

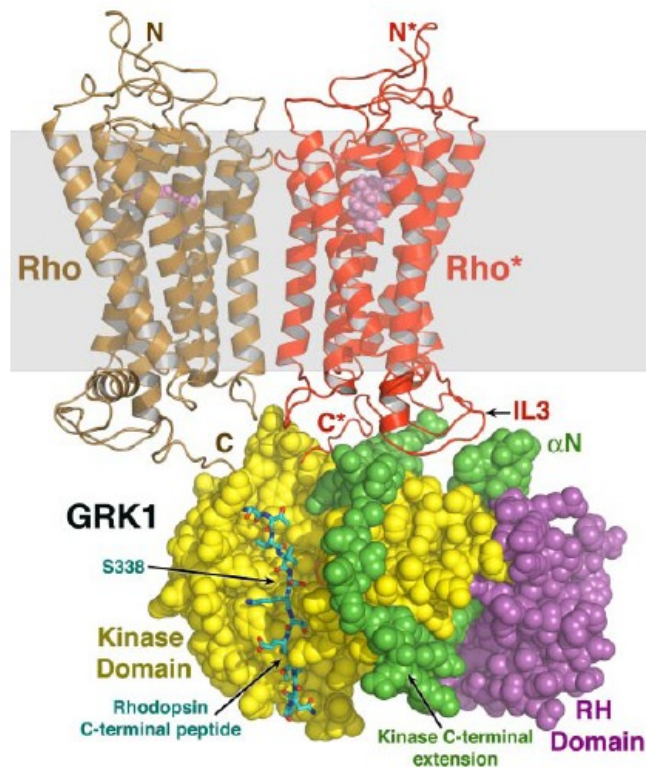


# Annual Report 2007-2008

*Center for Proteomics and Bioinformatics*

*Cleveland Foundation Center for Proteomics*

*Center for Synchrotron Biosciences*



Center helps reveal key elements involved in G protein-coupled receptor kinase activation

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## Director's Report for 2008

The Center for Proteomics and Bioinformatics (CPB) and Cleveland Foundation Center for Proteomics in the School of Medicine continues to grow and develop its vision as a world-leading center for proteomics, bioinformatics, and systems biology. This vision was dramatically altered quite recently, as the Dean of the School of Medicine approved a plan to rename the Center and raise the visibility of the Bioinformatics mission. The impact of these changes will be clearer in time for next year's report, however they emphasize the importance of computational biology to the research and education missions of the Center.

The faculty of the Center continue to build their research and funding portfolios; Dr. Jinsook Chang received an R21 grant from NIDDK entitled: "Vsca1, A Biomarker for Vascular Complications" and a pilot grant award from the NCI funded TREC program for her work in obesity and cancer titled: "Role of Genetic Susceptibility to Obesity and Tumorigenesis". Profs. Shi and Takamoto are important Co-investigators in a major program project awarded to the school as part of the NIAID funded HIV Vaccine Development program. Prof. Miyagi is playing a key role in the NIH funded Vision Sciences Center and in projects related to post-translational modifications of rapid response transcription factors. Dr. Kiselar is participating in NIDCR research related to beta-defensins and expanding the Center's involvement in HIV biology research overall. Center students and Post-Doctoral fellows have also received a number of training awards, including Dr. Gurkan Bebek and Dr. Jen Bohon and graduate students Vishal Patel and Rod Nibbe. Over the last year the Center launched a pilot grant program, funding five projects for \$10,000 each from seventeen applications. We expect these pilots to lead to additional extramural collaborative funding. Overall, the center's core and collaborative grant programs continue to grow dramatically, with \$43 million in grants awarded since 2005 and over \$30 million in funding currently pending.

The research portfolio of the faculty and staff continues to strengthen. We include six science highlights that showcase the best research of the CPB over the last year. These include research by the Palczewski group defining the mechanism by which a specific kinase quenches the signaling of the G-protein coupled receptor rhodopsin through specific phosphorylation events (published in *J. Biol. Chem.*). A second highlight (published in *Mol. Cell. Prot.*) explores the pathophysiology of diabetes related complications that involve the down regulation of structural and extra-cellular matrix proteins in bladder smooth muscle. This pathophysiology was revealed by expression proteomics studies coupled to protein interaction network modeling. Overall, the Center's faculty and staff have been actively publishing, with 44 papers published or in-press in 2008. They have also been quite active in presenting posters and giving talks at national meetings and giving invited lectures around the country; 70 presentations of faculty and staff are reported. We also report the publications of users who carried out service research within the cores of the Center; this activity resulted in 156 publications and is primarily derived from research at our synchrotron facilities. Overall, the record of 200 publications total indicates the strength of the research program.

An important goal of the CPB is to develop an infrastructure of sophisticated equipment that facilitates and maximizes shared equipment usage, as well as to offer a wide array of proteomics services. The Center now has seven major cores that are functioning at a high level; these include Expression Proteomics, Mass Spectrometry, Biostatistics, Systems Biology Data Analysis, Macromolecular Crystallography, X-ray Spectroscopy, and X-Ray Footprinting. The last three cores are available to a national community of users based on Case facilities that are operated at the National Synchrotron Light Source of Brookhaven Laboratories<sup>1</sup>. These cores serve hundreds of users in Cleveland and across the world. For example, the Mass Spectrometry Core routinely processes over 1500 samples each quarter on its instruments; this output is shown in the chart below. The Expression Proteomics Core offers 2-D gel, label-free, and O<sup>18</sup>-labeling methods of expression analysis; these approaches are optimized based the specific needs of the investigator.

The continued development of these cores is driving the overall research activity of the Center. Over the course of FY 2008, 107 Cleveland based PIs and investigators utilized the Center's facilities; these investigators come from 37 Departments and Divisions of the University. These users have interacted with the Center in a variety of ways, some projects have involved simple "drop-off" service, others have included close collaboration with Center faculty and staff in the design and execution of experiments, while a third class of interactions involve "independent use" of Center facilities. In this case, users are trained in the use of Center instruments and conduct and analyze their own experiments.

The Center continued to increase its personnel during its third year, currently the Center employs 48 faculty, Research Associates, Post-Docs, Research Assistants, support staff and students, including 11 faculty members with primary or secondary appointments. Additionally, Center faculties are training 3 graduate students as they pursue a Ph.D. degree. Our most recent faculty recruit, Dr. Rob Ewing joined the Center in March 2007 as an expert in Bioinformatics and Computational Biology; he also has a secondary appointment in Genetics. Dr. Ewing studies protein networks in human cells relevant to disease. He is leading the expansion of the Center's capabilities in identifying and exploring signaling networks in higher eukaryotes; this will result in the development of an Interaction Proteomics Core this year. The effort is essential to providing an advanced systems description of human disease. The Center also recently participated with the Department of Pharmacology in the recruitment of Dr. Chris Dealwis, who received a secondary appointment in Proteomics. Dr. Dealwis has expertise in cancer related crystallography and mass spectrometry studies and will be an institutional leader in structural biology. These faculty recruitments have been supported by the Cleveland Foundation.

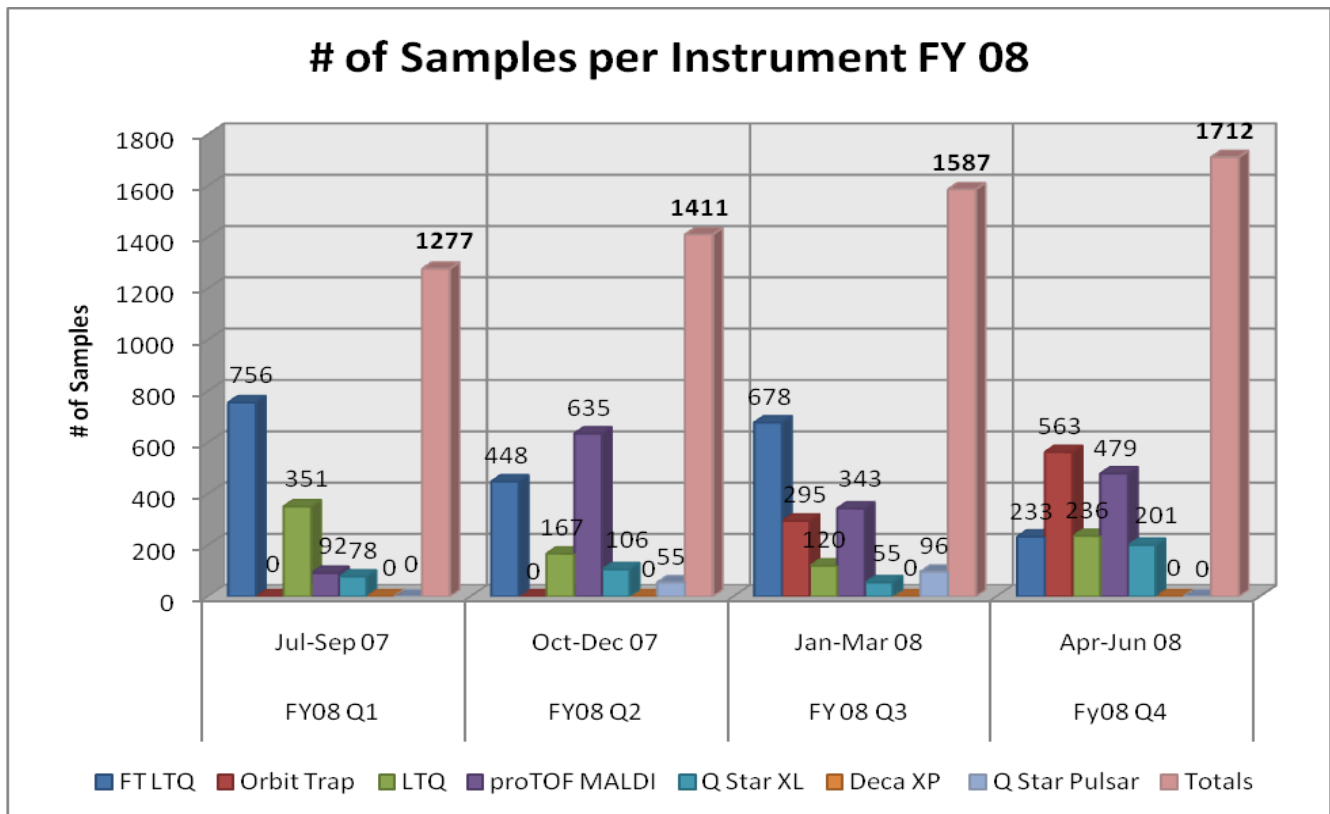
The Center has also become an important resource for training and dissemination of information on proteomics technologies and approaches. The Center continues its Thursday seminar series and 27 seminars were held from July 2007 through June 2008, with an average attendance of 40 people. Speakers included Center faculty and staff, nationally recognized scientists and instrument vendors. Dr. Chance recently edited a book published by Wiley on the topic of structural mass spectrometry that included twelve articles by leading experts in cross-linking, deuterium exchange, and footprinting. The Center also maintains a popular website that details services, publications, facilities, contact information and seminars.<sup>2</sup>

We expect the publication rate of Center staff and users to accelerate as results continue to flow through the technology pipelines and we expect to continue to recruit highly qualified faculty and staff, especially in the area of Bioinformatics. The coming year promises to provide exciting opportunities for the faculty and staff of the Center.

