

Case Center for Proteomics

&

Cleveland Foundation Center for Proteomics

Annual Report

2007



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Case Center for Proteomics: Report from the Director for 2007

The Center for Proteomics and Cleveland Foundation Center for Proteomics in the School of Medicine continues to grow and develop its missions to be a world-leading center for clinical, translational, and structural proteomics. This growth has been made possible by investments from the School of Medicine and the Case Research Institute funded through University Hospitals/Case Medical Center. This report highlights the major accomplishments of the Center after the second year, which represents the first full year of operation (2006-2007).

One of the primary goals of the Case Center for Proteomics 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 including 2D gel and mass spectrometry analyses. These goals have been accomplished. Eight mass spectrometry instruments are operating, including several very high resolution and high sensitivity instruments, such as the Thermo-Finnegan Fourier-Transform-LTQ mass spectrometer. A ninth instrument, an Orbitrap LTQ from Thermo-Finnegan will be installed in late 2007, keeping the Center at the forefront of modern instrumentation. During FY 2007 the Center fulfilled its goal of providing high-throughput proteomics services by processing nearly 1400 mass spectrometry samples per quarter on its instruments.

Over the course of the FY 2007, 98 PIs and investigators utilized the Center's facilities from 26 Departments and Divisions of the Medical school and hospital. A list of Departments using the Center, with distributions by number of investigators is provided in the report. 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, 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. Overall the collaborative research portfolio of the Center has grown dramatically since July 2005. Center staff and users have been awarded \$27.5 million in funding from the NIH, foundations, and other sources (see Highlight #1 and cover for an example). These grants are documented in the report. The funded programs include significant participation by the Center in R-type grants and well as core development for large center grants such as the Case Comprehensive Cancer Center renewal, the CORT grant in Psoriasis, and the Clinical and Translational Science Award. The major pending grants of the center are also listed, these proposals total in excess of \$34 million.

The Center continues to increase its personnel during its second year, currently the Center employs 56 faculty, Research Associates, Post-Docs, Research Assistants, support staff and students, including 11 faculty members with primary or secondary appointments. Additionally, the Center faculty are training 5 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. 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 will receive 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 28 seminars were held from July 2006 through June 2007, with an average attendance of 40 people. Speakers included center faculty and staff, nationally recognized scientists and instrument vendors. The Center has established a website that details services, publications, facilities, contact information and seminars.¹ The Center's faculty, staff, and users also have been actively publishing their work; 42 papers are reported for 2006-2007. They have also been quite active in presenting posters and giving talks at national meetings and giving invited lectures around the country; 63 presentations are reported.

In the field of structural proteomics the Center manages a National Institute of Health grant program of international scope with facilities located at Brookhaven National Laboratories. This Center for Synchrotron Biosciences (CSB)² continues to be highly productive as it operates five beamlines for structural molecular biology and imaging research at the National Synchrotron Light Source (NSLS). In its most recent year of operation, the CSB supported over 550 trained users who published 149 full papers. Twenty-five of these publications were co-authored by Case Center for Proteomics faculty, staff, and users (and are listed in this report) and the remaining 124 were authored by external users of the CSB facilities and are reported on the CSB and NSLS websites. The CSB continues to expand its unique research efforts in synchrotron footprinting of proteins to determine molecular structure in solution on beamline X-28C and has recently demonstrated valuable approaches to *in vivo* nucleic acids footprinting. This technology leverages the advanced mass spectrometry instrumentation of the Case Proteomics Center (see Highlights #5 & #6). In addition, the center is playing a leading role in the Protein Structure Initiative as a part of the New York Structural Genomics Research Consortium³. The development and operation of X-3A and X-29 beamlines for macromolecular crystallography are important continuing areas of research for the CSB and are available to Case investigators. The X-29 undulator facility in particular, is now one of the leading crystallography beamlines in the world (see Highlight #4).

The report also provides six science highlights showcasing the best research of the CSB and the CCP over the last year. In the coming year we expect continued progress in securing grant funding for the Center and its users. We expect the publication rate of Center staff and users to accelerate as results continue to flow through the technology pipelines. We anticipate the launch of a new systems biology interdisciplinary Ph.D. program at the University. This program is currently under review. Finally, we expect to validate a number of biomarkers for disease states of interest to diabetes researchers in the Cleveland health care community (see Highlight #2).

Website Links:

1-<http://casemed.case.edu/proteomics/index.html>

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

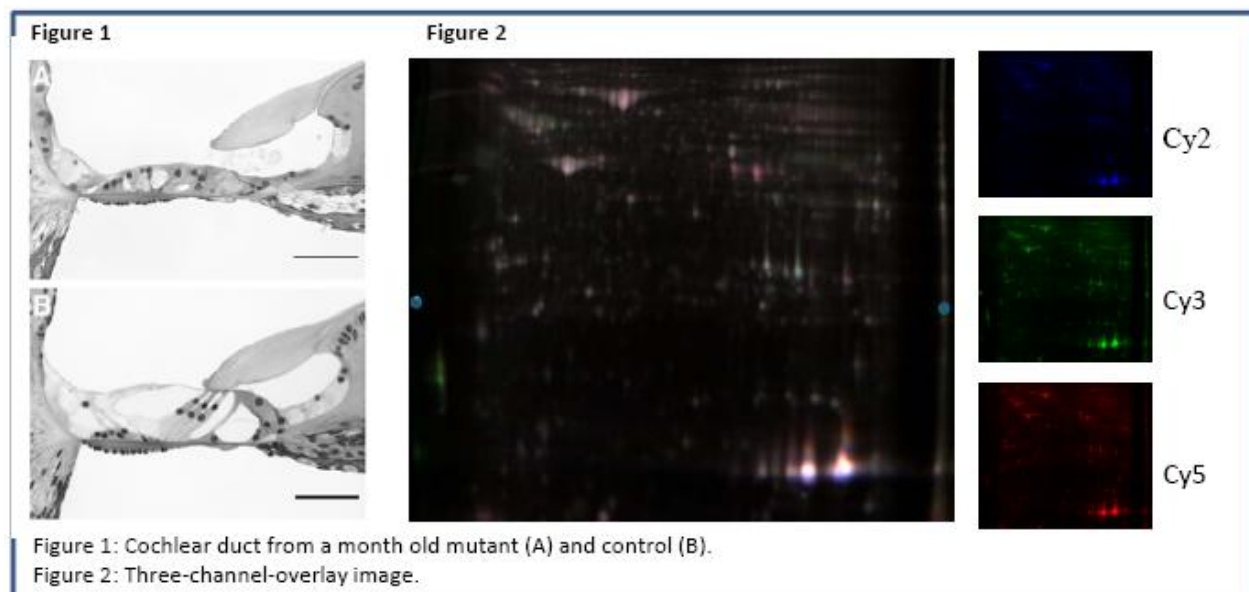
3- www.nysgxrc.org

Highlight #1: MAP: Mouse Auditory Proteomics

Introduction: Mouse mutants have served as excellent models to understand the genetic basis of hereditary inner ear disorders, including those linked to Usher syndromes. Though the Usher models have been available for many years now, none of them have been utilized for proteomic studies. The ultimate aim of this program is to establish a mouse auditory protein database and biomarkers for hearing impairment. Here we report data from a pilot study. The aim of this pilot study is to identify biomarkers of sensory cells and ear pathogenesis in the mouse model for deafness in Usher 1F model by comparing the global protein expression changes between normal and mutant mouse cochlea.

Method: The affected and normal cochlea of mice at 1 month of age were dissected on ice and homogenized with the aid of liquid nitrogen. The protein was then extracted by using 7M urea plus 2M thiourea and 4% chaps with the aid from water bath sonication. The soluble proteins extracted from the cochlea were then labeled by Cys-dye, prefractionated by the 2-D DIGE, digested by trypsin and analyzed by MALDI-OTOF (prOTOFM 2000) and MDLC LTQ systems. DeCyder software 6.5 was used to quantify the protein spots on the 2D gel.

Preliminary Data: In this pilot study, 2D-difference gel electrophoresis (DIGE) technique combined with mass spectrometry analysis was performed to compare protein expression profiles of the affected and normal cochlea at 1 month of age, a time point when most of the hair cells in the mutant cochlea have degenerated. A successful and reproducible method for protein extraction with stable yield has been established. The soluble proteins were analyzed by the 2D-DIGE system newly established at the Case Center for Proteomics and Mass Spectrometry. The analytic gel resolved more than 2500 protein spots. Over 20 protein spots showed significant changes by the difference in gel analysis (DIA). The biological variation analysis (BVA) experiments are in process. The interesting proteins will be picked, digested and identified both by MALDI-OTOF and MDLC LTQ, and the relevant results will be presented. The proteomic discovery of biomarkers and the establishment of potential regulation pathway are of clinical relevance to the prevention and treatment of hearing diseases.



Results from: Zheng, Q.Y., Rozanas, C.R., Thalmann, I., Chance, M.R., Alagramam, K.N. Inner ear proteomics of mouse models for deafness, a discovery strategy. *Brain Res.* 1091(1): 113-21, 2006.

Highlight #2: Quantitative Proteomic Method Utilizing Proteolytic ^{18}O Labeling

There are a multitude of applications for quantitative proteomics including identification of differentially-expressed proteins, biomarker discovery, signal transduction pathway characterization and quantitative interaction proteomics. Several methodologies for performing these experiments, including using stable isotope labeling with different masses to tag peptides from different samples have emerged. One such method is proteolytic ^{18}O labeling method that utilizes proteases to incorporate isotopically light ^{16}O or heavy ^{18}O atom into the C-terminal carboxyl group of peptides. The principle of quantification of ^{16}O - and ^{18}O -labeled peptides by mass spectrometry is shown schematically in Figure 1. In this method it is critical to achieve either single ^{18}O atom or a complete two ^{18}O atom incorporation into peptides to obtain accurate quantification results. We have established methods that can achieve single ^{18}O atom incorporation using peptidyl-Lys-metalloprotease (Lys-N) or complete two ^{18}O atom incorporation using trypsin or Lys-C. These methods are expected to be widely used for various quantitative proteomics applications.

