

Chad R. Borges Curriculum Vitae

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Address: Molecular Biomarkers
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Education

Michigan State University – **Postdoctoral research associate** under J. Throck Watson in the field of mass spectral analysis of biological macromolecules, 2001-2003.

University of Utah – **Ph.D. in Analytical Toxicology / Pharmacology**, December 2001—
emphases in analytical toxicology and drug metabolism. Cumulative GPA 3.97

Walla Walla College – **B.S. in Chemistry**, June 1997. Magna Cum Laude.

Experience

Professional History:

Assistant Research Professor, Molecular Biomarkers Unit, The Biodesign Institute at Arizona State University, 5/2008-PRESENT (Asst. Res. Scientist 1/2007 – 5/2008)

Research interests include:

- 1) Glycobiology of Human Vitamin D Binding Protein and other proteins carrying the Core 1 O-glycan.
- 2) Cysteine sulfenic acid as a posttranslational protein modification
- 3) Discovery, characterization, and verification of new protein markers of disease—particularly those based on protein posttranslational modifications relevant to diabetes and cancer.
- 4) Development of new bio-analytical modalities.

Funding: According to Internal Credit Allocation (RID, IIA, etc.) Currently Personally Responsible for Bringing in **\$558,631 per year (Total Costs to ASU), \$994,570 per year (Including Sub-contracts to Other Institutions).**

PI on NIH/NCRR **R21** 1R21RR024440-01 entitled *Site-specific analysis of human cysteine sulfenic acid protein modifications*, 12/2007 – 11/2010. (90% Internal Credit Allocation)

Co-Investigator on NIH/NIDDK **R24** 1R24DK090958-01A1 entitled Team Approach to Translate Novel Biomarkers for Diabetes, 8/2011 - 7/2015. (**75%** Internal Credit Allocation)

Co-Investigator on NIH/NIDDK **R01** DK082542 entitled *Population-Based Proteomic Investigation of Type 2 Diabetes Mellitus*, 3/2010 - 2/2015. (**20%** Internal Credit Allocation)

Pending Funding (Under Review at NIH)

PI on NIH **R01** Proposal entitled *Core 1 O-Glycan Anticancer Biology*. (**75%** Internal Credit Allocation)

Co-Investigator on NIH **U01** Proposal entitled, PTHRP Signature-Based Biomarkers for Common Cancers. (**100%?** Internal Credit Allocation)

Previous Positions

Data Analysis Consultant to Aegis Sciences Corporation (a forensic drug testing company), Nashville, TN, 2008-2009

Assistant Director, Center for Human Toxicology, University of Utah, Department of Pharmacology and Toxicology, 2005-2007

Research Assistant Professor of Pharmacology and Toxicology & Research Toxicologist, University of Utah, Department of Pharmacology and Toxicology, 12/2003 – 1/2007

Funded research projects included:

- 1) Co-Investigator** on NIH/NIGMS R01 GM074249-01 (GS Yost, PI) entitled *P450-mediated dehydrogenation mechanisms*, 20% effort, started 1/2006. Major responsibilities include overseeing the structural characterization of protein-suicide substrate covalent adducts.
- 2) Co-Investigator** on a University of Utah seed grant to develop methods to screen for novel allosteric modulators of target proteins (J Rutter, PI).
- 3) PI** on a 1-yr grant from the National Football League Charities entitled, *Application of Automated Chemometric Techniques for the Improved Detection of Steroids in Urine*.

Other responsibilities included:

- 1)** Development of mass spectrometry-based methods for the detection of anabolic agents in urine
- 2)** Oversee day-to-day mass spectrometer upkeep, operation, troubleshooting, and training. MS instruments include GC/MS, LC/MS, LC/MS/MS (QqQ and Q-TOF)
- 3)** Certify data in compliance with ISO 17025:2005 guidelines.

Postdoctoral Research Associate, Michigan State University, Department of Biochemistry under J. Throck Watson, 9/2001 – 5/2003.

Responsibilities (all involved **determination of posttranslational protein modifications**):

- 1)** Served as a general collaboration “point-man” for Prof. Watson.

