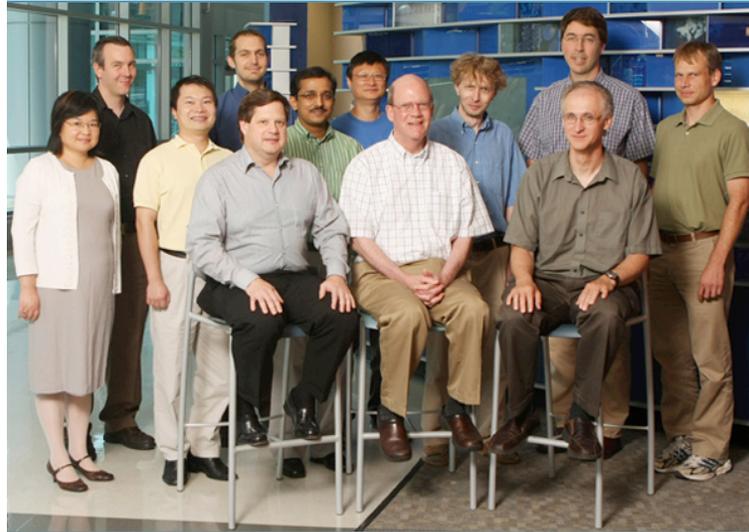


Division Photo



First Row: J. Pestian, J. Hutton, M. Medvedovic; Second Row: Y. Xu, J. Lu, A. Jegga, J. Meller, M. Wagner, M. Kouril; Third Row: E. Hall, K. Marsolo, J. Ma.

Division Data Summary

Research and Training Details

Number of Faculty	10
Number of Joint Appointment Faculty	5
Number of Research Fellows	3
Number of Research Students	14
Number of Support Personnel	58
Direct Annual Grant Support	\$857,549
Direct Annual Industry Support	\$0
Peer Reviewed Publications	28

Division Highlights

Mission

Biomedical informatics is the rapidly developing scientific field that deals with resources, devices, and formalized methods for optimizing the acquisition, storage, retrieval, communication, and use of biomedical information for problem solving and decision making. The Mission of the Division of Biomedical Informatics is: (1) To provide the core knowledge, skills, and equipment that are necessary for the acquisition, storage and analysis of biomedical data using high performance computational systems; (2) To educate graduate and medical students, residents, and fellows in the theory and practice of biomedical and healthcare informatics; (3) To develop new knowledge and technologies in informatics that support clinical practice and biomedical research, thereby accelerating improvements in human health. Providing expertise in data management and complex computing to clinically relevant research programs is the most common role for informatics faculty at the present time. External support of faculty research is generally through collaboration with other investigators.

Core Services: For the past few years, focus has been upon building the extensive informatics infrastructure

necessary to implement our institution's Five Year Strategic Plan. Demand for informatics support of both clinical and research programs has grown rapidly, as the world has become more "digital". To provide state-of-art informatics resources to faculty, the Division is organized into 3 service groups, each headed by a member of the faculty.

Data Management and Software Development

The data management and software development group is headed by Keith Marsolo. He has implemented the i2b2 research patient data warehouse at CCHMC and is a member of the national i2b2 Users Group based at Partner's Health Care and HarvardMedicalSchool. The CCHMC warehouse contains information on more than 500,000 patients and is essential to support of translational research at CCHMC. Dr. Eric Hall, who has a joint faculty appointment in Neonatology and Biomedical Informatics, has worked with Dr. Marsolo and our i2b2 staff to: (1) identify quality of care improvements associated with the post-surgical management of infants with gastroschisis; (2) examine the regional incidence of several foregut malformations; and (3) provide a confidential centralized repository of baseline and outcome data for all infants and their mothers born in the Greater Cincinnati area. Data will be collected with uniform definitions of prematurity and other morbidities and will be useful for: (1) monitoring time-related changes in neonatal care and outcomes; (2) identifying observational cohorts; and (3) benchmarking of neonatal outcomes. Dr. Marsolo worked with investigators in Adolescent Medicine to determine the incidence of Pelvic Inflammatory Disease in patients seen at CCHMC and in a separate study to examine socioeconomic factors that influenced whether the HPV vaccine was administered to adolescents.