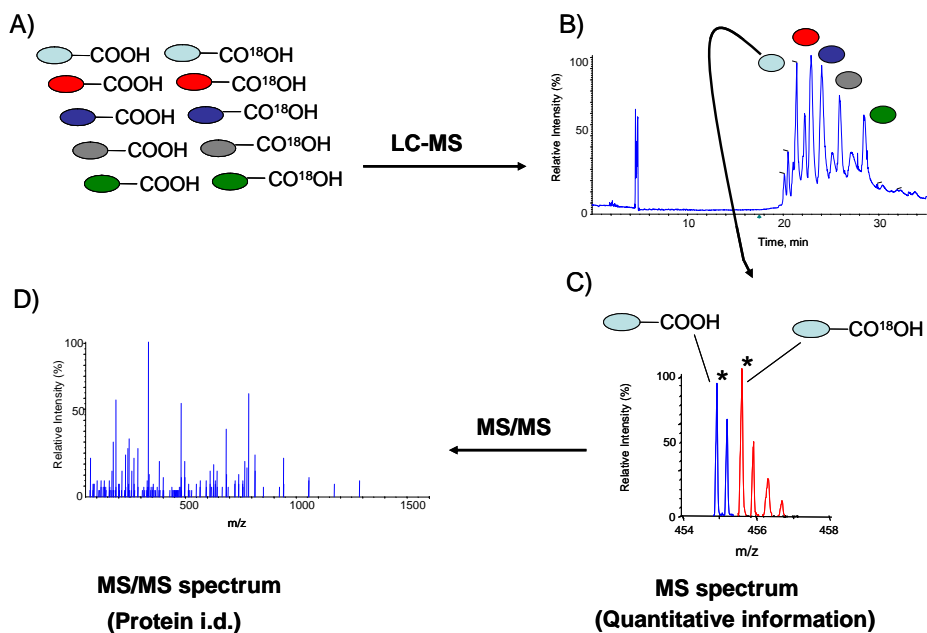


Figure 1. **Principle of quantification by mass spectrometry.** Each of the ^{16}O -labeled peptides from one sample and the corresponding ^{18}O -labeled peptides from the other sample (A) coelute from the chromatography step in the LC/MS/MS analysis step (B). By comparing the peak heights of the ^{16}O - and ^{18}O -labeled peptide in the obtained mass spectrum, the relative abundance of the two peptides (and thus the relative abundance of the particular parent protein in the two samples from which the peptides were generated) can be determined (C). By subjecting one of the peptide ions to MS/MS analysis, the identity of the peptide can be determined from the obtained MS/MS spectrum using database search tools for protein identification (D).

Results from: Miyagi, M. and Rao, K. C. S. (2007) Proteolytic ^{18}O Labeling Strategy for Quantitative Proteomics. Mass Spect. Rev. 26, 121-136

Highlight #3: Structural and Biological Biomarkers in Urine: Probes for Diabetic Complications

Diabetes mellitus (DM) is estimated to affect approximately 20 million people in the US and more than 150 million people worldwide. There are numerous end organ complications of diabetes the onset of which can be delayed by early diagnosis and treatment. Recently, studies have been conducted to develop accurate urine based diagnostic testing as conventional assays for diabetes and its complications lack specificity, sensitivity and accuracy. Utilizing both top-down proteomic applications (1D and 2D gel) and bottom-up applications (label free expression), we have extensively investigated the protein changes in a diabetic rat model to better understand the pathophysiological changes that occur in uro-genital dysfunction as a result of diabetes mellitus. Our results suggest that biological changes in kidney function due to diabetes result in specific structural differences in urinary protein isoforms due to changes in tissue histology as well as due to changes in cellular protein processing. These structural changes provide unique peptide signatures for control and diseased states which have been validated in individual samples via stable isotope dilution mass spectrometry. Our results suggest these peptides can be used as functional and structural biomarkers which could be used in specific diagnostic assays to “stage” the disease.

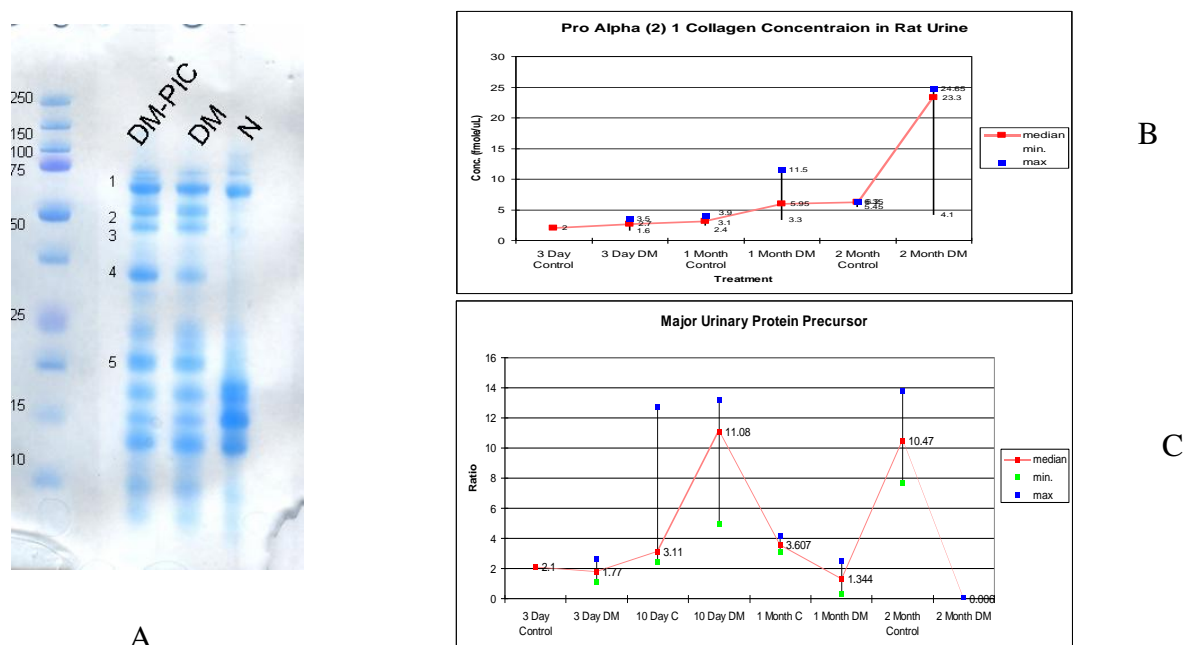
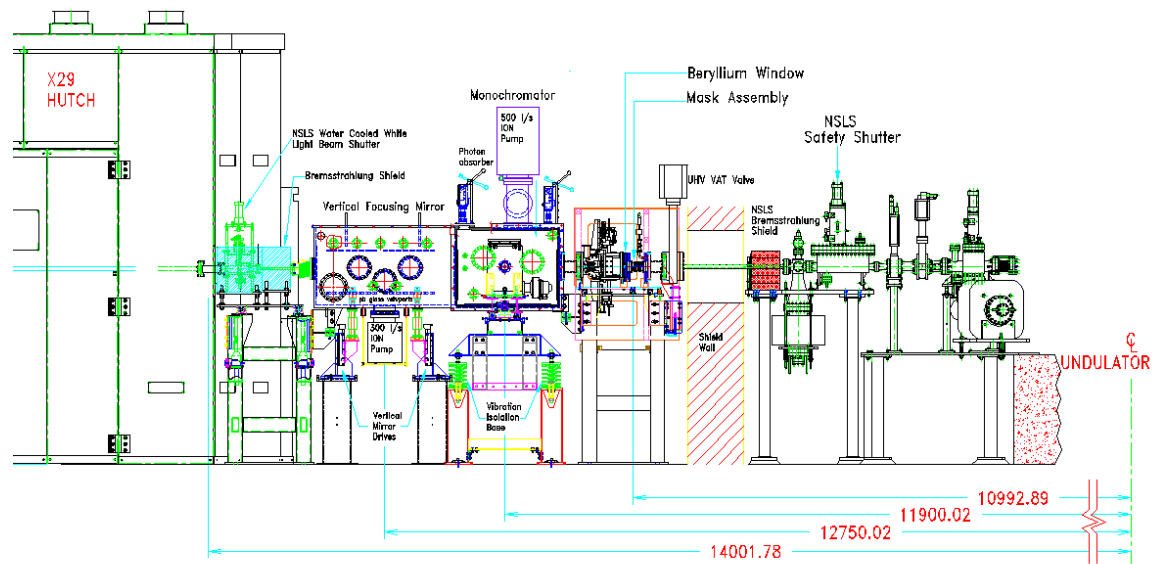


Figure 1. (A) One dimensional SDS gel of 20 micrograms of pooled normal and diabetic (DM) rat urine highlighting the protein isoform differences between DM and normal (N). **(B and C)** Absolute quantification of two putative biomarkers, pro-alpha (2) 1 collagen and major urinary protein precursor.