Website Links:

1-<http://casemed.case.edu/proteomics/CSB/INDEX.shtml>

2-<http://proteomics.case.edu>

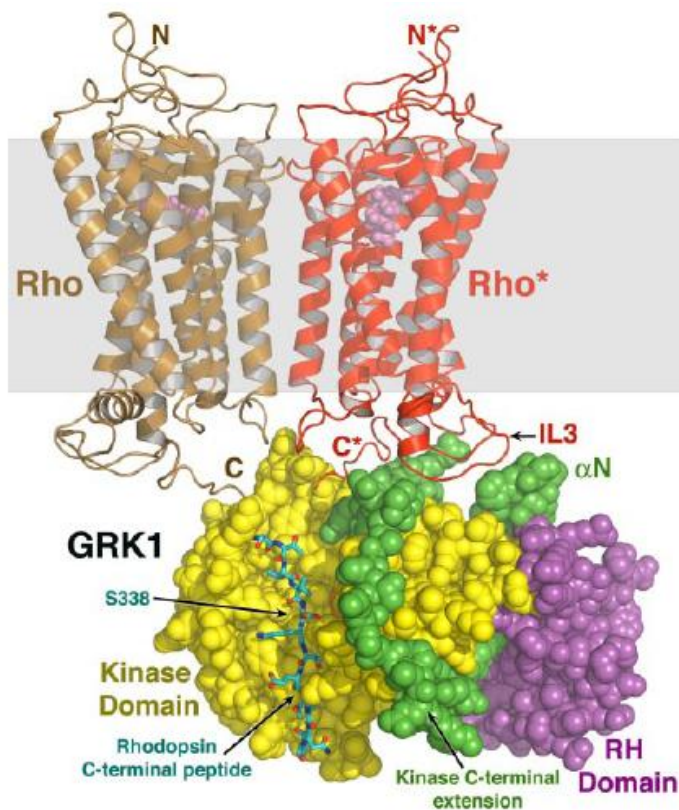


## Highlight #1: Structures of Rhodopsin Kinase in Different Ligand States Reveal Key Elements Involved in G Protein-coupled Receptor Kinase Activation

Rhodopsin (Rho) is the G protein-coupled receptor (GPCR) responsible for visual signal transduction in rod cells. Phosphorylation of light-activated Rho (Rho\*) by rhodopsin kinase, also known as GPCRkinase 1 (GRK1), initiates a series of events that rapidly quenches signaling by the receptor. This rapid desensitization is essential for scotopic vision and, in concert with the regeneration of visual pigment, protects rod cells from photodegeneration and permits rapid adaptation to changes in illumination. Phosphorylation of Rho\* at multiple sites by GRK1 is also believed to contribute to the reproducibility of the single photon visual response.

Liquid chromatography-tandem mass spectrometry analysis of digested GRK1 proteins was performed using a linear ion trap mass spectrometer (model LTQ) from Thermo-Finnigan coupled with an Ettan MDLC system (GE Healthcare). The obtained data were submitted to Bioworks (Thermo Scientific) by searching the phosphorylation on Ser, Thr, and Tyr. Phosphorylation sites were confirmed by tandem MS2 and/or MS3.

Here we report six crystal structures of rhodopsin kinase (GRK1), revealing not only three distinct nucleotide-binding states of a GRK but also two key structural elements believed to be involved in the recognition of activated GPCRs. The first is the C-terminal extension of the kinase domain, which was observed in all nucleotide-bound GRK1 structures. The second is residues 5–30 of the N terminus, observed in one of the GRK1\_(Mg<sup>2+</sup>)<sub>2</sub>\_ATP structures. The N-terminus was also clearly phosphorylated, leading to the identification of two novel phosphorylation sites by mass spectral analysis. Co-localization of the N-terminus and the C-terminal extension near the hinge of the kinase domain suggests that activated GPCRs stimulate kinase activity by binding to this region to facilitate full closure of the kinase domain.



**Figure 1. Conceptual model of GRK1 docked to Rho\*.** The closed composite model of GRK1 was docked with a model of an array of Rho molecules (Protein Data Bank code 1N3M) (50), of which two molecules are shown here for clarity. GRK1 is rendered as *spheres*, and the expected lipid bilayer plane is shown as a *transparent gray box*. A monomer of Rho\* (*red*) was modeled such that its third cytoplasmic loop (IL3) lies close to the proposed receptor-docking site. Using the PKB-GSK3<sub>3</sub> structure (1O6L) as a guide, the C-terminal peptide of Rho\* (carbons are colored *cyan*, oxygens are *red*, and nitrogens are *blue*) was modeled docked to the large lobe. The GRK1 active site would have easy access to the C-tail of Rho\* or of a neighboring unactivated Rho (*brown*) in the samemembraneplane, allowing high gain phosphorylation of ROS.

**Results from:** Singh, P., Wang, B., Maeda, T., Palczewski, K., Tesmer, J.J.D. Structures of rhodopsin kinase in different ligand states reveal key elements involved in G protein-coupled receptor kinase activation, *J Biol Chem*, 283: 14053-14062, 2008.

## Highlight #2: Proteomics Analysis Identifies Molecular Targets Related to Diabetes Mellitus Associated Bladder Dysfunction

Diabetic bladder dysfunction is among the most common complications associated with diabetes mellitus. The disease is not life threatening; however, it is associated with several debilitating urological symptoms. It appears that up to 80% of patients with diabetes may eventually develop some type of bladder dysfunction. Unfortunately, there are few systems biology studies focusing on the initiation, development, and progression of the bladder dysfunction in diabetic patients or relevant animal models.

In exploring the possible causes of bladder dysfunction at the proteome level during the initiation, and progression of the disease, protein expression profiles in rat bladder smooth muscles were compared between animal models of STZ-induced diabetes mellitus (STZ-DM) and age matched controls (AMC) at one week and two months after induction of hyperglycemia with STZ treatment. At each time point, protein samples from four STZ-DM and four AMC rat bladder tissues were prepared independently and analyzed together across multiple DIGE gels using a pooled internal standard sample to quantify expression changes with statistical confidence. A total of 100 spots were determined to be significantly changing among the four experimental groups. A subsequent mass spectrometry analysis of the 100 spots identified a total of 56 unique proteins.

A network analysis of these proteins using Metacore™ suggested induction of transcriptional factors that are too low to be detected by 2D-DIGE and identified an enriched cluster of down regulated proteins that are involved in cell adhesion, cell shape control and motility; including vinculin, intermediate filaments, Ppp2r1a, and extra cellular matrix (ECM) proteins. The proteins that are up-regulated include proteins involved in muscle contraction (eg., Mrlcb, and Ly-GDI), in glycolysis (eg.,  $\alpha$ -enolase, and Taldo1), in mRNA processing (eg., hnRNP A2/B1), in inflammatory response (eg., S-100A9, Annexin1, and ApoA-I), and in chromosome segregation and migration (eg., Tuba1, and Vil2).

Our results suggest that the development of diabetes related bladder complication in this model involves the down regulation of structural and ECM proteins in smooth muscle that are essential for the normal muscle contraction and relaxation but also induces proteins that are associated with cell proliferation and inflammation that may account for some of the functional deficits known to occur in diabetic complications of bladder.

**Results from:** Yohannes, E., Chang, J., Christ, G.J., Davies, K.P., Chance, M.R. Proteomics Analysis Identifies Molecular Targets Related to Diabetes Mellitus Associated Bladder Dysfunction. *Mol. Cell Prot.*, 7: 1270-1285, 2008.

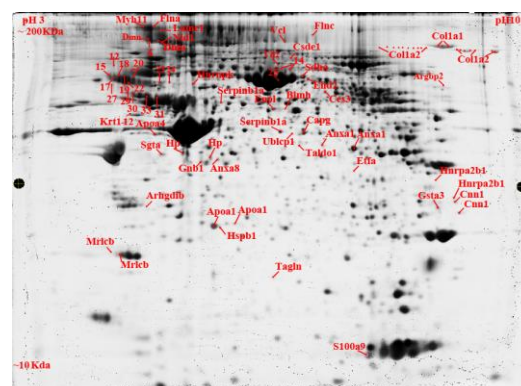


Figure 1

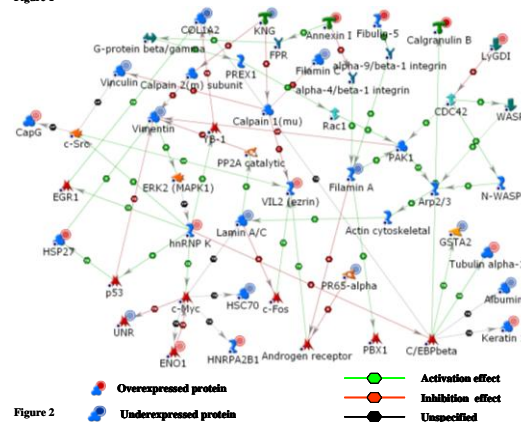


Figure 2

**Figure 1.** The 2D map of deep purple labeled bladder smooth muscle proteins indicating pick location of subset of proteins that changed in response to STZ-induced diabetes. Orientation of the pH gradients is indicated on the horizontal axes from 3 pH unit (left) to 10 pH unit (right), and approximate apparent molecular mass ranges are indicated along the vertical axes 10 kDa (bottom) to 200 kDa (top).

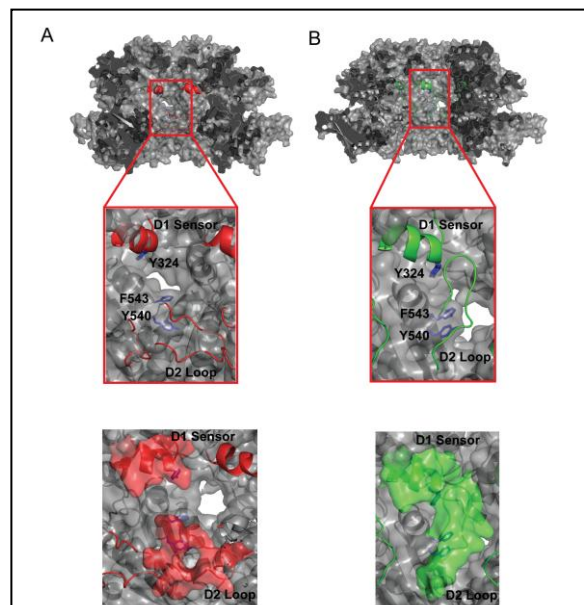
**Figure 2.** Protein networks associated with the proteins differentially expressed in response to STZ-induced diabetes. Individual proteins are represented as nodes, and the different shapes of the nodes represent the functional class of the proteins. The edges define the relationships of the nodes; the arrowheads indicate the direction of the interaction.