- 2) Determined the disulfide bond structure for the 12-cysteine-containing Transforming Growth Factor β Type II Receptor Extracellular Domain using mass spectrometry (related work published 2003 and 2004)
- 3) Determined tyrosine nitration patterns in Tyrosine Hydroxylase following toxic insult with peroxynitrite using mass spectrometry (published 2002 and 2003)
- 4) Determined cysteinyl glutathionylation patterns of Tyrosine Hydroxylase using mass spectrometry following oxidative insult and treatment with glutathione (published 2002)
- 5) Developed a methodology for producing a distinctive MALDI mass spectral fragmentation pattern from cysteinyl peptides by which they can be rapidly (and automatically, if desired) recognized within a single-stage MALDI mass spectrum, then mass mapped, allowing for easy, quick identification of cysteine-containing peptides (published 2003)

Teaching Experience

Lectures:

ASU – Mass Spectrometry and Immunoassays (BDE 598 Fundamentals of Biological Design [Oct. 2011])

University of Utah – Introduction to Analytical Toxicology (PHTX 7114)

Future Directions in Analytical Toxicology (PHTX 7114)

Introduction to Mass Spectrometry (PHTX 7114)

Plant & Animal Toxins (PHTX graduate level)

Endocrine Pharmacology (PHTX graduate level)

Thyroid Pharmacology (PHTX for pharmacy students)

Doctoral Student Committees: ASU – 1 student; **University of Utah** – 6 students

Teaching Assistant for American Chemical Society mass spectrometry short course

(2002): Chromatography / Mass Spectrometry: Principles & Practice, July 29-August 2.

Taught by O. David Sparkman, Frederick E. Klink, and Patrick R. Jones.

Teaching Assistant for undergraduate labs in Organic Chemistry and General Chemistry (1994-1997)

Patents / Innovations

2011: MIDAS: A method for systematic identification of small molecule/protein interactions (University of Utah, Under Review)

2010: A liquid buffer formulation to enhance detection sensitivity and oxidative stability of low-concentration protein solutions (~~Patent Pending~~ Under Revision)

2008: Single Assay Determination of Genotype and Protein Phenotype in the Assessment of Disease (Patent Pending)

2007: Concept for facilitating analyst-mediated interpretation of qualitative chromatographic-mass spectral data from batch-wise screening of “noisy” samples (University of Utah; Not pursued by Technology Commercialization Office, but basis of professional consulting work—see 2007 publication in *Analytical Chemistry*)

Scientific Review Services

Ad hoc reviewer for the following peer reviewed journals:

Analytical Biochemistry, Skin Pharmacology and Physiology, Journal of the American Society for Mass Spectrometry, Chemical Research in Toxicology, Analytical Chemistry, Toxicology Letters, Journal of Chromatography A, Journal of Proteome Research, Biochimica et Biophysica Acta, Journal of the American Chemical Society (JACS), and Clinical Chemistry and Laboratory Medicine.

Ad hoc Grant Proposal Reviewer for the National Science Foundation (NSF)

Selection of Invited or Competitively Selected Lectures at National Meetings

“Electrospray Ionization-based Mass Spectrometric Immunoassay” (GTCbio 5th Biomarker Discovery and Development Conference [Oct. 2011])

“Human Osteocalcin Characterization by Mass Spectrometric Immunoassay” (FASEB Summer Research Conference on Molecular, Structural & Clinical Aspects of Vitamin K & Vitamin K-Dependent Proteins, June 2011)

“Protein Biomarkers Beyond Fluctuations in Concentration (HUPO, Feb 2009)

“Escorting protein biomarkers down the discovery pipeline using mass spectrometry immunoassay: a case study of work in progress with Type 2 Diabetes biomarkers” (CHI conference on Proteomic Sample Preparation, Boston, May 2008)

This lecture also selected for highlight in a news article in the July 1, 2008 (Vol. 28 No. 13) issue of *Genetic Engineering and Biotechnology News* (pgs. 1; 40-42)

“Hyphenated Mass Spectrometric Techniques” (Agilent, July 2007)

“Time of Flight Mass Spectrometry: Forensic Applications” (American Academy of Forensic Science, Feb. 2007)

Awards

Abstract submitted to the 2008 Association of Biomolecular Resource Facilities (ABRF) selected as a semi-finalist in the annual poster competition and selected as an invited paper to the *Journal of Biomolecular Techniques*

Awarded “Best Student Platform Presentation” at the 18th annual (2000) Mountain West Society of Toxicology meeting.

Recipient of a 1999-2000 University of Utah Graduate Research Fellowship for the amount of \$10,000.

Recipient of a 1999 University of Utah Graduate Research Supplemental Travel Award to attend the 1999 Society of Toxicology meeting.

Finalist in the 1999 Society of Toxicology's Mechanisms Specialty Section's Carl C. Smith Fourteenth Annual Graduate Student Awards for Meritorious Research in Mechanisms of Toxicology.

Winner of the 1996 Walla Walla College Department of Chemistry Merit Award (included partial scholarship).

Professional Memberships

American Society for Mass Spectrometry, 2001-present

Society of Toxicology, 1998-2001

Mountain West Society of Toxicology (MWSOT), 1998 – 2001

Elected as a student counselor of MWSOT for the 1999-2000 school year

American Chemical Society, 1996-1997.

