Harvard Medical School
Curriculum Vitae

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Education

1991-1995	B.A.	Chemistry	Brandeis University
1995-1999	Ph.D.	Chemistry (PI: John Allison)	Michigan State University

Postdoctoral Training

1999-2002	Research Scientist	Proteomics (PI: William S. Lane)	Harvard University

Faculty Academic Appointments

2005-2008	Instructor	Dept. of Pathology	Harvard Medical School
2009-2009	Instructor	Dept. of Medicine	Harvard Medical School
2010-Present	Assistant Professor	Dept. of Medicine	Harvard Medical School
2017-Present	Associate Professor	Dept. of Medicine	Harvard Medical School

Other Professional Positions

2002-2004	Scientist	Beyond Genomics, Inc.

Major Administrative Leadership Positions

2004-Present	Director	Mass Spectrometry Core	Beth Israel Deaconess Medical Center

Professional Societies

1995-Present	American Chemical Society	Member
1996-Present	American Society for Mass Spectrometry	Member
2000-Present	Association of Biomolecular Resource Facilities (ABRF)	Member
2011-2015	Metabolomics Research Group for ABRF	Member
2007-Present	American Association for the Advancement of Science	Member
2008-Present	Human Proteome Organization	Delegate
2011-Present	American Association for Cancer Research	Member
2014-Present	Metabolomics Society	Member
2015-Present	Cancer Research Institute (CRI) at BIDMC Cancer Center	Member
2016-Present	SCIEX Innovation Advisory Board	Advisor
2017-Present	Metabolomics Association of North America	Advisory Board

Grant Review Activities

2016 National Science Foundation Research Proposal
-*CAREER: Discovering Upstream Effectors to Cell Fate Determination*

2017 Harvard Catalyst Reactor Program The Harvard Clinical and Translational Science Center
-Review pilot grants advance the design, development, and evaluation of novel targeted secretion inhibitors (TSIs) for their potential application in oncology, endocrinology, neurology, or pain management

2017 Barts Charity, London UK Strategic Research Grant Proposal
-*Creating a facility for Metabolic flux analysis*

Editorial Activities

- Ad hoc Reviewer

Science Magazine
Analytical Chemistry
Journal of Proteome Research
Proteomics
Cancer Research
Molecular Systems Biology

Scientific Reports
Medicinal Research Reviews
Molecular Biosystems
Metabolomics
Nature Protocols
Molecular Cancer Therapeutics
Protein Science
PLoS ONE
Proceedings of the National Academy of Sciences
Protein Science
Future Oncology
Medicinal Research Reviews
Cell Metabolism
Expert Opinion on Therapeutic Targets
International Journal of Veterinary Science & Technology

- Other Editorial Roles

2010-Present	Faculty Member, Biology	*Faculty of 1000*
2015-Present	Editorial Board Member	*Trends in Proteomics and Bioinformatics*
2016-Present	Editorial Board Member	*Biointerface Research in Applied Chemistry*
2017-Present	Editorial Board Member	*Annals of Proteomics and Bioinformatics*
2017-Present	Editorial Board Member	*International Journal of Genomics, Proteomics, Metabolomics & Bioinformatics*
2017-Present	Editorial Board Member	*Archives of Organic and Inorganic Chemical Sciences*
2018-Present	Editorial Board Member	*Current Trends in Metabolomics*
2018-Present	Editorial Board Member	*Methods and Protocols*
2019-Present	Editorial Board Member	*URINE*

Honors and Prizes

1994-1995	Undergraduate Fellowship	Brandeis University
1996	Roses Award in Teaching	Michigan State University
1998-1999	Tulinsky Endowed Fellowship	Michigan State University
2005	Outstanding Scientist Travel Award	Association of Biomolecular Resource Facilities
2007	Ranked #10 of the 100 Top Scientific	Discover Magazine

	Discoveries of the Year	
2009	Young Investigator Award	Human Proteome Organization
2010	Outstanding Poster Award	Association of Biomolecular Resource Facilities
2010	Faculty Member, Biology (Signal Transduction)	Faculty of 1000
2012	Shared Instrumentation Award	National Institutes of Health
2014	Capital Equipment Award	Beth Israel Deaconess Med Ctr
2015	Academic Partnership Award	AB/SCIEX
2018	Capital Equipment Award	Beth Israel Deaconess Med Ctr

Report of Funded and Unfunded Projects

Past Funding:

2007-2009 Principal Investigator NSF 0634136 $112,736
SGER: A Method to Sequence Novel Peptides from Unsequenced Taxa: Soft tissue of the 68M Year Old Tyrannosaurus rex

- Developed a mass spectrometry and informatics based method using ion trap technology to sequence novel peptide sequences from a well-preserved *T. rex* fossil bone

2012-2013 Principal Investigator NIH 1S10OD010612 $599,926
SIG: LTQ Orbitrap Elite Mass Spectrometer System

- Acquire a new generation and state-of-the art ultra-high resolution/high mass accuracy mass spectrometer for cancer research