Results From: Daniela Schaltzer, Elizabeth Yohannes, Serguei Ilchenko, George Christ and Mark. R. Chance. “Utilizing a Rat Model of Diabetes to Identify Urine Biomarkers for Early Diagnosis of Bladder Dysfunction”. 55th ASMS Conference of Mass Spectrometry, June 2007 and Cambridge Healthtech Institute Biomarkers Summit, September 2007

Highlight #4: Center for Synchrotron Biosciences Beamline X29: A Novel Undulator Source for X-ray Crystallography

A high flux insertion device and beamline for macromolecular crystallography has been built at the National Synchrotron Light Source that utilizes a mini-gap undulator source developed by the NSLS. The mini-gap undulator at X29 is a hybrid-magnet device of 12.5 mm period operating at proven gaps of 3.3-10 mm. The beamline provides hard X-rays for macromolecular crystallography experiments from the 2nd and 3rd harmonics over an energy range of 5-15 keV. The X-ray optics is designed to deliver intense and highly collimated X-ray for macromolecular crystallography experiments. Horizontal focusing is achieved by a cryogenically cooled sagittally focusing double crystal monochromator with ~ 4.1:1 demagnification. A vertical focusing mirror downstream from the monochromator is used for harmonic rejection and vertical focusing. The end station hosts an Area Detector Systems Corporation Quantum 315 CCD detector with 2.2 sec readout time between exposures and Crystal Logic Goniostat for omega crystal rotation and detector positioning. An auto-mounter crystal changer has been installed to facilitate the high throughput data collection required by the major users, who include structural genomics projects and a Fed-Ex Mail-in data collection program. X29 is 10³ times brighter than any existing bending magnet beamlines at NSLS with a maximum flux of 5 x 10¹¹ photons/sec through a 0.10 x 0.16 mm square aperture at 11.470keV. X29 is built and operated in collaboration between NSLS, BNL Biology Department and the Case Center for Synchrotron Biosciences. The user-friendly operation and convenient location of X29 attract a large number of productive user groups from the mid-Atlantic and New England regions. Over 400 users have been trained and have collected data at the beamline since June 2004. As of September, 239 structures have been deposited in the Protein Data Bank credited to X29 and 102 publications have resulted from these structures.



X-29 ELEVATION VIEW

Results from: Shi, W., Robinson, H., Sullivan, M., Abel, D., Toomey, J., Berman, L., Lynch, D., Rosenbaum, G., Rakowsky, G., et al. Beamline X29: A Novel Undulator Source for X-ray Crystallography. *J. Synch. Rad.* **13**: 365-372, 2006.

Highlight #5: Center for Synchrotron Biosciences Beamline X28C: Three-Dimensional Structure of Cofilin Bound to Monomeric Actin Derived by Structural Mass Spectrometry Data

Structure and function of the cytoskeletal protein, Actin, is regulated by cofilin. In the absence of an atomic resolution structure for the actin/cofilin complex, the mechanism of cofilin regulation is poorly understood. Theoretical studies based on the similarities of cofilin and gelsolin segment 1 proposed the cleft between subdomains 1 and 3 in actin as the cofilin binding site. Radiolytic protein footprinting with mass spectrometry is used to map the interactions between cofilin and monomeric actin complex. The rabbit G-actin and G-actin/cofilin complexes at 10 μ M concentration were exposed to X-ray at the X-28C beamline. Radiolyzed samples were subjected to enzymatic proteolysis and the resulting peptide mixtures were analyzed in a coupled, HPLC–electrospray ion source mass spectrometer equipped with a quadrupole ion trap. Footprinting data suggest that cofilin binds to the cleft between subdomains 1 and 2 in actin and that cofilin induces further closure of the actin nucleotide cleft. The molecular modeling base on the footprinting constraints is used to provide an atomic model of how cofilin binds to monomeric actin. The model identifies key ionic and hydrophobic interactions at the binding interface, including hydrogen-bonding between His-87 of actin to Ser-89 of cofilin that may control the charge dependence of cofilin binding. This model and its implications fill an especially important niche in the actin field, owing to the fact that ongoing crystallization efforts of the actin-cofilin complex have so far failed. This is the first 3D binary complex structure derived from a combination of solution footprinting data and computational approaches and outlines a general method for determining the structure of such complexes in solution.

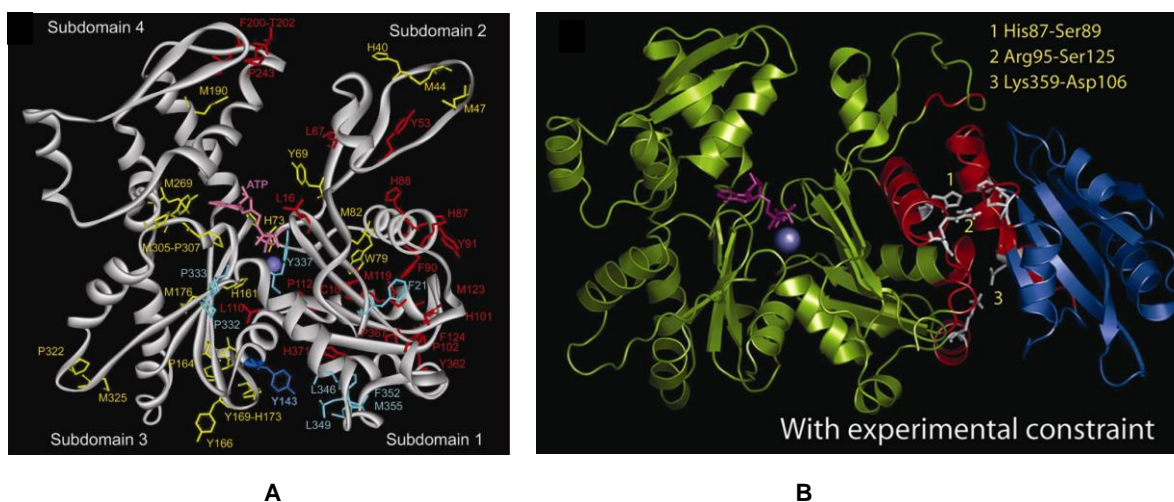
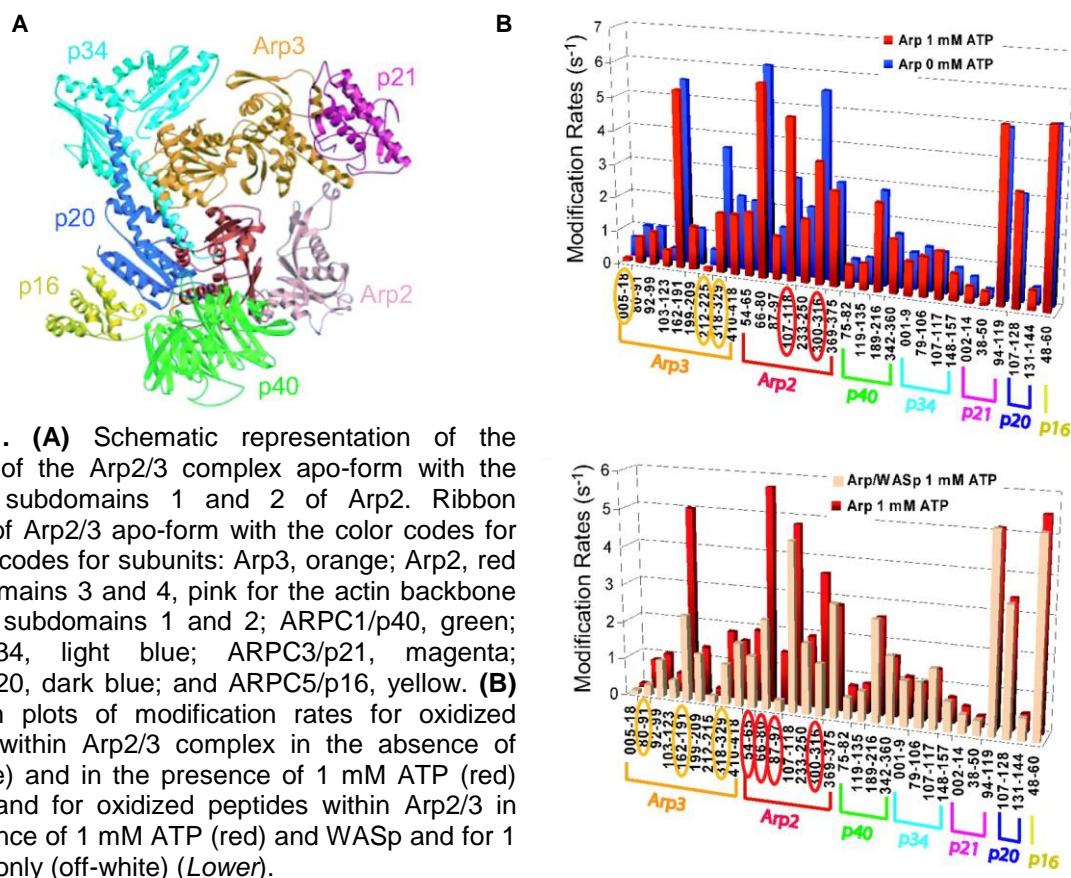


Figure 1. (A) G-actin structure indicating the protection sites revealed by radiolytic footprinting. Modified amino acids of various protected peptides are shown as stick models. Amino acids that show substantial protection (4.0-fold and beyond decrease in the modification rate) are colored in red, moderate protection (between 1.2- and 4.0-fold) are in yellow, and nearly no protection is in cyan (0.8- to 1.2-fold). The residue Tyr-143 shown as a blue stick model shows negative protection (increased modification). **(B)** Top-scored G-actin/cofilin model from the docking constrained with the footprinting data. Red-colored region marks the closely interacting segments. Hydrogen bonding/salt bridging at the interface is indicated as stick models.

