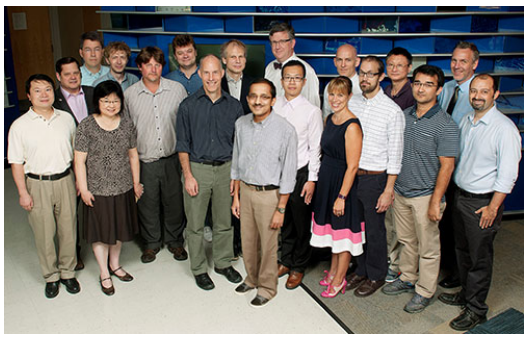
Biomedical Informatics

Division Details

RESEARCH AND TRAINING DETAILS	
Faculty	13
Joint Appointment Faculty	11
Research Fellows and Post Docs	1
Research Graduate Students	23
Total Annual Grant Award Dollars	$5,862,183
Total Publications	55



Row 1: L Lu, Y Xu, P White, A Jegga, Y Ni, J Dexheimer, K Marsolo, K Komurov, N Salomonis

Row 2: J Pestian, K Kaufman

Row 3: M Wagner, J Meller, A Porollo, M Kouril, A Spooner, E Kirkendall, J Ma, E Hall

Research Highlights

Bruce J. Aronow, PhD

Dr. Aronow, PhD, is a geneticist and computational and developmental biologist. His group carries out analyses, develops algorithms, and builds web databases that allow researchers from varying disciplines and backgrounds to access diverse types of biological data to better understand, model, and research complex biological processes in order to cure disease. The Aronow-Jegga Lab is highly collaborative with clinical and basic researchers involved in a broad range of research projects encompassing many areas of biology and disease, including normal and abnormal development, in vivo and in vitro disease models, and large-scale clinical studies based on genetic, genomic, proteomic, metabolomic and imaging data along with therapeutic agent response measures. Areas of high current interest include large-scale clinical sample analyses, single cell-based tissue dissection, and in vitro stem cell-based modeling of normal and abnormal neurological, immunological, cardiac, and cancer tissues and the prediction of new therapeutic approaches based on disease mechanism analysis. The labs recent efforts are focusing on the areas of inflammatory bowel disease, eosphinophilic esophagitis, sickle cell anemia, and neurological and psychiatric diseases; defining the transcriptome of the developing kidney, lung and brain; using stem cell-derived cells and organoids; and better understanding mechanisms that underlie cancers and the actions of therapeutic agents against disease.

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 help us 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 have been 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, PhD, 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 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. Research identifies genes with indispensable functions 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. In another research direction, Dr. Lu's lab developed a new computer program that analyzes functional brain MRIs in hearing-impaired children before cochlear implant and predicts whether they will develop effective language skills after surgery. The prediction algorithm, based on semi-supervised machine learning, can also evaluate how specific regions of the brain respond to auditory stimulus tests that hearing-impaired infants and toddlers receive before surgical implantation. With additional research and development, the computer model could become a practical tool that allows clinicians to reduce the number of children who undergo an invasive and costly procedure, only to be disappointed when implants do not deliver hoped-for results.

Jun Ma, PhD

Research performed by Dr. Ma’s team focuses on understanding developmental processes at a quantitative and systems level. They aim to establish quantitative models—with predictive power—of how embryonic patterns emerge in a manner that is proportional to embryo size. They perform experimental studies to facilitate model building, and use models to make predictions for experimental validations. They use Drosophila (fruit fly) embryos for their studies. The research by Dr. Ma’s team received support grants from the National Institutes of Health (NIH) and the National Science Foundation (NSF).

Keith Marsolo, PhD

Dr. Marsolo, and the learning networks informatics team, successfully completed an extension grant from the Agency for Healthcare Research and Quality (AHRQ) that builds on their implementation of an electronic health record (EHR)-linked registry for the ImproveCareNow Network, a 92-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 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.