2014-2016 Co-Investigator BIDMC CAO Pilot Grant Award $100,000
A novel multimodal molecular imaging of BRAFV600E-targeted therapy with vemurafenib in preclinical and translational models of human papillary thyroid cancer

- Developed mass spectrometry applications for phosphopeptide detection and quantification, protein-protein interactions as well as metabolomics targeted analyses from mouse models and cell lines

2015-2016 Site Co-Investigator NIH R01CA18139002 $28,142
Metabolic Control of Cell Growth by the MTOR Signaling Network

- Development of metabolomics and lipidomics technologies including stable isotope labeling strategies in the mTOR signaling pathway in cancers

Current Funding:

2005-2020 Site Director/Investigator BIDMC 01099980 $310,000
Development and Implementation of a Multi-Omics Mass Spectrometry Core Facility
- Development of new technologies and services for a mass spectrometry core serving the Longwood medical area and HMS community for lipidomics, proteomics and metabolomics analyses

2008-2020 Site Principal Investigator NIH 5P01CA120964 $172,953
Molecular Pathogenesis of the Hamartoma Syndromes-Core B: Mass Spectrometry, Proteomics and Metabolomics Core
- Support three cancer signaling projects studying Hamartoma syndromes and develop new mass spectrometry based strategies including metabolomics and proteomics for studying signal transduction

2009-2020 Site Co-Investigator NIH 5P30CA006516 $244,883
Cancer Center Support Grant: Cancer Proteomics Core
- Develop proteomics technologies to assist cancer researchers who are members of the Dana-Farber Harvard Cancer Center

2014-2020 Site Co-Investigator NIH R35CA19745902 $125,500
Decoding and Targeting the PI3K-mTor Signaling Network in Cancer
- Development of metabolomics and lipidomics technologies including stable isotope labeling strategies in the mTOR signaling pathway in cancers

2016-2020 Site Co-Investigator NIH 1R01AG051658 $117,000
Advancing the Understanding of Postoperative Delirium Mechanisms via Multi-Omics
- Develop and implement proteomic, metabolomic and lipidomic technologies from plasma of delirium patient populations for understanding pathway dysregulation in

Unfunded projects:

A Systems Biology Approach to Dissecting the Topology of the Insulin Signaling Network
- Uncover the protein-protein interaction network of the insulin signaling pathway by comparing immunoprecipitation-mass spectrometry bait-prey experiments from drosophila and human cancer cells

Proteomics and Molecular Phylogenetics of Ancient Fossil Bones
- Develop improved methods for sequencing ancient fossil material by mass spectrometry from several extinct and extant organisms and extend the ancient phylogenetic tree using bone and vessel protein data

Development of a Mass Spectrometry Based Lipidomics Platform to Study Human Disease
- Develop and implement quantitative lipidomics technology using a newly acquired high resolution mass spectrometer (QExactive Plus)

Report of Local Teaching and Training

Teaching of Students in Courses

2009-2014	Proteomics Nanocourse Open to faculty, students and staff	Harvard Catalyst Four hours per year

Formal Teaching of Residents, Clinical Fellows and Research Fellows

2010-Present	Small Molecule Mass Spectrometry Training HMS-affiliated postdocs	Beth Israel Deaconess Medical Center Thirty-five hours per year

Laboratory and Research Supervisory and Training

2005-Present Supervisor Beth Israel Deaconess Medical Center
Twelve hours per week

-Teaching activities involve training our staff in addition to students and post-doctoral research fellows from laboratories of collaborating investigators. Researchers are trained on the fundamental aspects of mass spectrometry (proteomics, metabolomics and lipidomics), sample preparation, instrumental analysis and data processing for biomedical applications.

Formally Supervised Trainees

2005	Robert Dorkin, Ph.D., Research Assistant (currently at CRISPR Therapeutics, Somerville, MA) -Robert helped to implement protocols for mass spectrometry service on proteins for protein identification and quantification as well as PTM mapping
2005-2008	Lisa Freimark, M.S., Research Associate (currently at Broad Institute, Cambridge MA) -Lisa helped to develop mass spectrometry sample preparation strategies for proteomics applications including relative quantification and PTM identification resulting in five peer reviewed publications
2007 – 2011	Shailender Nagpal, M.S., visiting scholar (currently at www.bioinformatics.net, Upton, MA) -Shailender developed bioinformatics algorithms and software to analyze label-free proteomics datasets and novel sequences resulting two peer reviewed publications
2007 - 2010	Xuemei Yang, M.S., Sr. Research Associate (currently at Merck & Co., Boston, MA) -Xuemei studied protein-protein interactions in signaling pathways and developed strategies to study protein complexes in the PI3K pathway using mass spectrometry, resulting in seven peer reviewed publications including two first authorships
2010 – 2017	Susanne B. Breitkopf, Ph.D., Postdoctoral Research Fellow (currently at Pfizer, Inc., Cambridge, MA)

-Susanne developed technological platforms and used mass spectrometry to study signaling networks in cancer via proteomics, phosphoproteomics, lipidomics and metabolomics, resulting in ten peer reviewed publications including seven first authorships

