

# Division of Biomedical Informatics

DIVISION PROFILE	
Number of Faculty	8
Number of Joint Appointment Faculty	3
Number of Fellows	
Research Fellows	6
Number of Graduate Students	17
Number of Support Personnel	31
Annual Total Grant Support (direct)	\$8,844,519
Number of Peer Reviewed Publications	20

## FACULTY LISTING

John J. Hutton, MD, Professor of Pediatrics, Director  
Bruce J. Aronow, PhD, Associate Professor of Pediatrics, Co-Director, Computational Medicine Center  
Anil Jegga, DVM, Research Instructor  
Jarek Meller, PhD, Associate Professor of Pediatrics  
John J. Pestian, PhD, MBA, Associate Professor of Pediatrics, Director, Computational Medicine Center  
Jerry L. Phillips, MS, SCSA, SCNA, Field Service Instructor  
Michael Wagner, PhD, Assistant Professor of Pediatrics  
Yan Xu, PhD, Associate Professor of Pediatrics, Dual Appointment: Pulmonary Biology and Biomedical Informatics

## FACULTY JOINT APPOINTMENT LISTING

Karen Davis, PhD, Associate Professor of Electrical & Computer Engineering and Computer Science, UC ECECS  
Michael Jansen, PhD, Research Instructor of Pediatrics, Experimental Hematology  
Mario Medvedovic, PhD, Assistant Professor of Pediatrics, UC Environmental Health

## OVERVIEW

The mission of the Division of Biomedical Informatics is to provide the core competencies, methods, and technologies that are necessary for the acquisition, storage, and analysis of biomedical data, using high performance computational systems. These resources are needed by investigators within Cincinnati Children's Research Foundation who are integrating the enormous quantities of new information about human genes and proteins with information about the health of individual children. The outcome of this research will be more effective ways of preventing, diagnosing, and treating diseases that affect children everywhere. The ultimate goal is to tailor health care to each person as an individual, taking into account the genetic and environmental factors that are unique to each of us.

## HIGHLIGHTS

### Core Support Highlights

Demand for core services in information technology has escalated. As is typical of maturing organizations, this has required the division to focus on management of workflow, cost control, training of staff, and quality assurance. The core services provided now or planned for the near future to the Research Foundation are more clearly defined and include:

- Purchase and maintenance of computer servers and data storage devices necessary to provide core informatics resources to investigators.
- Development of software to meet the needs of both the institution and individual investigators in basic and translational research.

- Assistance in defining the software and data management that would be required to carry out a research project. Assistance with writing informatics sections of grant applications is provided when requested.
- Assistance with installation, repair, and maintenance of software and other informatics resources used by investigators within the institution.
- Assistance with evaluation and selection of commercial software and other informatics resources as needed in research.

## Research Highlights

Much of the research conducted by the faculty of biomedical informatics is in collaboration with other divisions at Cincinnati Children's Hospital Medical Center and other institutions. Typically, this is through provision of expertise in gene identification, analyses of gene expression, development of algorithms, visualization of protein structure or integration of clinical and genomics data. Examples are listed below.

### Bruce Aronow

Focuses on analysis of biological systems in health and disease; comparisons of mouse models with human disease, comparative genomics of gene regulation, evolution, & polymorphism. Development of new web-based tools for understanding the structure and function of biological networks and systems, such as GenomeTraFaC and CisMols analyzer, which permit identification and analysis of transcription factor binding sites that regulate expression of genes; PolyDoms, which maps Synonymous and Non-Synonymous Single-Nucleotide Polymorphisms (or SNPs) of proteins and permits assessment of whether a specific mutation is likely to affect function of an encoded protein.



*Left to right: (1<sup>st</sup> row) B. Aronow, J. Hutton, A. Jegga, J. Pestian, J. Phillips (2<sup>nd</sup> row) A. Porollo, M. Medvedovic, M. Wagner, J. Meller*

### John Hutton

Major focus has been in three areas: (1) Developing a plan for an infrastructure in biomedical informatics (hardware, software, people) that will support the CCHMC Strategic Plan; (2) Restructuring and restaffing our software development group; (3) Assessing needs for faculty and beginning the process of recruiting.