### Highlight #3: Functional Consequences of Conformational Changes in the ClpA Hexamer and the ClpP N-terminus

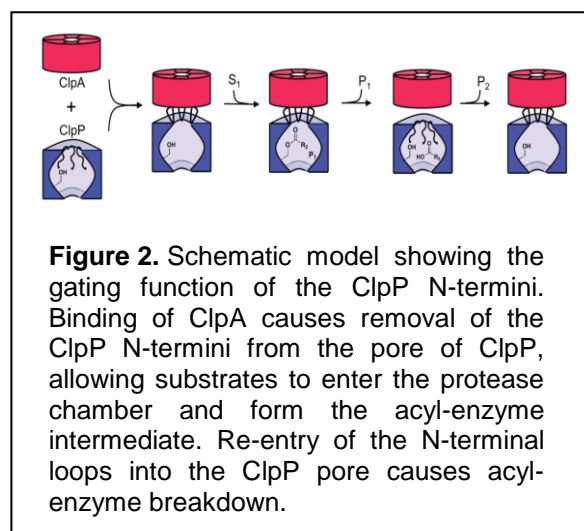
ATP-dependent proteases are responsible for a variety of essential cellular regulatory functions, the most notable of which are the dissolution of protein aggregates and the degradation of unwanted proteins. Understanding the conformational changes that enable these proteases to manipulate their substrates is a useful first step in designing agents to modulate bacterial physiology by activating or inhibiting these molecular machines. In a collaborative effort, the Case Western Reserve University Chance group and the Massachusetts Institute of Technology Licht group used x-ray synchrotron footprinting and kinetic studies to investigate these conformational changes in the ClpAP protease complex.

Existing hexameric models of the ClpA chaperone based on the ADP-bound monomeric crystal structure provided a basis for comparison for the footprinting data. The data differed substantially from the models in two parts of the structure: the D1 sensor 1 domain and the D2 loop region. The results suggest that these two regions can access alternate conformations in which they are significantly less solvent accessible. In combination with previously reported structural data, the footprinting data provide support for a revised model in which the D2 loop contacts the D1 sensor 1 domain in the ATP-bound form of the complex (figure 1). These data provide the first direct experimental support for the nucleotide-dependent D2 loop conformational change previously proposed to mediate substrate translocation.

Footprinting and kinetic studies were used to characterize functionally important conformational changes of the ClpP N-termini. The data suggest a model for proteolysis (figure 2) by wild-type ClpAP in which an interaction with the ATP-bound form of ClpA causes the ClpP N-termini to assume the “up” conformation. This conformational change opens the ClpP axial pore, providing substrate access to the active sites and enabling formation of the acyl-enzyme intermediate. Re-entry of the ClpP N-termini into the axial pore leads to hydrolysis of the acyl-enzyme intermediate and escape of the product via the equatorial pores. An important unresolved question is exactly how ATP-driven conformational changes of ClpA are coupled to the conformational changes of ClpP that regulate acyl-enzyme reactivity. It may be that motions of the ClpA D2 loop, proposed to drive substrate translocation, also drive ClpP conformational changes. Further footprinting and kinetic studies are expected to help resolve this question.



**Figure 1.** Cross-Section of the ClpA hexamer illustrating the pore region (A) a previous hexameric model (Hinnerwisch et al., 2005). (B) footprinting model. The sequences containing the D1 sensor 1 region (318–333) and the D2 loop (526–538) peptides are highlighted and labeled. Bottom figures depict the D1 Sensor 1 and D2 Loop regions in space-fill form.



**Figure 2.** Schematic model showing the gating function of the ClpP N-termini. Binding of ClpA causes removal of the ClpP N-termini from the pore of ClpP, allowing substrates to enter the protease chamber and form the acyl-enzyme intermediate. Re-entry of the N-terminal loops into the ClpP pore causes acyl-enzyme breakdown.

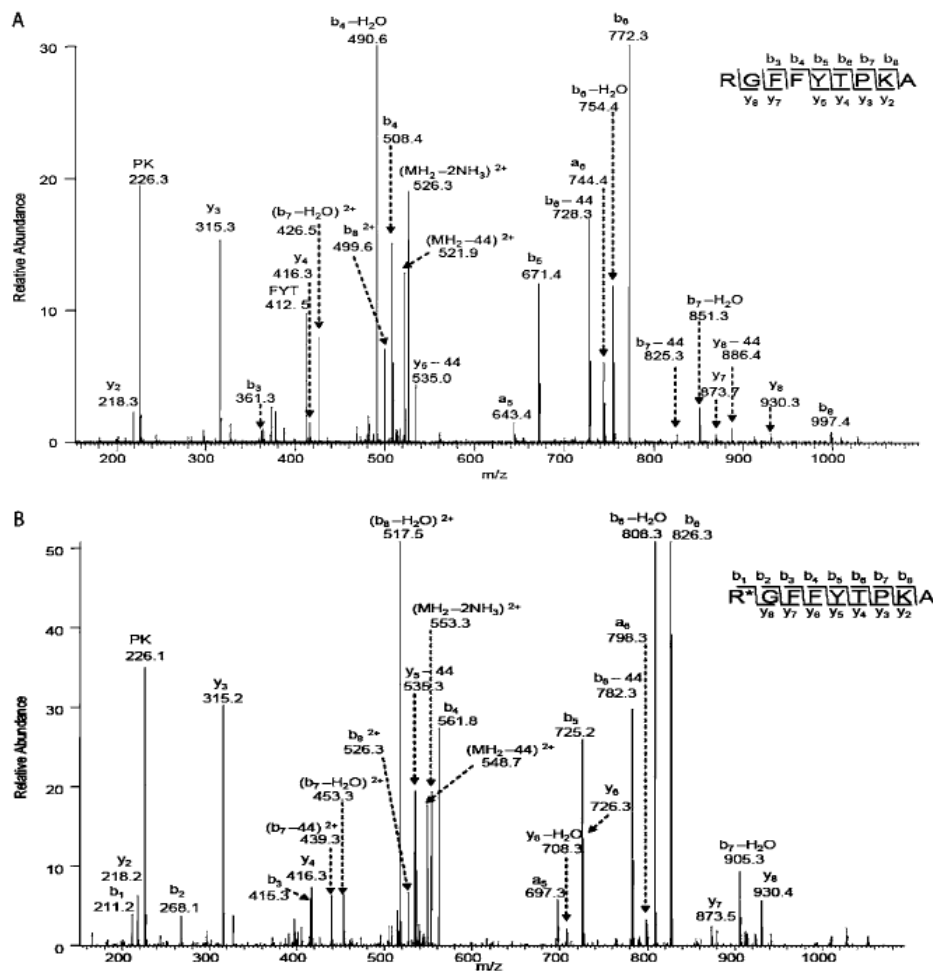
#### Results from:

Bohon J., Jennings, L.D., Phillips, C.M., Licht, S., Chance, M.R. (2008) Synchrotron Protein Footprinting Supports Substrate Translocation by ClpA via ATP-Induced Movements of the D2 Loop. *Structure* **16**, 1157-1165.

Jennings, L.D., Bohon, J., Chance, M.R., Licht, S. (2008) The ClpP N-terminus Coordinates Substrate Access with Protease Active Site Reactivity. *Biochemistry*, **47**:11031-40.

## Highlight #4: Effect of methylglyoxal modification on stress-induced aggregation of client proteins and their chaperoning by human $\alpha$ A-crystallin

$\alpha$ A-Crystallin prevents protein aggregation under various stress conditions through its chaperone-like properties. Previously, we demonstrated that MGO (methylglyoxal) modification of  $\alpha$ A-crystallin enhances its chaperone function and thus may affect transparency of the lens. During aging of the lens, not only  $\alpha$ A-crystallin, but its client proteins are also likely to be modified by MGO. We have investigated the role of MGO modification of four model client proteins (insulin,  $\alpha$ -lactalbumin, alcohol dehydrogenase and  $\gamma$ -crystallin) in their aggregation and structure and the ability of human  $\alpha$ A-crystallin to chaperone them. We found that MGO modification (10–1000  $\mu$ M) decreased the chemical aggregation of insulin and  $\alpha$ -lactalbumin and thermal aggregation of alcohol dehydrogenase and  $\gamma$ -crystallin. Surface hydrophobicity in MGO-modified proteins decreased slightly relative to unmodified proteins. HPLC and MS analyses revealed argpyrimidine and hydroimidazolone in MGO-modified client proteins. The degree of chaperoning by  $\alpha$ A-crystallin toward MGO-modified and unmodified client proteins was similar. Co-modification of client proteins and  $\alpha$ A-crystallin by MGO completely inhibited stress-induced aggregation of client proteins. Our results indicate that minor modifications of client proteins and  $\alpha$ A-crystallin by MGO might prevent protein aggregation and thus help maintain transparency of the aging lens.



**Figure 1. MS/MS spectra of peptides derived from MGO-treated and untreated insulin.** MS/MS spectra of (A) the peptide R22GFFYTPKA30 (with an m/z of 543.5) from untreated insulin and (B) R22\*GFFYTPKA30 (with an m/z of 570.9) from MGO-modified insulin. Both precursor ions are doubly charged.

**Results from:** Biswas, A., Wang, B., Miyagi, M., Nagaraj, R.H. Effect of methylglyoxal modification on stress-induced aggregation of client proteins and their chaperoning by human alphaA-crystallin, *Biochem J*, 409, 771-777, 2008.

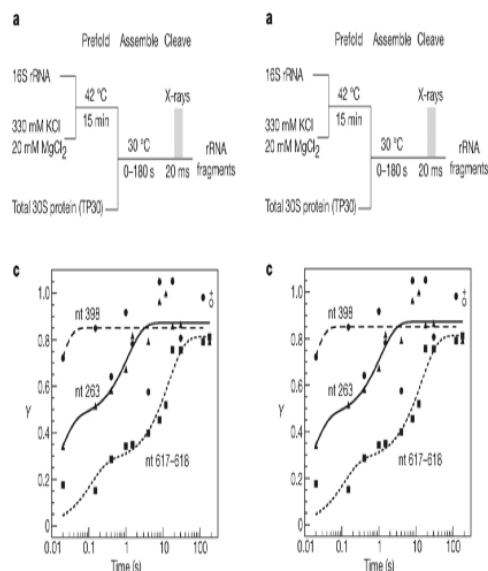
## Highlight #5: Concurrent Nucleation of 16S Folding and Induced Fit in 30S Ribosome Assembly

Rapidly growing cells produce thousands of new ribosomes each minute in a tightly regulated process that is essential to cell growth. How the *Escherichia coli* 16S ribosomal RNA and the 20 proteins that make up the 30S ribosomal subunit can assemble correctly in a few minutes remains a challenging problem, partly because of the lack of real-time data on the earliest stages of assembly.