Publications (Peer Reviewed; 30 Published, 2 Currently Under Review)

h-index = 10

Personal Impact Factor = 14.1 (average number of citations for all articles published in 2010 or earlier)

Under Review

Bley, C.J., Rand, D.P., Qi, X., **Borges, C.R.**, Nelson, R.W., Chen, J.J.L. Mapping the RNA-protein interface in telomerase RNP. *PNAS*, Under Review.

Orsak, T., Smith, T.L., Eckert, D., Lindsley, J.E., **Borges, C.R.**, Rutter, J. Revealing the Allosterome: Systematic Identification of Metabolite/Protein Interactions. *Biochemistry*, Under Review

Published

Oran, P.E., Jarvis, J.W., **Borges, C.R.**, Sherma, N.D., Nelson, R.W. Mass Spectrometric Immunoassay of Intact Insulin and Related Variants for Population Proteomics Studies. *Proteomics Clin Appl* **5**: 454-9, 2011.

Borges, C.R., Oran, P.E., Buddi, S., Jarvis, J.W., Schaab, M.R., Rehder, D.S., Rogers, S. P., Taylor, T. and Nelson, R.W. Building Multidimensional Biomarker Views of Type 2 Diabetes Based on Protein Microheterogeneity. *Clin. Chem* **57**: 719-728, 2011.

Nelson, R.W., **Borges, C.R.** Mass spectrometric immunoassay revisited. *J Am Soc Mass Spectrom* **22**: 960-968, 2011.

Rehder, D. S., **Borges, C. R.** Cysteine sulfenic Acid as an Intermediate in Disulfide Bond Formation and Nonenzymatic Protein Folding, *Biochemistry* **49**: 7748-7755, 2010.

Oran, P.E., Sherma, N.D., **Borges, C.R.**, Jarvis, J.W., Nelson, R.W. Intrapersonal and Populational Heterogeneity of the Chemokine RANTES. *Clin Chem* **56**: 1432-1441, 2010.

Rehder, D. S., **Borges, C. R.** Possibilities and pitfalls in quantifying the extent of cysteine sulfenic acid modification of specific proteins within complex biofluids. *BMC Biochemistry* **11**: 25, 2010.
– Achieved “Highly Accessed” Status.

Lopez, M.F., Rezai, T., Sarracino, D.A., Prakash, A., Krastins, B., Athanas, M., Singh, R.J., Barnidge, D.R., Oran, P.E., **Borges, C.R.**, Nelson, R.W. Selected Reaction Monitoring–Mass Spectrometric Immunoassay Responsive to Parathyroid Hormone and Related Variants *Clin Chem* **56**: 281-290, 2010. – Featured as one of *Clinical Chemistry*’s 2010 Journal Club articles

Borges, C.R., Rehder, D.S., Jarvis, J.W., Schaab, M.S., Oran, P.E., Nelson, R.W. Full length characterization of proteins in human populations *Clin Chem* **56**: 202-211, 2010.

Oran, P.E., Jarvis, J.W., **Borges, C.R.**, Nelson, R.W. C-peptide Microheterogeneity in Type 2 Diabetes Populations *Proteomics Clin Appl* **4**: 1-6, 2010.

Rehder, D. S., Nelson, R. W., **Borges, C. R.** Glycosylation status of vitamin D binding protein in cancer patients. *Protein Sci* **18**: 2036-2042, 2009.

Borges, C.R., Jarvis, J.W., Oran, P.E., Rogers, S.P., Nelson, R.W. “Population Studies of Vitamin D Binding Protein Microheterogeneity by Mass Spectrometry Lead to Characterization of its Genotype Dependent O-glycosylation Patterns” *J. Proteom. Res.* **7**:4143-53, 2008.

Borges, C.R., Jarvis, J.W., Oran, P.E., Rogers, S.P., Nelson, R.W. “Population studies of intact Vitamin D binding protein by affinity capture ESI-TOF-MS” *J Biomolecular Techniques* **19**(3): 167-176, 2008.

Hoggan, A.M., Shelby, M.K., Crouch, D.J., **Borges, C.R.**, Slawson, M.H. “Detection of bumetanide in an over-the-counter dietary supplement” *J. Anal. Toxicol.* **31**(9):601-4, 2007.

Borges C.R., “Concept for facilitating analyst-mediated interpretation of qualitative chromatographic-mass spectral data from batch-wise screening of “noisy” samples” *Anal. Chem.* **79**(13):4805-13, 2007.

Borges C.R., Miller N., Shelby M., Hansen M., White C., Slawson M.H., Monti K., and Crouch D.J. “Analysis of a challenging subset of World Anti-Doping Agency-banned steroids and anti-estrogens by LC/MS/MS” *J. Anal. Toxicol.* **31**(3):125-31, 2007.

