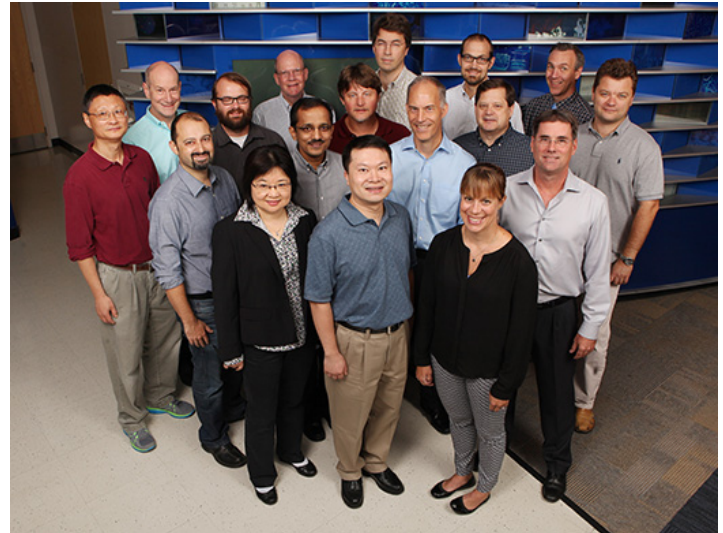


Biomedical Informatics

RESEARCH AND TRAINING DETAILS



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Joint Appointment Faculty	11
Research Fellows	6
Research Students	19
Support Personnel	117
Direct Annual Grant Support	\$2,928,278
Peer Reviewed Publications	60

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Research Highlights

Peter S. White, PhD

Dr. White is the director of the **Division of Biomedical Informatics** at Cincinnati Children's and the Rieveschl Chair of the **Department of Biomedical Informatics** at the University of Cincinnati College of Medicine. Dr. White also serves as co-director of Cincinnati Children's Center for Pediatric Genomics. In these roles, he oversees informatics research and resources at both institutions, including academic, educational, data services, technology development and research IT missions. In his research career, Dr. White has explored the development and application of novel approaches for disease

gene discovery, including identifying causative genes for neuroblastoma, ADHD, autism and congenital heart defects. He has also developed innovative methods and technologies for integration and use of clinical, phenotypic and molecular data in promoting discovery and hypothesis validation. Dr. White is playing a lead informatics role on a number of national data networks, including the [National Institute of Child Health and Human Development's \(NICHD\) Newborn Screening Translational Research Network](#), the [National Heart, Lung, and Blood Institute's \(NHLBI\) Bench to Bassinet Program](#) and the Genomic Research and Innovation Network.

Bruce J. Aronow, PhD

[Dr. Aronow](#) works toward unraveling both the role and mechanism by which the functional capabilities of the human genome shape human health and our ability to adapt to stressful challenges. [The Aronow Lab](#) focuses on collaborative research projects and the development of informatics systems that leverage multiple disciplines of knowledge, expertise and diverse data. The goal is to improve our collective ability to formulate high-impact inferences, hypotheses and next-stage experiments that could have the highest overall impact for biomedical research. The lab's current research focus is to find or support efforts to solve problems relevant to genomic medicine by developing, both independently and collaboratively, new algorithms, tools and methodologies in translational bioinformatics.

John J. Hutton, MD

Dr. Hutton continued his collaboration with [Dr. Keith Marsolo](#) and [Dr. Peter Margolis](#) ([James M. Anderson Center for Health Systems Excellence](#)) to publish the methods and results of the learning networks informatics team supported by a grant from the [Agency for Healthcare Research and Quality](#). The aims of the award were to develop and implement an electronic health record (EHR)-linked registry for the [ImproveCareNow Network](#), a quality improvement and research network that focuses on improving the outcomes of children with inflammatory bowel disease (IBD). For the past year Dr. Hutton has collaborated with [Dr. Melissa DelBello](#), chair of the [University of Cincinnati \(UC\) Department of Psychiatry](#), and others to prepare a [Patient-Centered Outcomes Research Institute \(PCORI\)](#) application to support a pragmatic clinical trial of therapy in childhood bipolar disorder. The award was funded to begin this year (2015). He continues to review applications for research support by the [National Library of Medicine](#) and to participate in the activities of the [Clinical and Translational Science Award](#) to UC. Dr. Hutton serves as a member of various UC committees that oversee information technology planning and services in the university including the College of Medicine Information Technology, [UC Information Technology \(UCit\)](#), and the UC Data Center Planning Committee.

