

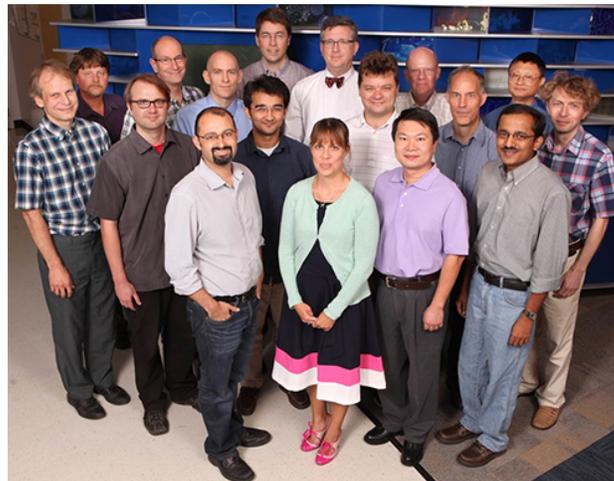
### Division Summary

#### RESEARCH AND TRAINING DETAILS

Number of Faculty	13
Number of Joint Appointment Faculty	11
Number of Research Fellows	6
Number of Research Students	11
Number of Support Personnel	107
Direct Annual Grant Support	\$2,182,122
Direct Annual Industry Support	\$414,547
Peer Reviewed Publications	54

#### CLINICAL ACTIVITIES AND TRAINING

### Division Photo



Row 1: N Salomonis, J Dexheimer, J Lu, A Jegga  
Row 2: M Kouril, M Weirauch, K Komurov, A Porollo,  
P White, J Meller  
Row 3: K Kaufman, B Aronow, E Kirkendall, M  
Wagner, A Spooner, J Hutton, J Ma

## Significant Accomplishments

### Novel methods for studying disease

**Bruce Aronow, PhD**, focuses on the 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.

**Anil Jegga, DVM**, focuses on the elucidation of gene regulatory networks and the interaction between genotype and phenotype using a variety of bioinformatics approaches. He has extensive experience in transcription factor and micro-RNA based gene regulatory mechanisms, gene polymorphism functional analysis, candidate disease gene identification and prioritization. His current interests include elucidating the regulatory mechanisms of p53 tumor suppressor network.

**Jason Lu, PhD**, is developing biomarkers to assess the risk of developing heart disease by combining proteomics experiments and computational prediction to discover subspecies in high density lipoproteins (HDL) that correlate with cardiovascular protection.

**Nathan Salomonis, PhD**, is breaking ground in pediatric cancer, cardiovascular disease and spinal cord injury by developing new software and algorithms to identify complex relationships from whole transcriptome data. The advent of single-cell genomic profiles has created many new opportunities for understanding how stem cells differentiate and how disease gene expression is regulated.

**Jun Ma, PhD**, is using computational tools to understand how cells in a developing embryo "know" where they

are located and what they will become.

### **Learning healthcare systems**

**Keith Marsolo, PhD**, and the learning networks informatics team have received a grant extension to expand and improve an electronic health record-linked registry they built for the ImproveCareNow Network. This 67-center group helps improve outcomes for children with Inflammatory Bowel Disease (IBD) by sharing learnings gleaned from collecting data at the point of care. The network's uses include identifying patients for clinical trials and supporting comparative effectiveness research. Marsolo and his team have also created several new versions of the pre-visit planning and population management reports that clinicians use for chronic care management.

### **Approaches for improving data-driven research, screening, and decision support**

**Michael Wagner, PhD**, and colleagues launched the C-MIND database, which contains MRI and neuropsychological evaluation data on normally developing children. This resource is available to the public and can be used as a healthy control group in clinical studies. His team is also developing methods to integrate and disseminate longitudinal clinical, observational, and genomic data for newborn screening disorders on a national scale through the Newborn Screening Translational Research Network.

**John Pestian, PhD, MBA**, and colleagues have been issued a patent for processes that optimize medication dosages for patients with refractory epilepsy. Their software application analyzes clinical linguistic characteristics of patients and their medical record to identify individuals who would best be treated by neurosurgery. Dr. Pestian has also launched a clinical trial to test a system that uses linguistics, acoustics and facial features to identify emergency room patients at very high risk of committing suicide.

**Imre Solti, MD, PhD**, and his team have applied the tools of natural language processing, machine learning and information extraction to develop an automated method for identifying patients for clinical trials and to detect medical errors in neonatal intensive care units. Solti's team also has developed algorithms linking genotypes and phenotypes in childhood obesity and autism.