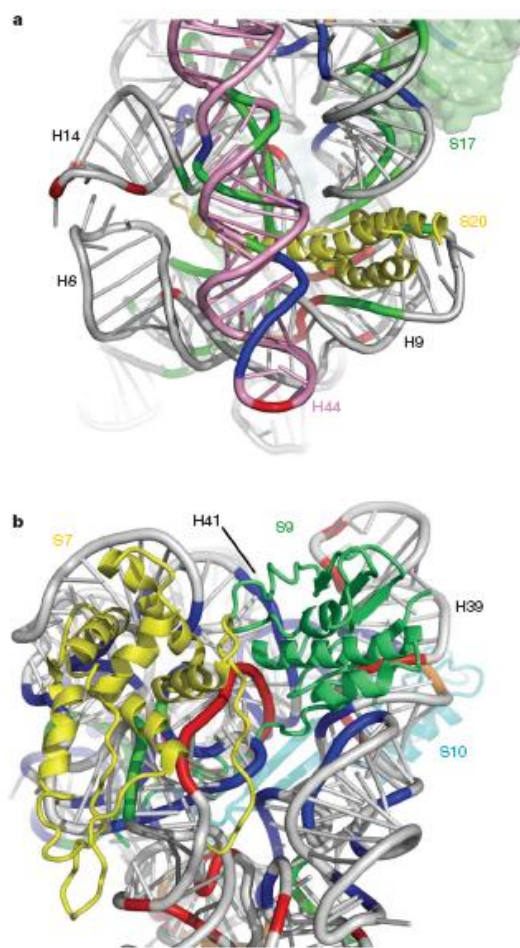
The Woodson group from Johns Hopkins University collected radiolytic footprinting data from the X28C beamline of Case Western Reserve University. Time-resolved hydroxyl radical footprinting was used to map changes in the structure of the rRNA within 20 milliseconds after the addition of total 30S proteins. Helical junctions in each domain fold within 100 ms. In contrast, interactions surrounding the decoding site and between the 59, the central and the 39 domains require 2–200 seconds to form. Figure 1 shows the overall experiment and sample RNA protection data.

Previous studies indicated that ribosome assembly is not completely cooperative, demonstrating the need for several nucleation sites. The lack of complete cooperativity, and the differences between the time-dependence of 16S folding and the assembly map revealed by kinetic footprinting of the nucleotide bases, support the conclusion that assembly proceeds in parallel through intermediates with different subsets of proteins (Figure 2). Radiolytic footprinting allows snapshots of individual RNA and protein interactions to be taken as they emerge in real time. Therefore, the Woodson group was able to show that 30S assembly nucleates concurrently from different points along the rRNA.

**Results from:** Adilakshmi, T., Bellur, D.L., Woodson, S.A. Concurrent nucleation of 16S folding and induced fit in 30S ribosome assembly, *Nature*, 2008, in press.



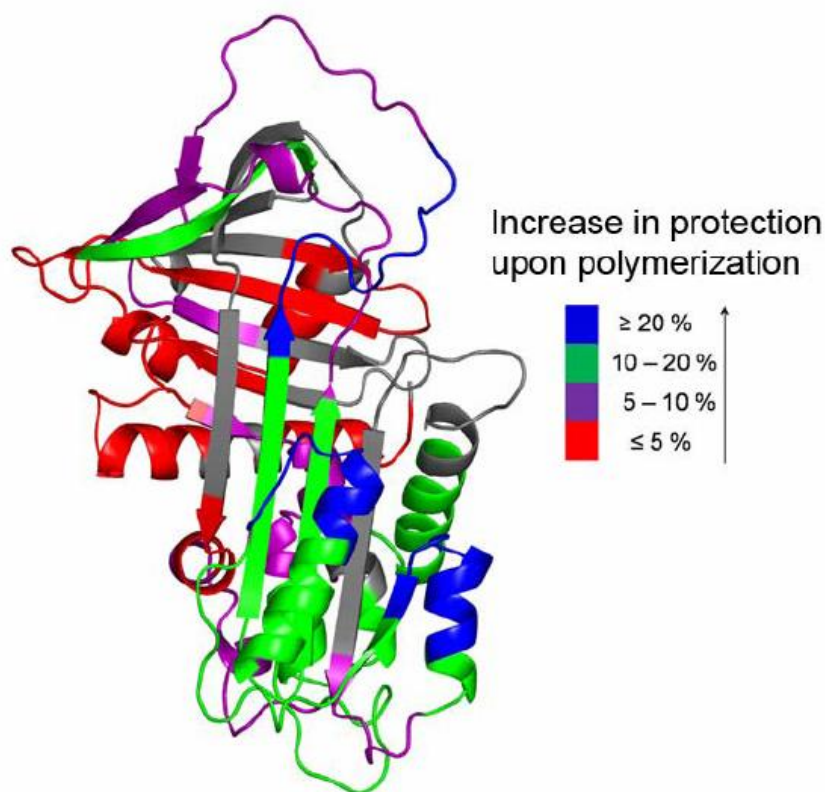
**Figure 1:** Ribosome Assembly experiment. (a) RNA is pre-folded by mixing with metal ions, then 30S ribosomal proteins and mixed rapidly with the RNA. X-ray pulses of 20 ms are then used to interrogate the sample and samples are collected from 100 ms to 180 seconds after mixing for analysis by gel electrophoresis. (b) Progress curves showing increasing protection of specific RNA sites as a function of time after the initiation of the reaction.



**Figure 2.** Stepwise assembly of RNA and protein interactions. **a.** Protein S20 (yellow ribbon) contacts the 30S body in the 59 domain (grey) earlier than helix H44 in the 39 minor domain (pink). **b.** Proteins S7 (yellow) and S9 (green) protect a segment of their binding site immediately (red), whereas nucleotides at the interface between the subdomains

## Highlight #6: The structural basis of serpin polymerization studied by hydrogen/deuterium exchange and mass spectrometry

The serpinopathies are a group of inherited disorders that share as their molecular basis the misfolding and polymerization of serpins – an important class of protease inhibitors. Depending on the identity of the serpin, conditions arising from polymerization include emphysema, thrombosis, and dementia. The structure of serpin polymers is thus of considerable medical interest. Wild type  $\alpha$ 1-antitrypsin will form polymers upon incubation at moderate temperatures and has been widely used as a model system for studying serpin polymerization. Using hydrogen/deuterium exchange and mass spectrometry, we have obtained molecular level structural information on the  $\alpha$ 1-antitrypsin polymer. We find that the flexible reactive center loop becomes strongly protected upon polymerization. We also find significant increases in protection in the center of  $\beta$ -sheet A and in helix F. These results support a model in which linkage between serpins is achieved through the insertion of the reactive center loop of one serpin into  $\beta$ -sheet A of another. We have also examined the heat induced conformational changes preceding polymerization. We find that polymerization is preceded by significant destabilization of  $\beta$ -sheet C. Based on our results, we propose a mechanism for polymerization in which  $\beta$ -strand 1C is displaced from the rest of  $\beta$ -sheet C through a binary serpin-serpin interaction. Displacement of strand 1C triggers further conformational changes, including the opening of  $\beta$ -sheet A, and allows for subsequent polymerization.



**Figure 1.** Differences in hydrogen exchange (at 5000 seconds) between monomeric and polymeric  $\alpha$ 1-AT mapped on to the 3 dimensional structure (1qlp). Darker colors represent larger decreases in observed exchange (i.e., increased protection) in the polymer as compared to the monomer.

**Results from:** Tsutsui, Y., Kuri, B., Sengupta, T., Wintrod, P.L. The structural basis of serpin polymerization studied by hydrogen/deuterium exchange and mass spectrometry, *J. Biol. Chem.*, in press.

## Center for Proteomics & Bioinformatics Faculty, Staff, and Students

### Center Members at Case Western Reserve School of Medicine

#### Faculty Members

Mark Chance, Ph.D., Director, Professor  
Jinsook Chang, Ph.D., Instructor  
Chris Dealwis, Ph.D., Associate Professor  
(secondary)  
Rob Ewing, Ph.D., Assistant Professor  
Reuben Gobezie, M.D., Assistant Professor  
(secondary)  
Janna Kiselar, Ph.D., Instructor  
Masaru Miyagi, Ph.D., Assistant Professor  
Joan Schenkel, M.S., Instructor  
Keiji Takamoto, Ph.D., Assistant Professor

#### Research Staff

Giri Gokulrangan, Ph.D. Research Associate  
Serguei Ilchenko, Ph.D., Research Associate  
Parminder Kaur, Ph.D., Research Associate  
Gaurav Rana, M.S., Research Associate  
Daniela Schlatzer, M.S., Sr. Research Associate  
Benlian Wang, Ph.D., Sr. Research Associate  
Elizabeth Yohannes, Ph.D., Sr. Research Associate  
Chao Yuan, Ph.D., Sr. Research Associate  
Xiaojing Zheng, Ph.D., Research Associate

#### Postdoctoral Research Fellow

Gurkan Bebek, Ph.D.

#### Postdoctoral Scholars

Sudipto Saha, Ph.D.  
Jing Song, Ph.D.  
Jianying Zhang Kiser, Ph.D.

#### Research Assistants

Jennifer Burgoyne, B.S.  
Katy Lundberg, M.S.  
Sunitha Shyam, M.S.  
Hong Zhao, M.S.

#### Graduate Students

Dasha Hajkova Leary, M.S.  
Rod Nibbe, M.S.  
Vishal Patel, B.S.  
Jackie Hill (Rotational)

#### Administrative Support

Maita Diaz, B.S., Department Assistant  
Shannon Swiatkowski, M.S., Department Assistant  
Jacek Szymanski, MIMI Developer  
Audrey Williams, B.S., IT Support

#### Interns

Rebekah Brown  
Eldra Daniels  
Harini Jogiraju  
Nicolle Patterson  
Eric Rodriguez  
Tim Yang

## Center Members located at the Case Center for Synchrotron Bioscience

### Faculty Members

Sayan Gupta, Ph.D., Instructor  
Wuxian Shi, Ph.D., Assistant Professor

### Research Staff

Michael Sullivan, Senior Research Associate  
Don Abel, Research Associate  
John Toomey, Research Associate

### Postdoctoral Scholar

Jen Bohon, Ph. D

### Research Assistants

Rhijuta D'Mello, M.S.