Results from: 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.

Highlight #6: Center for Synchrotron Biosciences Beamline X28C: Visualizing Arp2/3 Complex Activation Mediated by Binding of ATP and WASp Using Structural Mass Spectrometry

Actin-related protein (Arp) 2/3 complex nucleates new branches in actin filaments playing a key role in controlling eukaryotic cell motility. This process is tightly regulated by activating factors: ATP and WASp-family proteins. Radiolytic protein footprinting is used to probe the effects of nucleotide- and WASp-binding on Arp2/3 in solution. The free protein and its complexes in solution were exposed to X-rays at beamline X28C followed by proteolysis and mass spectrometric analysis using a coupled, HPLC–electrospray ion source mass spectrometer equipped with a quadrupole ion trap. Footprinting data suggest that ATP binding induces conformational changes only in the peptide segments of Arp3 and Arp2 within the Arp2/3 complex keeping other Arp subunits in native conformations. The protection map shows that the Arp2/3 complex binds to WASp within the C- and A-subdomain. Footprinting data also show a bivalent attachment of WASp to Arp3 and Arp2 subunits. WASp-dependent protections from oxidation within the peptides in Arp3 and Arp2 subunits suggest domain rearrangements of Arp2 and Arp3 resulting in a closed conformational state consistent with an "actin-dimer" model for the active state. Arp2/3 is the most complex macromolecular assembly yet examined in solution (MW. 220kD) by synchrotron footprinting experiments. The results of this study represent a significant advance in protein footprinting approaches for studying large macromolecular assemblies.



Results from: Kiselar, J., Mahaffy, R., Pollard, T., Almo, S., Chance, M.R. Visualizing Arp2/3 Complex Activation Mediated by Binding of ATP and WASp using Structural Mass Spectrometry. *Proc Natl Acad Sci USA*. **104**: 1552-1557, 2007.

Center for Proteomics Faculty, Staff, Students, and Advisory Committee Members

Advisory Committee

- Vernon Anderson, Ph.D. Professor, Biochemistry
- Henri Brunengraber, M.D., Ph.D. Chairman & Professor, Nutrition
- Mike Kinter, Ph.D. Associate Staff in Cell Biology, CCF & Associate Professor, Physiology and Biophysics
- Tom McCormick, Ph.D. Assistant Professor, Dermatology
- Krzysztof Palczewski, Ph.D., Chairman, Pharmacology & John H. Nord Professor
- Witold Surewicz, Ph.D., Professor, Physiology & Biophysics
- Assem Ziady, Ph.D., Assistant Professor, Pediatric Pulmunology

Center Members at Case Western Reserve School of Medicine

Faculty Members

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

Research Associates

Benlian Wang, Ph.D., Senior Research Associate
Jim Crish, Ph.D., Senior Research Associate
Daniela Schlatzer, M.S., Senior Research Associate
Chao Yuan, Ph.D. Senior Research Associate (begins October 15, 2007)
Giri Gokulrangan, Ph.D. Research Associate (begins September 15, 2007)
Serguei Ilchenko, Ph.D.
Amisha Kamal Kizhakkedathu, Ph.D.
Parminder Kaur, Ph.D.
Kelli Peterson, M.S.

Postdoctoral Scholars

Gurkan Bebek, Ph.D.
Adam Troy, Ph.D.
Elizabeth Yohannes, Ph.D.
Jianying Zhang, Ph. D.
Xiaojing Zheng, Ph.D.

Research Assistants

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

Graduate Students

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

Administrative Support

Beverly Montgomery, Department Assistant
Shannon Swiatkowski, M.S., Department Assistant
Audrey Williams, B.S., IT Support

Summer Interns

John Jimah
Brandon Szeto
Michael Bergen

Center Members located at the Case Center for Synchrotron Bioscience

Faculty Members

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

Research Associates

Babu Manjasetty, Ph.D., Senior Research Associate
Michael Sullivan, Senior Research Associate
Sandeep Rekhi, Ph. D., Research Associate
Don Abel, Research Associate
John Toomey, Research Associate

Postdoctoral Scholars

Jen Bohon, Ph. D

Research Assistants

Rhijuta D'Mello, M.S.

Summer Intern

Jacquelyn Cafasso

Faculty, Staff, and Student Summary

	Faculty Members	Research Associates	Postdoctoral Scholars	Research Assistants	Administrative Support	Graduate Students	Other Students	Total
	11	14	6	6	3	5	11	56

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
- we will be author on publications
- 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.

Number of Investigators by Department as of 06/30/2007

Department	Service	Collaborative	Independent	
Biochemistry	2		2	
Biological Sciences		1		
Biology	1	1		
Biomedical Engineering	4		1	
Cardiovascular Research Center	3			
Clinical and Molecular Endocrinology	1			
Dermatology	2	4		
Endocrinology		1		
Epidemiology and Biostatistics	1			
General Medicine	3		1	
Genetics	3			
Hematology/Oncology	4	2	1	
Infectious Disease	1	1		
Molecular Biology and Microbiology	2			
Neonatology	1			
Neuroscience	1			
Nutrition	2	1		
Ophthalmology		1		
Orthopedics	1			
Otolaryngology	1	1		
Pathology	4		4	
Pediatrics	3	2	1	
Pharmacology	4	2	2	
Physiology and Biophysics	2	1	1	
Proteomics			10	
Radiology	1		1	
Rheumatology		1		
Outside Case Community		7		
Cleveland Clinic Neuroscience		1		
	47	27	24	98

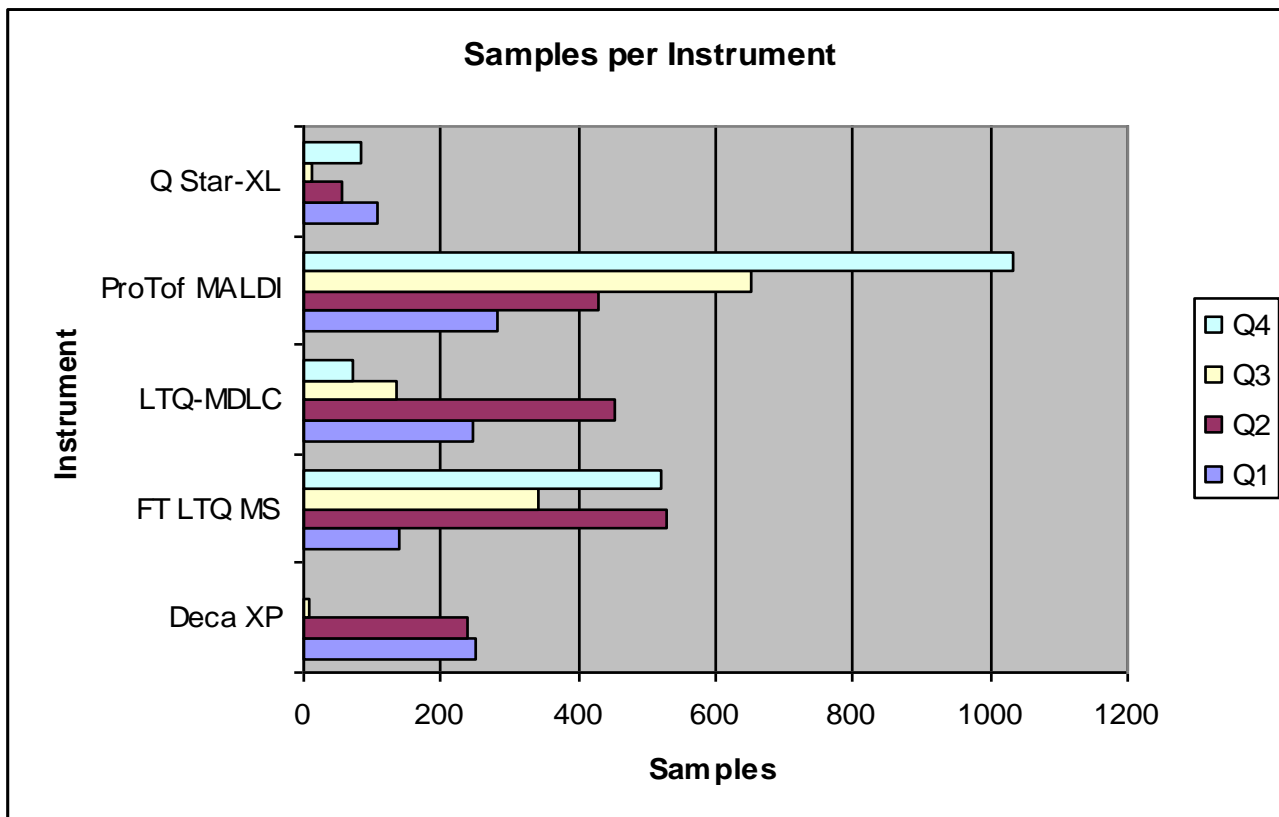
Key Services Performed During FY 2007

Service	Q1	Q2	Q3	Q4	Sum Of Samples
1-D Electrophoresis	6	12	4	2	24
96 Well Digestion Services	3	58	4	141	206
Data Analysis (hours)	167	263	24	236	690
Instrument Usage (Samples run for Center projects and independently)	455	386	1034	1236	3111
Protein ID Gel Bands	10	210	44	31	295
Protein ID Gel Spots	535	1078	59	399	2071
Protein Intact Mass	18	7	10	15	50
Spot Picking	424	222	29	131	806
Triple labeled gel	36	23	23	19	101