2011- Present Min Yuan, M.S., Sr. Research Associate
-Min is performing method development and implementing strategies for various aspects of lipidomics, metabolomics and proteomics in cancers, resulting in thirteen peer reviewed publications including one first authorship

2015 - 2016 Ying Xu, Ph.D., Postdoctoral Research Fellow (currently at Nuclear Biotechnologies, Boston, MA)
-Ying helped develop our current lipidomics platform that is used for many cancer biomarker studies, resulting in one peer reviewed publication

2017- Present He Huang, Ph.D., Postdoctoral Research Fellow
-He is developing technologies for labeled metabolic and lipidomics flux for biomarker discovery in cancers

Local Invited Presentations

2006 *Qualitative and Quantitative Proteomics Strategies in Cellular Signaling using LC/MS/MS*
Dept. of Surgery
Beth Israel Deaconess Medical Center

2009 *Mass Spectrometry Methods and Applications to Cancer Biology*
Dept. of Cancer Biology
Beth Israel Deaconess Medical Center

2010 *From Fossil Bones to Functional Assays in Cancer: Mass Spectrometry is an Indispensable Tool*
Research & Academic Affairs
Beth Israel Deaconess Medical Center

2011 *Mass Spectrometry in the Cretaceous*
Mass Spectrometry & Chromatography User's Group
Harvard University

2018 *Mass Spectrometry Core: Metabolomics, Lipidomics and Proteomics*
LMA Research Cores Showcase
Harvard Medical School

Report of Regional, National and International Invited Teaching and Presentations

Regional:

Those presentations below sponsored by outside entities are so noted and the sponsor(s) is (are) identified.

2007 *Using an LTQ Ion Trap and Orbitrap to Sequence and Assess the Phylogeny of Ancient Dinosaur Fossils*
Thermo Scientific Corporation User's Meeting
Cambridge, MA

2009 *Proteomics in the Cretaceous*
Northeastern University
Department of Biology
Boston, MA

2010 *Proteomics in the Cretaceous*
Acceleron Pharma
Greater Boston Mass Spectrometry Discussion Group
Cambridge, MA

2010 *A Platform for Quantifying Cancer Cell Metabolism*
Applied Biosystems / SCIEX
Cambridge, MA

2013 *Using ^{13}C and ^{15}N Isotopomer Metabolic Flux via Glucose and Glutamine to Understand Cancer's Metabolic Dependencies by SRM-LC-MS/MS*
Genzyme
Framingham, MA

National:

2007 *TiO2 and its Application to Phosphorylation in Cell Signaling Pathways*
Association of Biomolecular Resource Facilities/Perkin Elmer
Tampa, Florida

2008 *Dinosaur Molecules and Their Evolutionary Tale* (Plenary session)
Association of Biomolecular Resource Facilities
Salt Lake City, Utah

2008 *Dinosaur Sequences and Their Evolutionary Tale*
American Society for Mass Spectrometry
Denver, Colorado

2010 *A Platform for Quantifying Cancer Cell Metabolism*
U.S. Human Proteome Organization
Denver, Colorado

2010 *Getting the Best Data from your Proteomics Core: Facility Proteomics Strategies and Workflows*
Association of Biomolecular Resource Facilities
Sacramento, California

2010 *Proteomics in the Creataceous*
American Chemical Society (Eastern New York Section)

Albany, NY

2010 *A Targeted Protein-Protein "Interact-ome" of Components in the Insulin Signaling Pathway in Drosophila and Compared to Human Cancer Cells*
American Society for Mass Spectrometry
Salt Lake City, Utah

2011 *Using Tandem Mass Spectrometry to Choose Appropriate Kinase Inhibitor Drugs in Cancers: A Personalized Medicine Approach Based on Protein-Protein Interactions (PPI)*
American Society for Mass Spectrometry
Denver, Colorado

2012 *Fluxing Through Cancer: Tracking the Fate of 13C Labeled Energy Sources Glucose and Glutamine in Cancer Cells and Mouse Tumors*
U.S. Human Proteome Organization
San Francisco, California

2012 *Fluxing Through Cancer: Tracking the Fate of 13C Labeled Energy Sources Glucose and Glutamine in Cancer Cells and Mouse Tumors*
American Society for Mass Spectrometry
Vancouver, Canada

2013 *Using 13C and 15N Isotopomer Metabolic Flux via Glucose and Glutamine to Understand Cancer's Metabolic Dependencies by SRM-LC-MS/MS*
American Society for Mass Spectrometry
Minneapolis, Minnesota

2014 *CrossOmics: Integrating Quantitative Phosphoproteomics and Metabolomic Flux to Study Drug Effects on Cancer Cells*
Association of Biomolecular Resource Facilities
Albuquerque, New Mexico

2014 *Cross-Omics: Global Phosphoproteomics and Metabolomics Reveals a Connection Between Kinase Inhibition and RNA Processing in BCR-ABL H929 Myeloma Cells*
American Society for Mass Spectrometry
Baltimore, Maryland

2015 *Small Molecules in a Core Setting: Targeted Metabolic Flux to Untargeted Lipidomics*
Association of Biomolecular Resource Facilities
St. Louis, Missouri