Yiazhao Ni, PhD

Dr. Ni's team consists of experts in natural language processing (NLP), machine learning (ML) and information retrieval (IR). Leveraging NLP and IR technologies, the team successfully developed a prototype automated system for patient eligibility screening. Utilizing advanced ML methodology, they also developed an automated algorithm to predict patients' responses to clinical trial invitations to facilitate patient recruitment. Dr. Ni was awarded a grant under the CCHMC Innovation Fund to continue this line of research. Dr. Ni's team also develops electronic health record (EHR)-based data analytics to support clinical decision-making. His team has participated in a variety of research projects: 1) the Electronic Medical Records and Genomics Network (eMERGE, U01) project, where Dr. Ni and his team explored the EHR information and developed phenotype algorithms for specific diseases; 2) the NICU medication safety project (R01), where the team automated medication discrepancy detection between patients' medication administrations and medication orders; and 3) the sustainable surveillance of diabetes project (U18), where the team used NLP and ML technologies to ascertain if a patient had diabetes, and if so, the date of diagnosis. In addition to his research, Dr. Ni is serving as a ML specialist in multiple quality improvement projects such as the safety and situation awareness project.

John P. Pestian, PhD, MBA

Dr. Pestian's lab focuses 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 focuses on building computer systems 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 cues that will help a clinician decide if an adolescent will attempt suicide. Some of Cincinnati Public Schools are currently testing these algorithms. Recent highlights for Dr. Pestian, and his lab, include the issuance five patents. The Pestian Lab works with local and national entrepreneurs to disseminate their findings to the marketplace. From these collaborations, more than 500 jobs and $255 million have been generated. One invention, Optimization and Individualization of Medication Selection and Dosing, is used for optimal mental health drug selection on over 400,000 people. The other notable invention, Processing Text With Domain-Specific Spreading Activation Methods, is used for identification of suicide, and other mental illness, using "thought markers" like language, acoustics and facial characteristics. Dr. Pestian is an alumni of the NIH's standing Study Section, Biomedical Library and Informatics Review Committee (BLIRC) of the National Library of Medicine, as well as the National Institute for Mental Health's, Pathway to Independence (K99) study section.

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. Last year, they worked collaboratively with a dozen investigative research teams within Cincinnati Children's 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 and adult cancers, cardiovascular disease and spinal cord injury.

S. Andrew Spooner, MD, MS, FAAP

Dr. Spooner practices general academic pediatrics and serves as the chief medical information officer for Cincinnati Children's. He is also actively involved in patient-centered research. He, 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 the National Heart Lung and Blood Institute (NHLBI)-funded Pediatric Cardiology Genomics Consortium, part of the Bench to Bassinet project, he plays a leadership role in the development and maintenance of the Data Hub (a.k.a. HeartsMart), which now houses tens of thousands of whole exome and thousands of whole genome sequencing data sets. He is co-principal investigator on the Longitudinal Pediatric Data Resource (LPDR) project funded through the Newborn Screening Translational Research Network (NBSTRN) and Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD). The LPDR, used by researchers nationwide, mines health outcome data over the lifespan of children who screen positive for rare and often devastating genetic disorders. Dr. Wagner also leads the Rheumatology Disease Research Informatics Core of the Cincinnati Rheumatic Diseases Core Center, funded by the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS).

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 Eunice Kennedy Shriver 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.

Significant Publications

Wu H, Manu, Jiao R, **Ma J. Temporal and spatial dynamics of scaling-specific features of a gene regulatory network in Drosophila**. *Nat Commun*. 2015 Dec 8;6:10031.

A fruit fly's head is the right size for its body, and an elephant's head is the right size for its body. But how does nature ensure that living organisms develop proportionally–sized body parts? Jun Ma, PhD, and his colleagues report in Nature Communications find one can view an entire developing embryo as a single, unified dynamic system. The maternally derived, size-dependent information interpreted locally can spread in space and time throughout the embryo. A gene regulatory network governs this process when it decodes the size cues derived from a maternal protein gradient called Bicoid. The paper is among the latest work from Ma's team, which is working to experimentally reconstruct and computationally simulate how size-dependent patterns emerge in the fruit fly embryo. They hope that better understanding of how organisms develop at the earliest stages of life may provide important clues into typical human development and certain types of birth defects.

Lu Y, Lu Y, Deng J, Peng H, Lu H, **Lu LJ**. **A novel essential domain perspective for exploring gene essentiality**. *Bioinformatics*. 2015 Sep 15;31(18):2921-9.

Genes identified with indispensable functions are essential; however, the traditional gene-level studies of essentiality have several limitations. This study introduces a new perspective to characterize gene essentiality by analyzing protein domains, the independent structural or functional units of a polypeptide chain. The researchers developed an algorithm-based model to identify essential domains and used simulated datasets to test the model and applied the model to six microbial species. When utilizing these essential domains to reproduce the annotation of essential genes, they received accurate results that suggest protein domains are more basic units for the essentiality of genes. Furthermore, they presented several examples to illustrate how the combination of essential and non-essential domains can lead to genes with divergent essentiality. This paper describes the first systematic analysis on gene essentiality on the level of domains.