### Anil Jegga

- Elucidating gene regulatory networks through computational approaches.
- Systems biology based approaches to understand disease: Systems biology based approaches endeavor to understand the detailed coordinated workings of entire organisms, with the ultimate goal to detect differences between health and disease. We are currently focusing on integrating the genomics, transcriptomics, proteomics, and metabolomics together with medical domains (disease and anatomical features).
- Comparative phenomics: Understanding phenotypic-genotypic interactions. Currently, we are mining the mouse phenotype data and extending it to the humans to explore the similarities and differences in the underlying biological networks.

## Jarek Meller

Major efforts focused on the development of novel methods for the recognition of protein interactions and their applications. Two new Web servers related to these activities have been developed: the MINNOU server for transmembrane domain and lipid accessibility prediction in membrane proteins and the SPPIDER server for protein-protein interaction site prediction. We continued our projects focused on identification of genotype-phenotype correlations (with applications to JRA and other diseases, collaboration with Dr. Glass), genome annotations and gene finding in fungal organisms (with focus on *Pneumocystis carinii*, collaboration with Dr. Cushion) and docking studies in the context of infections caused by the Norwalk virus (collaboration with Dr. Jiang).

## John Pestian

A major effort is the continued development of the Computational Medicine Center. The center aims to support cutting-edge research in personalized predictive medicine and disease management. In collaboration with industry, the center is building a team of research physicians and experts in bioinformatics, systems biology modeling, genomics, genetics, proteomics, epidemiology, and statistics, with the goal of creating a favorable environment for expanding, attracting and retaining biomedical industry in Ohio.

## Michael Wagner

Major efforts focused on algorithmic developments for solvent and lipid accessibility prediction for proteins, as well as on machine learning approaches for peptide mass fingerprinting techniques for protein identification. A third thrust has been work on algorithms for the analysis of mass-spectrometry-based protein profiling methods, and in particular on the analysis of technical reproducibility.

## TRAINING

Walter J. Jessen, PhD	Texas A&M University
Sergio Kaiser, PhD	University of Bath, UK
Sue Kong, PhD	University of Miami
Mirosław Kordos, PhD	Silesian University of Technology, Poland
Anne McLachlan, PhD	Melbourne University, Australia
Aleksei A. Porollo, PhD	Tver State University, Russia

## GRANTS, CONTRACTS AND INDUSTRY AGREEMENTS

Grant and Contract Awards	Annual Direct/Project Period Direct
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Aronow, B	
Mouse Models of Gastrointestinal Cancer National Institutes of Health (University of Cincinnati subcontract) U01 CA 084291	04/01/04 – 03/31/09 \$77,373/\$448,993
Comparative Mouse Genomics Center National Institutes of Health (University of Cincinnati subcontract) U01 ES 011038	04/01/01 - 03/31/06 \$46,694/\$233,654
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Meller, J	
Optimization of Folding and Threading Potentials National Institutes of Health (Cornell University subcontract) R01 GM 067821	02/01/04 – 01/31/08 \$37,403/\$150,930
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Pestian, J	
Gene Expression in Pediatric Arthritis – Core B National Institutes of Health P01 AR 048929	08/22/03 – 07/31/08 \$162,507/\$639,883

Biomedical Research and Technology Transfer CMC/Wright Center of Innovation  
Ohio Department of Development

	12/15/03 – 06/15/07	\$7,621,807/\$27,701,076
Grabowski, G	\$392,938	Subproject
Greinwald, J	\$207,916	Subproject
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Sakthivel, B		
Implementing IAIMS at the University of Cincinnati National Institutes of Health (University of Cincinnati subcontract) G08 LM 007853	05/15/04 – 05/14/07	\$20,472/\$61,416
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Wagner, M		
Biomarkers for Amyotrophic Lateral Sclerosis in Active Military Duty Department of Defense (University of Cincinnati subcontract) W81XWH-06-2-0016	01/23/06 – 01/22/09	\$27,306/\$85,238
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	Current Year Direct	\$8,844,519
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Industry Contracts		
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	Current Year Direct Receipts	\$0
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	<b>TOTAL</b>	<b>\$8,844,519</b>