**Stephen Spooner, MD, MS; Michal Kouril, PhD; Eric Kirkendall, MD, MBI; and Judith Dexheimer, PhD**, have collaborated to create a data warehouse to address growing concerns about alert fatigue. The data can be used to study how clinicians manage the load of decision-support alerts they receive when prescribing medications in the Cincinnati Children's system.

## **Research Highlights**

**Bruce Aronow, PhD & Anil Jegga, DVM, MRes**

The mission of Aronow/Jegga Lab is to develop predictive models of development-, disease- and drug- related phenotypes. To this effect, the lab continue 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. 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.

A newest addition from this group is AERSMine, a powerful phenotypic data source that represents a large and extremely valuable resource to explore relations of multiple factors with respect to drug safety issues in the US Food and Drug Administration's (FDA) Adverse Event Reporting System (AERS) data. AERS makes

drug-related adverse event (AE) data available to the community through the US Freedom of Information Act, but in a format that is not easy to access and mine. Through AERSMine, a robust and powerful web-datamine, these challenges are addressed by generating analyzable data matrices that can be filtered, clustered, and scored by a variety of approaches.

#### Michal Kouril, PhD

Research IT, under the oversight of Dr. Kouril, expanded its capacity to meet the demand and is now maintaining Petabyte size storage in a number of performance tiers including the fastest SSD-based used for most demanding applications, such as research data warehousing, virtual desktop infrastructure and some of the production servers. They have also built out the Research Disaster Recovery (DR) infrastructure to accommodate applications that are required from the business continuity perspective in the event of a disaster. In addition they have expanded the computational cluster and added cutting edge technology such as large GPU processing capability and high-core density teraFLOPS speed Intel Phi cards.

Dr. Kouril has continued his collaborations with several divisions. One notable collaboration is the five year R01 grant with the Division of Behavioral Medicine and Clinical Psychology (Jennie Noll, PI). The project is looking at online behavior of adolescent abused and non-abused teens to look for inappropriate and risky behavior. They have outfitted almost 50 laptops with a 3G modem and external antenna to give participants Internet access anywhere as well as to allow the laptops to constantly upload the basic information about the teen's online whereabouts such as URLs, search words, content keywords, etc. The computers are rotated every month and constantly feeding tens of thousands of data points a day, evaluated and processed through a number of blacklist databases, crowd sourced coding, etc.

#### Long (Jason) Lu, PhD

Jason Lu, PhD, focused 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) and correlate them with cardiovascular protection function. If these subspecies are successfully identified, they may serve as more accurate biomarkers to assess the risk of developing cardiovascular diseases. The expression level of these subspecies can also be elevated to reduce the risk of cardiovascular diseases.

Dr. Lu has also expanded his research to study pediatric brain disorders through analyzing brain MRI images. He recently published two papers in this area. He developed a novel local SIFT feature based algorithm to analyze structural MRI images. In another study he developed a novel two-layer classifier to integrate the features extracted from both structural MRI and functional MRI images, and achieved superior performance than existing methods. These algorithms will be important tools in aiding physicians in diagnosis and developing treatment plans.

Dr. Lu has established several pipelines for analyzing next-generation sequencing data through intramural collaborations, such as with Drs. Morrow and Hostetter's labs. His lab is now capable of performing data analysis for whole-genome sequencing, RNA-seq, metagenomics, exome-sequencing and ChIA-PET to assist collaborating investigators.

#### Jun Ma, PhD

Research performed by Dr. Ma's team focuses on understanding how cells in a developing embryo "know" where they are located and what they will become. Through quantitative experimental measurements, the team analyzes the properties of a concentration gradient of the morphogenetic protein Bicoid in the fruit fly embryo, and investigates how cells in the embryo make location-appropriate decisions through sensing the

nuclear concentration of Bicoid. In their latest studies, which appeared in *Nature Communications* (2013) and *Development* (2014), the team reported their new findings about how cells' developmental fates are properly adjusted to the activity of the Bicoid protein and the size of the embryo. The research in Dr. Ma's team was supported by grants from NIH and NSF.

#### Keith Marsolo, PhD

Dr. Marsolo and the learning networks informatics team successfully completed a grant from the Agency for Healthcare Research and Quality (AHRQ; R01 HS020024 – Hutton, PI) to develop and implement an electronic health record (EHR)-linked registry for the ImproveCareNow Network, a 67-center quality improvement and research network that focuses on improving the outcomes of children with Inflammatory Bowel Disease (IBD). Data are collected at point of care and uploaded to the registry, reducing the need for double data entry. This success was rewarded with an grant extension to increase the number of centers that are collecting data in the EHR, as well as develop methods to increase the amount of data that can be transferred, further reducing the need for double data entry. Dr. Marsolo and his team have created several new versions of the pre-visit planning and population management reports that are used for chronic care management, which have been well-received by the network.