Center Performance by Quarter FY 2007

Number of Samples Processed on Each Instrument

Instrument	Q1	Q2	Q3	Q4	Sum Of samples
Deca XP	251	237	8	0	496
FT LTQ MS	139	528	340	522	1529
LTQ-MDLC	245	454	137	72	908
ProTof MALDI	284	428	651	1033	2396
Q Star-XL	107	57	12	82	258
	1026	1704	1148	1709	5587



Hours Each Instrument Processed Samples

Instrument	Q1	Q2	Q3	Q4	Number of Hours
Deca XP	384	385	25	0	794
FT LTQ MS	184	733	457	624	1998
LTQ-MDLC	393	679	275	89	1436
ProTof MALDI	20	131	55	70	276
Q Star-XL	84	47	4	32	167
	1065	1975	816	815	4671

Center for Proteomics Funding Profile (2005 to Present)

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	07/30/08
Chance, Mark		OH	Board of Regents Action Fund	\$125,000	09/01/08	08/31/09
Chance, Mark	P41	NIH	Center for Synchrotron Biosciences-Supplement	\$216,000	03/01/06	08/31/08
Chance, Mark	P41	NIH	Center for Synchrotron Biosciences	\$4,635,000	09/01/05	08/31/08
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	CTSA	NIH	CTSA: Translational Technology Core	\$3,862,500	09/01/07	08/31/12
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	U54	NIH	Genomics and Structural Proteomics Core	\$54,000	11/01/06	07/31/07
Chance, Mark	U54	NIH	New York Structural Genomics Research Consortium	\$494,400	07/01/05	08/31/10
Alagramam, Kumar	R21	NIH	Noise Induced Hearing Loss Proteomics	\$436,000	03/01/07	02/28/09
Bebek, Gurkan	TRN	NIH	Cancer Epidemiology Fellowship	\$287,370	08/31/07	07/30/11
Chang, Jinsook	TREC	NIH	Role of Genetic Susceptibility to Obesity and Tumorigenesis	\$50,000	03/07/07	03/06/08
Chang, Jinsook	R21	NIH	Vsca1 Biomarker Vascular Complications	\$118,500	07/01/07	06/30/09
Cooper, Kevin	P30	NIH	Cort in Psorias: Genomics Core	\$401,700	09/24/07	08/31/12
Dearborn, Dorr	R21	NIH	Biomarkers for Exposure to Stachybotrys	\$419,000	05/01/06	04/30/08
Ghannoum, Mahmoud	R01	NIH	Identification of Early Phase C. albicans Biofilm	\$1,791,000	12/01/06	11/30/11
Haqqi, Tariq	R01	NIH	Mechanisms of chondroprotection by Pomegranate	\$1,920,000	09/01/07	08/31/12
Maguire, Mike	R01	NIH	Magnesium Homeostatis in Microorganisms	\$1,399,000	01/01/07	06/01/10
Nibbe, Rod		AMS	Discovery Proteomics of Colorectal Cancer	\$2,000	07/01/07	10/31/07
Palczewski, Krzysztof	P30	NIH	Core Grant Vision Research-Proteomics Core	\$441,000	04/01/07	03/31/12
Qu, Cheng-Kui	R01	NIH	Tyrosine phosphatases	\$1,930,000	12/01/07	11/30/12
Weinberg, Aaron	R01	NIH	Ontogeny of Oral Epithelial Antimicrobial Peptides	\$1,299,000	04/01/07	03/31/11
Wintrode, Patrick	R01	NIH	Molecular Basis of Serpin Function and Dysfunction	\$1,545,000	06/01/07	05/31/12
Case Center for Proteomics			Center for Proteomics and Center for Synchrotron Biosciences User Fees	\$2,500,000	07/01/05	06/30/10
				\$27,813,470		

Selected Pending Proposals

Principal Investigator	Type of Grant	Agency	Title	Total Cost	Start Date	End Date
Chance, Mark	P41	NIH	Case Center for Synchrotron Bioscience	\$5,995,000	09/01/08	08/31/13
Cho, Michael	P01	NIH	HIV Vaccine Development	\$6,025,019	01/01/08	12/31/12
Cho, Michael	U01	NIH	Development of HIV Related Antigens	\$2,869,155	01/01/08	12/31/12
Haqqi, Tariq	R21	NIH	Chondroprotective Activity in Pomegranate Extract	\$424,000	12/01/07	11/30/09
Liedtke, Carole	R01	NIH	Differential Regulation of NKCC1-Cotransplant	\$1,931,250	12/01/07	11/30/12
Liedtke, Carole	R21	NIH	CFTR regulation of Scaffold proteins	\$424,875	12/01/07	11/30/09
Liedtke, Carole	R01	NIH	Molecular Regulation of Epithelial Na-K-Cl	\$1,962,500	07/01/08	06/30/12
Miyagi, Masaru & Rob Ewing		NSF	Quantitative Tools for Proteomics	\$654,473	04/01/08	03/30/11
Miyagi, Masaru		AMS	Quantification Colon Cancer Secreted Proteins by	\$29,997	01/01/08	12/31/08
Miyagi, Masaru	R21	NIH	Quantification of Colon Cancer Secreted Proteins	\$417,500	07/01/08	06/30/10
Miyagi, Masaru & Rob Ewing	R01	NIH	Tools for Quantitative Proteomics	\$1,177,500	07/01/08	06/30/11
Miyagi, Masaru	R21	NIH	Proteome Analysis of Photoreceptor	\$424,875	12/01/07	11/30/09
Mukherjee, Pranab	R21	NIH	Role of Extracellular Matrix Proteins in Candida	\$424,875	12/01/07	11/30/09
Qu, Cheng-Kui	R01	NIH	PTPMT1 Phosphatases and oxidative stress	\$1,962,500	07/01/08	06/30/13
Swain, James		AICR	Iron Supplementation and Intestinal Tumors	\$163,735	12/01/07	11/30/09
Weinberg, Aaron	P30	NIH	Epithelial Immunity and Oral Complications of HIV	\$6,470,680	07/01/08	06/30/13
Whittaker, Jonathan	R01	NIH	Molecular Biology of Insulin Binding	\$1,931,000	12/01/07	11/30/12
Zhang, Guo-Qiang	R01	NIH	Bench to Book: A vertically integrated MIMI	\$1,611,671	01/01/08	12/31/12
				\$34,900,605		

Invention Disclosures Since 2005

1. Method to enhance qualitative and quantitative analysis of 2-D Gels- 2/28/06- Chance and Takamoto
2. Mediators that isolate and establish adult human mesenchymal stem cells- 8/11/06- Chance, Caplan and Yohannes
3. Expression and Purification of Streptomyces Erythraeus Trypsin- 10/24/06- Miyagi
4. Peptide Separation Technique Using Catalytically Inactive Proteases- 10/25/06- Miyagi
5. Biomarkers Differentiating Two Subtypes of Osteoarthritis- 10/31/06- Gobezie and Lee
6. Collaborative Software for Integrating Data Management, Sharing, Archiving and Distribution- 11/14/06- Zhang, Wilson, Muzic, Szymanski, Flask, Kelley, Janet, Troy, Takamoto, and Schenkel
7. Proteomic biomarkers of diabetic complications of bladder discovered in a rat model of diabetes- 11/28/06- Chance, Christ, and Yohannes
8. 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
9. 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
10. Urinary Proteomic Biomarkers of Diabetic Complication Discovered in a Rat Model of Diabetes – 8/10/07 – Chance, Schaltzer, Christ

Community Outreach Seminar Series

2006

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|-------------------------|--|
| July 10 th | Brian Halligan, Ph.D., Medical College of Wisconsin
“New Approaches to Proteomics Data Analysis” |
| August 8 th | Rob Ewing, Ph.D., (Faculty Candidate) Protana Inc., Toronto Canada
“Computational Proteomics: Tools, Methodologies & Discovery” |
| August 14 th | Simin Hu, Ph.D., (Candidate)
“Penalized Weighted Least Squares Method for Variable Selection
In Survival Analysis with High Dimensional Covariates” |
| August 15 th | Lei Liu, Ph.D., (Candidate)
“Biological Networks: Modularity, Function and Evolution” |
| Sept. 8 th | Mark Michael Yore, Ph.D., (Candidate)
“Synthetic Triterpenoids: Molecular Targets & Mechanisms of Action” |
| Sept. 21 st | Corey Smith, Ph.D., Case Physiology and Biophysics
“Activity-Dependent Differential Transmitter Release From Adrenal Chromaffin
Cells” |
| Sept. 28 th | Reuben Gobezie, M.D., Case Center for Proteomics & University Hospitals,
Department of Orthopaedic Surgery
“Biomarkers for Osteoarthritis: Pearls and Cons...” |
| October 5 th | J. Andrew Keightley, Ph.D., University of Missouri Kansas City
“Protein Identified? Scoring, Confidence and a Novel Solution for Sequence Not in
Database” |