Funded Collaborative Efforts

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Aronow, B.		
Therapeutic Targets for Neurofibromatosis Identification by Cross-Species Gene Expression Analysis National Institutes of Health		
PI: Ratner, N	02/01/04 – 02/28/07	5%
Physiology of Placental Lactogen National Institutes of Health		
PI: Handwerker, S	04/01/04 – 3/31/07	5%
Vector Insertion and Mutagenesis in Human Hematopoiesis National Institutes of Health		
PI: Von Kalle, C	04/01/04 – 3/31/08	5%
Genomic Analysis of Pediatric SIRS National Institutes of Health		
PI: Wong, H	08/01/03 – 07/31/06	5%
Genetic Analysis of Hyperoxia-Induced Acute Lung Injury National Institutes of Health		
PI: Prows, D	02/15/03 – 11/30/07	5%
Genomic Landscapes in Large Scale Integrated JRA Studies National Institutes of Health		
PI: Thompson, S	09/15/03 – 08/31/07	5%
Cincinnati DDRDC: Center for Growth and Development National Institutes of Health		
PI: Cohen, M	04/01/04 – 03/31/08	7%
Decidual Prolactin in Normal and Pathogenic Pregnancies National Institutes of Health		
PI: Handwerker, S	04/1/03 – 03/31/08	3%
HLA-B27 Misfolding in Spondyloarthritis Pathogenesis National Institutes of Health		
PI: Colbert, R	09/01/03 – 08/31/06	3%

Mechanisms of Tropomyosin Induced Hypertrophy National Institutes of Health PI: Prows, D	8/1/03 – 6/30/07	4%
Gene Expression in Pediatric Arthritis National Institutes of Health PI: Glass, D	08/22/03 – 07/31/08	10%
Biomedical Research and Technology Transfer CMC/Wright Center of Innovation Ohio Department of Development PI: Pestian, J	07/01/04 – 06/30/07	30%
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Jegga, A.		
Therapeutic Targets for Neurofibromatosis Identification by Cross-Species Gene Expression Analysis National Institutes of Health PI: Ratner, N	07/01/07 – 06/30/07	10%
Cincinnati DDRDC: Center for Growth and Development National Institutes of Health PI: Cohen, M	04/1/04 – 8/31/07	8%
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Meller, J		
Genomic Landscapes in Large Scale Integrated JRA Studies National Institutes of Health PI: Thompson, S	09/15/03 – 08/31/07	30%
Cincinnati DDRDC: Center for Growth and Development National Institutes of Health PI: Cohen, M	04/01/04 – 03/31/08	8%
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Pestian, J		
Genomic Analysis of Pediatric SIRS National Institutes of Health PI: Wong, H	08/01/03 – 07/31/06	5%
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Wagner, M		
Genomic Landscapes in Large Scale Integrated JRA Studies National Institutes of Health PI: Thompson, S	08/01/03 – 07/31/06	25%
Optimization of Threading and Folding Proteins National Institutes of Health PI: Eber, R	02/01/04 – 01/31/08	15%

## PUBLICATIONS

1. Blanchard C, Wang N, Stringer KF, Mishra A, Fulkerson PC, Abonia JP, Jameson SC, Kirby C, Konikoff MR, Collins MH, Cohen MB, Akers R, Hogan SP, Assa'ad AH, Putnam PE, Aronow BJ, Rothenberg ME. Eotaxin-3 and a uniquely conserved gene-expression profile in eosinophilic esophagitis. *J Clin Invest* 2006;116(2):536-47.
2. Kong S, Aronow BJ, Handwerger S. Gene expression microarray data analysis of decidual and placental cell differentiation. *Methods Mol Med* 2006;121:425-38.
3. Mallakin A, Kutcher LW, McDowell SA, Kong S, Schuster R, Lentsch AB, Aronow BJ, Leikauf GD, Waltz SE. Gene expression profiles of Mst1r-deficient mice during nickel-induced acute lung injury. *Am J Respir Cell Mol Biol* 2006;34(1):15-27.