Research IT Services

Research IT Services are directed by Michal Kouril. He manages the ResearchDataCenter (hardware such as servers, computers, data storage) and serves as the primary liaison between BMI and technical groups in CCHMC Information Services and the University of Cincinnati. He is presently working with CCHMC Information Services to upgrade and reorganize our networks and servers with the intent of improving connectivity to the University of Cincinnati, while maintaining security for sensitive data in our medical center. His group is also implementing a new identity management system for research so that a single password will provide an individual with access to the computational resources they are authorized to use. The new network and identity management systems are in response to the need for investigators at CCHMC and the University of Cincinnati to exchange data more readily, as required by the Clinical Translational Research Award (CTSA) the institutions recently received from the NIH.

Faculty Liaison

The key BMI liaison to faculty is Michael Wagner. He works with both BMI and IS to meet needs of individual faculty in all divisions of CCHMC in terms of IT support of their research. In an effort to streamline basic research data management at CCHMC, BMI staff have developed web-based portals for flow cytometry, genotyping and expression microarray data files with enhanced search, permissions management and (cluster-based) processing capabilities. As these tools are rolled out, investigators will have a single web-accessible portal for all their (typically large) primary data files. Furthermore, BMI is providing web-based equipment scheduling tools for various cores (including flow cytometry and confocal microscopy), which facilitate the process of scheduling instrument time greatly and help the cores with capacity planning.

Graduate Education

Currently, the PhD granting graduate program in bioinformatics is based in the UC Department of Biomedical Engineering. The Department is uniquely affiliated with both the UC College of Medicine and the College of Engineering. Dr. Jarek Meller leads the program in close collaboration with other faculty from Biomedical Informatics (Drs. Aronow, Jegga, Wagner and Liu), and Environmental Health (Drs. Rao and Medvedovic). Currently fifteen PhD candidates are enrolled and 2 new students are to be admitted in the Fall, 2009. Courses offered include Introduction to Functional Genomics, Introduction to Bioinformatics, and Advanced Computational Biology They cover basic material such as genomic databases, algorithms and methods in bioinformatics, molecular simulation techniques, as well as their specific applications. In addition, interdisciplinary workshops and multimedia educational materials are being developed for medical students and professionals, building on our cross-institutional efforts in the form of seminar series and journal club, summer workshops and other training initiatives. Thanks to the strength of the program, several Choose Ohio First scholarships have been secured this year for our current and prospective students.

Faculty Members

John Hutton, MD, Professor ; *Director, Division Chief*

Bruce Aronow, PhD, Professor ; *Co-Director, Computational Medicine Center*

Research Interests: Gene Expression Analysis, Gene Regulation, Clinical Genomics, Functional Genomics of Development and Disease

Anil Jegga, MS, DVM, Research Assistant Professor

Research Interests: Gene Regulatory Networks, Biomedical Ontologies, Integrative Genomics

Michal Kouril, PhD, Research Instructor ; *Director, Research IT*

Research Interests: Computational Support, High-performance computing, Parallel Programming, High-end Data Storage

Long Jason Lu, PhD, Assistant Professor

Research Interests: Bioinformatics, Machine Learning, Integrative Genomics, Biological Networks, Computational Modeling, Software Development

Jun Ma, PhD, Associate Professor

Research Interests: Development, Transcription, Morphogen Gradient, Embryo, Robustness, Quantitative Studies

Keith Marsolo, PhD, Research Instructor ; *Director, Software Development and Data Warehouse*

Research Interests: i2b2, Data Integration, Data Warehousing and Data Management

John Pestian, PhD, MBA, Associate Professor ; *Director, Computational Medicine Center*

Research Interests: Natural Language Processing, Clinical Decision Support, Suicide Research, Pathology Research, Psychiatric Research

S. Andrew Spooner, MD, FAAP, Associate Professor Clinical ; *Chief Medical Information Officer*

Research Interests: Decision Support, Pharmacy Information Systems

Michael Wagner, PhD, Research Associate Professor ; *Faculty Liaison*

Research Interests: Machine Learning, Proteomics, Genome-wide Association, Parallel Computing, Computational Infrastructure, Bioinformatics

Joint Appointment Faculty Members

Karen Davis, PhD, Associate Professor

UC ECECS

Electrical & Computer Engineering and Computer Science

Eric Hall, PhD, Research Instructor

Neonatology & Pulmonary Biology

Clinical Informatics, Knowledge Discovery Tools, Data Mining and Warehousing

Mario Medvedovic, PhD, Associate Professor

UC Environmental Health

Biostatistics

Jarek Meller, PhD, Associate Professor

UC Environmental Health

Protein Modeling

Yan Xu, PhD, Associate Professor

Pulmonary Medicine

Trainees

- **Jacek Biesiada, PhD**, University of Silesia, Poland
- **Junbo Liu, PhD**, Fudan University, Shanghai, China
- **Julia Taylor, PhD**, University of Cincinnati, Cincinnati, OH