- October 12th Janna Kiselar, Ph.D., Case Center for Proteomics
"ProToF 2000: An Orthogonal MALDI-TOF Analyzer for High Mass Accuracy and High Throughput Capability"
- October 16th Donna Lee Dinnes, Ph.D., (Candidate)
"The Influence of Material Surface Chemistry on the Inflammatory, Degradative and Differentiation Capacity of Human Macrophages"
- October 19th Pranab Mukherjee, Ph.D., Case Department of Dermatology
"Proteomic Analysis of Candida Biofilms"
- Nov. 6th Abhay Golhar, (Post Doc Candidate)
"Intron Evolution in Chicken, Human and Mouse"
- Nov. 16th John Lowe, M.D., Case Department of Pathology
"Control of Mammalian T Cell Development By Fucosylated Glycans"
- Nov. 30th Henri Brunengraber, M.D., Ph.D., Case Department of Nutrition
"Pathway Discovery Via Isotopomics"
- Dec. 14th Amisha Kamal, Ph.D., Case Center for Proteomics
"The Rigor State of The Acto-Myosin Motor: Revelations From X-Ray Protein Footprinting"
- Dec. 21st Timothy S. Kern, Ph.D., Case Western Reserve University
"Pathogenesis of Diabetic Retinopathy"
- 2007
- Jan. 11th Babu A. Manjasetty, Ph.D., Case Center for Proteomics and Center for Synchrotron Biosciences, New York
"Case Proteomics Center Beamlines For Structural Proteomics"
- Jan. 22nd Bruce Lyeth, Ph.D., University of California, Neurological Surgery
"Traumatic Brain Injury: Laboratory Studies of Acute Astrocyte Pathology"
- Feb. 8th Askar Kuchumov, Ph.D., BD Diagnostics
"Reduction of Biological Complexity with Free Flow Electrophoresis: Novel High Resolution Separation of Organelles and Complex Protein Mixtures"
- April 19th Fan Xiang, Ph.D., Shimadzu Biotech
"Unique MALDI Tandem Mass Spectrometers for Structural and Cellular Proteomics"
- April 26th Xiaojing Zheng, Ph.D., Case Center for Proteomics
"Complementary Study of Two Structural Mass Spectrometry Methodologies: Synchrotron Footprinting and Hydrogen Exchange Mass Spectrometry"
- May 3rd Timothy Croley, Ph.D., Virginia State Laboratory
"Automated LC/MS Strategies for Identification of Biomarkers, Metabolites and Poisons"
- May 17th Rhiju Das, Ph.D., University of Washington
"What Protein Structure Prediction Can Do For You"
- May 31st Dan Pu, Ph.D., University of Alabama
"Mass Spectrometric Studies of Peptides: Negative Dissociation of Peptides Containing Hydroxyl Side Chains and Investigation on Complexes of Chromium (III) with Acidic Peptides"
- June 12th Risto Renkonen, CEO, M.D., Ph.D., Antti Kankkunen, VP, Sakari Joenvaara, M.Sc., Medice Oy
"Proteomics Tools of Medice Integrator Systems Biology Software Platform"
- June 13th Brahmananda Reddy Chitteti, Ph.D., Mississippi State University
"Proteome and Phosphoproteome Dynamic Change During Cell Dedifferentiation in Arabidopsis"
- June 14th Chao Yuan, Ph.D., University of Illinois
"Quantitative Comparison of Myofilament Phospho-Proteomes of Neonatal and Adult Rat Hearts"
- June 29th Giridharan Gokulrangan, Ph.D., University of Kansas
"Proteomic Analysis of Protein Nitration: Effect of Biological Aging"

Publications by Center Members and Users since July 2006 (bold names indicate members)

1. Thomson, J.M., Distler, A.M., Prati, F., Bonomo, R.A. Probing active site chemistry in SHV beta-lactamase variants at Ambler position 244. Understanding unique properties of inhibitor resistance. *J Biol Chem.* **281(36)**: 26734-44, 2006.
2. Yike, I., Distler, A.M., Ziady, A.G., Dearborn, D.G. Mycotoxin Adducts on Human Serum Albumin: Biomarkers of Exposure to *Stachybotrys chartarum*. *Environ. Hlth. Perspect.* **114**: 1221-1226, 2006.
3. Zheng, Q.Y., Rozanas, C.R., Thalmann, I., **Chance, M.R.**, Alagramam, K.N. Inner ear proteomics of mouse models for deafness, a discovery strategy. *Brain Res.* **1091(1)**: 113-21, 2006.
4. **Manjasetty, B.**, Bussow, K., Fieber-Erdman, M., Roske, Y., Gobam, J., Scheich, C., Gotz, F., Niesen, F., Heinemann, U. Crystal Structure of Homo Sapiens PTD012 Reveals a Zinc-Containing Hydrolase Fold. *Protein Sci.* **15**: 914-920, 2006.
5. Davies, K.P., Zhao, W., Tar, M., Figueroa, J.C., Desai, P., Verselis, V.K., Kronengold, J., Wang, H.-Z., Melman, A., Christ, G. Diabetes-Induced Changes in the Alternative Splicing of the *Slo* Gene in Corporal Tissue. *Euro. Urol.* 2006.
6. Palamalai, V., Darrow, R. M., Organisciak, D. T. and **Miyagi, M.** "Light-Induced Changes of Protein Nitration in Photoreceptor Rod Outer Segments," *Mol Vis.*, **12**: 1543-1551, 2006.
7. Singh, V., **Shi, W.**, Almo, S., Evans, G., Furneaux, R., Tyler, P., Painter, G., Lenz, D., Mee, S., et al. Structure and Inhibition of Quorum Sensing Target from *Streptococcus pneumoniae*. *Biochemistry.* **45**: 12929-12941, 2006.
8. Murkin, A., Birck, M., Rinaldo-Matthis, A., **Shi, W.**, Taylor, E., Almo, S., Schramm, V. Neighboring Group Participation in the Transition State of Human Purine Nucleoside Phosphorylase, *Biochemistry*, **46**: 5038-5049, 2007.
9. **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.
10. Davies, K.P., Stanevsky, Y., Moses, T., **Chang, J.S.**, **Chance, M.R.**, Melman, A. Ageing causes cytoplasmic retention of MaxiK channels in rat corporal smooth muscle cells. *Int. J. Impotence Res.* **19(4)**: 371-7, 2007.
11. Bharti, A., Ma, P.C., Salgia, R. Biomarker Discovery in Lung Cancer – Promises and Challenges of Clinical Proteomics. *Mass Spec. Rev.* **00**: 1-15, 2007.
12. **Takamoto, K.**, **Amisha Kamal, J.K.**, **Chance, M.R.** "Biological and Chemical Implications of a Three Dimensional Model of Monomeric Actin Bound to Magnesium Chelated ATP" *Structure*, **15(1)**: 39-51, 2007.
13. **Chang, J.**, Cornell, J.E., Van Remmen, H., Hakala, K., Ward, W.F., Richardson, A. "Effect of aging and caloric restriction on mitochondrial proteome," *J. Gerontol. A. Biol. Sci. Med. Sci.*, **62**: 223-34, 2007.
14. **Wang, B.**, Sun, G., Anderson, D.R., Jia, M., Previs, S., Anderson, V.E. "Isotopologue distributions of peptide product ions by tandem mass spectrometry: Quantitation of low levels of deuterium incorporation," *Anal. Biochem.*, **367(1)**: 40-48, 2007
15. Cassano, A.G., **Wang, B.**, Anderson, D.R., Previs, S., Harris, M.E., Anderson, V.E. "Inaccuracies in selected ion monitoring determination of isotope ratios obviated by profile acquisition: nucleotide (18)O/(16)O measurements," *Anal. Biochem.*, **367(1)**: 28-39, 2007.
16. **Miyagi, M.** and Rao, K. C. S. "Proteolytic 18O Labeling Strategy for Quantitative Proteomics," *Mass Spect. Rev.*, **26**: 121-136, 2007.

17. **Kiselar, J.**, Mahaffy, R., Pollard, T.D., Almo, S.C., **Chance, M.R.** "Arp2/3 activation mediated by binding of nucleotides and WASp: Structural mass spectrometry approaches to large macromolecular complexes" *Proc. Nat. Acad. Sci.*, **104**(5): 1552-7, 2007.
18. **Gupta, S., Sullivan, M., Toomey, J., Kiselar, J., Chance, M.R.** "The Beamline X28C of the Center for Synchrotron Biosciences: a National Resource for Biomolecular Structure and Dynamics Experiments Using Synchrotron Footprinting," *J. Synchrotron Rad.*, **14**(Pt 3): 233-43, 2007.
19. **Ilchenko, S.A.**, Cotter, R.J. "Collision Energetics in a Tandem Time-of-Flight (TOF/TOF) Mass Spectrometer with a Curved-Field Reflectron," *Int. J. Mass Spectrometry*, Printed online June, 6, 2007.
20. Garai, J., Haggerty, S., **Rekhi, S., Chance, M.R.** "Infrared Absorption Spectroscopy Investigations Confirm the Extraterrestrial Origin of Coronado-Diamonds." *Astrophysical J.* 653, L153, 2007.
21. **Shi, W., Chance, M.R.** Structural Genomics-High Throughput Structure Determination of Protein Domains, in *Comprehensive Medicinal Chemistry II*, Volume 3: Drug Discovery Technologies, J.B. Taylor and D.J. Triggle, Eds., Elsevier, 2007.
22. **Manjasetty, B.A., Shi, W.** Zhan, C., Fiser, A., **Chance, M.R.** "A High-Throughput Approach to Protein Structure Analysis," *Genetic Engineering*, Vol. 28: 105-128, 2007.
23. 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.
24. **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.
25. Zhu, W. "Crystal Structure of Mn²⁺ bound Escherichia coli L-arabinose Isomerase (ECAI): Its implications in Protein Catalytic Mechanism and Thermo-Stability", *J. of Young Investigators*, 17(3): 2007.
26. 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.
27. **Gupta, S.**, Cheng, H., Mollah, A.K.M.M., 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*, Epub ahead of print, 2007 Aug 7.
28. Yoo, B., Raam, M., Rosenblum, R., Pagel, M.D. "Enzyme-responsive PARACEST MRI contrast agents: A new biomedical imaging approach for studies of the proteasome", *Contrast Media and Molecular Imaging*, 2007, 2:189-198.
29. Yoo, B., Pagel, M.D. "Peptidyl Molecular Imaging Contrast Agents Using a New Solid Phase Peptide Synthesis Approach," *Bioconj. Chem.*, 2007 18:903-11.
30. Mader, D., Yike, I., Distler, A.M., Dearborn, D.G. "Acute pulmonary hemorrhage in two cats during anesthesia associated with exposure to toxic black mold (*Stachybotrys chartarum*)," *J. Am. Vet. Med. Assoc.*, in press.
31. **Shi, W., Chance, M.R.** "Metalloproteomics: A Pfam 500 Strategy for Metalloprotein Annotation", *Cellular and Molecular Life Sciences*, in press.
32. **Manjasetty, B.A.**, Turnbull, A., Panjekar, S., Bussow, K., **Chance, M.R.** "Automated Technologies and Novel Techniques to Accelerate Protein Crystallography for Structural Genomics", *Proteomics*, in press.
33. **Chance, M.R.** "Chapter 1: Overview of Mass Spectrometry Technologies for Examining Protein Structure: Current and Future Directions", in *Mass Spectrometry Analysis for Protein-Protein Interactions and Dynamics*, M. Chance, Ed., Wiley-Blackwell Publishing, in press.