2015-2017 Metabolomics/Lipidomics Workshop Training Course
Association of Biomolecular Resource Facilities

2016 *Preparing Biological Samples for Metabolomics and Lipidomics, Can We Start with Just One Sample?*
Association of Biomolecular Resource Facilities
Ft. Lauderdale, Florida

2016 *A Quantitative Positive/Negative Switching Method for Shotgun Lipidomics via High*

Resolution LC-MS/MS from any Biological Source
American Society for Mass Spectrometry
San Antonio, Texas

2016 *Metabolomics and Lipidomics in Cancer Research*
3rd Metabolomics: Advances & Applications in Human Disease
GTCBio
Cambridge, MA

2016 *Dealing with Lipid ID and Informatics in the Triome Era*
American Society for Mass Spectrometry
San Antonio, Texas

2017 *Lipidomics in Systems Biology – Untargeted Pos/Neg Switching LC-MS/MS Platform*
Association of Biomolecular Resource Facilities
San Diego, California

2018 *Serial-Omics: From Breast Tumors to Bodily Fluids to Dried Blood Spots*
American Society for Mass Spectrometry
San Diego, California

2018 *FluxSearch: A Strategy for 13C/15N Metabolic and Lipid Flux Analysis from Untargeted High Resolution LC-MS/MS*
American Society for Mass Spectrometry
San Diego, California

2018 *Serial-Omics Characterization of Equine Urine and Mane Hair by LC-MS/MS*
American Society for Mass Spectrometry
San Diego, California

International:

2008 *Splitless nano-LC Technology for Biomolecular Research: Proteomics to Fossilomics*
Human Proteome Organization World Congress
Amsterdam, Netherlands

2008 *Dinosaur Sequences and Their Evolutionary Tale*
London Biological Mass Spectrometry Discussion Group
London, England

2009 *A Targeted Protein-Protein "Interact-ome" of the Insulin Signaling Pathway in Drosophila and Compared to Human Cells*
Human Proteome Organization World Congress
Toronto, Canada

2012 *Fluxing Through Cancer: Tracking the Fate of ^{13}C Labeled Energy Sources Glucose and Glutamine in Cancer Cells and Mouse Tumors*
Human Proteome Organization World Congress
Boston, MA

Report of Technological and Other Scientific Innovations

US Patent 20140193920 A1 7/10/2014
Metabolomics of human biological fluids identify signatures of malignant glioma
-A method of identifying a patient in need of therapy to treat a malignant glioma comprising measuring a panel of polar metabolite levels in a biological sample taken from the patient and implementing a therapy to treat the malignant glioma in the patient.

Report of Education of Patients and Service to the Community

Activities:

2013-2017 Local High School Mass Spectrometry Technology Overview course

Report of Scholarship:

Peer-Reviewed Scholarship in print or other media (212):

1. **Asara, J.M.;** Uzelmeier, C.E.; Dunbar, K.R.; Allison, J. Analysis of transition-metal compounds containing tetrathiafulvalene phosphine ligands by fast atom bombardment mass spectrometry: limitations and the development of matrix additives for the desorption of multiply charged complexes. ***Inorg. Chem***. 1998;37:1833-40.

2. **Asara, J.M.;** Allison, J. Enhanced detection of phosphopeptides in matrix-assisted laser desorption/ionization mass spectrometry using ammonium salts. ***J. Am. Soc. Mass Spectrom***. 1999;10:35-44.

3. **Asara, J.M.;** Allison, J. Enhanced detection of oligonucleotides in UV MALDI MS using the tetraamine spermine as a matrix additive. ***Anal. Chem***. 1999;71:2866-70.

4. **Asara, J.M.;** Hess, J.S.; Lozada, E.; Dunbar, K.R.; Allison, J. Evidence for binding of dirhodium acetate units to adjacent GG and AA sites on single-stranded DNA. ***J. Am. Chem. Soc***. 2000;122:8-13.

5. Oh, M.-H.; Huber, S.; **Asara, J.M.;** Gage, D.A.; Clouse, S. Putative phosphorylation recognition sequences of the arabidopsis Bri1 receptor kinase. ***Plant Phys***. 2000, 124:751-65.

6. Ivan, M.; Kondo K.; Yang, H.F.; Kim, W.; Valiando, J.; Ohh, M.; Salic, A.; **Asara, J.M**.; Lane, W.S.; Kaelin, W.G. HIFalpha targeted for VHL-mediated destruction by proline hydroxylation: implications for O2 sensing. ***Science.*** 2001;292:464-68.

7. Kane, S.; Sano, H.; Liu, S.C.H.; **Asara, J.M.;** Lane, W.S.; Garner, C.C.; Lienhard, G.E. a new method to identify serine kinase substrates: Akt phosphorylates a novel adipocyte protein with a Rab gap domain. ***J. Biol. Chem***. 2002;277:22115-118.

8. Schweitzer, M.H.; Hill, C.H.; Chiappe, L.M.; **Asara, J.M.;** Lane, W.S.; Pincus, S.H. Identification of immunoreactive material in mammoth fossils. ***J. Mol. Evol***. 2002;55:696-705.

