

PIERRE R. BUSHEL

EDUCATION

B.S., Zoology, May 1984

University of Massachusetts Amherst, MA

M.S., Molecular and Cellular Biology, September 1989

Long Island University Brooklyn, NY

Ph.D., Bioinformatics, May 2005

North Carolina State University Raleigh, NC

Research Experience

September 2006-Present National Institute of Environmental Health Sciences, RTP, NC

Staff Scientist

Biostatistics Branch, Clarice Weinberg

Development of computational algorithms for microarray gene expression and genomic data analysis.

September 2008-December 2008 Harvard School of Public Health, Cambridge, MA

Assistant Professor

Department of Biostatistics, Louise Ryan

Department of Environmental Health, Douglas Dockery

Yerby Visiting professorship in bioinformatics and computational biology.

April 2000-September 2006 National Institute of Environmental Health Sciences, RTP, NC

Staff Scientist

Microarray Group, Cindy Afshari and Richard S. Paules

Development of bioinformatics tools for microarray gene expression data analysis.

November 1998-April 2000 OAO Corporation, Durham, NC

Bioinformatics Scientist

NIEHS Microarray Center, Hunter Robinson

Development of databases for microarray gene expression data management and analysis.

June 1998-August 1998 SYNAPTIC, Paramus, NJ

Manager/Genome Analyst

Automated DNA Sequencing, T.V. Venkatesh

Managed the DNA sequencing core facility.

April 1996-February 1998 NOVARTIS, RTP, NC

Scientist/Genome Analyst

Automated DNA Sequencing, Steve Goff

Performed DNA sequencing and analyzed the sequence reads.

August 1990-April 1996 SCHERING-PLOUGH, Kenilworth, NJ

Associate Scientist

Tumor Biology Department, Chandra Kumar

Developed DNA-protein binding assays to screen for anti-cancer therapeutics and investigated transcriptional regulatory elements involved in rho- and ras –mediated signaling.

September 1986-August 1990 COLUMBIA UNIVERSITY, New York, NY

Technician

Human Genetics and Medicine, Arthur Bank and Maggie Allan

Screen for sickle cell anemia, performed haplotyping and investigated transcriptional regulatory elements involved in erythroid differentiation and development.

HONORS AND AWARDS

- National Institutes of Health Award of Merit, NIEHS, December 2000, 2001 & 2003
- National Institutes of Health Director's Award, NIH, Bethesda Maryland June 2002

PROFESSIONAL ACTIVITIES

Member, Scientific Advisory Committee for the Carolina Environmental Bioinformatics Center, at the University of North Carolina- Chapel Hill. 2008 and 2009

Ph.D. Dissertation Committees:

Lingkang Huang - Variable Selection in Multiclass Support Vector Machine and Applications in Genomic Data Analysis. 2004 – 2008.

Member, Society of Toxicology

PUBLICATIONS IN PEER-REVIEWED JOURNALS

Bushel, P.R., Nielsen, D, Tong, W. Proceedings of the First International Conference on Toxicogenomics Integrated with Environmental Sciences (TIES-2007). BMC Proceedings 2009 3(Suppl 2):S1.

Bushel, P.R., Clustering of Gene Expression Data and End-Point Measurements by Simulated Annealing. JBCB 2009 7(1): 193-215.

Lobenhofer E.K., Auman J.T., Blackshear P.E., Boorman G.A., **Bushel P.R.**, Cunningham M.L., Fostel J.M., Gerrish K., Heinloth A.N., Irwin R.D., Malarkey D.E., Merrick B.A., Sieber S.O., Tucker C.J., Ward S.M., Wilson R.E., Hurban P., Tennant R.W., Paules R.S. Gene Expression Response in Target Organ and Whole Blood Varies as a Function of Target Organ Injury Phenotype. Genome Biol. 2008 Jun 20;9(6):R100.

Huang L., Heinloth A.N., Zeng Z.B., Paules R.S., **Bushel P.R.** Genes Related to Apoptosis Predict Necrosis of the Liver as a Phenotype Observed in Rats Exposed to a Compendium of Hepatotoxicants. BMC Genomics. 2008 Jun 16;9(1):288.

Boedigheimer M.J., Wolfinger R.D., Bass M.B., **Bushel P.R.**, Chou J.W, Cooper M., Corton J.C., Fostel J., Hester S., Lee J.S., Liu F., Liu J., Qian H.R., Quackenbush J., Pettit S., Thompson K.L. Sources of Variation in Baseline Gene Expression Levels from Toxicogenomics Study Control Animals Across Multiple Laboratories. BMC Genomics. 2008 Jun 12;9(1):285.