34. **Kiselar, J., Takamoto, K.** "Chapter 3: Covalent labeling Methods for Examining Protein Structure and Protein Interactions", in *Mass Spectrometry Analysis for Protein-Protein Interactions and Dynamics*, M. Chance, Ed., Wiley-Blackwell Publishing, in press.
35. **Zheng, X.**, Wintrode, P. "Chapter 5: Transferrin: Receptor Complex formation Examined by Hydroxyl Radical Footprinting", in *Mass Spectrometry Analysis for Protein-Protein Interactions and Dynamics*, M. Chance, Ed., Wiley-Blackwell Publishing, in press.
36. **Amisha Kamal, J.K., Takamoto, K.** "Chapter 10: Computational Approaches to Examining Protein-Protein Interactions: Combining Experimental and Computational Data in the Era of Structural Genomics", in *Mass Spectrometry Analysis for Protein-Protein Interactions and Dynamics*, M. Chance, Ed., Wiley-Blackwell Publishing, in press.
37. **Amisha Kamal, J.K.**, Chance, M.R. "Modeling protein binary complexes from structural mass spectrometry data," *Prot. Sci.*, in press.
38. Biswas, S. Lewis, **B. Wang, M. Miyagi**, P. Santoshkumar, R.H. Nagaraj. "Revival and augmentation of the chaperone-like activity of guanidinated human α A-crystallin by methylglyoxal modification", *Biochemistry*, submitted.
39. Biswas, **B. Wang, M. Miyagi**, R.H. Nagaraj. "Effect of Methylglyoxal Modification on Stress-Induced Aggregation of Substrate Proteins and their Chaperoning by Human α A-crystallin", *Prot. Sci.*, submitted.
40. **Chang, J., Chance, M.R.**, Nicholas, C., Byun, D.-S., Nasser, S., Albanese, A., Corner, G.A., Tanaka, K., Wilson, A.J., Augenlicht, L.H., Mariadason, J.M. "Proteomic changes during intestinal cell maturation *in vivo*" *Mol. Cell. Prot.*, submitted.
41. **Sullivan, M.R., Rekhi, S., Bohon, J., Gupta, S., Abel, D., Toomey, J., Chance, M.R.** "Installation of a Focusing Mirror at Beamline X28C for High Flux X-ray Radiolysis of Biological Macromolecules." *Rev. Sci. Inst.*, submitted.
42. **Zheng, X.**, Tsutsui, Y., Wintrode, P.L., **Chance, M.R.** "Complementary Structural Mass Spectrometry Techniques Reveal Local Dynamics in Functionally Important Regions of a Metastable Serpin." *Structure*, submitted.

Abstracts, Posters, and Presentations by Center Members and Users since July 2006 (bold names indicate members)

1. **M. Chance.** Workshop Leader, *Medical Scientist Training Program Proteomics Workshop Summer Retreat*, Lodge and Conference Center at Geneva State Park, Geneva, OH, oral presentation, 2006.
2. **M. Chance.** "Structural Proteomics of Macromolecular Complexes", *Amgen*, Thousand Oaks, CA, oral presentation, 2006.
3. **M. Chance.** "Present and Future Plans for the Case Center for Proteomics and Mass Spectrometry", *Center for Proteomics*, Case Western Reserve University, Cleveland, OH, oral presentation, 2006.
4. **M. Chance.** "Structural and Cellular Proteomics in the Post-Genomic Era", *Wake Forest University Health Sciences Institute for Regenerative Medicine, Seminar Series*, Wake Forest University, Winston-Salem, NC, oral presentation, 2006.
5. **M. Chance, S. Liu, M.-Z. Sun**, D. Chen, Q.Y. Zheng, K. Alagramam. "Auditory Proteomics of Mouse Model for Usher Syndrome 1F", *ASM Meeting*, abstract, 2006.
6. **Bohon J.**, Jennings, L., **Gupta, S., Kiselar, J.**, S. Licht and Chance, M.R. "Inside of a Molecular Machine: Examination of the ClpAP Protease via Synchrotron X-ray Hydroxyl-Radical Protein Footprinting and Mass Spectrometry," 54th ASMS Conference on Mass Spectrometry, Seattle, Washington, poster, 2006.
7. Bohon J., L. "ClpAP Protease: Synchrotron Protein Footprinting of a 1.3MDa Molecular Machine", MIT, oral presentation, 2006.
8. **E. Yohannes**, J. Chang, G. Christ, K. Davies, and M. R. Chance. "Differential Proteome Approach to identify Molecular Targets: Signatures for Bladder Dysfunction Associated with Diabetes Mellitus," *Diabetes Research Retreat*, Case School of Medicine and DAGC's Dietrich Diabetes Research Institute, poster, 2006.

9. **J.G. Kiselar.** "prOTOF 2000: An orthogonal MALDI-TOF analyzer for high mass accuracy and high throughput capability," *Case Center for Proteomics Seminar Series*, Case Western Reserve University, Cleveland, OH, presentation, 2006.
10. **J. K. Amisha Kamal**, S. Benchaar, E. Reisler, and **M.R. Chance.** Conformational Dynamics of the Actin Filament Bound to Myosin Head, as Revealed by X-ray Protein Footprinting. **Mol. Cell Proteomics**, 5, S1-S20, abstract, 2006.
11. **J.K. Amisha Kamal**, "The Rigor State of the Acto-Myosin Motor: Revelations From X-Ray Protein Footprinting," *Center for Proteomics*, Case Western Reserve University Cleveland, OH, oral presentation, 2006.
12. **J.K. Amisha Kamal**, "Probing Actin in the Rigor State of the Acto-Myosin Motor by using X-Ray Protein Footprinting," *Center for Proteomics*, Case Western Reserve University Cleveland, OH, oral presentation, 2006.
13. **J.K. Amisha Kamal**, "Three Dimensional Structure of G-actin/Cofilin Binary Complex: Protein Footprinting and Computational Modeling," University of California Los Angeles, Department of Chemistry and Biochemistry, Los Angeles, CA, oral presentation, 2006.
14. **J.K. Amisha Kamal**, "Conformational Dynamics of Actin Filament Bound to Myosin Head," *5th Annual World Congress on Human Proteome Organization (HUPO)*, Long Beach, CA, oral presentation, 2006.
15. **X.J. Zheng**, Y. Tsutsui, P.L. Wintrode and **M.R. Chance.** "Comparison of radiolytic footprinting and hydrogen/deuterium exchange methodologies on the structure of human alpha1-antitrypsin" *HUPO 5th Annual World Congress*, Long Beach, California, poster, 2006.
16. **Shi, W.**, "Metalloproteomics: High-throughput Structural and Functional Annotation of Proteins in Structural Genomics." Department of Biology, Brookhaven National Laboratory, oral presentation, 2006.
17. **Shi, W.**, "Beamline X29 Operation and Metalloproteomics. "Case Center for Proteomics and Mass spectrometry. Oral presentation, 2006.
18. **Shi, W.** Structure Assisted Inhibitor Design and Structure Genomics, Case Center for Proteomics and Mass spectrometry, oral presentation, 2006.
19. **J. K. Amisha Kamal**, S. Benchaar, E. Reisler, and **M.R. Chance.** " Visualizing actin in the rigor state of the acto-myosin motor by using structural mass spectrometry," *55th ASMS Conference on Mass Spectrometry*, Indianapolis, IN, poster, 2007.
20. **R.K. Nibbe** and **M.R. Chance.** "Discovery Proteomics in Colorectal Cancer", *American Association of Cancer Research (AACR) Annual Convention*, Los Angeles, poster, 2007.
21. **R.K. Nibbe** and **M.R. Chance.** "Discovery Proteomics in Colorectal Cancer", *Case Research Showcase*, poster, 2007.
22. **M. Chance.** "Structural and Cellular Proteomics in the Post-Genomic Era", *Case Cardiovascular Research Institute*, Cleveland, OH, oral presentation, 2007.
23. **M. Chance.** "Structural and Cellular Proteomics in the Post-Genomic Era", *USB Corporation*, Cleveland, OH, oral presentation, 2007.
24. **M. Chance.** "Structural and Cellular Proteomics in the Post-Genomic Era", *CRISS Meeting*, Cleveland, OH, oral presentation, 2007.
25. **M. Chance.** "Structural Genomics and Macromolecular Complexes", *NHLBI Systems Medicine Workshop*, Bethesda, MD, oral presentation, 2007.
26. **M. Chance.** "Top-Down Proteomics Using 2D DIGE-Digging Deep for Markers of Diabetic Complications", *2007 Pittsburgh Conference (PITTCON)*, Pittsburgh, PA, oral presentation, 2007.
27. **M. Chance.** "Paradigm Shifts in Structural Genomics: Computational and Experimental Approaches in High-throughput Structure Determination", *SGX Pharmaceuticals*, San Diego, CA, oral presentation, 2007.
28. **M. Chance.** "Three Dimensional Structure of Cofilin Bound to Monomeric Actin Derived by Structural Mass Spectrometry Data", *ASMS Meeting*, Indianapolis, IN, oral presentation, 2007.