Anil Goud Jegga, DVM, MRes

The mission of the [Jegga Lab](#) is to design, develop and apply novel and robust computational approaches that will accelerate the diffusion of genomics into biomedical research and education and convert the genomics data deluge into systematized knowledge to understand the molecular basis of disease. To this effect, the lab continues with their focus on integration and mining of multiple sources of genomic, genetic and biomedical data to derive models for pathways and processes underlying development, disease and drug response. Independently and collaboratively, they have previously developed and published tools that allow biologists with minimal computational experience to integrate diverse data types and synthesize hypotheses about gene and pathway function in human and mouse. These tools are designed to answer several straightforward questions that biologists frequently encounter while trying to apply systems-level analyses to specific biological problems. The lab is currently focusing on developing and implementing systems biology-based novel computational approaches to identify drug candidates for rare lung disorders. The lab is integrating and mining genomic and compound screening-based big data to identify drug repositioning and novel drug candidates.

Michal Kouril, PhD

[Dr. Kouril](#) collaborates with several Cincinnati Children's divisions on a number of innovative technology-related projects. One notable collaboration is the five-year R01 grant with the [Division of Behavioral Medicine and Clinical Psychology](#) ([Jennie Noll, PI](#)). The project is monitoring online behavior of abused and non-abused adolescents to look for

inappropriate and risky behavior. In addition, Dr. Kouril oversees the Cincinnati Children's Research IT group, which maintains petabyte-size storage in a number of performance tiers including the fastest SSD-based systems used for the most demanding applications, such as research data warehousing, virtual desktop infrastructure and some production servers. His team built out the research disaster recovery infrastructure to accommodate applications that are required from the business continuity perspective. In addition, they have expanded the computational cluster and added cutting-edge technology such as large graphics processing unit capability and high-core density teraFLOPS-speed Intel Phi cards.

Long (Jason) Lu, PhD

Dr. Lu focuses on developing innovative computational approaches to study a variety of human diseases. He developed a network-based approach that combines proteomics experiments and computational predictions to discover the subspecies in high-density lipoprotein (HDL) cholesterol and correlate them with cardiovascular protection function. His approach identified 38 candidate HDL subparticles. Further biochemical characterization of these putative subspecies may facilitate the mechanistic research of cardiovascular disease and guide targeted therapeutics aimed at its mitigation. Dr. Lu has also introduced a new perspective to characterize gene essentiality from protein domains, the independent structural or functional units of a polypeptide chain. Genes with indispensable functions are identified as essential; however, the traditional gene-level studies of essentiality have several limitations. To identify such essential domains, Dr. Lu's lab developed an Expectation-Maximization (EM) algorithm-based Essential Domain Prediction (EDP) Model and presented the first systematic analysis on gene essentiality on the level of domains.

Jun Ma, PhD

Research performed by **Dr. Ma's** team focuses on understanding developmental processes at a quantitative and systems level. In a recent study that the team reported in a *Nature Communications* paper (2015), they establish a mathematical model to quantitatively connect two different stages of the life cycle of the fruit fly *Drosophila*: oocyte formation and embryonic pattern specification. They perform experimental measurements to determine parameters of their model and validate their model predictions. Their reported study provides a fresh view of how the resources are accumulated by the mother for the purpose of instructing robust development of the future embryo. The research in Dr. Ma's team was supported by grants from the [National Institutes of Health](#) and the [National Science Foundation](#).

Keith Marsolo, PhD

Dr. Marsolo and the learning networks informatics team successfully completed an extension grant from the [Agency for Healthcare Research and Quality](#) that builds on their implementation of an electronic health record (EHR)-linked registry for the [ImproveCareNow Network](#), a 77-center quality improvement and research network that focuses on improving the care and outcomes of children with inflammatory bowel disease (IBD). Data on 75% of the patients in the network (at the time of submission) are now being automatically uploaded to the registry, which has significantly reduced the overall data entry burden for the network. Marsolo's team is participating in three projects that are part of the [Patient Centered Outcomes Research Institute's \(PCORI\) National Patient-Centered Clinical Research Network \(PCORnet\)](#). They are part of two [Clinical Data Research Network \(CDRN\)](#) awards, as well as a [Patient-Powered Research Network \(PPRN\)](#). Among the various required tasks of these awards, Dr. Marsolo and his team will create standardized extracts of EHR data for Cincinnati Children's and ImproveCareNow patients and use that information to respond to analytical queries that have been developed by patients and investigators within PCORnet. This network will also be used to identify and recruit patients for clinical trials and to conduct observational and comparative effectiveness research. In addition, Dr. Marsolo is serving as one of the co-chairs of the PCORnet's Data Standards, Security and Network Infrastructure (DSSNI) Task Force.