Tan L, Holland S, Deshpande A, Chen Y, Choo D, **Lu LJ**. **A semi-supervised SVM model for predicting the language outcomes following cochlear implantation based on pre-implant brain fMRI imaging**. *Brain Behav*. 2015 Oct 12;5(12):e00391.

A new computer program that analyzes functional brain MRI scans of hearing-impaired children may help predict whether the children will develop effective language skills within two years of cochlear implant surgery. This study describes a computer program that evaluates how specific regions of the brain respond to auditory stimulus tests that hearing-impaired infants and toddlers receive before surgical implantation. The study included 44 infants and toddlers (aged 8 to 67 months), 23 of whom received cochlear implant surgery. Two years following surgery, the team measured language performance. The study identified two features from the computer analysis that are potential biomarkers for predicting cochlear implant outcomes. With additional research and development, the computer model could become a practical tool that allows clinicians to reduce the number of children who undergo an invasive and costly procedure and are then disappointed when the implants do not deliver hoped-for results.

Connolly N, Anixt J, Manning P, Ping-I Lin D, **Marsolo KA,** Bowers K. **Maternal metabolic risk factors for autism spectrum disorder-An analysis of electronic medical records and linked birth data**. *Autism Res*. 2016 Aug;9(8):829-37.

An estimated one out of 45 children are affected by autism spectrum disorder (ASD). Suspected causal factors are genetics, environment and the interaction of both. This study strengthens evidence linking autism to maternal obesity and diabetes and demonstrates that electronic medical data can verify and establish the extent of this link across large populations. The researchers analyzed a variety medical record and birth data from patients and mothers to help identify risk factors. Using birth records from Southwest Ohio (part of the Cincinnati Children's primary service area), the researchers compared mothers who had a child diagnosed with ASD to mothers of children with a non-autism developmental disorder. They also included in their comparison mothers with children having no developmental disorders. According to study data, pregnant mothers with obesity or gestational diabetes were 1.5 times more likely to have a child with ASD compared to mothers of children without developmental disorders. The increased risk of ASD for pregnant mothers with both obesity and gestational diabetes was two-fold. The findings fit well into an increasing body of evidence associating obesity and gestational diabetes with the development of autism.

Venek V, Scherer S, Morency L-P, Rizzo A, **Pestian J**. **Adolescent Suicidal Risk Assessment in Clinician-Patient Interaction**. *IEEE Transactions on Affective Computing*. 2016 Jan:18;Volume: PP Issue: 99.

Suicide among adolescents is a major public health problem and the third leading cause of death in the United States for children from ages 13-18. This paper presents work to investigate if suicidal risk is determinable by observing a patient-clinician conversation including the communicated verbal information, conversational dynamics, and vocal characteristics. The researchers studied the verbal and nonverbal acoustic information related to 60 audio-recorded interviews of 30 suicidal and 30 non-suicidal adolescents interviewed by a case worker. The researchers analyzed the recordings to reveal statistical differences between suicidal v. non-suicidal adolescents, and to investigate the behaviors of those who attempted suicide repeatedly v. those who attempted it once. Variables analyzed included conversation dynamics (such as speak and pause times), verbal information (such as use of personal pronouns), and acoustic information (such as pitch and volume). The study identified significant statistical differences between the three groups of patients: non-suicidal patients, suicidal repeaters and suicidal non-repeaters. Using hierarchical classification methods, the researchers were able to successfully discriminate between the three groups of patients.

Division Publications

1. Adams AK, Bolanos LC, Dexheimer PJ, Karns RA, Aronow BJ, Komurov K, Jegga AG, Casper KA, Patil YJ, Wilson KM, Starczynowski DT, Wells SI. **Irak1 Is a Novel Dek Transcriptional Target and Is Essential for Head and Neck Cancer Cell Survival.** *Oncotarget*. 2015; 6:43395-407.

2. Arya R, Gillespie CW, Cnaan A, Devarajan M, Clark P, Shinnar S, Vinks AA, Mizuno K, Glauser TA, Childhood Absence Epilepsy Study Group. **Obesity and Overweight as Cae Comorbidities and Differential Drug Response Modifiers.** *Neurology*. 2016; 86:1613-21.