9. Sano, H; Kane, S; Sano, E; Miinea, C.P.; **Asara, J.M.;** Lane, W.S.; Garner, C.W.; Lienhard, G.E. Insulin-stimulated phosphorylation of a Rab GTPase-activating protein regulates GLUT4 translocation. ***J. Biol. Chem***. 2003;278**:**14599-602.

10. Levine, M.Z.; Sanchez, C.C.; Wilkins, P.P.; Lane, W.S.; **Asara, J.M.;** Hancock, K.; Gonzalez, A.E.; Garcia, H.H.; Gilman, R.H.; Tsang, V.C.W. Characterization, cloning and expression of two diagnostic antigens for *Taenia solium*. tapeworm infection. ***J. Parasitol***. 2004;90:631-38.

11. Abbott, D.A.; Wilkins, A.; **Asara, J.M.;** Cantley, L.C. The Crohn's disease gene, NOD2, requires RIP2 to induce ubiquitinylation of a novel site on NEMO. ***Curr. Biol.*** 2004;14:2217-27.

12. Zhang, X.; Hines, W.; Adamec, J.; **Asara, J.M.;** Naylor, S.; Regnier, F.E. An automated method for the analysis of stable-isotope labeling data in proteomics. ***J. Am. Soc. Mass Spectrom***. 2005;16:1181-91.

13. Zhang, X; **Asara, J.M**.; Adamec, J; Ouzzani, M; Elmagarmid, A.K. Data pre-processing in liquid chromatography-mass spectrometry based proteomics. ***Bioinformatics***. 2005;21*:*4054-4059.

14. **Asara, J.M.;** Zhang, X.; Zheng, B.; Christofk, H.H.; Wu, N.; Cantley, L.C. In-gel stable isotope labeling (ISIL): A strategy for mass spectrometry-based relative quantification. ***J. Proteome Res.*** 2006; 5:155-163.

15. **Asara, J.M.;** Zhang, X.; Zheng, B.; Maroney, L.A.; Christofk, H.R.; Wu, N.; Cantley, L.C. In-gel stable isotope labeling for relative quantification by mass spectrometry. ***Nature Protoc***. 2006;1:46-51.

16. **Asara, J.M.**; Schweitzer, M.H.; Freimark, L.M.; Phillips, M.; Cantley, L.C. Protein sequences from Mastodon and *Tyrannosaurus rex* revealed by mass spectrometry. ***Science*.** 2007;316:280-285.

17. Schweitzer. M.H.; Suo, Z.; Avci, R.; **Asara, J.M.**; Allen, M.A.; Arce, F.T.; Horner, J.R. Analysis of soft tissue from *Tyrannosaurus rex* suggest the presence of protein. ***Science*.** 2007;316:277-280.

18. Hutti, JE, Turk, BE, **Asara, JM**, Ma, A, Cantley, LC, and Abbott, DW A screen for IKKB substrates identifies IKKB-mediated phosphorylation of A20 as a mechanism of feedback inhibition in the NFkB pathway. ***Mol Cell Biol.*** 2007;27:7451-61.

19. Zinkin, N.T.; Grall, F.; Bhaskar, K.; Otu, H.H.; Spentzos, D.; Kalmowitz, B.; Wells, M.; Guerrero, M.; **Asara, J.M.;** Libermann, T.A.; Afdhal, N.H. Serum Proteomics and Biomarkers in Hepatocellular Carcinoma and Chronic Liver Disease. ***Clin. Cancer. Res.*** 2008;14:470-477.

20. **Asara, J.M**.; Christofk, H.R.; Freimark, L.M.; Cantley, L.C. Label-free relative quantification by MS/MS TIC compared to stable-isotope labeling and spectral counting in a proteomics screen. ***Proteomics***. 2008:8:994-999.

21. Christofk, H.R.; Vander Heiden, M.V.; Wu, N.; **Asara, J.M.**; Cantley, L.C. Pyruvate kinase M2 is a novel phosphotyrosine binding protein**.** ***Nature*.** 2008:452:181-186.

22. Organ, C.L.; Schweitzer, M.H.; Zheng, W.; Freimark, L.M.; Cantley, L.C.; **Asara, J.M.** Molecular phylogenetics of Mastodon and *Tyrannosaurus rex*. ***Science***. 2008:320:499.

23. Clements, R.T.; Smejkal, G.; Sodha, N.R.; Ivanov, A.R.; **Asara, J.M.**; Feng, J.; Lazarev , A.; Senthilnathan, V.; Khabbaz , K.R.; Bianchi, C.; Sellke, F.W. Proteomic profile of differentially regulated proteins in human myocardium before and after cardiac surgery utilizing cardioplegia and cardiopulmonary bypass. ***Circulation***, 2008:30:118.

24. Zheng, B.; Jeong, J.H.; **Asara, J.M**.; Yuan, Y.Y.; Granter, S.R.; Chin, L.; Cantley, L.C. Oncogenic B-RAF negatively regulates the tumor suppressor LKB1 to promote melanoma cell proliferation. ***Mol. Cell***, 2008:33:237-47.