John P. Pestian, PhD, MBA

Dr. Pestian's lab is focused on using the science of natural language understanding in biomedical settings with the goal of developing advanced technology for the care of neuropsychiatric illness. Recently they have begun to integrate genetics, language, voice and facial features for identifying epilepsy surgery candidates and those at risk for depression, anxiety

and suicide. The lab's epilepsy studies are focused on building computer systems that will be used to understand the quality of epilepsy care. They have also developed methods for predicting neurosurgery for epileptic patients. The goal of their suicide research is to develop a system that will identify suicidal adolescents. Here they are trying to combine the linguistic, acoustic, and visual queues that will help a clinician decide if an adolescent will attempt suicide. [Dr. Pestian](#) and his lab had several highlights for this past year including the issuance five patents. One invention, [Optimization and Individualization of Medication Selection and Dosing](#), has been used for optimal mental health drug selection on over 250,000 people. The other notable invention, [Processing Text With Domain-Specific Spreading Activation Methods](#), is being used for identification of suicide and other mental illness using Thought Markers like language, acoustics, and facial characteristics. Dr. Pestian is a member of the NIH's standing Study Section, Biomedical Library and Informatics Review Committee (BLIRC) that serves the [National Library of Medicine](#).

Nathan Salomonis, PhD

[Dr. Salomonis](#) and his group are on the cutting edge of developing new software and algorithms to identify complex functional relationships from whole transcriptome data. They have developed several open source analysis tools including AltAnalyze, LineageProfiler, GO-Elite, and NetPerspective. The advent of single-cell genomic profiles has created many new opportunities for understanding stochastic decisions mediating stem cell differentiation to distinct cell fates and the regulation of distinct gene expression and splicing programs. They are capitalizing on this new technology to explore these decision-making processes at a resolution never previously possible. They have worked collaboratively with a dozen investigative research teams within Cincinnati Children's last year to develop new methods for evaluating whole genome transcriptome datasets. These methods include: 1) the detection of distinct gene and splicing populations from bulk and single cell genome profiles, 2) predicting implicated cell types present in complex fetal maternal biological samples and 3) identifying new disease regulatory networks related to pediatric cancer, cardiovascular disease and spinal cord injury.

Imre Solti, MD, PhD

The Solti Lab consists of experts in natural language processing (NLP), machine learning (ML), and information extraction (IE). Members of the Solti Lab automated the process of eligibility screening for clinical trials. In collaboration with [Boston Children's Hospital](#), using NLP techniques, they successfully developed two phenotyping algorithms for early childhood obesity and autism. An R21 electronic health record-based patient safety grant is aimed to automate the detection of medical errors in the Cincinnati Children's neonatal intensive care units. Leveraging NLP and ML algorithms, a medication reconciliation project automated medication discrepancy detection between patients' discharge medication lists and medications in discharge summaries. A project of predictive modeling for patients' clinical status utilized advanced ML methodology to predict the possibility of a patient's 24-hour PICU transfer and 30-day unplanned readmission.

S. Andrew Spooner, MD, MS, FAAP

[Dr. Spooner](#) and his research group have created a data warehouse focusing on medication alerts stretching back five years, into which they have built several metrics of user alert-response behavior. They are using this warehouse to answer questions about how clinical users manage the load of decision-support alerts in the system and how they detect potential harmful overdose errors. They are collaborating with an external machine-learning vendor that is working with the hospital's safety leaders on safety analytics to bring more powerful tools to bear on the problem of alert fatigue and user overload. On other fronts, Dr. Spooner is researching decision support for weight data-entry errors that can have profound effects on medication safety. His group is working with business intelligence systems interfaced to the electronic medical record to tune decision support to unprecedented specificity and sensitivity.