4. Oka T, Mailliet M, Watt AJ, Schwartz RJ, Aronow BJ, Duncan SA, Molkentin JD. Cardiac-specific deletion of Gata4 reveals its requirement for hypertrophy, compensation, and myocyte viability. *Circ Res* 2006;98(6):837-45.
5. Robins JC, Akeno N, Mukherjee A, Dalal RR, Aronow BJ, Koopman P, Clemens TL. Hypoxia induces chondrocyte-specific gene expression in mesenchymal cells in association with transcriptional activation of Sox9. *Bone* 2005;37(3):313-22.
6. Schwab K, Hartman HA, Liang HC, Aronow BJ, Patterson LT, Potter SS. Comprehensive microarray analysis of Hoxa11/Hoxd11 mutant kidney development. *Dev Biol* 2006;293(2):540-54.
7. Smiley AK, Klingenberg JM, Aronow BJ, Boyce ST, Kitzmiller WJ, Supp DM. Microarray analysis of gene expression in cultured skin substitutes compared with native human skin. *J Invest Dermatol* 2005;125(6):1286-301.
8. Xu J, Gong NL, Bodi I, Aronow BJ, Backx PH, Molkentin JD. Myocyte enhancer factors 2A and 2C induce dilated cardiomyopathy in transgenic mice. *J Biol Chem* 2006;281(14):9152-62.
9. Jegga AG, Gupta A, Gowrisankar S, Deshmukh MA, Connolly S, Finley K, Aronow BJ. CisMols Analyzer: identification of compositionally similar cis-element clusters in ortholog conserved regions of coordinately expressed genes. *Nucleic Acids Res* 2005;33(Web Server issue):W408-11.
10. Jegga AG, Kong S, Zhang J, Moseley A, Gupta A, Williams SS, Genter MB, Aronow BJ. Comparative genomics of tissue specific gene expression In: Ma J, editor. *Gene expression and regulation*: Springer; 2005. p. 393-408.
11. Miller SJ, Rangwala F, Williams J, Ackerman P, Kong S, Jegga AG, Kaiser S, Aronow BJ, Frahm S, Kluwe L, Mautner V, Upadhyaya M, Muir D, Wallace M, Hagen J, Quelle DE, Watson MA, Perry A, Gutmann DH, Ratner N. Large-scale molecular comparison of human schwann cells to malignant peripheral nerve sheath tumor cell lines and tissues. *Cancer Res* 2006;66(5):2584-91.
12. Erwin CR, Jarboe MD, Sartor MA, Medvedovic M, Stringer KF, Warner BW, Bates MD. Developmental characteristics of adapting mouse small intestine crypt cells. *Gastroenterology* 2006;130(4):1324-32.
13. Gandhi M, Medvedovic M, Stringer JR, Nikiforov YE. Interphase chromosome folding determines spatial proximity of genes participating in carcinogenic RET/PTC rearrangements. *Oncogene* 2006;25(16):2360-6.
14. Icenhour CR, Arnold J, Medvedovic M, Cushion MT. Competitive coexistence of two *Pneumocystis* species. *Infect Genet Evol* 2006;6(3):177-86.
15. Medvedovic M, Tomlinson CR, Call MK, Grogg M, Tsonis PA. Gene expression and discovery during lens regeneration in mouse: regulation of epithelial to mesenchymal transition and lens differentiation. *Mol Vis* 2006;12:422-40.
16. Sartor MA, Zorn AM, Schwanekamp JA, Halbleib D, Karyala S, Howell ML, Dean GE, 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* 2006;34(1):185-200.
17. 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 transforming growth factor beta. *Am J Respir Crit Care Med* 2005;172(11):1399-411.
18. Wesselkamper SC, McDowell SA, Medvedovic M, Dalton TP, Deshmukh HS, Sartor MA, Case LM, 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* 2006;34(1):73-82.
19. Cao B, Porollo A, Adamczak R, Jarrell M, Meller J. Enhanced recognition of protein transmembrane domains with prediction-based structural profiles. *Bioinformatics* 2006;22(3):303-9.
20. Wade SL, Wolfe C, Brown TM, Pestian JP. Putting the pieces together: preliminary efficacy of a web-based family intervention for children with traumatic brain injury. *J Pediatr Psychol* 2005;30(5):437-42.