BIOGRAPHICAL SKETCH

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NAME Mario Medvedovic	POSITION TITLE Associate Professor
eRA COMMONS USER NAME medvedm	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
University of Zagreb, Zagreb, Croatia	B.S.	1992	App. Math./ Comp. Sci
Bowling Green State Univ., Ohio	M.S.	1994	Applied Statistics
University of Cincinnati, Cincinnati, OH	Ph.D.	1998	Biostatistics

RESEARCH AND PROFESSIONAL EXPERIENCE

1992 - 1994	Graduate Teaching Assistant, Depart. of Mathematics and Statistics, Bowling Green St. Univ.
1994 – 1998	Graduate Research Assistant, Department of Environmental Health, University of Cincinnati.
1999 – 2000	Senior Research Associate, Department of Environmental Health, University of Cincinnati.
2000 – 2004	Research Assistant Professor, Department of Environmental Health, University of Cincinnati.
2001-Present	Associate Director for Bioinformatics, Center for Biostatistical Services, University of Cincinnati.
2004-2007	Assistant Professor, Department of Environmental Health, University of Cincinnati
2004-Present	(Secondary Appointment) Assistant Professor, Division of Biomedical Informatics, CCHMC
2007-Present	Associate Professor, Department of Environmental Health, University of Cincinnati

POSTDOCTORAL TRAINING

Summer School in Computational Biology. June 1999, Lipari, Italy.

SELECTED PEER REVIEWED PUBLICATIONS (out of 57)

Nikiforova M., Stringer J.R., Blough R., **Medvedovic M.**, Fagin J.A., Nikiforov Y.A. Proximity of Chromosomal Loci That Participate in Radiation-Induced Translocations in Human Cells. *Science*, 290: 138-141. 2000.

Puga A., Maier A., **Medvedovic M.** The transcriptional signature of dioxin in human hepatoma HepG2 cells. *Biochemical Pharmacology*, 60: 1129-1142. 2000.

Medvedovic M., Succop P., Dixon K., Shukla R. Clustering mutational spectra via classification likelihood and Markov Chain Monte Carlo Algorithm. *J. of Agricultural, Biological and Env. Statistics*, 6: 19-37. 2001.

Medvedovic M., Sivaganesan S. Bayesian infinite mixture model based clustering of gene expression profiles. *Bioinformatics* 18: 1194-1206, 2002.

Yeung, K.Y., **Medvedovic,M.** Bumgarner, R.E. Clustering Gene Expression Data With Repeated Measurements. *Genome Biology* 4(5): R34. 2003

Medvedovic, M., Yeung, K.Y., Bumgarner, R.E. Bayesian Mixtures for Clustering Replicated Microarray Data. *Bioinformatics* 20: 1222-1232, 2004.

Sartor, M, Schwanekamp, J, Halbleib, D, Mohamed, I, Karyala, S, **Medvedovic, M**, Tomlinson, CR. Microarray results improve significantly as hybridization approaches equilibrium. *Biotechniques* 36: 790-796, 2004.

Yeung KY, **Medvedovic M**, and Bumgarner RE, From co-expression to co-regulation: how many microarray experiments do we need? *Genome Biol.* 5: R48, 2004.

Zhang J., Moseley A., Jegga A.G., Gupta A., Witte D.P., Sartor M., **Medvedovic M.**, Williams S.S., Ley-Ebert C., Coolen L., Egnaczyk G., Genter M.B., Lehman M., Lingrel J., Maggio J., Parysek L., Walsh R., Xu M., Aronow B.J. Neural system-enriched gene expression, relationship to biological pathways and neurological diseases. *Physiologic Genomics* 18: 167-183, 2004.

Puga, A., Sartor, M.A., Huang, M., Kerzee, K.J., Wei, Y.D., Tomlinson, C.R., Baxter, C.S., **Medvedovic, M.** Gene Expression Profiles of Mouse Aorta and Cultured Vascular Smooth Muscle Cells are Widely Different, yet Show Common Responses to Dioxin Exposure. *Cardiovascular Toxicology* 4: 385-404. 2004.

Medvedovic M and Guo J, Bayesian Model-Averaging in Unsupervised Learning From Microarray Data. *BIOKDD 2004,* 2004.

Stringer JR, Larson JS, Fischer JM**, Medvedovic M**, Hersh MN, Boivin GP, Stringer SL. Modeling variation in tumors in vivo. *Proc Natl Acad Sci U S A.* 2005 Feb 3; [Epub ahead of print].

Puxeddu, E, Knauf, JA, Sartor, MA, Mitsutake N, Smith, EP, **Medvedovic M.**, Tomlinson, CR, Moretti, S, Fagin, JA. RET/PTC-induced gene expression in thyroid PCCL3 cells reveals early activation of genes involved in regulation of the immune response *Endocr Relat Cancer*. 2005 Jun;12(2):319-34.