Michael Wagner, PhD

[Dr. Wagner](#) has a long-standing interest in applications of machine learning techniques to bioinformatics problems such as protein structure prediction, disease classification and protein identification. He is also involved in a number of projects that

implement complex software and data infrastructure. For example, he is co-principal investigator on the [Longitudinal Pediatric Data Resource \(LPDR\)](#) project funded through the [Newborn Screening Translational Research Network \(NBSTRN\)](#). The LPDR will be used by researchers nationwide to mine health outcome data over the lifespan of children who screen positive for a large number of rare and often devastating genetic disorders. Furthermore, Dr. Wagner is overseeing the development of genomic data management and analysis tools both for the Center for Pediatric Genomics (CpG) at Cincinnati Children's and in his role as director of the [Rheumatic Disease Research Informatics Core](#) of the [Cincinnati Rheumatic Diseases Core Center](#), which is funded by the [National Institute of Arthritis and Musculoskeletal and Skin Diseases](#).

Significant Publications

Ni Y, Kennebeck S, [Dexheimer JW](#), McAneney CM, Tang H, Lingren T, Li Q, Zhai H, Solti I. [Automated clinical trial eligibility prescreening: increasing the efficiency of patient identification for clinical trials in the emergency department.](#) *J Am Med Inform Assoc.* 2015 Jan;22(1):166-78.

Clinical trials are critical to the progress of medical science; however, awareness and access to clinical trials pose significant challenges to both patients and physicians. Efforts are underway to leverage electronic health record (EHR) information to aid in trial recruitment. Study authors developed a natural language processing- and machine learning-based system, Automated Clinical Trial Eligibility Screener (ACTES), to automatically screen patients' EHR data and determine their suitability for clinical trials. In a gold-standard based retrospective evaluation of 13 diverse clinical trials actively enrolling in the Emergency Department, the ACTES achieved statistically significant improvement in screening efficiency and showed a potential of 75% reduction in staff screening effort. This is the first, known to us, introduction of machine learning techniques to patient screening for enhancing trial-patient matching.

[Salomonis N](#). [Systems-Level Perspective of Sudden Infant Death Syndrome.](#) *Pediatr Res.* 2014 Sep;76(3):220-9.

Research into causes and treatments for Sudden Infant Death Syndrome or SIDS, a poorly understood pediatric disease, requires a comprehensive and evolving systems-level model of the disease. This article describes the creation of a living biological review that integrates prior experimental and genomic research into a WikiPathway model of SIDS. Unlike a normal review article or even pathways produced by other tools such as KEGG or Ingenuity, a WikiPathway can be expanded and improved over time by the research community; includes embedded links to the literature; has machine readable interactions, genes, proteins and metabolites; and is available for integrated analyses with any collected large-scale datasets. The author used this tool to perform a comprehensive analysis of existing proteomics data from brainstem samples of infants with SIDS and found new targets for further consideration that can enrich this pathway model. This model, over time, can improve as a wiki-based, community curation project.

Connolly B, Matykiewicz P, Bretonnel Cohen K, Standridge SM, Glauser TA, Dlugos DJ, Koh S, Tham E, [Pestian J](#). [Assessing the similarity of surface linguistic features related to epilepsy across pediatric hospitals.](#) *J Am Med Inform Assoc.* 2014 Sep-Oct;21(5):866-70.

A diagnosis of epilepsy significantly affects a person's quality of life and imposes a considerable medical and economic burden; yet, a proportion of people with epilepsy need treatment but do not receive it. Computational linguistic methods provide opportunities for discovering information in clinical text and allow researchers to explore novel approaches to care for disorders such as epilepsy. In this study, an automated system using support vector machine (SVM)-based natural language processing (NLP) was developed to compare descriptions of epilepsy patients at three children's hospitals to allow evaluation of epilepsy progress notes in support of quality measures. The authors found that an NLP-based algorithm can effectively classify epilepsy progress notes and support automated comparisons of patient conditions, treatments, and diagnoses across different healthcare settings.

Masino AJ, Dechene ET, Dulik MC, Wilkens A, Spinner NB, Krantz ID, Pennington JW, Robinson PN, **White PS**. **Clinical phenotype-based gene prioritization: an initial study using semantic similarity and the human phenotype ontology**. *BMC Bioinformatics*. 2014 Jul 21;15:248.