3. Berry RL, Ozdemir DD, Aronow B, Lindstrom NO, Dudnakova T, Thornburn A, Perry P, Baldock R, Armit C, Joshi A, Jeanpierre C, Shan J, Vainio S, Baily J, Brownstein D, Davies J, Hastie ND, Hohenstein P. **Deducing the Stage of Origin of Wilms' Tumours from a Developmental Series of Wt1-Mutant Mice.** *Dis Model Mech*. 2015; 8:903-17.

4. Bian F, Gao F, Kartashov AV, Jegga AG, Barski A, Das SK. **Polycomb Repressive Complex 1 Controls Uterine Decidualization.** *Sci Rep*. 2016; 6:26061.

5. Cai WF, Liu GS, Lam CK, Florea S, Qian J, Zhao W, Pritchard T, Haghighi K, Lebeche D, Lu LJ, Deng J, Fan GC, Hajjar RJ, Kranias EG. **Up-Regulation of Micro-Rna765 in Human Failing Hearts Is Associated with Post-Transcriptional Regulation of Protein Phosphatase Inhibitor-1 and Depressed Contractility.** *Eur J Heart Fail*. 2015; 17:782-93.

6. Chen S, Brunskill EW, Potter SS, Dexheimer PJ, Salomonis N, Aronow BJ, Hong CI, Zhang T, Kopan R. **Intrinsic Age-Dependent Changes and Cell-Cell Contacts Regulate Nephron Progenitor Lifespan.** *Dev Cell*. 2015; 35:49-62.

7. Chen Y, Mazlack LJ, Minai AA, Lu LJ. **Inferring Causal Networks Using Fuzzy Cognitive Maps and Evolutionary Algorithms with Application to Gene Regulatory Network Reconstruction.** *Appl Soft Comput*. 2015; 37:667-79.

8. Cheung D, Ma J. **Probing the Impact of Temperature on Molecular Events in a Developmental System.** *Sci Rep*. 2015; 5:13124.

9. Cohen K, Glass B, Greiner H, Holland-Bouley K, Standridge S, Arya R, Faist R, Morita D, Mangano F, Connolly B. **Methodological Issues in Predicting Pediatric Epilepsy Surgery Candidates through Natural Language Processing and Machine Learning.** pmc/PMC4876984. *Biomed Inform Insights*. 2016; 8:11-8.

10. Connolly N, Anixt J, Manning P, Ping ILD, Marsolo KA, Bowers K. **Maternal Metabolic Risk Factors for Autism Spectrum Disorder-an Analysis of Electronic Medical Records and Linked Birth Data.** *Autism Res*. 2016; 9:829-37.

11. Cooke JP, Meng S, Wong WT, Sayed N, Ospino F, Lee J, Jha A, Dexheimer P, Aronow B. **Response to Letter Regarding Article Transdifferentiation of Human Fibroblasts to Endothelial Cells: Role of Innate Immunity.** *Circulation*. 2015; 132:e197.

12. Davis J, Salomonis N, Ghearing N, Lin SC, Kwong JQ, Mohan A, Swanson MS, Molkentin JD. **Mbnl1-Mediated Regulation of Differentiation Rnas Promotes Myofibroblast Transformation and the Fibrotic Response.** *Nat Commun*. 2015; 6:10084.

13. Fukuma K, Kawanaka H, Prasath S, Aronow BJ, Takase H. **Feature Extraction and Disease Stage Classification for Glioma Histopathology Images.** *2015 17th International Conference on E-Health Networking, Application & Services (Healthcom)*. 2015:598-99.

14. Fulford L, Milewski D, Ustiyan V, Ravishankar N, Cai Y, Le T, Masineni S, Kasper S, Aronow B, Kalinichenko VV, Kalin TV. **The Transcription Factor Foxf1 Promotes Prostate Cancer by Stimulating the Mitogen-Activated Protein Kinase Erk5.** *Sci Signal*. 2016; 9:ra48.

15. Hawrylycz M, Miller JA, Menon V, Feng D, Dolbeare T, Guillozet-Bongaarts AL, Jegga AG, Aronow BJ, Lee CK, Bernard A, Glasser MF, Dierker DL, Menche J, Szafer A, Collman F, Grange P, Berman KA, Mihalas S, Yao Z, Stewart L, et al. **Canonical Genetic Signatures of the Adult Human Brain.** *Nat Neurosci*. 2015; 18:1832-44.