This group is participating in three projects that are part of the Patient Centered Outcomes Research Institute's (PCORI) National Patient-Centered Clinical Research Network (PCORnet). The informatics team is participating in 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 CCHMC 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.

#### John Pestian, PhD, MBA

Dr. Pestian and his lab had several highlights for this past year. A major accomplishment is the issuance of US Patent Number 8,589,175 B2 - Optimization and Individualization of Medication Selection and Dosage. The invention provides population models, methods, and algorithms for targeting a dosing regimen or compound selection to an individual patient.

Other successes for the Pestian lab include: (1) the testing of spreading activation divergence by analyzing clinical linguistic characteristics to identify potential epilepsy neurosurgery candidates and, (2) the initiation of the nation's first prospective clinical trial testing a multimodal approach of linguistics, acoustics and facial features to identify suicidal patients.

#### 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 (AltAnalyze, LineageProfiler, GO-Elite, 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 Children's Hospital 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. The R21 EHR-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, the medication reconciliation project automated medication discrepancy detection between patients' discharge medication lists and medications in discharge summaries. The 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 alert data stretching back five years, into which we 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 our 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.

Michael Wagner, PhD

For Dr. Wagner, this last year marked the official launch of the C-MIND database, which was developed under contract for NICHD (Scott Holland, PI) with significant involvement from developers in the Division of Biomedical Informatics. C-MIND contains functional and anatomical MRI data as well as neuropsychological evaluation data on normally developing children ages 0-18. This resource is now available to the public and can be used, for example, as a healthy control group in clinical studies.

## Division Publications

1. Abonia JP, Wen T, Stucke EM, Grotjan T, Griffith MS, Kemme KA, Collins MH, Putnam PE, Franciosi JP, von Tiehl KF, Tinkle BT, Marsolo KA, Martin LJ, Ware SM, Rothenberg ME. **High prevalence of eosinophilic esophagitis in patients with inherited connective tissue disorders.** *J Allergy Clin Immunol.* 2013; 132:378-86.
2. Akdemir KC, Jain AK, Allton K, Aronow B, Xu X, Cooney AJ, Li W, Barton MC. **Genome-wide profiling reveals stimulus-specific functions of p53 during differentiation and DNA damage of human embryonic stem cells.** *Nucleic Acids Res.* 2014; 42:205-23.
3. Bessho K, Shanmukhappa K, Sheridan R, Shivakumar P, Mourya R, Walters S, Kaimal V, Dilbone E, Jegga AG, Bezerra JA. **Integrative genomics identifies candidate microRNAs for pathogenesis of experimental biliary atresia.** *BMC Syst Biol.* 2013; 7:104.
4. Bisio A, De Sanctis V, Del Vescovo V, Denti MA, Jegga AG, Inga A, Ciribilli Y. **Identification of new p53 target microRNAs by bioinformatics and functional analysis.** *BMC Cancer.* 2013; 13:552.
5. Brown EB, Layne JE, Zhu C, Jegga AG, Rollmann SM. **Genome-wide association mapping of natural variation in odour-guided behaviour in *Drosophila*.** *Genes Brain Behav.* 2013; 12:503-15.
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- perivascular adipocytes overexpress genes responsible for regulating vascular morphology, inflammation, and hemostasis.** *Physiol Genomics*. 2013; 45:697-709.
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  8. Cheung D, Miles C, Kreitman M, Ma J. **Adaptation of the length scale and amplitude of the Bicoid gradient profile to achieve robust patterning in abnormally large *Drosophila melanogaster* embryos.** *Development*. 2014; 141:124-35.
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  11. Feng Y, Huang W, Meng W, Jegga AG, Wang Y, Cai W, Kim HW, Pasha Z, Wen Z, Rao F, Modi RM, Yu X, Ashraf M. **Heat shock improves Sca-1+ stem cell survival and directs ischemic cardiomyocytes toward a prosurvival phenotype via exosomal transfer: a critical role for HSF1/miR-34a/HSP70 pathway.** *Stem Cells*. 2014; 32:462-72.
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  13. Gan Z, Wang J, Salomonis N, Stowe JC, Haddad GG, McCulloch AD, Altintas I, Zambon AC. **MAAMD: a workflow to standardize meta-analyses and comparison of affymetrix microarray data.** *BMC Bioinformatics*. 2014; 15:69.
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  17. Gordon SM, Deng J, Tomann AB, Shah AS, Lu LJ, Davidson WS. **Multi-dimensional co-separation analysis reveals protein-protein interactions defining plasma lipoprotein subspecies.** *Mol Cell Proteomics*. 2013; 12:3123-34.
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- pathology.** *Wound Repair Regen.* 2013; 21:530-44.
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26. Kirkendall ES, Spooner SA, Logan JR. **Evaluating the accuracy of electronic pediatric drug dosing rules.** *J Am Med Inform Assoc.* 2014; 21:e43-9.
27. Krishnan K, Ren Z, Losada L, Nierman WC, Lu LJ, Askew DS. **Polysome profiling reveals broad translome remodeling during endoplasmic reticulum (ER) stress in the pathogenic fungus *Aspergillus fumigatus*.** *BMC Genomics.* 2014; 15:159.
28. Lingren T, Deleger L, Molnar K, Zhai H, Meinzen-Derr J, Kaiser M, Stoutenborough L, Li Q, Solti I. **Evaluating the impact of pre-annotation on annotation speed and potential bias: natural language processing gold standard development for clinical named entity recognition in clinical trial announcements.** *J Am Med Inform Assoc.* 2014; 21:406-13.
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## Faculty, Staff, and Trainees