Significant Accomplishments

Studying human diseases using computational approaches

Bruce Aronow, Anil Jegga, and Jason Lu focus on studying human diseases using computational approaches. Jegga and Aronow have developed a unique one-stop suite of online software tools called “ToppGene Suite” and GATACA that enable biomedical researchers to explore, analyze, and hypothesize genetic pathways responsible for disease. Using these tools investigators can also prioritize causal genes for further genetic and biochemical studies. ToppGene Suite and other tools such as GATACA, also developed by this group, permit researchers to both focus their laboratory and clinical research on specific genes and molecular pathways more quickly and productively than would otherwise be possible—and further—to identify underlying regulatory mechanisms that could be exploited to develop new disease treatments or preventives. Lu has developed a novel computational algorithm that can systematically identify a compendium of essential genes in *Pseudomonas aeruginosa*, an opportunistic pathogen that causes chronic infection of the lungs of

more than 80% of cystic fibrosis patients. These genes are essential to the viability of the pathogen and are the most obvious targets for new drugs designed to kill the organism and to treat infection.

Clinical Linguistic Group

John Pestian has built a Clinical Linguistic Group within the Division of Biomedical Informatics and continues to focus on the analysis of neurological and psychiatric free-text. In collaboration with faculty from the Divisions of Psychiatry and Emergency Medicine, the Clinical Linguistic group is developing a suicide risk index. This index combines biomarkers and thought markers with the intent of measuring the likelihood of repeated suicide attempts. The group has compiled what is thought to be the world's largest database of notes from those who have completed suicide. These notes have been loaded into the natural language processing framework and initial analyses have been completed. These will provide the preliminary data necessary to apply for NIH funding to support the research.

Studying development of the embryo using computational resources

Jun Ma continues to use computational tools to study development of the embryo, using *Drosophila* as a model. A remarkable feature of development is its reproducibility, the ability to correct embryo-to-embryo variations and instruct precise patterning. One unavoidable variation is the size of embryos. Ma's group performed quantitative studies to evaluate the properties of a *Drosophila* gradient protein called Bicoid, a maternally-deposited master control protein that instructs the development of anterior structures including the head. His analyses traced the origin of proportionate development of body parts in early embryos to scaling properties of the Bicoid gradient. These results demonstrate that developmental proportionality, an ability to correct embryo-to-embryo differences in size, can be understood at a molecular level.

Division Publications

1. Haffey WD, Mikhaylova O, Meller J, Yi Y, Greis KD, Czyzyk-Krzeska MF. [ITRAQ proteomic identification of pVHL-dependent and -independent targets of Eglin1 prolyl hydroxylase knockdown in renal carcinoma cells](#). *Adv Enzyme Regul.* 2009; 49: 121-32.
2. Tan M, Xia M, Chen Y, Bu W, Hegde RS, Meller J, Li X, Jiang X. [Conservation of carbohydrate binding interfaces: evidence of human HBGA selection in norovirus evolution](#). *PLoS One.* 2009; 4: e5058.
3. Nishijo K, Chen QR, Zhang L, McCleish AT, Rodriguez A, Cho MJ, Prajapati SI, Gelfond JA, Chisholm GB, Michalek JE, Aronow BJ, Barr FG, Randall RL, Ladanyi M, Qualman SJ, Rubin BP, LeGallo RD, Wang C, Khan J, Keller C. [Credentialing a preclinical mouse model of alveolar rhabdomyosarcoma](#). *Cancer Res.* 2009; 69: 2902-11.
4. Gu Y, Harley IT, Henderson LB, Aronow BJ, Vietor I, Huber LA, Harley JB, Kilpatrick JR, Langefeld CD, Williams AH, Jegga AG, Chen J, Wills-Karp M, Arshad SH, Ewart SL, Thio CL, Flick LM, Filippi MD, Grimes HL, Drumm ML, Cutting GR, Knowles MR, Karp CL. [Identification of IFRD1 as a modifier gene for cystic fibrosis lung disease](#). *Nature.* 2009; 458: 1039-42.
5. Chen J, Aronow BJ, Jegga AG. [Disease candidate gene identification and prioritization using protein interaction networks](#). *BMC Bioinformatics.* 2009; 10: 73.
6. Besnard V, Wert SE, Stahlman MT, Postle AD, Xu Y, Ikegami M, Whitsett JA. [Deletion of Scap in alveolar type II cells influences lung lipid homeostasis and identifies a compensatory role for pulmonary lipofibroblasts](#). *J Biol Chem.* 2009; 284: 4018-30.
7. Vallat BK, Pillardy J, Majek P, Meller J, Blom T, Cao B, Elber R. [Building and assessing atomic models of proteins from structural templates: Learning and benchmarks](#). *Proteins.* 2009; 76: 930-945.
8. Spooner SA, Classen DC. [Data standards and improvement of quality and safety in child health care](#). *Pediatrics.* 2009; 123 Suppl 2: S74-9.
9. Barnes MG, Grom AA, Thompson SD, Griffin TA, Pavlidis P, Itert L, Fall N, Sowders DP, Hinze CH, Aronow BJ, Luyrink LK, Srivastava S, Ilowite NT, Gottlieb BS, Olson JC, Sherry DD, Glass DN, Colbert RA. [Subtype-specific peripheral blood gene expression profiles in recent-onset juvenile idiopathic arthritis](#). *Arthritis Rheum.* 2009; 60: 2102-12.
10. Qu XA, Gudivada RC, Jegga AG, Neumann EK, Aronow BJ. [Inferring novel disease indications for known drugs by semantically linking drug action and disease mechanism relationships](#). *BMC Bioinformatics.* 2009; 10 Suppl 5: S4.
11. Sun Y, Jia L, Williams MT, Zamzow M, Ran H, Quinn B, Aronow BJ, Vorhees CV, Witte DP, Grabowski GA. [Temporal gene expression profiling reveals CEBPD as a candidate regulator of brain disease in prosaposin deficient mice](#). *BMC Neurosci.* 2008; 9: 76.
12. Wan H, Luo F, Wert SE, Zhang L, Xu Y, Ikegami M, Maeda Y, Bell SM, Whitsett JA. [Kruppel-like factor 5 is required for perinatal lung morphogenesis and function](#). *Development.* 2008; 135: 2563-72.