16. Heink A, Davidson WS, Swertfeger DK, Lu LJ, Shah AS. **A Comparison of Methods to Enhance Protein Detection of Lipoproteins by Mass Spectrometry.** *J Proteome Res*. 2015; 14:2943-50.

17. Herr TM, Bielinski SJ, Bottinger E, Brautbar A, Brilliant M, Chute CG, Cobb BL, Denny JC, Hakonarson H, Hartzler AL, Hripcsak G, Kannry J, Kohane IS, Kullo IJ, Lin S, Manzi S, Marsolo K, Overby CL, Pathak J, Peissig P, et al. **Practical Considerations in Genomic Decision Support: The Emerge Experience.** *J Pathol Inform*. 2015; 6:50.

18. Hoffman L, DeWire M, Ryall S, Buczkowicz P, Leach J, Miles L, Ramani A, Brudno M, Kumar S, Drissi R. **Spatial Genomic Heterogeneity in Diffuse Intrinsic Pontine and Midline High-Grade Glioma: Implications for Diagnostic Biopsy and Targeted Therapeutics.** *Acta Neuropathol Commun*. 2016; 4:1.

19. Hutton JS, Horowitz-Kraus T, Mendelsohn AL, DeWitt T, Holland SK, C-Mind Authorship Consortium. **Home Reading Environment and Brain Activation in Preschool Children Listening to Stories.** *Pediatrics*. 2015; 136:466-78.

20. Jin X, Khatwani C, Niu N, Wagner M, Savolainen J. **Pragmatic Software Reuse in Bioinformatics: How Can Social Network Information Help?** In: G Kapitsaki, E DeAlmeida, eds. *Software Reuse: Bridging with Social-Awareness*. Switzerland: Springer; 2016:247-64.

21. Kamath-Rayne BD, Du Y, Hughes M, Wagner EA, Muglia LJ, DeFranco EA, Whitsett JA, Salomonis N, Xu Y. **Systems Biology Evaluation of Cell-Free Amniotic Fluid Transcriptome of Term and Preterm Infants to Detect Fetal Maturity.** *BMC Med Genomics*. 2015; 8:67.

22. Kouril M. **Leveraging Fpga Clusters for Sat Computations.** *Adv Parallel Computing*. 2016; 27:525-32.

23. Li H, Gordon SM, Zhu X, Deng J, Swertfeger DK, Davidson WS, Lu LJ. **Network-Based Analysis on Orthogonal Separation of Human Plasma Uncovers Distinct High Density Lipoprotein Complexes.** *J Proteome Res*. 2015; 14:3082-94.

24. Li MH, Abrudan JL, Dulik MC, Sasson A, Brunton J, Jayaraman V, Dugan N, Haley D, Rajagopalan R, Biswas S, Sarmady M, DeChene ET, Deardorff MA, Wilkens A, Noon SE, Scarano MI, Santani AB, White PS, Pennington J, Conlin LK, et al. **Utility and Limitations of Exome Sequencing as a Genetic Diagnostic Tool for Conditions Associated with Pediatric Sudden Cardiac Arrest/Sudden Cardiac Death.** *Hum Genomics*. 2015; 9:15.

25. Li Q, Kirkendall ES, Hall ES, Ni Y, Lingren T, Kaiser M, Lingren N, Zhai H, Solti I, Melton K. **Automated Detection of Medication Administration Errors in Neonatal Intensive Care.** *J Biomed Inform*. 2015; 57:124-33.

26. Liu J, Ma J. **Modulation of Temporal Dynamics of Gene Transcription by Activator Potency in the Drosophila Embryo.** *Development*. 2015; 142:3781-90.

27. Lu Y, Lu Y, Deng J, Peng H, Lu H, Lu LJ. **A Novel Essential Domain Perspective for Exploring Gene Essentiality.** *Bioinformatics*. 2015; 31:2921-9.

28. Ma J, He F, Xie G, Deng WM. **Maternal Ap Determinants in the Drosophila Oocyte and Embryo.** *Wiley Interdiscip Rev Dev Biol*. 2016; 5:562-81.

29. Marsolo K, Margolis PA, Forrest CB, Colletti RB, Hutton JJ. **A Digital Architecture for a Network-Based Learning Health System: Integrating Chronic Care Management, Quality Improvement, and Research.** *EGEMS (Wash DC)*. 2015; 3:1168.