Jin Y.H., Dunlap P.E., McBride S.J., Al-Refai H., **Bushel P.R.**, Freedman J.H. Global Transcriptome and Deletome Profiles of Yeast Exposed to Transition Metals. PLoS Genetics 2008 Apr 25;4(4):e1000053.

Bushel, P.R., Heinloth, A.N., Li, J., Huang, L., Chou, J.W., Boorman, G.A., Malarkey, D.E., Houle C.D., Ward S.M., Wilson R.E., Tennant R.W., Paules, R.S. Blood Gene Expression

Signatures Predict Exposure Levels. PNAS 2007 Nov;104(46):18211-18216. Epub 2007 November 2.

Bushel P.R., Wolfinger R.D., Gibson G.C. “Simultaneous Clustering of Gene Expression Data with Clinical Chemistry and Pathological Evaluations Reveals Phenotypic Prototypes”. BMC Systems Biology 2007, 1:15.

Chou J.W., Zhou, T., Kaufmann, W.K., Paules R.S., **Bushel P.R.** “Extracting gene expression patterns and identifying co-expressed genes from microarray data reveals biologically responsive processes”. BMC Bioinformatics 2007, 8:427.

Zhou T., Chou J., Zhou Y., Simpson D.A., Cao F., **Bushel P.R.**, Paules R.S., Kaufmann W.K. Ataxia telangiectasia-mutated dependent DNA damage checkpoint functions regulate gene expression in human fibroblasts. Mol Cancer Res. 2007 Aug;5(8):813-22.

Fostel J.M., Burgoon L., Zwickl C., Lord P., Corton J.C., **Bushel P.R.**, Cunningham M., Fan L., Edwards S.W., Hester S., Stevens J., Tong W., Waters M., Yang C., Tennant R. Toward a checklist for exchange and interpretation of data from a toxicology study. Toxicol Sci. 2007 Sep;99(1):26-34. Epub 2007 Apr 17.

Zhou T., Chou J., Mullen T.E., Elkon R., Zhou Y., Simpson D.A., **Bushel P.R.**, Paules R.S., Lobenhofer E.K., Hurban P., Kaufmann W.K. Identification of primary transcriptional regulation of cell cycle-regulated genes upon DNA damage. Cell Cycle. 2007 Apr 15;6(8):972-81. Epub 2007 Apr 19.

Zhou T, Chou JW, Simpson DA, Zhou Y, Mullen TE, Medeiros M, **Bushel PR**, Paules RS, Yang X, Hurban P, Lobenhofer EK, Kaufmann WK. Profiles of global gene expression in ionizing-radiation-damaged human diploid fibroblasts reveal synchronization behind the G1 checkpoint in a G0-like state of quiescence. EHP. 2006 Apr;114(4):553-9.

Innes CL, Heinloth AN, Flores KG, Sieber SO, Deming PB, **Bushel PR**, Kaufmann WK, Paules RS. ATM requirement in gene expression responses to ionizing radiation in human lymphoblasts and fibroblasts. Mol Cancer Res. 2006 Mar;4(3):197-207.

Xirasagar S, Gustafson SF, Huang CC, Pan Q, Fostel J, Boyer P, Merrick BA, Tomer KB, Chan DD, Yost KJ 3rd, Choi D, Xiao N, Stasiewicz S, **Bushel P**, Waters MD. Chemical effects in biological systems (CEBS) object model for toxicology data, SysTox-OM: design and application. Bioinformatics. 2006 Apr 1;22(7):874-82. Epub 2006 Jan 12.

Chou J.W, Paules R.S., **Bushel P.R.** “Systematic Variation Normalization in Microarray Data to Get Gene Expression Comparison Unbiased”. JBCB 3, 1-17, 2005.

Leung E, **Bushel PR**. PAGE: phase-shifted analysis of gene expression. Bioinformatics. 2006 Feb 1;22(3):367-8. Epub 2005 Dec 1.