29. **M. Chance.** "Differential Expression of Fibulin Family Proteins in Mechanically Strong vs. Weak Fetal Membrane Fragments", *ASME 2007 Summer Bioengineering Conference*, Keystone, CO, oral presentation, 2007.
30. **M. Chance.** "Bladder Complications of Diabetes: Pathophysiology & Biomarkers of Disease", *NIDDK Workshop "Clinical Proteomics in Diabetes and its Complications"*, Bethesda, MD, oral presentation, 2007.
31. **X.J. Zheng**, Y. Tsutsui, P.L. Wintrode and **M.R. Chance.** "Structural study of serpin and its unique mechanism of inhibition" *15th Conversation*, Albany, NY, poster, 2007.
32. **X.J. Zheng**, Y. Tsutsui, P.L. Wintrode and **M.R. Chance.** "MS characterization of serpin and its complex structures" *ASMS*, Indianapolis, IN, poster, 2007.
33. **X.J. Zheng**, Y. Tsutsui, P.L. Wintrode and **M.R. Chance.** "Structural study of serpin and its unique mechanism of inhibition" *Research ShowCASE 2007*, Case Western Reserve University, Cleveland, OH, poster, 2007.
34. **Shi, W.**, "Metalloproteomics: High-throughput Determination of Transition Metal Content in Proteins." NYSGXRC Strategy Meeting, SGX Pharmaceuticals, San Diego, CA, oral presentation, 2007.
35. R.T. Strachan, D.J. Sheffler, B. Willard, M. Kinter, **J.G. Kiselar**, B.L. Roth. "Ribosomal S6 kinase 2 exerts a "tonic brake" on 5-hydroxytryptamine 2A receptor signaling: potential role of direct receptor phosphorylation", *Gordon Research Conference, Phosphorylation and G-Protein Mediated Signaling Networks*, Biddeford, ME, abstract, 2007.
36. Biswas, S. Lewis, **B. Wang**, **M. Miyagi**, R.H. Nagaraj. "Revival and Augmentation of the Chaperone Function of Guanidinated Human α A-Crystallin by Methylglyoxal", *ARVO Meeting*, abstract, 2007.
37. **J. K. Amisha Kamal**, S. Benchaar, E. Reisler, and **M.R. Chance.** Conformational Dynamics of Actomyosin Motor as Revealed by X-ray Protein Footprinting. *J. Biomol. Struct. Dyn.*, 609-772, abstract and oral presentation, 2007.
38. **G. Bebek**, **K. Takamoto.** Accurate Elimination of False Protein-Protein Interactions, *RECOMB 2007*, Oakland, CA, accepted poster, 2007.
39. **Wang, B.**, Biswas, A., **Miyagi, M.**, Nagaraj, R.H., Chance, M.R., Palczewski, K. "Proteomics in Vision Research," *Research ShowCASE 2007*, Case Western Reserve University, Cleveland, OH, poster, 2007.
40. **Wang, B.**, Biswas, A., **Miyagi, M.**, Nagaraj, R.H., Chance, M.R., Palczewski, K. "Proteomics in Vision Research," *Ninth Annual Visual Sciences Research Center Symposium*, poster, 2007.
41. **M. Miyagi**, V. Palamalai, D. Hajkova, K.C. S. Rao, R.M. Darrow, D.T. Organisciak. "Comparative Proteome Analysis of Light Exposed and Unexposed Photoreceptor Outer Segments," *Annual meeting of the Association for Research in Vision and Ophthalmology*, Fort Lauderdale, FL, poster, 2007.
42. **D. Hajkova**, **V. Palamalai**, K.C.S. Rao, R.M. Darrow, D.T. Organisciak, **M. Miyagi.** "Comparative Proteomic Analysis of Light Exposed and Unexposed Photoreceptor Rod Outer Segments by Proteolytic ^{18}O Labeling Strategy," *Annual meeting of the American Society for Mass Spectrometry*, Indianapolis, IN, poster, 2007.
43. **V. Palamalai**, **M. Miyagi.** "The site of modification and mechanism of inactivation of glyceraldehyde-3-phosphate dehydrogenase upon nitration," *Annual meeting of the American Society for Mass Spectrometry*, Indianapolis, IN, poster, 2007.
44. **M. Miyagi.** "O-18 Labeling for Quantitative Proteomics of Photoreceptor Outer Segments," *PITTCON*, Chicago, IL, presentation, 2007.
45. **M. Miyagi.** "A Strategy to Study Photoreceptor Outer Segments Proteome," *9th Annual Case Visual Sciences Research Center Symposium*, Cleveland, OH, presentation, 2007.
46. **M. Miyagi.** "Research and Resources at the Case Proteomics Center," *3rd Annual Resident Research Day*, Department of Otolaryngology, Head and Neck Surgery, University Hospital of Cleveland, OH, presentation, 2007.

47. **R. Gobezie.** "Osteoarthritis: Where We've Been, Where We Are and Where We Hope to Go," *New Faculty Symposium*, Case Western Reserve University School of Medicine, presentation, 2007.
48. **R. Gobezie, J. Crish, S. Kertesy, L. Prebill, M.R. Chance.** "High Abundance Synovial Fluid Proteome In Health and Osteoarthritis," *Research ShowCASE 2007*, Case Western Reserve University, Cleveland, OH, poster, 2007.
49. **E. Yohannes, J. Chang, G. Christ, K. Davies, and M. R. Chance.** "Differential Proteome Approach to identify Molecular Targets: Signatures for Bladder Dysfunction Associated with Diabetes Mellitus," *2007 DIGE Users Meeting*, presentation, 2007.
50. **E. Yohannes, J. Chang, G. Christ, K. Davies, and M. R. Chance.** "Differential Proteome Approach to identify Molecular Targets: Signatures for Bladder Dysfunction Associated with Diabetes Mellitus," *US HUPO 3rd Annual Conference*, Seattle, WA, poster, 2007.
51. **R.M. Moore, E. Yohannes, M.R. Chance, D. Kumar, B.M. Mercer, J.J. Moore** "Proteomic Assessment of Mechanically Strong vs. Weak Amnion Fragments from Vaginally Delivered Fetal Membranes", *53rd Annual meeting of the Society for Gynecological Investigation*, presentation, 2007. Abstract form in the Supplement to Reproductive Sciences, V14, No. 1 (Suppl) January, 2007.
52. **A.V. Dagdanova, S.A. Ilchenko, Q. Yang, P. Gambetti, S.G. Chen.** "Mass Spectrometry Characterization of Urinary Prion Protein", *ASMS Meeting*, Indianapolis, IN, poster, 2007.
53. **A.V. Dagdanova, S.A. Ilchenko, Q. Yang, P. Gambetti, S.G. Chen.** "Mass Spectrometry Characterization of Urinary Prion Protein", *Research ShowCASE 2007*, Case Western Reserve University, Cleveland, OH, poster, 2007.
54. **D.M. Schlatzer, S.A. Ilchenko, E. Yohannes, B. Wang, G. Christ, M.R. Chance.** "Utilizing a Rat Model of Diabetes to Identify Urine Biomarkers for Early Diagnosis of Bladder Dysfunction", *ASMS Meeting*, Indianapolis, IN, poster, 2007.
55. **L. Dubois, D. Dalmas, M. Scicchitano, D.M. Schlatzer, M. Moyer, J. Liu, A. Moseley, N. Cariello, M. Darfler, K. Blackburn.** "Biomarker Proteomics from Formalin-Fixed Paraffin-Embedded Liver and Breast Tissue Sections", *ASMS Meeting*, Indianapolis, IN, poster, 2007.
56. **Bohon J., L.** "Synchrotron Protein Footprinting of the ClpAP Protease Complex at X28C." National Synchrotron Light Source, oral presentation, 2007.
57. **Bohon J., Jennings, L., Gupta, S., Kiselar, J., S. Licht and Chance, M.R.** "Synchrotron Protein Footprinting of the ClpAP Protease." *Research ShowCASE 2007*, Case Western Reserve University, Cleveland, OH, poster, 2007.
58. **Gupta S, Sullivan M, D'Mello R, Bohon J, Abel D, Toomey J, Chance MR.** Synchrotron Footprinting at Beamline X28C of Case Center for Proteomics and Mass Spectrometry: A National Resource for Mapping the Structure and Dynamics of Macromolecular Complexes in Solution. *Research Showcase Case Western Reserve University*, poster, 2007.
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61. **Gupta S, Jastrzebska B, D'Mello R, Palczewski K, Chance MR,** Mapping the structure and dynamics of dark- and light-state bovine rhodopsin by synchrotron radiolysis and high resolution mass spectrometry. *55th ASMS Conference on Mass Spectrometry*, Indianapolis, IN, poster, 2007.
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63. **J. Moore, R. Moore, D. Kumar, J. Mansour, B. Mercer, E. Yohannes, J. Novak, M. Chance.** "Differential Expression of Fibulin Family Proteins in Mechanically Strong vs. Weak Fetal Membrane Fragments", *ASME Summer Bioengineering Conference*, Keystone, CO, PODIUM presentation, 2007.