Contemporary DNA sequencing techniques such as next generation sequencing (NGS) now enable rapid and inexpensive exome and whole genome sequencing, but clinical interpretation of results is difficult due to the scale and complexity of the test output data. Each patient's sequence reveals many possibly damaging variants that must be individually assessed to establish clear association with patient phenotype. The study authors developed an algorithm that ranks a given set of genes relative to patient phenotype using semantic similarity and tested it by using simulation with clinical data. They found that using semantic similarity combined with variant analysis holds promise to increase accuracy and decrease effort for identifying pathogenic variants for clinical genetic diagnosis.

Wu C, Bardes EE, Jegga AG, **Aronow BJ**. **ToppMiR: ranking microRNAs and their mRNA targets based on biological functions and context**. *Nucleic Acids Res*. 2014 Jul;42:W107-13.

The functional characterization of microRNAs (miRs) and their target messenger RNAs (mRNAs), especially in specific biological contexts, is fundamental to improve our understanding of molecular mechanisms underlying organismal development, physiology and disease. The authors have developed **ToppMiR**, a web-based analytical workbench that uses intrinsic and hidden biological and genomic knowledge from the user-specified biological context to recognize and rank miR-mRNA interactions. The results from ToppMiR can be exported in a variety of formats to facilitate further analyses with other open source bioinformatics applications.

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54. Vannest J, Rajagopal A, Cicchino ND, Franks-Henry J, Simpson SM, Lee G, Altaye M, Sroka C, Holland SK, Consortium CA. **Factors determining success of awake and asleep magnetic resonance imaging scans in nonsedated children**. *Neuropediatrics.* 2014; 45:370-7.
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56. Ward MJ, Marsolo KA, Froehle CM. **Applications of Business Analytics in Healthcare**. *Bus Horiz.* 2014; 57:571-582.
57. White PS, Xie HM, Werner P, Glessner J, Latney B, Hakonarson H, Goldmuntz E. **Analysis of chromosomal structural variation in patients with congenital left-sided cardiac lesions**. *Birth Defects Res A Clin Mol Teratol.* 2014; 100:951-64.
58. Wu C, Bardes EE, Jegga AG, Aronow BJ. **ToppMiR: ranking microRNAs and their mRNA targets based on biological functions and context**. *Nucleic Acids Res.* 2014; 42:W107-13.
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60. Zhu C, Wu C, Jegga AG. **Network Biology Methods for Drug Repositioning**. In: KR Sakharkar, MK Sakharkar, R Chandra, eds. *Post-Genomic Approaches in Drug and Vaccine Development*. Denmark: Rivers Publishers; 2015:115-132.

Faculty Members

Peter S. White, PhD, Professor

Leadership Director, Department Chair

Research Interests Discovery Genomics, Clinical Genomics, Decision Support, Phenotype Capture, Data Integration, Data Discovery, Data Utilization

Bruce J. Aronow, PhD, Professor

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

John J. Hutton, MD, Professor

Research Interests Federated Data Sharing Networks to Support Translational Research

Anil Goud Jegga, DVM, MRes, Associate Professor

Research Interests Systems Biology, Biological Networks, Biomedical Ontologies, Integrative Genomics, Drug Discovery and Repositioning

Michal Kouril, PhD, Assistant Professor

Leadership Director, Research IT

Research Interests Computational Support, High-Performance Computing, Parallel Programming, High-End Data Storage

Long (Jason) Lu, PhD, Associate Professor

Research Interests Bioinformatics, Machine Learning, Integrative Genomics, Biological Networks, Computational Modeling, Software Development, Next Gen Sequencing Analysis

Jun Ma, PhD, Professor

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

Keith Marsolo, PhD, Associate Professor

Research Interests i2b2, Data Integration, Data Warehousing and Data Management, Electronic Health Records, Learning Networks, Distributed Research Networks

John P. Pestian, PhD, MBA, Professor

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

Nathan Salomonis, PhD, Assistant Professor

Research Interests Bioinformatics, Genomics, Alternative Splicing, MicroRNA Biology, Pathway Analysis, Pathway Visualization, Pathway Curation, SIDS, Stem Cell Biology, Cardiac Specification, Renal Graft Dysfunction