13. Duch W, Matykiewicz P, Pestian J. [Neurolinguistic approach to natural language processing with applications to medical text analysis](#). *Neural Netw.* 2008; 21: 1500-10.
14. Kim GR, Lehmann CU, Spooner SA. [Pediatric aspects of inpatient health information technology systems](#). *Pediatrics.* 2008; 122: e1287-96.
15. Shen H, Powers N, Saini N, Comstock CE, Sharma A, Weaver K, Revelo MP, Gerald W, Williams E, Jessen WJ, Aronow BJ, Rosson G, Weissman B, Muchardt C, Yaniv M, Knudsen KE. [The SWI/SNF ATPase Brm is a gatekeeper of proliferative control in prostate cancer](#). *Cancer Res.* 2008; 68: 10154-62.
16. Sinha AU, Kaimal V, Chen J, Jegga AG. [Dissecting microregulation of a master regulatory network](#). *BMC Genomics.* 2008; 9: 88.
17. Glasser SW, Senft AP, Whitsett JA, Maxfield MD, Ross GF, Richardson TR, Prows DR, Xu Y, Korfhagen TR. [Macrophage dysfunction and susceptibility to pulmonary Pseudomonas aeruginosa infection in surfactant protein C-deficient mice](#). *J Immunol.* 2008; 181: 621-8.
18. Takemoto CM, Lee YN, Jegga AG, Zablocki D, Brandal S, Shahlaee A, Huang S, Ye Y, Gowrisankar S, Huynh J, McDevitt MA. [Mast cell transcriptional networks](#). *Blood Cells Mol Dis.* 2008; 41: 82-90.
19. Brunskill EW, Aronow BJ, Georgas K, Rumballe B, Valerius MT, Aronow J, Kaimal V, Jegga AG, Yu J, Grimmond S, McMahon AP, Patterson LT, Little MH, Potter SS. [Atlas of gene expression in the developing kidney at microanatomic resolution](#). *Dev Cell.* 2008; 15: 781-91.
20. Demner-Fushman D, Ananiadou S, Cohen KB, Pestian J, Tsujii J, Webber B. [Themes in biomedical natural language processing: BioNLP08](#). *BMC Bioinformatics.* 2008; 9 Suppl 11: S1.
21. Hall ES, Thornton SN. [Generating nurse profiles from computerized labor and delivery documentation](#). *AMIA Annu Symp Proc.* 2008; : 268-72.
22. Gudivada RC, Qu XA, Chen J, Jegga AG, Neumann EK, Aronow BJ. [Identifying disease-causal genes using Semantic Web-based representation of integrated genomic and phenomic knowledge](#). *J Biomed Inform.* 2008; 41: 717-29.
23. He F, Wen Y, Deng J, Lin X, Lu LJ, Jiao R, Ma J. [Probing intrinsic properties of a robust morphogen gradient in Drosophila](#). *Dev Cell.* 2008; 15: 558-67.
24. Kardina SL, Kelly RJ, Keddache MA, Aronow BJ, Grabowski GA, Hahn HS, Case KL, Wagoner LE, Dorn GW, 2nd, Liggett SB. [Multiple interactions between the alpha 2C- and beta1-adrenergic receptors influence heart failure survival](#). *BMC Med Genet.* 2008; 9: 93.
25. Kucherlapati MH, Yang K, Fan K, Kuraguchi M, Sonkin D, Rosulek A, Lipkin M, Bronson RT, Aronow BJ, Kucherlapati R. [Loss of Rb1 in the gastrointestinal tract of Apc1638N mice promotes tumors of the cecum and proximal colon](#). *Proc Natl Acad Sci U S A.* 2008; 105: 15493-8.
26. Chakraborty S, Cheek J, Sakthivel B, Aronow BJ, Yutzey KE. [Shared gene expression profiles in developing heart valves and osteoblast progenitor cells](#). *Physiol Genomics.* 2008; 35: 75-85.
27. Swift SM, Gaume BR, Small KM, Aronow BJ, Liggett SB. [Differential coupling of Arg- and Gly389 polymorphic forms of the beta1-adrenergic receptor leads to pathogenic cardiac gene regulatory programs](#). *Physiol Genomics.* 2008; 35: 123-31.
28. Tan M, Xia M, Cao S, Huang P, Farkas T, Meller J, Hegde RS, Li X, Rao Z, Jiang X. [Elucidation of strain-specific interaction of a GII-4 norovirus with HBGA receptors by site-directed mutagenesis study](#). *Virology.* 2008; 379: 324-34.