Bammler T, Beyer RP, Bhattacharya S, Boorman GA, Boyles A, Bradford BU, Bumgarner RE, **Bushel PR**, Chaturvedi K, Choi D, Cunningham ML, Deng S, Dressman HK, Fannin RD, Farin FM, Freedman JH, Fry RC, Harper A, Humble MC, Hurban P, Kavanagh TJ, Kaufmann WK,

Kerr KF, Jing L, Lapidus JA, Lasarev MR, Li J, Li YJ, Lobenhofer EK, Lu X, Malek RL, Milton S, Nagalla SR, O'malley JP, Palmer VS, Pattee P, Paules RS, Perou CM, Phillips K, Qin LX, Qiu Y, Quigley SD, Rodland M, Rusyn I, Samson LD, Schwartz DA, Shi Y, Shin JL, Sieber SO, Slifer S, Speer MC, Spencer PS, Sproles DI, Swenberg JA, Suk WA, Sullivan RC, Tian R, Tennant RW, Todd SA, Tucker CJ, Van Houten B, Weis BK, Xuan S, Zarbl H; Members of the Toxicogenomics Research Consortium. "Standardizing global gene expression analysis between laboratories and across platforms". *Nat Methods*. 2005 May;2(5):351-6.

Fostel J, Choi D, Zwickl C, Morrison N, Rashid A, Hasan A, Bao W, Richard A, Tong W, **Bushel PR**, Brown R, Bruno M, Cunningham ML, Dix D, Eastin W, Frade C, Garcia A, Heinloth A, Irwin R, Madenspacher J, Merrick BA, Papoian T, Paules R, Rocca-Serra P, Sansone AS, Stevens J, Tomer K, Yang C, Waters M. Chemical effects in biological systems--data dictionary (CEBS-DD): a compendium of terms for the capture and integration of biological study design description, conventional phenotypes, and 'omics data. *Toxicol Sci*. 2005 Dec;88(2):585-601. Epub 2005 Sep 8.

Mattes, W.B., Pettit, S.D., Sansone, S., **Bushel, P.R.**, Waters, M.D." Database Development in Toxicogenomics: Issues and Efforts ". *EHP Toxicogenomics* 112(4) 495-505, 2004.

Hamadeh HK, Jayadev S, Gaillard ET, Huang Q, Stoll R, Blanchard K, Chou J, Tucker CJ, Collins J, Maronpot R, **Bushel P**, Afshari CA. "Integration of clinical and gene expression endpoints to explore furan-mediated hepatotoxicity". *Mutat Res*. 2004 May 18;549(1-2):169-83.

Bushel, P.R., Hamadeh, H.K., Bennett, L., Green, J., Albeson, A., Misener, S., Afshari, C.A., Paules, R.S. "Computational Selection of Distinct Class- and Subclass- Specific Gene Expression Signatures". *Journal of Biomedical Informatics* 35: 160-170, 2003.

Hodges, L.C., Cook, J.D., Lobenhofer, E.K., Li, L., Bennett, L., **Bushel, P.R.**, Aldaz, C.M., Afshari, C.A., Walker, C.L. "Tamoxifen Functions As a Molecular Agonist Inducing Cell Cycle-Associated Genes in Breast Cancer Cells". *Molecular Cancer Research* 1: 300-311, 2003.

Steenbergen, C., Afshari, C.A., Petranka, J.G., Collins, J., Martin, K., Bennett, L., Haugen, A., **Bushel, P.**, Murphy, E. "Altered Gene Expression in Human Idiopathic Cardiomyopathic Hearts in Failure: A Pro-Apoptotic Shift in the Tumor Necrosis Factor- α Signaling Pathway". *Am J Physiol Heart Circ Physiol* 284(1): H268-276, 2003.

Heinloth A.N., Shackelford R.E., Innes C.L., Bennett L., Li L., Amin R.P., Sieber S.O., Flores K.G., **Bushel P.R.**, Paules R.S. "Identification of Distinct and Common Gene Expression Changes after Oxidative Stress, g- and Ultraviolet-Radiation". *Molecular Carcinogenesis*, 37(2): 65-82, 2003.

Heinloth A.N., Shackelford R.E., Innes C.L., Bennett L., Li L., Amin R.P., Sieber S.O., Flores K.G., **Bushel P.R.**, Paules R.S. "ATM-Dependent and -Independent Gene Expression Changes in Response to Oxidative stress, g- and UV-Radiation". *Radiation Research* 160, 273-290, 2003.

Waters M, Boorman G, **Bushel P**, Cunningham M, Irwin R, Merrick A, Olden K, Paules R, Selkirk J, Stasiewicz S, Weis B, Van Houten B, Walker N, Tennant R. "Systems toxicology and

the Chemical Effects in Biological Systems (CEBS) knowledge base". EHP Toxicogenomics. 2003 Jan;111(1T):15-28.