Wesselkamper SC, Case LM, Henning LN, Borchers MT, Tichelaar JW, Mason JM, Dragin N, **Medvedovic M**, Sartor MA, Tomlinson CR, Leikauf GD. Gene Expression Changes During the Development of Acute Lung Injury: Role of TGF-{beta}. *Am J Respir Cell Mol Biol.* 172(11):1399-411. 2005

Wesselkamper SC, Mcdowell SA, **Medvedovic M,** Dalton TP,Deshmuch HS, Sartor MA, Case L, Henning LN, Borchers MT, Tomlinson CR, Prows DR, Leikauf GD. The Role of Metallothionein in the Pathogenesis of Acute Lung Injury. *Am J Respir Cell Mol Biol.* 34(1):73-82. 2006.

Gandhi M., **Medvedovic M.**, Stringer J.R., Nikiforov, Y. Interphase chromosome folding determines spatial proximity of genes participating in carcinogenic ret/ptc rearrangements. *Oncogene.* 25(16):2360-6. 2006.

Sartor MA, Zorn AM, Schwanekamp J, Halbleib D, Karyala S, Howell ML, **Medvedovic M**, Tomlinson CR. A new method to remove hybridization bias for interspecies comparison of global gene expression profiles uncovers an association between mRNA sequence divergence and differential gene expression in Xenopus. *Nucleic Acids Res.* 5;34(1):185-200. 2006

Medvedovic M, Tomlinson CR, Call MK, Grogg M, Tsonis PA. Gene Expression and Discovery during Lens Regeneration in Mouse: Regulation of EMT and Lens Differentiation. *Mol Vis.* 12:422-40. 2006

Mesa C.Jr, Mirza M, Mitsutake N, Sartor M, **Medvedovic M**, Tomlinson C, Knauf JA, Weber G, Fagin JA. Conditional activation of the RET/PTC3 and B-RAFV600E oncoproteins in thyroid cells is associated with unique patterns of gene expression that predict distinct functional properties and a preferential role of BRAF in extracellular matrix remodeling. *Cancer Research,* 66(13):6521-9. 2006.

Liu X, Sivaganesan S, Yeung K.Y., Bumgarner RE**, Medvedovic M.** Bayesian context-specific infinite mixture model for clustering of gene expression profiles across diverse microarray datasets. *Bioinformatics*, 22(14):1737-44. 2006.

Sartor MA, Tomlinson CR, Wesselkamper SC, Sivaganesan S, Leikauf GD**, Medvedovic M.** Intensity-based hierarchical Bayes method improves testing for differentially expressed genes in microarray experiments. *BMC Bioinformatics* 7: 538, 2006.

Liu X, Jessen W, Sivaganesan S, Aronow B, **Medvedovic M**. Bayesian hierarchical models for learning transcriptional modules from expression and binding data. *BMC Bioinformatics 2007* Aug 3;8(1):283 [Epub ahead of print].

Popa I, Zubkova I, **Medvedovic M**, Romantseva T, Mostowski H, Boyd R, and Zaitseva M, Regeneration of the adult thymus is preceded by the expansion of K5+K8+ epithelial cell progenitors and by increased expression of Trp63, cMyc and Tcf3 transcription factors in the thymic stroma. *Int.Immunol.* 19(11):1249-60, 2007.

Tam NN, Szeto CY, Sartor MA, **Medvedovic M**, and Ho SM, Gene expression profiling identifies lobe-specific and common disruptions of multiple gene networks in testosterone-supported, 17beta-estradiol- or diethylstilbestrol-induced prostate dysplasia in Noble rats. Neoplasia. 10: 20-40, 2008.

Bakshi S, Zhang X, Godoy-Tundidor S, Cheng RYS, Sartor MA**, Medvedovic M**, and Ho SM. Transcriptome Analyses in Normal Prostate Epithelial Cells Exposed to Low-Dose Cadmium: Oncogenic and Immunomodulations Involving the Action of TNF. *Environ Health Perspect* Jun;116(6):769-76. 2008.

Tang,WY, Newbold, R, Mardilovich, K, Jefferson, W, Cheng, R, Szeto, C, **Medvedovic, M**, Shuk-Mei Ho. Identification of nucleosomal binding protein 1 (Nsbp1) as a gene susceptible to diethylstilbestrol- or genistein-induced developmental reprogramming via DNA methylation in the mouse uterus. *Endocrinology*. 2008 Jul 31. [Epub ahead of print].

Sartor MA, Leikauf GD, and **Medvedovic M.** LRpath: A logistic regression approach for identifying enriched biological groups in gene expression data. *Bioinformatics* 25(2):211-7, 2009.

Zhang X, Leav I, Revelo MP, Deka R, **Medvedovic M**, Jiang Z, and Ho SM. Deletion Hotspots in AMACR Promoter CpG Island Are cis-Regulatory Elements Controlling the Gene Expression in the Colon. PLoS Genet 5: e1000334, 2009.