Grants, Contracts, and Industry Agreements

Grant and Contract Awards

Annual Direct / Project Period Direct

ARONOW, B

CTSA - Enabling Tehnologies: Ctr for Translational & Molecular Disease Modeling

National Institutes of Health (University of Cincinnati)

UL1 RR 026314

04/03/09 - 03/31/14

\$24,238 / \$24,238

Murine Atlas of Genitourinary Smooth Muscle Development

National Institutes of Health

U01 DK 070219

04/01/09 - 03/31/10

\$137,231 / \$137,231

Digestive Health Center: Bench to Bedside Research in Pediatric Digestive Disease

National Institutes of Health

P30 DK 078392

06/01/09 - 05/31/10

\$106,171 / \$106,171

HUTTON, J**CTSA - Biomedical Informatics**

National Institutes of Health (University of Cincinnati)

UL1 RR 026314

04/03/09 - 03/31/14

\$72,175 / \$72,175

JEGGA, A**Functional Polymorphisms in P53 Response Elements**

Ohio Cancer Research Association

5408

07/01/08 - 06/30/10

\$22,727 / \$45,454

Murine Atlas of Genitourinary Smooth Cell Muscle Development

National Institutes of Health

U01 DK 070219

04/01/09 - 03/31/10

\$24,490 / \$24,490

MA, J**Activities of the Bicoid Gradient in Drosophila Embryos**

National Institutes of Health

R01 GM 072812

07/01/05 - 06/30/09

\$180,154 / \$760,000

Probing the Robustness of a Developmental System

National Science Foundation

IOS-0843424

05/15/09 - 04/30/13

\$203,556 / \$861,735

SPOONER, A**Step Tools: Developing Web Services for Safe Pediatric Dosing**

National Institutes of Health (Vanderbilt University)

R18 HS 017216

09/01/08 - 08/31/09

\$12,068 / \$12,068

WAGNER, M.**Bayesian Mixture Modeling of Functional Genomics Data**

National Institutes of Health (University of Cincinnati)

R01 HG 003749

07/01/06 - 06/30/10

\$14,103 / \$53,679

Optimization of Structures and Networks of Proteins

National Institutes of Health (The University of Texas at Austin)

R01 GM 067823

06/01/08 - 05/31/11

\$19,141 / \$57,535

Cincinnati Rheumatic Disease Core Center

National Institutes of Health

P30 AR 047363

07/01/08 - 06/30/09

\$41,495 / \$41,495

Current Year Direct**\$ 857,549****Total \$ 857,549**