### Faculty Members

**John Hutton, MD**, Professor

**Leadership** Director, Division Chief

**Research Interests** Federated data sharing networks to support translational research

**Peter White, PhD**, Professor

**Leadership** Director, Department Chair

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

**Bruce Aronow, PhD**, Professor

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

**Anil Jegga, MS, DVM**, Associate Professor

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

**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

**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

**John 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, MA**, Assistant Professor

**Research Interests** Computational Linguistics

**S. Andrew Spooner, MD, FAAP**, Associate 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 Dexheimer, PhD**, Instructor (Emergency Medicine)

**Research Interests** Clinical Decision Support, Informatics

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

**Research Interests** Clinical Informatics, Knowledge Discovery Tools, Data Mining and Warehousing

**Kenneth Kaufman, PhD**, Professor (Center for Autoimmune Genomics – CAGE)

**Eric Kirkendall, MD**, Assistant Professor (Hospital Medicine)

**Research Interests** General Pediatrics, Clinical Informatics

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

**Research Interests** Bioinformatics, Cancer Biology

**Mario Medvedovic, PhD**, Associate Professor (UC Environmental Health)

**Research Interests** Biostatistics

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

**Research Interests** Computational biology; bioinformatics

**Alexander Towbin, MD**, Assistant Professor (Radiology and Medical Imaging)

**Research Interests** Radiology informatics; cancer imaging; abdominal imaging

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

**Research Interests** Protein Modeling

**Matthew Weirauch, PhD**, Assistant Professor (Rheumatology)

**Research Interests** Transcriptional Regulation, Bioinformatics, Functional Genomics

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

**Research Interests** Bioinformatics; Systems Biology

#### Trainees

- **Jacek Biesiada, PhD**, 2000, University of Silesia, Poland
- **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

- **Junbo Liu, PhD**, 2000, Fudan University, Shanghai, China
- **Yizhao Ni, PhD**, 2010, University of Southampton, Southampton, UK
- **Mayur Sarangdhar, PhD**, 2011, University of Hull, Hull, UK
- **Haijun Zhai, PhD**, 2010, University of Science and Technology of China, Hefei, Anhui Province, China

## Division Collaboration

Dr. Marsolo and his team are developing a web application that will facilitate the communication and pre-visit planning activities for patients within the Cancer and Blood Diseases Institute that are being seen by the Psychosocial Care Team. (Keith Marsolo, PhD)

**Center for Adherence and Self-Management** » Ahna Pai, PhD

Dr. Salomonis is collaborating with Dr. Barski with the analysis and functional interpretation of distinct human T-cell subsets using RNA-Seq. (Nathan Salomonis, PhD)

**Allergy and Immunology** » Artem Barski, PhD

Dr. Kouril, as Co-Investigator on an R01 grant studying Internet and media use in the teenage population is leading efforts to develop hardware and software that will allow naturalistic observation of adolescents' "Internet Footprint". (Michal Kouril, PhD)

**Behavioral Medicine and Clinical Psychology** » Jennie Noll, PhD

Drs. Hutton, Marsolo, Solti, and Wagner are providing informatics support for Cincinnati Children's participation in the electronic MEical Records and GENomics (eMERGE) Network. Cincinnati Children's Hospital Medical Center, in collaboration with colleagues from Boston Children's, is looking at correlations between EMR-derived phenotypes and genotypes. Dr. Marsolo and his team have been working to establish a federated SHRINE network between Cincinnati Children's and Boston Children's, allowing de-identified queries to be executed between the two institutions.