### Intern

Jacquelyn Cafasso

## Faculty, Staff, and Student Summary

	Faculty Members	Research Associates	Postdoctoral Scholars and Fellows	Research Assistants	Administrative Support	Graduate Students	Other Students	Total
	11	12	5	5	4	4	7	48

## Types of Research Conducted at the Center for Proteomics

**Center Research**-Research that is conducted and charged to grants where Center for Proteomics Member is PI

**Collaborative Research**- Research conducted with other departments. Research is considered collaborative when:

- there is an agreement to submit a collaborative grant
- a collaborative staff member has been identified
- a fraction of staff members salary will be paid by grant or pending grant
- co-authorship on publications is expected
- the grant will provide on-going financial support to Center
- the collaborative grants pays for use of center facilities

**Service**- Research conducted by Center according to specifications on Sample Submission Form. PI pays for this service.

**Independent Research**- Research conducted by **non-center staff** using Case Center for Proteomics facilities.

**Center for Proteomics Funding Profile**  
**Active Projects**

Principal Investigator	Type of Grant	Agency	Title	Total Cost	Start Date	End Date
Chance, Mark		CF	Cleveland Foundation Faculty Recruitment	\$1,500,000	08/01/05	03/31/11
Chance, Mark	U54	NIH	New York Structural Genomics Research Consortium	\$880,000	07/01/05	08/31/10
Chance, Mark	P41	NIH	Center for Synchrotron Biosciences	\$5,175,000	09/01/05	08/31/09
Chance, Mark		OH	Board of Regents Action Fund	\$125,000	09/01/09	08/31/10
Chance, Mark	R01	NIH	Identification and Validation of Alcohol Biomarkers	\$602,000	05/01/06	04/30/11
Chance, Mark	P30	NIH	Comprehensive Cancer Center- Proteomics Core	\$726,000	07/01/07	06/30/12
Chance, Mark	CTSA	NIH	CTSA: Translational Technology Core	\$3,862,500	09/01/07	08/31/12
Chance, Mark		Ohio	Choose Ohio First Engaged Scholarship Program	\$355,000	09/01/08	08/31/13
Alagramam, Kumar	R21	NIH	Proteome and Transcriptome of Defined Cell Types in the Ear Following Noise Exposure	\$436,000	03/01/07	02/28/09
Chang, Jinsook	TREC	NIH	Role of Genetic Susceptibility to Obesity and Tumorigenesis	\$154,500	07/01/07	08/31/09
Chang, Jinsook	R21	NIH	Vsca1 Biomarker Vascular Complications	\$118,500	07/01/07	06/30/09
Cho, Michael	P01	NIH	Development of a Subunit Envelope Vaccine Against- HIV1	\$6,001,000	05/01/08	04/30/13
Cooper, Kevin	P30	NIH	Cort in Psorias: Genomics Core	\$655,000	09/24/07	08/31/12
Dearborn, Dorr	R21	NIH	Biomarkers for Exposure to Stachybotrys	\$419,000	05/01/06	04/30/09
Ghannoum, Mahmoud	R01	NIH	Identification of Early Phase C. albicans Biofilm Proteins	\$1,757,000	05/15/07	04/30/12
Liedtke, Carole	R01	NIH	Differential Regulation of NKCC1- Cotransplant	\$1,545,000	02/01/08	01/31/12
Maguire, Mike	R01	NIH	Magnesium Homeostatis in Microorganisms	\$1,388,000	01/01/07	06/01/10
Miyagi, Masaru	R01	NIH/CCF	Activators and Repressors of NFkappaBand IRF3/7 Innate Immunity	\$23,735	07/01/08	05/31/09
Miyagi, Masaru	R01	NIH/CCF	IFNS and Cytokines: Signalling	\$41,550	06/01/08	04/30/09
Palczewski, Krzysztof	P30	NIH	Core Grant Vision Research- Proteomics Core	\$441,000	04/01/07	03/31/12
Palczewski, Krzysztof	R01	NIH	Phototransduction Enzymes	\$3,680,000	01/01/09	12/31/14
Qu, Cheng-Kui	R01	NIH	Tyrosine phosphatases	\$1,930,000	12/01/07	11/30/12
Ramachandra, Lakshmi	R21	NIH	Mycobacterium Tuberculosis Phagosome Maturation	\$431,750	09/24/08	02/28/11
Rote, Neal	R21	NIH	Trophoblast Intercellular Fusion	\$428,000	07/01/08	06/30/10
Rote, Neal	R01	NIH	Apoptosis and Trophoblast Fusion	\$1,962,500	12/01/08	11/30/13
Weinberg, Aaron	R01	NIH	Ontogeny of Oral Epithelial Antimicrobial Peptides	\$1,296,000	04/01/07	03/31/11

Weinberg, Aaron	P01	NIH	Epithelial Immunity and Oral Complications of HIV	\$527,500	08/01/08	07/31/09
Weinberg, Aaron	R01	NIH	Beta Defensin Protection of Human Oral Epithelial Cells	\$1,400,000	08/01/05	07/31/09
Wintrode, Patrick	R01	NIH	Molecular Basis of Serpin Function and Dysfunction	\$1,545,000	06/01/07	05/31/12
			Other Federal and Non-Federal Revenue	\$1,931,423	07/01/05	09/30/08
				\$41,337,958		

### Completed Projects

Principal Investigator	Type of Grant	Agency	Title	Total Cost	Start Date	End Date
Chance, Mark	R21	NIH	Cellular Footprinting of the Transferrin: Receptor	\$431,000	09/01/05	08/31/07
Chance, Mark	R21	NIH	Proteomics of Type 1 Diabetes Progression	\$628,000	09/01/05	08/31/07
Chance, Mark	P41	NIH	Center for Synchrotron Biosciences-Supplement	\$216,000	03/01/06	08/31/08
Chance, Mark	U54	NIH	Genomics and Structural Proteomics Core	\$54,000	11/01/06	07/31/07
Nibbe, Rod		AMS	Discovery Proteomics of Colorectal Cancer	\$2,000	07/01/07	10/31/07
				\$1,331,000		

### Training Grant Summary

Trainee	Type of Grant	Agency	Title	Trainee Support	Start Date	End Date
Bohon, Jennifer	T32	NIH	Cell Physiology Project: Examination of the ClpAP Protease via Synchrotron X-ray Hydroxyl-Radical Protein Footprinting and Mass Spectrometry	\$39,000	07/1/06	03/01/07
Bebek, Gurkan	TRN	NIH	Training in Computational Genomics: Biological Protein Interaction Networks	\$160,000	08/31/07	07/30/09
Bohon, Jennifer	T32	NIH	Heart Lung Physiology Project: Structural Mapping of the ClpAP Protease and its Assembly	\$45,000	07/1/08	06/30/09
Patel, Vishal	T32	NIH	Genetics Project: Network Crosstalk in Complex Genetic Models of Colon Cancer	\$83,000	07/01/07	06/30/09
Rod Nibbe	T32	NIH	Predoctural Training Program Project: Late Stage Human Colon Cancer	\$45,000	08/01/08	07/31/09
				\$372,000		

### Pilot Projects funded by the Center for Proteomics and Bioinformatics

PI	Title of Project	Amount	Year
Betapudi, Venk	A Proteomics approach to understand the regulatory mechanisms of nonmuscle myosin II mediated breast cancer cell migration	\$10,000	2008
Lee, Hyoung-Gon	Pathogenic mechanism of MYC cardiomyopathy	\$10,000	2008
Nock, Nora	Genotype-Phenotype Modeling of Polycyclic Aromatic Hydrocarbon Response System Pathways in Prostrate Carcinogenesis	\$10,000	2008
Ramachandra, Lakshmi	Analyses of Mycobacterium tuberculosis phagosomes by proteomics	\$10,000	2008
Romani, Andrea	Proteomic Identification of Proteins Modified by HNE in the Heart of type-1 diabetic rats	\$10,000	2008
		\$50,000	

### Selected Pending Proposals

Principal Investigator	Type of Grant	Agency	Title	Total Cost	Start Date	End Date
Chance, Mark	P30	NIH	Case Center for Synchrotron Biosciences	\$4,667,000	09/01/09	08/31/14
Chance, Mark	R01	NIH	Radiolytic Footprinting Methods for Structural Mass Spectrometry	\$1,962,500	07/01/09	06/30/14
Adams, Mark	R01	NIH	Mechanism of colistin resistance in <i>Acinetobacter baumannii</i>	\$1,570,000	03/01/09	02/28/13
Caplan, Arnold	R41	NIH	Proteomics to Optimize Adult MSC Cultures	\$250,000	04/01/09	03/31/11
Cho, Michael (Young Kim)		KOSEF	Center for Excellence on Zoonotic & Human Viral Diseases	\$5,310,000	12/1/08	11/30/13
Cobb, Brian	R01	NIH/NIH/GMS	Antigenic Carbohydrate Structure, Function and Specificity	\$1,962,500	10/01/08	09/30/13
Cobb, Brian	R01	NIH/NIH/GMS	Structure and Function Relationships in carbohydrate antigen recognition	\$1,766,250	07/01/09	06/30/14
Fulton, Scott	R03	NIH/NIH/AID	<i>M. bovis</i> BCG antigen identification using bronchoalveolar antibodies	\$157,000	01/01/09	12/31/10
Guda, Kishore	K99-R00	NIH/NIH/CI	Functional analysis of novel O-glycosylation gene(s) mutations in colon cancer	\$927,000	07/01/09	07/1/14
Jackson, Mark	R01	NIH	Identification of a novel oncogene using validation-based insertional mutagenesis	\$1,962,500	10/01/08	09/30/13
Chandra, Jyotsna		AHA	Interactions between Host Immune Cells and Intravascular Catheter-associated <i>Candida albicans</i> Biofilms	\$308,000	01/1/09	12/31/12
Karnik, Pratima	R01	NCI	Deciphering Gene-Environment Interactions in Melanoma: A Systems Genetic Approach	\$1,875,000	09/01/08	08/30/13
Koyuturk, Mehmet		NSF Career	CAREER: Computational Models and Algorithms for Differential Network Analysis in Systems Biology	\$424,000	07/01/09	06/30/11
Maguire, Mike	R01	NIH	Structure-Function of the MgtE Mg <sup>2+</sup> Transporter	\$1,962,500	04/01/09	03/31/13
Qu, Cheng-Kui	R01	NIH	PTPMT1 Phosphatases and oxidative stress	\$1,962,500	07/01/08	06/30/13
Surewicz, Witold	R01	NIH	Confrontational conversions of prion protein	\$1,695,000	12/01/08	11/30/13
Whittaker, Jonathan	R01	NIH	Molecular Aspects of IGF-I Receptor Interactions with its Cognate Ligands	\$1,535,972	02/01/09	01/31/13
				\$30,297,722		