25. Karnchanaphanurach, P.; Mirchev, R.; Ghiran, I.; **Asara, J.M**.; Papahadjopoulos-Sternberg, B.; Nicholson-Weller, A.; Golan, D.E. Membrane skeleton-linked protein complex induced by C3b deposition on human erythrocytes. ***J. Clin. Invest***., 2009:119:788-801.

26. Schweitzer, M.H.; Zheng, W.; Organ, C.L.; Avci, R.; Suo, Z.; Freimark, L.M.; Lebleu, V.S.; Duncan II, M.B.; Vander Heiden, M.G.; Neveu, J.M.; Lane, W.S.; Cottrell, J.S.; Horner, J.R.; Cantley, L.C.; Kalluri, R.; **Asara, J.M.** Biomolecular Characterization and Protein Sequences of the Campanian Hadrosaur *Brachylophosaurus canadensis*. ***Science***, 2009:324:626-31.

27. Hutti, J.E.; Shen, R.R.; Abbott, D.W.; Zhou, A.Y.; Sprott, K.M.; **Asara, J.M.**; Hahn, W.C.; Cantley, L.C. Phosphorylation of the tumor suppressor CYLD by the breast cancer oncogene IKK epsilon promotes cell transformation. ***Mol. Cell***, 2009:14:461-72.

28. Dibble, C.C.; **Asara, J.M.**; Manning, B.D. Characterization of Rictor phosphorylation sites reveals direct regulation of mTOR complex 2 by S6K1. ***Mol. Cell. Biol.***, 2009:29:5657-70.

29. Chen, Y.J.; Dominguez-Brauer, C.; Wang, Z.; **Asara, J.M.**; Costa, R.H.; Tyner, A.L.; Lau, L.F.; Raychaudhuri, P. A. conserved phosphorylation site within the forkhead domain of FoxM1B is required for its activation by cyclin-CDK1. ***J. Biol. Chem.*** 2009:284:30695-707.

30. Yang, X.; Friedman, A.; Nagpal, S.; Perrimon, N.; **Asara, J.M.** Use of a label-free quantitative platform based on MS/MS average TIC to calculate dynamics of protein complexes in insulin signaling. ***J. Biomol. Tech.*** 2009:20:272-7.

31. Palka-Hamblin, H.L.; Gierut, J.J.; Bie, W.; Brauer, P.M.; Zheng, Y.; **Asara, J.M.**; Tyner, A.L. Identification of beta-catenin as a target of the intracellular tyrosine kinase PTK6. ***J. Cell Sci.*** 2010:123(Pt 2):236-45.

32. Li, M.; Aliotta, J.M.; **Asara, J.M.**; Wu, Q.; Dooner, M.S.; Tucker, L.D.; Wells, A.; Quesenberry, P.J.; Ramratnam, B. Intercellular transfer of proteins as identified by stable isotope labeling of amino acids in cell culture (SILAC). ***J. Biol. Chem.*** 2009:[Epub ahead of print].

33. Kesavan, K.; Ratliff, J.; Johnson, E.W.; Dahlberg, W.; **Asara, J.M.**; Misra, P.; Frangioni, J.V.; Jacoby, D.B. Annexin A2 Is a Molecular Target for TM601, a Peptide with Tumor-targeting and Anti-angiogenic Effects. ***J. Biol. Chem.*** 2010:285:4366-74.

34. Li M, Aliotta JM, **Asara JM**, Wu Q, Dooner MS, Tucker LD, Wells A, Quesenberry PJ, Ramratnam B. Intercellular transfer of proteins as identified by stable isotope labeling of amino acids in cell culture. ***J. Biol. Chem.*** 2010:285:6285-97.

35. Palka-Hamblin HL, Gierut JJ, Bie W, Brauer PM, Zheng Y, **Asara JM**, Tyner AL. Identification of beta-catenin as a target of the intracellular tyrosine kinase PTK6. ***J. Cell Sci.*** 2010:123(Pt 2):236-45.

36. Gwinn DM, **Asara JM**, Shaw RJ. Raptor is phosphorylated by cdc2 during mitosis. ***PLoS One.*** 2010:5:e9197.

37. Jiang X, Chen S, **Asara JM**, Balk SP. Phosphoinositide 3-kinase pathway activation in phosphate and tensin homolog (PTEN)-deficient prostate cancer cells is independent of receptor tyrosine kinases and mediated by the p110beta and p110delta catalytic subunits. ***J. Biol. Chem.*** 2010:285:14980-9.

38. Nhek S, Ngo M, Yang X, Ng MM, Field SJ, **Asara JM**, Ridgway ND, Toker A. Regulation of oxysterol-binding protein golgi localization through protein kinase D-mediated phosphorylation. ***Mol. Biol. Cell***. 2010:21:2327-37.

39. Zheng Y, Peng M, Wang Z, **Asara JM**, Tyner AL. Protein tyrosine kinase 6 directly phosphorylates AKT and promotes AKT activation in response to epidermal growth factor. ***Mol. Cell Biol.*** 2010, 30:4280-92.