Borges C.R., Taccogno J., Crouch D.J., Le L., Truong T.N. “Structure and Mechanism of Formation of an Important Ion in Doping Control.” *Int. J. Mass Spectrom.* **247**: 48-54, 2005.

Borges C.R., Qi J., Wu W, Torng E., Hinck A.P., and Watson J.T. “Algorithm-Assisted Elucidation of Disulfide Structure: Application of the Negative Signature Mass Algorithm to Mass-Mapping the Disulfide Structure of the 12-Cysteine Transforming Growth Factor β Type II Receptor Extracellular Domain.” *Anal Biochem.* **329**(1):91-103, 2004.

Rollins, D.E., Wilkins, D.G., Krueger, G.G., Augsburger, M.P., Mizuno, A., O’neal, C., **Borges, C.R.**, Slawson, M.H. “The Effect of Hair Color on the Incorporation of Codeine into Hair.” *J. Anal. Toxicol.* **27**: 545-551, 2003.

Qi, J., Hang, D., Rupp, M., **Borges, C.R.**, Wu, W., Torng E., and Watson, J.T. "Automated Data Interpretation Based on the Concept of 'Negative Signature Mass' for Mass-Mapping Disulfide Structures of Cystinyl Proteins." *J. Amer. Soc. Mass Spectrom.* **14**(9): 1032-1038, 2003. – This manuscript also selected for inclusion in (Issue 18, 29 August 2003) of "Proteomics Select – The Virtual Journal of Proteomics", <http://www.proteomicsvj.com>

Borges, C.R., and Watson, J.T., "Recognition of Cysteine-Containing Peptides through Prompt Fragmentation of the 4-Dimethylaminophenylazophenyl-4'-maleimide Derivative During Analysis by MALDI-MS" *Protein Sci.* **12**(7): 1567-72, 2003.

Borges, C.R., Kuhn, D.M., and Watson, J.T. "Mass Mapping Sites of Nitration in Tyrosine Hydroxylase: Random versus Selective Nitration of Three Tyrosine Residues" *Chem. Res. Toxicol.* **16**(4): 536-40, 2003.

Borges, C.R., Roberts, J.C., Wilkins, D.G., and Rollins, D.E. "Cocaine, Benzoylecgonine, Amphetamine, and N-acetylamphetamine Binding to Melanin Subtypes." *J. Anal. Toxicol.* **27**(3): 125-34, 2003.

Wilkins, D.G., Mizuno, A., **Borges, C.R.**, Slawson, M.H., and Rollins, D.E., "Ofloxacin as a reference marker in hair of various colors." *J. Anal. Toxicol.* **27**(3): 149-55, 2003.

Borges, C.R., Geddes, T., Watson, J.T., and Kuhn, D.M. "Dopamine biosynthesis is regulated by S-glutathionylation: Potential mechanism of tyrosine hydroxylase inhibition during oxidative stress." *J. Biol. Chem.* **277**(50): 48295-302, 2002.

Kuhn D.M., Sadidi M., Lu X., Kriepke C., Geddes T., **Borges C.**, Watson J.T. "Peroxynitrite-induced nitration of tyrosine hydroxylase: identification of tyrosines 423, 428, and 432 as sites of modification by MALDI-TOF mass spectrometry and tyrosine-scanning mutagenesis." *J. Biol. Chem.* **277**(16): 14336-42, 2002.

Borges, C.R., Martin, S.D., Meyer, L.J., Wilkins, D.G., and Rollins, D.E. "Influx and Efflux of Amphetamine and N-acetylamphetamine in Keratinocytes, Pigmented Melanocytes, and Non-Pigmented Melanocytes." *J. Pharm. Sci.* **91**(6): 1523-35, 2002.

Borges, C.R., Wilkins, D.G., and Rollins, D.E. "Amphetamine and N-acetylamphetamine incorporation into hair: an investigation of the potential role of drug basicity in hair color bias." *J. Anal. Toxicol.* **25**: 221-227, 2001.

Borges, C.R., Roberts, J.C., Wilkins, D.G., and Rollins, D.E. "Relationship of melanin degradation products to actual melanin content: Application to human hair." *Anal. Biochem.* **290**: 116-125, 2001.

Denkinger, D.J., **Borges, C.R.**, Butler, C.L., Cushman, A.M., and Kawahara, R.S. "Genomic organization and regulation of the *vav* proto-oncogene." *Biochim. Biophys. Acta* **1491**: 253-262, 2000.

Hold, K.M., **Borges, C.R.**, Wilkins, D.G., Rollins, D.E., and Joseph, R.E. Jr. "Detection of nandrolone, testosterone and their esters in rat and human hair samples." *J. Anal. Toxicol.* **23**: 416-423, 1999.

Dissertation Title: Roles of drug basicity, melanin binding, and hair cell transport in drug incorporation into hair.