## Invention Disclosures and Patent Applications in FY 2008

1. A Fully Integrated Data Management Environment for Small Animal Imaging Core Facilities – Zhang, Wilson, Muzic, Szymanski, Troy, Flask, Schiclano, Covey, Takamoto, Schenkel – 01/05/07
2. Novel method to fix and stain dissolvable gels under non-acidic conditions and maximize protein and peptide extractions from dissolved gel matrix- Takamoto, Chance- 5/10/07
3. Urinary Proteomic Biomarkers of Diabetic Complication Discovered in a Rat Model of Diabetes – 8/10/07 – Chance, Schaltzer, Christ
4. SYSTEMS AND METHODS OF ANALYZING TWO DIMENSIONAL GELS Wipo Patent application, WO/2008/016912, Takamoto and Chance

## Community Outreach Seminar Series

### 2007

- 08/14/2007 Understanding and Addressing the Challenges of Differential Expression Analysis of Proteomics Data  
Steve Noblitt – Nonlinear Dynamics, Ltd
- 08/16/2007 Drug Testing in the Racehorse: Analytical Toxicology's Leading Edge  
Andreas Lehner – Univ of Kentucky
- 08/29/2007 Analyzing High-Throughput Protein-Protein Interaction by Machine Learning Methods  
Xuejian Xiong - University of Toronto
- 10/17/2007 Determining the Architectures of Macromolecular Assemblies by Integrating Spatial Restraints from Proteomic Data (SB)  
Andrej Sali – UC San Francisco
- 10/19/2007 Structure Guided Discovery of Target Oncology Therapeutics  
Stephen Burley – SGX Pharmaceuticals
- 11/1/2007 Proteomic Data Management at CWRU  
Jason Attanucci – Genomics Life Sciences Software
- 11/8/2007 External User Training for Project Submission and Sample Tracking  
Adam Troy and Katy Lundberg
- 11/19/2007 An *in silico* Approach to Construct Transcriptional Regulatory Networks  
Amitava Karmaker - University of Texas at San Antonio
- 11/27/2007 Glycoproteins in Cancer Detection  
Hui Zhang – John Hopkins Univ
- 11/28/2007 Cardiac Systems Biology (SB)  
Andrew McCulloch – UC San Diego
- 11/29/2007 Thermo Scientific's Workshop on Label Free Quantitation Using Mass Spectrometry  
Rob Ewing and Danie Schlatzer  
Susan Abbatiello – Univ of Pittsburgh  
Michael Freitas – OSU  
Michael Kinter – CCF

Scott Peterman & Amy Zumwalt- Thermo Fisher

12/4/2007 Application of Proteomics to Investigate Age-Related Macular Degeneration: Hypothesis Testing and Generating  
Deborah Ferrington – Univ of Minnesota

12/6/2007 Discovering Commonalities in Interaction Networks: From Alignment to Canonical Modules  
Mehmet Koyuturk – CWRU EECS

## **2008**

01/17/2008 New Methods for Improved Protein Sample Preparation  
Dustin Hoylman – Protea Biosciences

01/24/2008 The Role of Flanking Sequences in Polyglutamine Aggregation – A Glimpse behind the Veil of Intrinsic Disorder  
Ronald Wetzel - Pittsburgh Institute of Neurodegenerative Diseases

01/29/2008 Expression Systems and Database Developed for Biological, Structural, Bioinformatic Studies and Clinical Development of Antimicrobial Peptides  
Yi-feng Li – Univ of Nebraska

01/31/2008 Computational Methods for Improving Protein Identification and Quantification in Shotgun Proteomics  
Haixu Tang – Indiana School of Informatics

02/21/2008 Introduction to Milliplexing and Luminex Technology  
Collin Mitchell – Millipore Corp.

03/13/2008 Tissue Fractionation by Hydrostatic Pressure Cycling Technology - A Unified Sample Preparation Method for Systems Biology Studies  
Alexander Lazarev – Pressure Biosciences

03/18/2008 Enzyme function prediction on Machine Learning approach  
Ying Huang – Georgia Institute of Technology

03/27/08 Nonmuscle Myosin II Takes Center Stage in Cancer Spread  
Venk Betapudi – CWRU Physiology & Biophysics

04/10/2008 Development of Cardiomyopathy Cell Cycle Re-entry  
Hyoung-gon Lee - CWRU Pathology

04/17/2008 Computer-aided Prediction of Potential Vaccine Candidates based on B-cell Epitopes  
Sudipto Saha - University of Indiana

04/22/2008 An Automated Analysis Architecture for Mass Spectrometry based Proteomics  
Gaurav Rana - Philip Morris U.S.A.

04/24/2008 Modifications of Cellular and Mitochondrial Proteins by HNE in Cardiac Tissues of Type-I Diabetic Rats  
Andrea Romani – CWRU Physiology & Biophysics

04/30/2008 Protein Dynamics & Allostery: Insights for Metabolic Models (SB)  
Ivet Bahar – Univ of Pittsburgh

**Publications (bold names indicate Center members)**

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**Center & Collaborative Research**

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1. Amisha Kamal, J.K., Benchaar, S., **Takamoto, K.**, Reisler, E., **Chance, M.R.** Three-dimensional structure of cofilin bound to monomeric actin derived by structural mass spectrometry data, *Proc. Nat. Acad. Sci.*, 104(19): 7910-7915, 2007.
2. Anni, H., **Yohannes, E.**, Niculescu, R., Gonye, G.E., **Chance, M.R.**, and Rubin, E. Expression Proteomics of Alcoholism in rat sera, *Alcohol. Clin. Exp. Res.* 31(S2) 338, 2007.
3. Gardberg, A.S., Dice, L.T., Helmbrecht, E., Ko, J., Ou, S., Patterson, P.H., Rich, R., Myszk, D., Wetzel, R., **Dealwis, C.** Molecular basis for passive immunotherapy of Alzheimer's disease, *Proc. Nat. Acad. Sci.*, 104, 15659-64, 2007.
4. **Gupta, S.**, Cheng, H., Mollah, A., Jamison, E., Morris, S., **Chance, M.R.**, Khrapunov, S., Brenowitz, M. DNA and Protein Footprinting Analysis of the Modulation of DNA Binding by the N-Terminal Domain of the *Saccharomyces cerevisiae* TATA Binding Protein, *Biochemistry*, 46: 9886-9898, 2007.
5. Johnson, E., Lyndaker, A., Deyhim, A., **Sullivan, M.**, **Chance, M.R.**, **Abel, D.**, **Toomey, J.**, Hulbert, S. White Light Focusing Mirror. *AIP Conference Proceedings*, 879: 675-678, 2007.
6. Xu, G., **Chance, M.R.** Hydroxyl Radical-Mediated Modification of Amino Acid Side Chains as Probes for Structural Proteomics. *Chemical Reviews*, 107(8): 3514-43, 2007.
7. Zhu, W., Manjasetty, B.A., **Chance, M.R.** "Crystal Structure of Mn<sup>2+</sup> bound Escherichia coli L-arabinose Isomerase (ECAI): Its implications in Protein Catalytic Mechanism and Thermo-Stability", *J. of Young Investigators*, 17(3): 2007.
8. Almo, S.C., Bonanno, J.B., Sauder, J.M., Emtage, S., Dilorenzo, T.P., Malashkevich, V., Wasserman, S.R., Swaminathan, S., Eswaramoorthy, S., Agarwal, R., Kumaran, D., Madegowda, M., Ragumani, S., Patskovsky, Y., Alvarado, J., Ramagopal, U.A., Faber-Barata, J., **Chance, M.R.**, Sali, A., Fiser, A., Zhang, Z.Y., Lawrence, D.S., Burley, S.K. Structural genomics of protein phosphatases, *J. Struct Funct Genomics*, 8(2-3):121-40, 2007.
9. **Yohannes, E.**, **Chang, J.**, Christ, G.J., Davies, K.P., **Chance, M.R.** Proteomics analysis identifies molecular targets related to diabetes mellitus associated bladder dysfunction, *Mol. Cell. Proteomics*, 7: 1270-1285, 2008.
10. Xu, H., Fairman, J.W., Wijerathna., Kreischer, N.R., LaMacchia, J., Helmbrecht, E., Cooperman, B.S and **Dealwis, C.** The Structural Basis for Peptidomimetic Inhibition of Eukaryotic Ribonucleotide Reductase: a Conformationally Flexible Pharmacophore, *J. Med Chem.*, 51, 5653-9, 2008.
11. Bennett, B.C., Gardberg, A.S., Blair, M., **Dealwis, C.** On the determinants of amide backbone exchange in proteins: a neutron crystallographic comparative study, *Acta. Cryst. D.*, 64, 764-83, 2008.
12. Langan, P., Fisher, Z., Kovalevsky, A., Mustyakimov, A., Sutcliffe, V., Afonine, A.V., Bennett, B., **Dealwis, C.**, Schoenborn, B. Protein structures by Spallation neutron crystallography, *J. Synch. Rad*, 15, 215-218, 2008.
13. Cooperman, B.S, **Dealwis, C.** Allosteric Regulation and Inhibition of Class 1a Ribonucleotide Reductase Activity. *Ribonucleotide Reductase*, Kristoffer Anderson Ed., Noa Publishing, p. 99-134, 2008.
14. **Zheng, X.**, Wintode, P.L., **Chance, M.R.** Complementary structural mass spectrometry techniques reveal local dynamics in functionally important regions of a metastable serpin, *Structure* 16: 38-51, 2008.
15. **Swiatkowski, S.M.**, **Chance, M.R.** Chapter 1: Overview of Mass Spectrometry Technologies for Examining Protein Structure: Current and Future Directions, *Mass Spectrometry Analysis for Protein-Protein Interactions and Dynamics*, p. 1-9, Wiley, Hoboken, 2008.
16. **Kiselar, J.**, **Takamoto, K.** Covalent labeling Methods for Examining Protein Structure and Protein Interactions, *Mass Spectrometry Analysis for Protein-Protein Interactions and Dynamics*, p. 45-68, Wiley, Hoboken, 2008.
17. **Zheng, X.**, Wintode, P.L. Chapter 4: Complementary methods for structural determination: hydroxyl radical-mediated footprinting and deuterium exchange mass spectrometry as applied to serpin structure, in *Mass spectrometry analysis for protein-protein interactions and dynamics*, p. 69-90, Wiley, Hoboken, 2008.