Imre Solti, MD, PhD, Assistant Professor

Research Interests Computational Linguistics, Machine Learning, Expert Systems, Natural Language Processing, Clinical Decision Support, Precision Medicine

S. Andrew Spooner, MD, MS, FAAP, Professor

Leadership Chief Medical Information Officer

Research Interests Decision Support, Pharmacy Information Systems

Michael Wagner, PhD, Associate Professor

Leadership Faculty Liaison

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

Joint Appointment Faculty Members

Judith W. Dexheimer, PhD, Assistant Professor (Emergency Medicine)

Research Interests Clinical Decision Support, Informatics, Natural Language Processing, Artificial Intelligence

Eric Hall, PhD, Assistant Professor (Neonatology & Pulmonary Biology)

Research Interests Clinical Informatics, Public Health Informatics, Record Linkage, Data Mining and Warehousing

Kenneth M. Kaufman, PhD, Professor (Center for Autoimmune Genomics and Etiology – CAGE)

Research Interests Genotyping, Next-Generation DNA Technologies

Eric S. Kirkendall, MD, MBI, FAAP, Assistant Professor (Hospital Medicine)

Research Interests Clinical Informatics, Healthcare Information Technology, Clinical Decision Support, Patient Safety, Quality Improvement, Data Management, Application/Software Development

Kakajan Komurov, PhD, Assistant Professor (Experimental Hematology & Cancer Biology)

Research Interests Bioinformatics, Cancer Biology

Mario Medvedovic, PhD, Professor (UC Environmental Health)

Research Interests Biostatistics, Bioinformatics

Jarek Meller, PhD, Associate Professor (UC Environmental Health)

Research Interests Protein Modeling

Alexey Porollo, PhD, Assistant Professor (Center for Autoimmune Genomics and Etiology – CAGE)

Research Interests Computational Biology, Bioinformatics

Alexander Towbin, MD, Associate Professor (Radiology and Medical Imaging)

Research Interests Radiology Informatics, Cancer Imaging, Abdominal Imaging

Matthew Weirauch, PhD, Assistant Professor (Center for Autoimmune Genomics and Etiology - CAGE)

Research Interests Transcriptional Regulation, Bioinformatics, Functional Genomics

Yan Xu, PhD, Professor (Neonatology & Pulmonary Biology)

Research Interests Bioinformatics, Systems Biology

Trainees

- **Brian Connolly, PhD**, 2002, Florida State University, Gainesville, FL, USA
- **Rebekah Karns, PhD**, 2012, University of Cincinnati, Cincinnati, OH, USA
- **Hailong Li, PhD**, 2013, University of Cincinnati, Cincinnati, OH, USA
- **Qi Li, PhD**, 2011, University of Pittsburgh, Pittsburgh, PA, USA
- **Mayur Sarangdhar, PhD**, 2011, University of Hull, Hull, UK
- **Haijun Zhai, PhD**, 2010, University of Science and Technology of China, Hefei, Anhui Province, China

Grants, Contracts, and Industry Agreements

Grant and Contract Awards

Annual Direct

Aronow, B

RNA Deep Sequencing and Metabolomic Profiling of Microgravity-Induced Regulation of the Host-Pathogen Interaction: An Integrated Systems Approach

National Aeronautics and Space Administration(Arizona Board of Regents)

NNX13AM01G	7/1/2013-6/30/2016	\$13,072
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A Genitourinary Development Molecular Anatomy Project - Database and Website

National Institutes of Health(Western General Hospital)

U01 DK092983	9/15/2011-8/31/2016	\$34,640
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Multimodal Analysis of High-Risk Psychosis Mutations in Induced Neuronal Cells

National Institutes of Health(Stanford University)

U19 MH104172	9/9/2014-7/31/2019	\$150,000
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Digestive Health Center: Bench to Bedside Research in Pediatric Digestive Disease

National Institutes of Health

P30 DK078392	6/01/2012-5/31/2017	\$94,377
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Kouril, M

Data Coordination and Integration Center for LINCS-BD2K

National Institutes of Health(Mount Sinai Hospital)

U54 HL127624	9/29/2014-4/30/2019	\$10,452
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Lu, L

A Network-based Approach to Associate HDL Subspeciation with Function

National Institutes of Health

R01 HL111829	8/1/2012-6/30/2017	\$405,292
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Targeting the Blood-Brain Barrier in Ischemic Stroke