40. Vander Heiden, MG; Locasale, JW; Swanson, KD; Sharfi, H; Heffron, GJ; Amador-Noguez, D; Christofk, HR; Wagner, G; Rabinowitz, JD; Asara, JM; Cantley, LC. Evidence for an alternative glycolytic pathway in rapidly proliferating cells. ***Science***. 2010, 329:1492-9.

41. Tigno-Aranjuez JT, **Asara JM**, Abbott DW. Inhibition of RIP2's tyrosine kinase activity limits NOD2-driven cytokine responses. ***Genes Dev.*** 2010, 24:2666-77.

42. Simabuco FM, **Asara JM**, Guerrero MC, Libermann TA, Zerbini LF, Ventura AM.Structural analysis of human respiratory syncytial virus p protein:identification of intrinsically disordered domains. Braz ***J Microbiol***. 2011Jan;42(1):340-5.

43. Egan DF, Shackelford DB, Mihaylova MM, Gelino S, Kohnz RA, Mair W, Vasquez DS, Joshi A, Gwinn DM, Taylor R, **Asara JM**, Fitzpatrick J, Dillin A, Viollet B, Kundu M, Hansen M, Shaw RJ. Phosphorylation of ULK1 (hATG1) by AMP-activated protein kinase connects energy sensing to mitophagy. ***Science***. 2011 Jan 28;331(6016):456-61.

44. Aboulaich N, Chui PC, **Asara JM**, Flier JS, Maratos-Flier E. Polymerase I and transcript release factor regulates lipolysis via a phosphorylation-dependent mechanism. ***Diabetes***. 2011 Mar;60(3):757-65

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Non-peer Reviewed Scholarship:

Letters to the Editor

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Thesis

1999 Michigan State University *"Enhancing spectra in desorption/ionization mass spectrometry through the use of chemical additives"*

- Developed methods for mass spectral signal enhancement of highly charged biological molecules such as oligonucleotides, phosphopeptides, and DNA-metal complexes

Narrative Report

As an Associate Professor in the Division of Signal Transduction in Harvard Medical School's Department of Medicine and the Director of the Mass Spectrometry Core at Beth Israel Deaconess Medical Center, I have collaborated with nearly 200 investigators over the last fifteen years and have developed a state-of-the-art mass spectrometry facility that attracts local, national and international researchers. In addition to core collaborative and service based projects, I lead several research efforts externally funded by the NIH. These internal research efforts in combination with external collaborations have resulted in more than 220 peer reviewed national publications and invitations to speak at national and international mass spectrometry, -omics, health and biotechnology conferences. Most notably, I improved the lab dramatically over the last several years by securing three grants (NIH and BIDMC capital funds) to fund ultra-high resolution and mass accuracy Orbitrap mass spectrometers (QExactive HF and QExactive Plus), the gold standard in high resolution mass spectrometry instrumentation, dedicated to non-targeted lipidomics, metabolomics and phosphoproteomics. We also incorporated hybrid triple quadrupole (5500 and 6500 QTRAP) that we use exclusively for quantitative targeted metabolomics and 13C/15N metabolic flux analysis, technology that we incorporated five years ago.

The main area of my research involves the use of various mass spectrometry technologies to study the integration of metabolomics, lipidomics and phosphoproteomics (*Triomics*) as well as the study of protein complexes in signaling pathways for diseases such as cancer and the goal is to identify new targets for "smart" drugs that specifically inhibit the pathways that are driving cell growth, proliferation and metastasis rather than a chemotherapy approach. The lab is gaining a national reputation for the integration of different –omics technologies as demonstrated by several publications and invited seminars. We recently used a combination of metabolomics, metabolomics flux, global phosphoproteomics and lipidomics from BCR/ABL positive H929 multiple myeloma cells to assemble a model showing that only does imatinib abrogate signaling via the BCR/ABL-ERK-TOR pathway, but a collection of phosphosites are elevated in the spliceosome which block transcription and result in an accumulation of free RNA nucleotides. This also results in a decrease in fatty acid synthesis and lipid biosynthesis. The nuclear phosphorylation events and metabolic consequences were unexpected (Breitkopf et al., ***Anal. Chem***., 2015). The study included triple SILAC stable isotope labeling for IMAC purified phosphopeptides as well as 13C glucose and glutamine labeled metabolites. We are extending this research to include *Serial-Omics*, a technology platform that we developed recently which begins with a single piece of tissue and a liquid-liquid extraction is performed whereby we use three different layers for proteomics, metabolomics and lipidomics (Breitkopf *et. al.*, ***Sci. Reports***, 2017; Yuan *et. al.*, ***PLoS One***, 2017).

We are also very interested in studying protein-protein interactions from model species and human disease models to find novel interactions that may conserved through evolution. To that end, we recently published a study where we analyzed PI3K immunoprecipitations from a variety of human cancers under various drugs and stimuli and compared those to drosophila cells under various stimuli using a label-free quantitative technology that we developed several years ago (Asara et. al., ***Proteomics***, 2008) to discover that the P85 regulatory subunit of PI3K binds directly to the tyrosine phosphatase SHP2 in an AKT independent manner. We believe that the pool of free P85 that is not bound to P110 (catalytic subunit of PI3K) when activating AKT is tied up with SHP2 and not truly free (Breitkopf et. al. ***Sci. Reports***, 2016).