Kerr, M.K., Afshari, C., Bennett, L., **Bushel, P.**, Martinez, J., Walker, N., and Churchill, G.A. "Statistical Analysis of a Gene Expression Microarray Experiment". Statistica Sinica 12(1): 203-217, 2002.

Hamadeh, H.K., **Bushel, P.**, Tucker, C.J., Martin, K., Paules, R., and Afshari, C.A. "Detection of Diluted Gene Expression Alterations Using cDNA Microarrays". Biotechniques 32: 322-329, 2002.

Hamadeh, H.K., **Bushel, P.R.**, Jayadev, J., Martin, K., DiSorbo, O., Sieber, S., Bennett, L., Tennant, R., Stoll, R., Barrett, J.C., Blanchard, K., Paules, R.S., Afshari, C.A. "Prediction of Compound Signature Using High Density Gene Expression Profiling". Toxicological Sciences, 67: 232-240, 2002.

Oh, J.S., Kucab, J.E., **Bushel, P.R.**, Martin, K., Bennett, L., Collins, J., DiAugustine, R.P., Barrett, J.C., Afshari, C.A., Dunn, S.E. "Insulin like growth factor-1 inscribes a gene expression profile for angiogenic factors and cancer progression". Neoplasia, 4(3): 204-217, 2002.

Hamadeh, H.K., **Bushel, P.R.**, Jayadev, S., Martin, K., DiSorbo, O., Sieber, S., Bennett, L., Tennant, R., Stoll, R., Barrett, J.C., Blanchard, K., Paules, R.S., Afshari, C.A. "Gene Expression Analysis Reveals Chemical-Specific Profiles". Toxicological Sciences 67: 219-231, 2002.

Amin, R.P., Hamadeh, H.K., **Bushel, P.R.**, Bennett, L., Afshari, C.A., Paules, R.S. "Genomic Interrogation of Mechanism(s) Underlying Cellular Responses to Toxicants". Toxicology 181-182:555-63, 2002.

Lobenhofer, E.K., Bennett, L., Cable, P.L., Li, L., **Bushel, P.**, Afshari, C.A. "Regulation of DNA Replication Fork Genes by 17 β -Estradiol". Molecular Endocrinology 16(6): 1215-1229, 2002.

Martinez, J. M., Afshari, C.A., **Bushel, P.**, Masuda, A., Takahashi, T., and Walker, N. J. "Differential toxicogenomic responses to 2,3,7,8-tetrachlorodibenzo-p-dioxin in malignant and nonmalignant human airway epithelial cells". Toxicological Sciences 69: 409-423, 2002

Hamadeh, H.K., Li, L., Stoltz, J., **Bushel, P.R.**, Stoll, R., Blanchard, K., Jayadev, S., Afshari, C.A. "Elucidation of signal versus effect in toxicogenomic studies". Applied Genomics and Proteomics, 2002.

Hamadeh, H.K., Knight, B.L., Haugen, A.C., Sieber, S., Amin, R.P., **Bushel, P.R.**, Stoll, R., Blanchard, K., Jayadev, S., Tennant, R.W., Cunningham, M.L., Afshari, C.A., Paules, R.S. "Methapyrilene Toxicity: Anchorage of Pathologic Observations to Gene Expression Alterations". Toxicologic Pathology 30(4): 470-482, 2002.

Wolfinger, R.D., Gibson, G., Wolfinger, E.D., Bennett, L., Hamadeh, H., **Bushel, P.**, Afshari, C., Paules, R.S. "Assessing gene significance from cDNA microarray expression data via mixed models". Journal of Computational Biology 8(6): 625-637, 2001.

Hamadeh, H., **Bushel, P.**, Nuwaysir, E., Barrett, J.C., Afshari, C.A. cDNA "Microarray Technology: Bringing Toxicology and Genomics Closer". *Comments on Toxicology* 7(4): 361-379, 2001.

Shcherbakova, P.V., Hall, M.C., Lewis, M.S., Bennett, S.E., Martin, K.J., **Bushel, P.R.**, Afshari, C.A., and Kunkel, T.A. "Inactivation of DNA Mismatch Repair by Increased Expression of Yeast MLH1". *Molecular and Cellular Biology* 21(3): 940-951, 2001.

Bushel, P.R., Hamadeh, H., Bennett, L., Sieber, S., Martin, K., Nuwaysir, E.F., Hayes, K., Reynolds, K., Paules, R., and Afshari, C.A. "MAPS: A MicroArray Project System for Gene Expression Experiment Information and Data Validation". *Bioinformatics* 17(6): 564-565, 2001.