National Institutes of Health(University of Cincinnati)

R15 NS088384	4/01/2015-3/31/2018	\$24,808
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Translational Repression & Aspergillus Fumigatus Virulence

National Institutes of Health(University of Cincinnati)

R21 AI111062	2/01/2014-1/31/2016	\$7,659
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Ma, J

Regulation and Scaling of a Morphogen Gradient

National Institutes of Health

R01 GM101373	8/15/2012-6/30/2016	\$190,000
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Marsolo, K

CMS Partnership for Patients Initiative

Department of Health and Human Services(Ohio Children's Hospitals' Solutions for Patient Safety)

12/9/2011-12/8/2019

\$402,532

University of Pittsburgh Clinical and Translational Science Institute

National Institutes of Health(University of Pittsburgh)

UL1 TR000005

1/1/2015-8/31/2015

\$92,400

Implementation of the BEACON Quality Improvement Data Infrastructure

Ohio Depart of Jobs and Family Services(Ohio State University)

9/23/2011-6/30/2016

\$238,544

Implementation of the BEACON Quality Improvement Data Infrastructure

Ohio Department of Health(Ohio State University)

7/1/2012-6/30/2016

\$119,633

MEDTAPP Neonatal Abstinence Syndrome (NAS) - State

Ohio Department of Medicaid (ODM)(Ohio State University)

1/14/2014-6/30/2015

\$5,418

MEDTAPP Neonatal Abstinence Syndrome (NAS) - Federal

Ohio Department of Medicaid (ODM)(Ohio State University)

1/14/2014-6/30/2015

\$12,764

A National Pediatric Learning Health System

Patient-Center Outcomes Research Institute(Children's Hospital of Philadelphia)

4/15/2014-10/14/2015

\$402,532

Scalable Collaborative Infrastructure for a Learning Healthcare System

Patient-Center Outcomes Research Institute(Harvard Medical School)

4/14/2014-9/30/2015

\$71,350

Salomonis, N

NHLBI Progenitor Cell Biology BioinformaticsCore

National Institutes of Health(University of Maryland)

U01 HL099997

7/1/2013-4/30/2016

\$51,203

Dissecting the role of RBM20 in Dilated Cardiomyopathy Using Isogenic iPSCs

National Institutes of Health(University of Maryland)

U01 HL099997 8/1/2014-4/30/2016 \$115,697

Wagner, M

Gene Expression in Pediatric Arthritis

National Institutes of Health

P01 AR048929 9/01/2002-8/31/2016 \$184,820

Cincinnati Rheumatic Disease Core Center

National Institutes of Health

P30 AR047363 3/15/2001-6/30/2016 \$62,548

White, P

NBSTRN: Newborn Screening Translational Research Network

National Institutes of Health(American College of Medical Genetics Fdn)

HHSN275201300011C:00 6/1/2014-9/25/2018 \$238,537

Current Year Direct \$2,928,278

Total \$2,928,278

Quantitative Model Provides Big Clues Into How Tiny Embryos Develop



Jun Ma, PhD

PUBLISHED MARCH 26, 2015

Nature Communications

A biological-mathematical-genetic model called TEMS, or Tissue Expansion-Modulated Maternal Morphogen Scaling, is providing insights into one of nature’s most intriguing genetic questions about scaling — the proportional growth of tissues, organs and structures from tiny ovaries, eggs and embryos.

The model provides new insights into the delicate connections between ovarian tissue and ensuing embryonic development, and it can be applied to future research into birth defects.

Developed by Biomedical Informatics scientist Jun Ma, PhD, and published March 26, 2015, in *Nature Communications*, the TEMS model was applied to fruit flies from development of the ovary through embryo. Ma’s team focused on two developmental components: morphogens — proteins that form concentration gradients along the axis of an embryo and instruct the genes that control the proportional formation of body parts and organs; and ovary-active genes that produce messengers delivered to the egg for instructing the production of morphogen proteins in the embryo.

His team studied front-to-back proportional scaling in embryos before organs start to develop, and found that the size of embryos was influenced by the quantity of initial tissue in the female’s ovary, particularly the size of the ovarian egg chamber and the expansion of the copy numbers of an ovary-active gene called bicoid.