Sartor, M.A., Schnekenburger, M., Marlowe, J.L., Reichard, J.F., Wang, Y., Fan, Y., Ma, C., Karyala, S., Halbleib, D., Liu, X., **Medvedovic, M**., and Puga, A. The aryl hydrocarbon receptor regulatory network controls multiple morphogenetic and developmental programs. *Environ Health Perspect. (In Press).*

ONGOING RESEARCH SUPPORT:

R01HG003749 PI: Medvedovic 07/01/06-06/31/10
NHGRI
Bayesian mixtures for modeling functional genomics data

The objective of this proposal is to develop a comprehensive framework for identifying statistically significant patterns in functional genomics data. Based on the Bayesian infinite mixture models, mathematical models will be developed that accommodate incorporation of prior knowledge and identifying contexts in the context-specific framework. Corresponding computational tools for fitting these models will be developed, optimized and delivered to biomedical community by developing a Bioconductor package and as stand-alone command-line applications.

R21LM009662 PI: Medvedovic 10/01/08-09/31/10
NLM
Integrative Probabilistic Models for Identifying Transcriptional Modules

We propose to develop Infinite Transcriptional Modules (ITM) framework consisting of a novel probabilistic model and related computational tools for identifying transcriptional modules by jointly modeling gene expression and regulatory data. Each different data type will be modeled separately within different context of a Context Specific Infinite Mixture Model. Such modular approach will facilitate the use of the most appropriate probabilistic models for representing different types of data. **We hypothesize that our unifying modeling approach will result in significantly higher precision of identified transcriptional modules than it would be achieved by either separately analyzing different data types, or by applying currently available algorithms for joint analysis.** We also expect that the posterior distribution of co-membership in a TM, based on our model, will offer credible assessment of statistical significance of identified TMs. Using real world data; we will construct datasets and protocols for objectively comparing key performance aspects of different methods for TM reconstruction.

P30 ES06096-10 PI: Ho 4/1/08 - 3/31/13
NIEHS
Center for Environmental Genetics
Bioinformatics Support Core (**Medvedovic, Core Director**)

The goal of the center is to investigate in various species, including humans, the role of genetic diversity on the response of the individual to toxic environmental agents. The role of the Bioinformatics core is to provide center researchers with statistical and computational expertise and hands on assistance in analyzing complex genomic and proteomic data.

U01 ES12770-01 PI: Anderson 09/01/03-08/31/10
NIEHS/NCI
Puberty and Cancer Initiation.

The major aim of this research is to study the link between obesity and breast cancer using a multi-pronged method of investigations. Part of the project is concerned with using DNA microarrays in identifying molecular signatures of tumor initiation.

U01ES015675-01 PI: Leikauf 09/29/06 - 05/31/11
NIEHS
Growth Factor Protection in Acute Lung Injury

The major goals of this project are to: 1) Identify the common genetic determinants and molecular mechanisms controlling acute lung injury following exposure to 5 leading hazardous chemicals: chlorine, phosgene, sulfuric acid, ammonia, and acrolein, 2) Evaluate the therapeutic efficacy of TGFalpha and FGF7 induction, and 3) Identify the molecular mechanisms that are unique to each hazardous chemical.

1U01ES016003 PI: Lamartiniere 08/15/2007-05/31/2011
NIEHS
Genomic and Proteomic Biomarkers of Biological Responses to Exposure

The goal of the project is to develop genomic and proteomic technologies for identification of biomarkers of exposure in girls and rats exposed to bisphenol A (BPA), butyl benzyl phthalate (BBP), di-2-ethylhexyl phthalate (DEHP) and genistein that are measurable in the population.

SELECTED COMPLETED:

R03LM8248 PI: Medvedovic 04/01/04-03/31/06
NLM
Joint modeling of genomic and functional genomic data

The objective of this study is to develop mathematical models and corresponding computational tools for efficient and reproducible extraction of relevant expression patterns, related regulatory motifs and genomic aberrations by jointly modeling genomic and functional genomic data.

R21HG002849 PI: Medvedovic 09/30/03 - 06/30/05
NHGRI
Computational Tools for Bayesian Mixture Modeling of Functional Genomic Data

The objective of this study is to develop computational tools for efficient and reproducible extraction of biologically significant patterns from functional genomic data.

P40 ES04908-12 PI: P. Bishop 4/01/01 – 03/31/05
NIEHS
Health Effects and Biodegradation of Complex Mixtures
Biostatistics Support Core **(M. Medvedovic, PI)**

The goal of Biostatistics Core is to provide research projects in the program with the statistical and computational support that will help them achieve their research goals. In addition, members of the core are developing novel statistical methods for analyzing challenging data such as microarray and Big-blue assay data.