering of alkaline phosphatase mutants with higher catalyic efficiency. Automation methods for protein crystallography. Use of Synchrotron radiation in structural biology, structure-based drug design and protein engineering. Structural genomics.

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