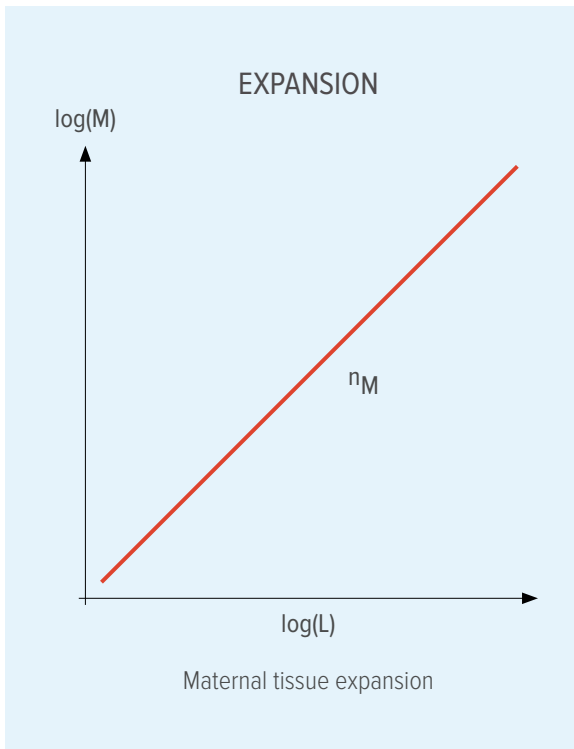
“The model provides a new perspective of embryonic development and contributes to our fundamental knowledge that may ultimately lead to an improved understanding of the basis of birth defects,” says Ma.

Of particular interest for future research, according to Ma, is the similarity between the peak number of bicoid gene copies in a female fly’s nurse cells and the peak number of cell nuclei in the offspring blastoderm, or early-stage embryo. Aided by TEMS, Ma and his team hope to better understand, quantify and predict how life forms grow and develop, and to explore the interplay between biology and evolution.

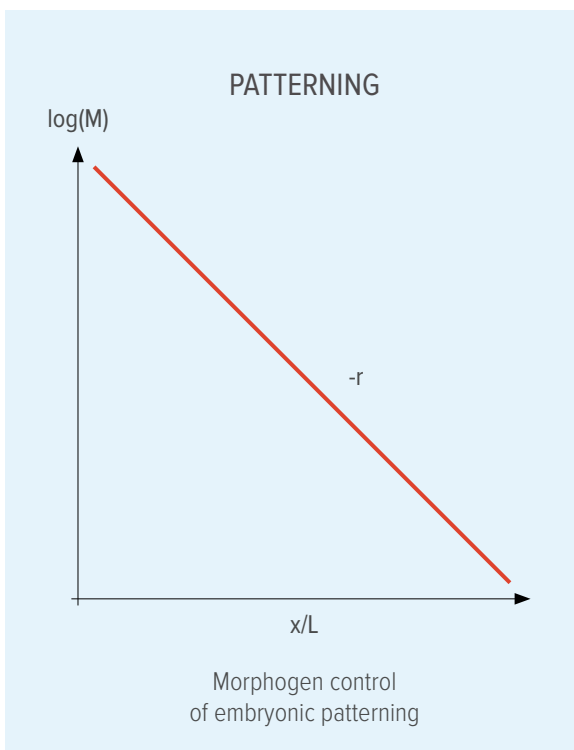
RESEARCH AND TRAINING DETAILS

Faculty	13
Joint Appointment Faculty	11
Research Fellows	6
Research Students	19
Support Personnel	117
Direct Annual Grant Support	\$2.9M
Peer Reviewed Publications	60

He F, Wei C, Wu H, Cheung D, Jiao R, Ma J. Fundamental origins and limits for scaling a maternal morphogen gradient. *Nat Commun.* 2015;6:6679.



A biological-mathematical-genetic model developed at Cincinnati Children's called Tissue Expansion-Modulated Maternal Morphogen Scaling (TEMS) provides new insights into the delicate connections between ovarian tissue and ensuing embryonic development. This study shows that embryo size is influenced by the quantity of initial ovary tissue, particularly the size of the ovarian egg chamber and the expansion of the copy numbers of the ovary-active gene bicoid. The figures here depict the mathematical relationships governing maternal tissue expansion (left) and morphogen control of embryonic patterning (below).



“The model provides a new perspective of embryonic development and contributes to our fundamental knowledge that may ultimately lead to an improved understanding of the basis of birth defects.”