18. **Amisha Kamal, J.K.**, Computational Approaches to Examining Protein-Protein Interactions: Combining Experimental and Computational Data in the Era of Structural Genomics, *Mass Spectrometry Analysis for Protein-Protein Interactions and Dynamics*, p. 189-215, Wiley, Hoboken, 2008.
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32. **Sullivan, M.**, Rekhi, S., **Bohon, J.**, **Gupta, S.**, **Abel, D.**, **Toomey, J.**, **Chance, M.R.** Installation and Testing of a Focusing Mirror at Beamline X28C for High Flux X-ray Radiolysis of Biological Macromolecules, *Rev. Sci. Instrum.*, 79: 025101, 2008.
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34. Manjasetty, B., Turnbull, A., Panjikar, S., Bussow, K., **Chance, M.R.**, Automated Technologies and Novel Techniques to Accelerate Protein Crystallography for Structural Genomics, *Proteomics*, 8: 612-625, 2008. [premier]
35. Smedley, J., Ben-Zvi, I., **Bohon, J.**, Chang, X., Grover, R., Isakovic, A., Evans-Lutterodt, K., Rao, T., Wu, Q. Diamond Amplified Photocathodes, in *Diamond Electronics-Fundamentals to Applications II*, 2007 MRS Fall Meeting, Vol. 1039, p. P09-02, sponsored by MRS, 2008.
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40. **Szymanski, J.**, Wilson, D.W., Zhang, G.-Q. MIMI: an integrated information management system for biomedical core facilities, *Journal of Digital Imaging*, in press.
41. **Chao, Y.**, Solaro Ross, J. Myofilament proteins: from cardiac disorder to proteomic changes, *Proteomics-Clinical Applications*, in press.
42. **Chance, M.R., Chang, J.S., Schlatzer, D.M., Miyagi, M.** Quantitative Proteomics, in *Encyclopedia of Analytical Chemistry*, R.A. Meyers, Ed., Wiley Publishing, in press.
43. Pieper, U., Chiang, R., Seffernick, J.J., Brown, S.D., Glasner, M.E., Kelly, L., Eswar, N., Sauder, J.M., Bonanno, J.B., Swaminathan, S., Burley, S.K., **Zheng, X., Chance, M.R.**, Almo, S.C., Gerlt, J.A., Raushel, F., Shoichet, B.K., Jacobson, M.P., Babbitt, P.C., Sali, A. Target Selection and Annotation for the Structural Genomics of the Amidohydrolase and Enolase Superfamilies, *J Struct Funct Genomics*, in press.
44. Zheng, L., Liu, S., Sun, M.-Z., **Chang, J., Chance, M.R.**, Kern, T.S. Pharmacologic intervention targeting glycolytic pathways protects against retinal injury due to ischemia and reperfusion, *J. Proteomics*, in press.

## Service Research

### Proteomics

45. Mader, D., Yike, I., Distler, A.M., Dearborn, D.G. Acute pulmonary hemorrhage during isoflurane anesthesia in two cats exposed to toxic black mold (*Stachybotrys chartarum*), *J Am Vet Med Assoc*, 231:731-735, 2007.
46. Lin, J. Novel Lithium Salt and Polymer Electrolytes for Polymer Lithium Batteries, Ph.D. Thesis. Department of Macromolecular Science and Engineering, Case Western Reserve University, Cleveland, OH, 2008.
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### Radiolytic Footprinting

48. Lease, R., Adilakshmi, T., Heilman-Miller, S., Woodson, S. Communication Between RNA Folding Domains Revealed by Folding of Circularly Permuted Ribozymes, *J. Mol. Biol.*, 373: 197-210, 2007.
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### X-ray Absorption Spectroscopy

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### Infrared Spectroscopy

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### **Posters and Presentations by Center Members since July 2007** (underlined names represent summer students)

1. **Bohon, J.** Oligomerization and Gating in the ClpAP Protease, *Advisory Board Meeting*, presentation, Case Western Reserve University, Cleveland, OH, August 2007.
2. Cafasso, J., Sandman, K., Karr, E., Reeve, J., Manjasetty, B.A., **Chance, M.R.** Crystallization and Preliminary X-ray Crystallographic Analysis of the Archaeal Tryptophan Regulator, TrpY, *2007 Summer Internship Symposium and Poster session*, poster, Office of Educational Programs, Brookhaven National Laboratory, NY, August 2007.
3. **Chang, J., Zhao, H., Chance, M.R.**, Swain, J. Proteomic analysis of effect of iron supplementation on intestinal tumorigenesis in ApcMin/+ mice, *International HUPO*, presentation, Seoul, Korea, 2007.
4. **Chance, M.R.** Systems Biology to Diagnostic Testing for Diabetic Complications, *Cambridge Healthtech Institute Biomarkers Symposium*, presentation, Philadelphia, PA, September 2007.
5. **Chance, M.R.** Systems Biology to Clinical Diagnostics: A Proteomics Approach, Lerner Research Institute Retreat, Keynote Speaker, Geneva, OH, September 2007.
6. **Chance, M.R.** Merging Computational and Experimental Data in Structural Mass Spectrometry Experiments, *Modeling of Protein Interactions Conference*, presentation, Lawrence, KS, September 2007.
7. **Kiser, J.Z.**, Post, M., **Wang, B., Miyagi, M.** *Streptomyces erythraeus* trypsin and its application in proteomics, *Department of Pharmacology Retreat*, Case Western Reserve University, poster, Geneva, OH, October 2007.

8. **Dealwis, C.** Structural studies of RNR and Alzheimer's causing A-beta, presentation, Yale University, Department of Pharmacology, November 2007.
9. **Chance, M.R.** How to Sell your Science, presentation, Professional Skills Program, Dept. Physiology & Biophysics, Case Western Reserve University, Cleveland, OH, December 2007.
10. **Dealwis, C.** Neutron diffraction, presentation, University of Pittsburgh, Department of Structural Biology, December 2007.
11. **Miyagi, M.** Quantitative Proteomics of Photoreceptor Outer Segments, presentation, Department of Anatomy and Cell Biology, Wayne State University, December 12, 2007.
12. **Takamoto, K.**, Combining hydroxyl radical protein footprinting and Rosetta: towards a new tool for rapid structural inference, presentation, Hokkaido University, Japan, December 20, 2007.
13. Zheng, L, Liu, S., Sun, M.-Z., **Chang, J.**, Howell, S.J., Mishra, R., **Chance, M.R.**, Kern, T.S. Alteration of transcriptional machinery in the retina of diabetic rats, *American Diabetes Association 68<sup>th</sup> Scientific Sessions*, 2008.
14. **Shi, W.**, Rekhi, S., **Sullivan, M.**, **Abel, D.**, Passerini, A., Ceroni, A., Frasconi, P., Punta, M., Rost, B. and **Chance, M.R.** Metalloproteomics-high throughput metal analysis of proteins, *Keystone Symposia in Structural Biology & Structure Genomics*, poster, Steamboat Springs, CO, Jan 6-11, 2008.
15. **Shi, W.** Metalloproteomics: High-throughput Determination of Transition Metal Content in Proteins, *Keystone Symposia in Structural Biology & Structure Genomics*, presentation, Steamboat Springs, CO, Jan 6-11, 2008.
16. **Takamoto, K.**, Das, R., Vernon, R., **Zheng, X.**, **Gupta, S.**, **Bohon, J.**, Baker, D., **Chance, M.R.** Combining hydroxyl radical protein footprinting and Rosetta: towards a new tool for rapid structural inference, *Keystone Symposia in Structural Biology & Structure Genomics*, poster, Steamboat Springs, CO, Jan 6-11, 2008.
17. **Gupta, S.** X-ray footprinting at NSLS-II, *Workshop on Strategic Planning for Life Sciences at NSLS and NSLS-II*, presentation, Brookhaven National Laboratory, NY, Jan 15-16, 2008.
18. Rekhi, S. Diamonds from outer space, *Long Island Mineral and Gem Association*, presentation, Central Islip, NY, Jan. 28, 2008.
19. Rekhi, S. 'Black' Diamond Research at BNL's Light Source among *Discover's* Top 100 Sciences Stories of 2007, press release, Jan-Feb 2008.
20. **D'Mello, R.**, **Gupta, S.**, Jastrzebska, B., Palczewski, K., **Chance, M.R.** Local Structural Changes on Photoactivation of Bovine Rhodopsin, *New York Structural Biology Discussion Group, 3rd Annual Winter Meeting*, poster, New York, NY, Feb 29, 2008.
21. **Bohon, J.** Oligomerization and Gating in the ClpAP Protease, *NIBIB Site Visit*, presentation, BNL, NY, March 2008.
22. **Bohon, J.** Beamline U2B, *Science Advisory Committee Beamline Tenure Review*, presentation, BNL, NY, March 2008.
23. **Zheng X.**, Wintrode, P.L., Chance, M.R., Structural and dynamic study of serpin using two complementary mass spectrometry methods, *5<sup>th</sup> Annual Ohio Mass Spectrometry Symposium*, presentation, Columbus, OH, March 2008.
24. **Yohannes, E.**, **Chang, J.**, Davies, K.P., **Chance, M.R.** Proteomics Analysis to Identified Molecular Signatures for Diabetes Mellitus Associated Erectile Dysfunction, *US HUPO 4<sup>th</sup> Annual Conference*, poster, North Bethesda, Maryland, March 16 - 19, 2008.
25. **Miyagi, M.** Mass Spectrometric Method to Determine pKa Values of Individual Histidine Residues in Proteins, *Fifth Annual Ohio Valley Mass Spectrometry Symposium*, presentation, Columbus, OH, March 24, 2008.
26. **Chance, M.R.** Proteomic Biomarkers of Diabetes Complications, presentation, Dean's Research Symposium, Case Western Reserve University, Cleveland, OH, April 2008.
27. **Miyagi, M.** Proteolytic O-18 labeling for Quantitative Proteomics, presentation, Department of Chemistry, St. Olaf College, April 10, 2008.
28. Gheyi, T., **Takamoto, K.**, Bain, K., Emtage, S., Thompson, D., Raushel, F., Gerlt, J., Burley, S.K., Zhang, F., Rodgers, L., **Zheng, X.**, **Chance, M.R.**, Sauder, J.M. Identifying Bottlenecks and Solutions in a Specific Protein Family: the Amidohydrolases, *NIH Protein Structure Initiative "Bottlenecks" Workshop*, poster, Bethesda, MD, April 14-16, 2008.