Approximately six years ago, we developed and implemented a hybrid triple quadrupole (QTRAP) mass spectrometry based platform for profiling more than 300 endogenous cellular metabolites in a single LC-MS/MS run using selected reaction monitoring (SRM) and pos/neg polarity switching (Yuan et. al., ***Nature Protoc***., 2012) that covers all major and metabolic pathways in cancers. We are studying the effects of various stimulations and drug treatments on cancer cells both mutant and endogenous and the metabolic consequences of such events to search for new metabolic pathway drug targets. We are also profiling metabolites from clinical tissues to search for biomarkers. This platform has resulting in major research publications in the journals ***Nature***, ***Science***, ***Cell***, ***Cancer Discovery***, ***Mol. Cell***, etc. We are actively using both steady-state and 13C/15N stable isotope labeling for targeted metabolomics and

lipidomics. A couple of studies where we developed significant custom sets of both 15N and 13C labeling methods from glucose, glutamine, etc. were in collaboration Dr. Brendan Manning's lab at Harvard School of Public Health where we identified novel mTOR and S6K control of pyrimidine synthesis via (Ben-Sahra et al., ***Science***, 2013) and also mTORC1's control in purine synthesis (Ben-Sahra et. al., ***Science***, 2016).

We also have shown that a signaling strategy using co-immunoprecipitation and LC-MS/MS or IP-MS can be used to identify key signaling events controlling particular cancers. We use a combination of a pTyr IP, p85 IP and Grb2 IP and integrate the resulting network. We used this strategy to identify a novel BCR/ABL mutation in H929 multiple myeloma cells (Breitkopf et. al., ***Proc. Nat. Acad. Sci. U.S.A***., 2012). This is an extension of work that showed that we can quantify the binding partners of PI3K using label free mass spectrometry in a variety of human cancers and under various treatment conditions to assess the adaptor use and activation state of each PI3K driven tumor (Yang et. al., ***Cancer Res***., 2011).

We have shown over the last few years that metabolism plays a key role in cancer progression and we have been performing mass spectrometry based non-labeled and ^{13}C and ^{15}N labeled metabolic flux experiments to help find altered metabolism in cancers and their response to drug treatments. To follow this, we published a detailed protocol on how to use tandem mass spectrometry to profile 13C and 15N labeled cells and organisms for targeted metabolic flux analysis by polarity switching and SRM (Yuan et. al., ***Nat. Protoc.***, 2019). This can be used in mice for in vivo studies and from cell culture studies.

Several articles in *Science* over the last ten years received national media attention as they discussed the sequencing of multi-million year collagen proteins extracted from *Tyrannosaurus rex* and *B. canadensis* fossil bones (Asara et. al., ***Science***, 2007; Asara et. al., ***Science*** 2008, Schweitzer et. al., ***Science***, 2009) and showed a molecular phylogenetic relationship to birds for the first time. I remain active in the development of new methods to sequence ancient fossils and uncovering the phylogenetics of both extinct and extant organisms as these applications continue to challenge our sensitivity capabilities needed for studying low level signaling proteins from tumors. Additionally, software that has been developed for finding subtle sequence changes in conserved proteins such as collagen in ancient species is now used by our laboratory for finding protein level mutations in human cancers.

Our newest technology using high resolution QExactive Orbitrap mass spectrometers focusses on the global untargeted lipidome from cells, tissues, bodily fluids, etc. We can identify more 1500 lipid molecules using this LC-MS/MS based strategy, not just lipid classes and fatty acid content but the actual composition of each individual lipid. Our latest endeavor involves labeling lipid molecules with ^{13}C and ^{15}N tracers to study lipid biochemistry in cancers and related diseases. These applications involve both targeted and untargeted approaches. We have shown progress in understanding the pathways affecting metabolism and fatty acid synthesis in TSC2-/- cells, critical for Hamartoma syndromes and we have assessed lipid profiles in multiple human and mouse tumors (Breitkopf et. al., ***Metabolomics***, 2017).

Teaching is an important focus of my lab and in that regard; I have taken part in numerous workshops on mass spectrometry technology including proteomics and metabolomics teaching seminars for the DF/HCC, HMS and BIDMC to teach both faculty and students. In addition, I personally formally supervise senior researchers, students and postdoctoral fellows in my laboratory. In addition, I teach students and post-docs from collaborating laboratories how to operate mass spectrometry instrumentation and how to prepare samples in order to answer biological questions related to diseases such as cancer, diabetes, etc. I also teach workshops in national conferences on various mass spectrometry topics and am heavily involved in research groups for biotechnology societies that involve teaching and tutorial components.

In addition to research and teaching activities, as the director of one of the medical center's core facilities, I provide daily service (50% of my effort) to local researchers in their quest to cure and treat debilitating diseases such as cancer. The service goes beyond instrumental analyses but extends to help in grant writing and presentations to local laboratories and investigators. I am committed to this endeavor of providing service to the academic and clinical research community.