Lobenhofer, E.K., **Bushel, P.R.**, Afshari, C.A., and Hamadeh, H.K. "Progress in the Application of DNA Microarrays". *EHP* 109(9): 881-891, 2001.

Hamadeh, H.K., **Bushel, P.**, Paules, R., and Afshari, C.A. "Discovery in Toxicology: Mediation by Gene Expression Array Technology". *J Biochem and Mol Tox* 15(5): 231-242, 2001.

Bushel P, Kim JH, Chang W, Catino JJ, Ruley HE, Kumar CC. Two serum response elements mediate transcriptional repression of human smooth muscle alpha-actin promoter in ras-transformed cells. *Oncogene* 10:1361-70 1995.

Simonson MS, Walsh K, Kumar CC, **Bushel P**, Herman WH. Two proximal CArG elements regulate SM alpha-actin promoter, a genetic marker of activated phenotype of mesangial cells. *Am J Physiol* 268:F760-9 1995.

Kim JH, **Bushel PR**, Kumar CC. Smooth muscle alpha-actin promoter activity is induced by serum stimulation of fibroblast cells. *Biochem Biophys Res Commun* 190:1115-21 1993.

Kumar CC, **Bushel P**, Mohan-Peterson S, Ramirez F. Regulation of smooth muscle alpha-actin promoter in ras-transformed cells: usefulness for setting up reporter gene-based assay system for drug screening. *Cancer Res.* 52:6877-84, 1992.

Bushel P, Rego, K, Mendelsohn, L, Allan, M. Correlation between patterns of DNase I-hypersensitive sites and upstream promoter activity of the human epsilon globin gene at different stages of erythroid development. *Mol. Cell. Biol.* 10:1199-1208, 1990.

Lowndes NF, **Bushel P**, Mendelsohn L, Wu J, Yen M-Y, Allan M. A short, highly repetitive element in intron-1 of the human c-Ha-ras gene acts as a block to transcriptional read through by a viral promoter. *Mol. Cell. Biol.* 10: 4990-4995, 1990.

Wu J, Grindlay J, **Bushel P**, Mendelsohn L, Allan M. Negative regulation of the human epsilon globin gene by transcriptional interference: Role of an Alu repetitive element. *Mol. Cell. Biol.* 10:1209-1216, 1990.

PAPERS SUBMITTED OR IN PREPARATION

Chou J.W. and **Bushel P.R.** Coherent Co-expression Biclustering Constrained by Study Design. Submitted

Bushel, P.R., Heard, N.A., Liu, L., Gutman, R., Peddada, S.D., and Pyne, S. Dissecting a Fission Yeast Regulatory Network for Phase-Specific Control Elements of its Cell Cycle. Submitted

Huang, et al. & **Bushel, P.R.** Genomic Indicators of Hepatotoxicity Conferred through Perturbed Biological Processes and Pathways in the Blood. Submitted

BOOK CHAPTERS

Bushel, P.R. " Toxicogenomics: Principles and Applications, Chapter 5 - Databases for Toxicogenomics ". Editors: Hisham K. Hamadeh and Cynthia A. Afshari, John Wiley and Sons, Inc. 2004.

INVITED TALKS

“A Bioinformatics Approach to Identify Microarray Gene Expression Toxicant Signature Patterns”. TestSmart- Pharmaceuticals: An Efficient and Humane Approach to Predictors of Potential Toxic Effects of Drugs, Pier 5 Hotel, Baltimore, Maryland, May 7, 2001.

“Informatics Implementations for Microarray Gene Expression and Toxicogenomics Efforts”. Department of Toxicoinformatics, Functional Genomics and Toxicoinformatics Centers, National Center for Toxicological Research, Jefferson, Arkansas, July 24, 2002.

“Classification and Prediction of Gene Expression Profiles for Toxicogenomics”. 10th Annual Hewitt Symposium and Toxicology Colloquium. Department of Pharmaceutical Sciences, University of Connecticut, Storres, Connecticut, May 16, 2003.

“Bioinformatics from a Toxicogenomics Perspective”. Training Initiative for Biomedical and Biological Sciences. Molecular Biology Department, University of North Carolina- Chapel Hill, Chapel Hill, North Carolina, March 20, 2007

“Delineation of Perturbed Biological Systems that Govern Hepatotoxic Potential”. Bioinformatics Core Forum. Department of Biostatistics, Harvard School of Public Health, Harvard University, December 16, 2008.