30. Matrka MC, Hennigan RF, Kappes F, DeLay ML, Lambert PF, Aronow BJ, Wells SI. **Dek over-Expression Promotes Mitotic Defects and Micronucleus Formation.** *Cell Cycle*. 2015; 14:3939-53.

31. Meyer SE, Qin T, Muench DE, Masuda K, Venkatasubramanian M, Orr E, Suarez L, Gore SD, Delwel R, Paietta E, Tallman MS, Fernandez H, Melnick A, Le Beau MM, Kogan S, Salomonis N, Figueroa ME, Grimes HL. **Dnmt3a Haploinsufficiency Transforms Flt3itd Myeloproliferative Disease into a Rapid, Spontaneous, and Fully Penetrant Acute Myeloid Leukemia.** *Cancer Discov*. 2016; 6:501-15.

32. Miethke AG, Zhang W, Simmons J, Taylor AE, Shi T, Shanmukhappa SK, Karns R, White S, Jegga AG, Lages CS, Nkinin S, Keller BT, Setchell KD. **Pharmacological Inhibition of Apical Sodium-Dependent Bile Acid Transporter Changes Bile Composition and Blocks Progression of Sclerosing Cholangitis in Multidrug Resistance 2 Knockout Mice.** *Hepatology*. 2016; 63:512-23.

33. Mo H, Thompson WK, Rasmussen LV, Pacheco JA, Jiang G, Kiefer R, Zhu Q, Xu J, Montague E, Carrell DS, Lingren T, Mentch FD, Ni Y, Wehbe FH, Peissig PL, Tromp G, Larson EB, Chute CG, Pathak J, Denny JC, et al. **Desiderata for Computable Representations of Electronic Health Records-Driven Phenotype Algorithms.** *J Am Med Inform Assoc*. 2015; 22:1220-30.

34. Morgan A, Mooney S, Aronow B, Brenner S. **Precision Medicine: Data and Discovery for Improved Health and Therapy.** *Pac Symp Biocomput*. 2016; 21:243-48.

35. Mrug M, Zhou J, Yang C, Aronow BJ, Cui X, Schoeb TR, Siegal GP, Yoder BK, Guay-Woodford LM. **Genetic and Informatic Analyses Implicate Kif12 as a Candidate Gene within the Mpkd2 Locus That Modulates Renal Cystic Disease Severity in the Cys1cpk Mouse.** *PLoS One*. 2015; 10:e0135678.

36. Namjou B, Marsolo K, Lingren T, Ritchie MD, Verma SS, Cobb BL, Perry C, Kitchner TE, Brilliant MH, Peissig PL, Borthwick KM, Williams MS, Grafton J, Jarvik GP, Holm IA, Harley JB. **A Gwas Study on Liver Function Test Using Emerge Network Participants.** *PLoS One*. 2015; 10:e0138677.

37. Nayak RC, Trump LR, Aronow BJ, Myers K, Mehta P, Kalfa T, Wellendorf AM, Valencia CA, Paddison PJ, Horwitz MS, Grimes HL, Lutzko C, Cancelas JA. **Pathogenesis of Elane-Mutant Severe Neutropenia Revealed by Induced Pluripotent Stem Cells.** *J Clin Invest*. 2015; 125:3103-16.

38. Pestian JP, Grupp-Phelan J, Bretonnel Cohen K, Meyers G, Richey LA, Matykiewicz P, Sorter MT. **A Controlled Trial Using Natural Language Processing to Examine the Language of Suicidal Adolescents in the Emergency Department.** *Suicide Life Threat Behav*. 2016; 46:154-9.

39. Pfluger PT, Kabra DG, Aichler M, Schriever SC, Pfuhlmann K, Garcia VC, Lehti M, Weber J, Kutschke M, Rozman J, Elrod JW, Hevener AL, Feuchtinger A, Hrabe de Angelis M, Walch A, Rollmann SM, Aronow BJ, Muller TD, Perez-Tilve D, Jastroch M, et al. **Calcineurin Links Mitochondrial Elongation with Energy Metabolism.** *Cell Metab*. 2015; 22:838-50.

40. Pogacar R, Plant E, Rosulek LF, Kouril M. **Sounds Good: Phonetic Sound Patterns in Top Brand Names.** *Mark Lett*. 2015; 26:549-63.