29. **Kiser, J.Z.**, Post, M., **Wang, B.**, **Miyagi, M.** Expression, Purification, and Characterization of *Streptomyces erythraeus* Trypsin, *Research ShowCASE*, poster, Case Western Reserve University, Cleveland, OH, April 16, 2008.
30. Crish, J. Proteomic Analysis of Human Synovial Fluid in Osteoarthritis Patients, presentation, Department of Orthopaedics seminar series, Case Western Reserve University, Cleveland, OH, April 22, 2008.
31. **Chang, J.** Proteomics analysis identifies molecular targets related to diabetes mellitus associated bladder and corpora dysfunction, presentation, Albert Einstein College of Medicine, Bronx, NY, May 2008.
32. **Chance, M.R.** Clinical Proteomic Analysis of Diabetes: Biomarker Discovery for End Organ Complications, *Proteomic Tools for Diagnostics Conference (GOT Summit)*, presentation, Boston, MA, May 2008.
33. **D'Mello, R.**, **Gupta, S.**, **Chance, M.R.** Synchrotron X-ray mediated hydroxyl radical structural probing of snap-freeze protein samples, *NSLS and CFN User Meeting*, poster, BNL, NY, May 19-21, 2008.
34. **Gupta, S.** X-ray Footprinting at Beamline X28C, *NSLS and CFN User Meeting*, poster, BNL, NY, May 19-21, 2008.
35. Manjasetty, B., **Sullivan, M.**, **Toomey, J.**, **Abel, D.**, **Chance, M.R.** Biomolecular Structure and Function: Macromolecular Crystallography (MX) Beamline X3A, *Joint NSLS and CFN Users' Meeting*, poster, BNL, NY, May 19-21, 2008.
36. **Sullivan, M.**, Rekhi, S., **Bohon, J.**, **Gupta, S.**, **Abel, D.**, **Toomey, J.**, **Chance, M.R.** Installation and Testing of a Focusing Mirror at Beamline X28C for High Flux X-ray Radiolysis of Biological Macromolecules, *Joint NSLS and CFN Users' Meeting*, poster, BNL, NY, May 19-21, 2008.
37. Datta, S., Hartmann, J., Rekhi, S., Protus, T., Mihalic, J., Rule, A., Ramos-Bonilla, J., Geyh, A., Breyse, P., Chillrud, S.N. New sample holder for mass limited samples for speciation studies of Fe, Mn, Ni by XANES, *27<sup>th</sup> American Association for Aerosol Research*, presentation, May 2008.
38. **Bohon, J.**, Jennings, L.D., Phillips, C.M., Licht, S. and **Chance M.R.** Synchrotron Footprinting Studies of Oligomerization and Gating in the ClpAP Protease, *Joint NSLS and CFN Annual Users' Meeting*, poster, BNL, NY, May 2008.
39. **Dealwis, C.** Hydrogen deuterium exchange patterns in proteins, *American Crystallography Association Conference*, presentation, Knoxville, TN, May 2008.
40. **Chance, M.R.** Processing of Urinary Proteins as Biomarkers for Diabetic Complications, *56<sup>th</sup> ASMS Conference on Mass Spectrometry*, presentation, Denver, CO, June 2008.
41. **Gokulrangan, G.**, **Chang, J.**, **Kiselar, J.**, Davies, K., **Chance, M.R.** Peptide products of Vsca1 and hSMR3A as markers for erectile dysfunction (ED) in diabetic and non-diabetic etiologies, *56<sup>th</sup> ASMS Conference on Mass Spectrometry*, poster, Denver, CO, June 2008.
42. **Ilchenko, S.A.**, **Chance, M.R.**, Whittaker, L.J., Whittaker, J. Determination of the Glycopeptide Structure of Insulin and IGF-I Receptors, *56<sup>th</sup> ASMS Conference on Mass Spectrometry*, poster, Denver, CO, June 2008.
43. **Kiselar, J.G.**, **Gupta, S.**, **Chance, M.R.** Quantitation of tandem MS ion data for hypothesis driven structural MS in protein footprinting experiments, *56<sup>th</sup> ASMS Conference on Mass Spectrometry*, poster, Denver, CO, June 2008.
44. **Kaur, P.**, Amisha Kamal, J.K., **Chance, M.R.** Computational Methods for Probing Biomolecular Structures using Protein Footprinting, *56<sup>th</sup> ASMS Conference on Mass Spectrometry*, poster, Denver, CO, June 2008.
45. **Lundberg, K.C.**, Christ, G., **Kiselar, J.**, **Schatzler, D.**, **Chance, M.R.** Single Reaction Monitoring (SRM) of Pro-Alpha (2) 1 Collagen: Validation of a Novel Biomarker of Uro-Genital Complications from Diabetes, *56<sup>th</sup> ASMS Conference on Mass Spectrometry*, poster, Denver, CO, June 2008.
46. **Miyagi, M.**, Nakazawa, T. Mass Spectrometric Method to Determine pKa Values of Individual Histidine Residues in Proteins, *56<sup>th</sup> ASMS Conference on Mass Spectrometry*, poster, Denver, CO, June 2008.
47. **Schatzler, D.M.**, Christ, G., Dazard, J.-E., **Ewing, R.**, **Ilchenko, S.A.**, **Chance, M.R.** Processing of Urinary Proteins as Biomarkers for Diabetic Complications, *56<sup>th</sup> ASMS Conference on Mass Spectrometry*, poster, Denver, CO, June 2008.
48. **Takamoto, K.**, **Zheng, X.**, **Kiselar, J.**, Das, R., Vernon, R., Baker, D., and **Chance, M.R.** Combining structural mass spectrometry and Rosetta: experimental data constrained *de novo* structure inference, *56<sup>th</sup> ASMS Conference on Mass Spectrometry*, poster, Denver, CO, June 2008.
49. **Takamoto, K.**, **Zheng, X.**, **Kiselar, J.**, Das, R., Vernon, R., Baker, D., and **Chance, M.R.** Probing the structure of serpin/protease complexes by structural mass spectrometry method, *56<sup>th</sup> ASMS Conference on Mass Spectrometry*, poster, Denver, CO, June 2008.

50. **Yohannes, E., Chang, J.,** Davies, K.P., **Chance, M.R.** Proteomics Analysis Identified Molecular Signatures for Diabetes Mellitus Associated Erectile Dysfunction, *56<sup>th</sup> ASMS Conference on Mass Spectrometry*, poster, Denver, CO, June 2008.
51. **Yuan, C.,** Yan, M., Markowitz, S.D., **Chance, M.R., Chang, J.** Proteome changes induced by knock-out of the prostaglandin-degrading enzyme, 15-PGDH. *56<sup>th</sup> ASMS Conference on Mass Spectrometry*, poster, Denver, CO, June 2008.
52. **Wang, B., Miyagi, M.,** Nagaraj, R.H., Palczewski, K., **Chance, M.R.** Posttranslational modifications of proteins identified by LC-mass spectrometry, *56<sup>th</sup> ASMS Conference on Mass Spectrometry*, poster, Denver, CO, June 2008.
53. **Zheng X.,** Wintrode P.L., **Chance M. R.** Probing the structure of serpin/protease complexes by structural mass spectrometry method, *56<sup>th</sup> ASMS Conference on Mass Spectrometry*, poster, Denver, CO, June 2008.
54. **Gupta, S., D'Mello, R., Chance, M.R.** Structural Probing of Snap-Freeze Protein Samples by X-ray Mediated Hydroxyl Radical Footprinting, *56<sup>th</sup> ASMS Conference on Mass Spectrometry*, poster, Denver, CO, June 1-5, 2008.
55. **Bohon, J.** Functional Consequences of Conformational Changes in the ClpP N-terminus and Ligand-driven ClpA Hexamer Formation: Structural MS of a Molecular Machine, *56<sup>th</sup> ASMS Conference on Mass Spectrometry and Allied Topics*, presentation, Denver, CO, June 2008.
56. **Yohannes, E.** Molecular Signature for Diabetes Mellitus Associated Bladder Dysfunction, Pathology-Anatomy & Cell Biology Department seminar series, presentation, Jefferson Medical College, Thomas Jefferson University, Philadelphia, PA, June 13, 2008.
57. **Miyagi, M.,** Nakazawa, T. Sensitive and Unequivocal Determination of pKa Values of Individual Histidine Residues in Proteins Using Mass Spectrometry, *56<sup>th</sup> ASMS Conference on Mass Spectrometry*, poster, Denver, CO, June 2008. (Also *17<sup>th</sup> Meeting of Methods in Protein Structure Analysis*, poster, Sapporo, Japan, August 26-29, 2008.)
58. Ghosh, S.K., **Yohannes, E.,** McCormick, T., **Chance, M.R.,** Weinberg, A. Proteomic profiling of oral epithelial cells from HIV-positive and healthy subjects, *IADR-2008*, abstract, Toronto, Canada, July 2-5, 2008.
59. **Rodriguez, E., Brown, R.C.,** Crish, J., **Chance, M.R., Gobezie, R.** Proteomic Analysis of the Human Synovium from Patients Clinically Diagnosed with Early and Late Osteoarthritis, *Summer Research Symposium for Undergraduate Research*, poster, Athens, OH, August 2008.
60. **Daniels, E.W., Brown, R.C.,** Crish, J., **Chance, M.R.,** Grant, R.E., **Gobezie, R.** Proteomic Analysis of Synovial Fluid of Healthy vs Osteoarthritic Patients Using 2D-DIGE and Mass Spectrometry (Validation of Putative Protein Markers Gelsolin and Afamin), *Nth Dimensions Education Solutions meeting*, poster, Miami, FL, August 2008.
61. **Gupta, S., D'Mello, R., Chance, M.R.,** Structural Probing of Snap-Freeze Protein Samples by Synchrotron Footprinting: Radiation Damage at Work, *New York Structural Biology Discussion Group, Summer Session*, poster, Cold Spring Harbor Laboratory, New York, NY, August 6, 2008.
62. **Gupta, S.,** X-ray Footprinting at Beamline X28C, *New York Structural Biology Discussion Group, Summer Session*, poster, Cold Spring Harbor Laboratory, New York, NY, August 6, 2008.
63. Berman, L.E., Allaire, M., **Chance, M.R.,** Hendrickson, W., Heroux, A., Manjasetty, B., Orville, A. Robinson, H., Saxena, A., Schneider, D., **Shi, W.,** Soares, A., Stojanoff, V., Sweet, R. A suite of macromolecular crystallography facilities being planned for NSLS-II, *XXI Congress and General Assembly of the IUCr*, poster, Osaka, Japan, August 23-31, 2008.
64. **Ewing, R.M.** Refining network topology through mining human AP-MS data. *CSHL/Wellcome Trust Network Biology meeting*, presentation, Hinxton, Cambridge, GB, August 2008.
65. **Dealwis, C.** Passive immunotherapy of Alzheimer's disease, presentation, Roskamp Institute, Sarasota, Florida, August 2008.
66. **Chance, M.R.** Integrating Gene and Protein Expression Biomarkers in a Systems Biology Approach to Colon Cancer, *Cambridge Healthtech Institute Biomarker Discovery Summit*, Philadelphia, PA, September 2008.
67. **Ewing, R.M.** Large-scale protein interaction mapping: moving towards dynamic networks, presentation, Department of Genetics, CWRU, Sept. 2008.

68. Manjasetty B.A., Zhu, W., **Chance, M.R.** Structure and function analysis of *E.coli* L-Arabinose Isomerase through structural genomics approach, *Genomics, Proteomics and Systems Biology*, presentation, J.N Tata Auditorium, Indian Institute of Science, Bangalore, India, October 1-3, 2008.
69. Azizi, F., Wan, Q., Radivoyevitch, T., **Dealwis, C.**, Mastrangelo, C.H. A Combinatorial Multicomponent Plug Mixer for Systems Chemistry, *MicroTAS2008*, poster, October 12-17, 2008.
70. Patterson, N., **Zheng, X.**, **Chance, M.R.** Advancing Computational Methods for Protein Structure Determination: Rosetta + Footprinting, *ABRCMS Conference*, poster, Orlando, FL, November 5-8, 2008.