41. Prasath VBS, Fukuma K, Aronow BJ, Kawanaka H. **Cell Nuclei Segmentation in Glioma Histopathology Images with Color Decomposition Based Active Contours.** *Proceedings (IEEE Int Conf Bioinformatics Biomed)*. 2015:1734-36.

42. Ren S, Hinzman AA, Kang EL, Szczesniak RD, Lu LJ. **Computational and Statistical Analysis of Metabolomics Data.** *Metabolomics*. 2015; 11:1492-513.

43. Shinnar S, Cnaan A, Hu F, Clark P, Dlugos D, Hirtz DG, Masur D, Mizrahi EM, Moshe SL, Glauser TA, Childhood Absence Epilepsy Study Group. **Long-Term Outcomes of Generalized Tonic-Clonic Seizures in a Childhood Absence Epilepsy Trial.** *Neurology*. 2015; 85:1108-14.

44. Sigdel T, Bestard O, Salomonis N, Hsieh S, Torras J, Naesens M, Tran T, Roedder S, Sarwal M. **Intragraft Antiviral-Specific Gene Expression as a Distinctive Transcriptional Signature for Studies in Polyomavirus-Associated Nephropathy.** *Transplantation*. 2016.

45. Soreq L, Salomonis N, Israel Z, Bergman H, Soreq H. **Analyzing Alternative Splicing Data of Splice Junction Arrays from Parkinson Patients' Leukocytes before and after Deep Brain Stimulation as Compared with Control Donors.** *Genom Data*. 2015; 5:340-3.

46. Sumegi J, Nestheide S, Aronow B, Fletcher D, Keddache M, Villanueva J, Zhang K, Filipovich AH. **Microrna Activation Signature in Patients with Hemophagocytic Lymphohistiocytosis and Reversibility with Disease-Specific Therapy.** *J Allergy Clin Immunol*. 2016; 137:309-12.

47. Tan L, Holland SK, Deshpande AK, Chen Y, Choo DI, Lu LJ. **A Semi-Supervised Support Vector Machine Model for Predicting the Language Outcomes Following Cochlear Implantation Based on Pre-Implant Brain Fmri Imaging.** *Brain Behav*. 2015; 5:e00391.

48. Toledo CM, Ding Y, Hoellerbauer P, Davis RJ, Basom R, Girard EJ, Lee E, Corrin P, Hart T, Bolouri H, Davison J, Zhang Q, Hardcastle J, Aronow BJ, Plaisier CL, Baliga NS, Moffat J, Lin Q, Li XN, Nam DH, et al. **Genome-Wide Crispr-Cas9 Screens Reveal Loss of Redundancy between Pkmyt1 and Wee1 in Glioblastoma Stem-Like Cells.** *Cell Rep*. 2015; 13:2425-39.

49. Topol A, English JA, Flaherty E, Rajarajan P, Hartley BJ, Gupta S, Desland F, Zhu S, Goff T, Friedman L, Rapoport J, Felsenfeld D, Cagney G, Mackay-Sim A, Savas JN, Aronow B, Fang G, Zhang B, Cotter D, Brennand KJ. **Increased Abundance of Translation Machinery in Stem Cell-Derived Neural Progenitor Cells from Four Schizophrenia Patients.** *Transl Psychiatry*. 2015; 5:e662.

50. Unruh D, Srinivasan R, Benson T, Haigh S, Coyle D, Batra N, Keil R, Sturm R, Blanco V, Palascak M, Franco RS, Tong W, Chatterjee T, Hui DY, Davidson WS, Aronow BJ, Kalfa T, Manka D, Peairs A, Blomkalns A, et al. **Red Blood Cell Dysfunction Induced by High-Fat Diet: Potential Implications for Obesity-Related Atherosclerosis.** *Circulation*. 2015; 132:1898-908.

51. Venek V, Scherer S, Morency LP, Rizzo A, Pestian J. **Adolescent Suicidal Risk Assessment in Clinician-Patient Interaction: A Study of Verbal and Acoustic Behaviors.** *IEEE Trans Affect Comput*. 2016; PP.

52. Vitalone MJ, Sigdel TK, Salomonis N, Sarwal RD, Hsieh SC, Sarwal MM. **Transcriptional Perturbations in Graft Rejection.** *Transplantation*. 2015; 99:1882-93.

53. Watson J, Kinstler A, Vidonish WP, 3rd, Wagner M, Lin L, Davis KG, Kotowski SE, Daraiseh NM. **Impact of Noise on Nurses in Pediatric Intensive Care Units.** *Am J Crit Care*. 2015; 24:377-84.

54. Wu H, Manu, Jiao R, Ma J. **Temporal and Spatial Dynamics of Scaling-Specific Features of a Gene Regulatory Network in Drosophila.** *Nat Commun*. 2015; 6:10031.

55. Xu J, Liu H, Lan Y, Aronow BJ, Kalinichenko VV, Jiang R. **A Shh-Foxf-Fgf18-Shh Molecular Circuit Regulating Palate Development.** *PLoS Genet*. 2016; 12:e1005769.

Grants, Contracts, and Industry Agreements

Annual Grant Award Dollars

Investigator	Title	Sponsor	ID	Dates	Amount
Bruce Aronow, PHD	UDMAP) - Database and Website	National Institutes of Health (Western General Hospital, Human Genetics)	U01 DK092983	9/15/2011 - 8/31/2016	$53,000
Bruce Aronow, PHD	NHLBI Progenitor Cell Biology Consortium Bioinformatics	National Institutes of Health (University of Maryland (College Park))	U01 HL099997	5/1/2013 - 4/30/2016	$235,371
Bruce Aronow, PHD	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	$206,550
Michal Kouril, PHD	Data Coordination and Integration Center for LINCS-BD2K	National Institutes of Health (Mount Sinai Hospital)	U54 HL127624	9/29/2014 - 4/30/2019	$27,179
Long Lu, PHD	A Network-based Approach to Associate HDL	National Institutes of Health	R01 HL111829	8/1/2012 - 6/30/2016	$514,439

	Subspeciation with Function				
Long Lu, PHD	Targeting the Blood-Brain Barrier in Ischemic Stroke	National Institutes of Health (University of Cincinnati)	R15 NS088384	4/1/2015 - 3/31/2018	$38,700
Long Lu, PHD	Translational Repression and Aspergillus Fumigatus Virulence	National Institutes of Health (University of Cincinnati)	R21 AI111062	2/1/2015 - 1/31/2016	$11,718
Jun Ma, PHD	Regulation and Scaling of a Morphogen Gradient	National Institutes of Health	R01 GM101373	8/15/2012 - 7/31/2017	$290,700
Keith Marsolo, PHD	MEDTAPP Neonatal Abstinence Syndrome (NAS) - State	Ohio Department of Medicaid (ODM) (Ohio State University)	G-1617-05-0003	7/1/2015 - 6/30/2016	$6,596
Keith Marsolo, PHD	MedTapp Data Infrastructure (ODM Federal)	Ohio Depart of Jobs and Family Services (Ohio State University)	G-1617-05-0003	7/1/2015 - 6/30/2016	$257,175
Keith Marsolo, PHD	MedTapp Data Infrastructure (ODH State)	Ohio Department of Health (Ohio State University)	G-1617-05-0003	9/5/2015 - 6/30/2016	$147,811
Keith Marsolo, PHD	MEDTAPP Neonatal Abstinence Syndrome (NAS) - Federal	Ohio Department of Medicaid (ODM) (Ohio State University)	ODM201636	7/1/2015 - 6/30/2016	$15,400
Keith Marsolo, PHD	University of Pittsburgh Clinical and Translational Science Institute	National Institutes of Health (University of Pittsburgh)	UL1TR000005-09S1	1/1/2015 - 8/31/2015	$48,048
Nathan Salomonis, PHD	NHLBI Progenitor Cell Biology BioinformaticsCore	National Institutes of Health (University of Maryland (College Park))	U01 HL099997	7/1/2013 - 4/30/2016	$79,629
Nathan Salomonis, PHD	Dissecting the Role of RBM20 in Dilated Cardiomyopathy Using Isogenic iPSCs	National Institutes of Health (University of Maryland (College Park))	U01 HL099997; 10567	8/1/2014 - 4/30/2016	$149,712
Peter S. White;Eileen King, PHD	Administrative Coordinating Center: Cardiovascular Development and Pediatric Cardiac Genomics Consortia	National Institutes of Health	U01 HL131003	1/1/2016 - 12/31/2020	$3,252,500
Peter S. White	NBSTRN: Newborn Screening Translational Research Network	National Institutes of Health (American College of Medical Genetics Fdn)	HHSN275201300011C:00	6/1/2014 - 9/25/2018	$527,655

Total Annual Grant Award Dollars	**$5,862,183**