Dr. Marsolo continues to provide consultation and advice to the Biomedical Informatics staff that support the institutional biorepository software used by the Cincinnati Children's biobank as well as other investigators. Included in this effort has been the development of tools to support the Better Outcomes for Children (BOfC) project, which collects residual clinical samples for research purposes from patients who have provided consent. Dr. Marsolo and his team created an application that allows biobank staff to scan a clinical sample and determine whether it can be retained for research purposes. This functionality was added to allow investigators to search for and request samples using the institution's de-identified i2b2 warehouse. (John Hutton, PhD, Keith Marsolo, PhD, Imre Solti MD, PhD, Michael Wagner, PhD)

**Center for Autoimmune Genomics and Etiology (CAGE)** » John B. Harley, MD, PhD

Dr. Pestian collaborates with the CTC looking for novel approaches to disseminate the laboratories innovations. (John P. Pestian, PhD, MBA)

**Center for Technology Commercialization** » Nicole Robinson, PhD

Dr. Ma collaborates with Dr. Kopan to study individual cells' decisions of gene transcription in response to Notch. (Jun Ma, PhD)

**Developmental Biology** » Rafi Kopan, PhD

Dr. Salomonis is collaborating with Dr. Yoshida in the analysis of distinct nervous system cell populations using RNA-Seq. (Nathan Salomonis, PhD)

**Developmental Biology** » Yutaka Yoshida, PhD

Dr. Salomonis is collaborating with Dr. Kopan in the evaluation of single-cell kidney progenitor profiles using RNA-Seq to identify cell subsets defined by distinct gene and splicing profiles. (Nathan Salomonis, PhD)

**Developmental Biology** » Rafi Kopan, PhD

Dr. Aronow's group collaborates with Drs. Potter and Lessard along with an international consortium on the use of genomics analyses to gain insight into the normal or abnormal development of the kidney and lower urinary tract. (Bruce J. Aronow, PhD)

**Developmental Biology** » James Lessard, PhD and S. Steven Potter, PhD

Dr. Spooner collaborates with the Emergency Medicine Department to develop a program where users can forward proposed edits to drug-dosing data in order to demonstrate the efficacy of user feedback as a part of the prescribing process. (Stephen A. Spooner, MD, MS, FAAP)

**Emergency Medicine** »

Dr. Pestian and his team are collaborating with Dr. Grupp-Phelan in the development of decision support tools to measure the likelihood of repeated suicide attempts. (John P. Pestian, PhD, MBA)

**Emergency Medicine** » Jacqueline M. Grupp-Phelan, MD, MPH

Dr. Salomonis is a collaborator via the Progenitor Cell Biology Consortium and the associated cell characterization core. The goal of the consortium is to evaluate bulk and single cell transcriptomes, genomes and epigenomes across distinct induced pluripotent stem cell lines and their differentiated lineage derivatives. Outside of the consortium, Dr. Salomonis collaborates with Dr. Lutzko's group to prototype a new experimental assay using single cell RNA profiling for cells with disease implicated mutations. (Nathan Salomonis, PhD)

**Experimental Hematology** » Carolyn Lutzko, PhD

Dr. Salomonis is collaborating with Dr. Grimes to evaluate single-cell monocyte progenitor profiles using RNA-Seq to identify cell subsets defined by distinct gene and splicing profiles. (Nathan Salomonis, PhD)

**Experimental Hematology** » Leighton Grimes, PhD

Dr. Salomonis is collaborating with Dr. Starczynowski in the analysis of alternative splicing microarray expression data and splicing factor regulation prediction analysis relevant to MDS. (Nathan Salomonis, PhD)

**Experimental Hematology** » Daniel Starczynowski, PhD

Dr. Jegga collaborates with Bezerra Lab to understand the molecular basis of biliary atresia, a rare condition in newborn infants which if unrecognized could lead to liver failure. He provides bioinformatic support that includes data analysis, data-mining and hypothesis generation using systems biology-based approaches. (Anil Goud Jegga, DVM, MRes)

**Gastroenterology, Hepatology and Nutrition** » Jorge Bezerra, MD

Dr. Aronow serves as the Bioinformatics Core Director on the Digestive Health Center: Bench to Bedside Research in Pediatric Digestive Disease grant project. His role is to aid or supervise in strategic planning,

experimental designs, data analysis, and to generate a data portal for the genomics data and sample characterizations. (Bruce J. Aronow, PhD)

**Gastroenterology, Hepatology and Nutrition** » Jorge Bezerra, MD

Dr. Jegga collaborates with the Hinton Lab in their mission to understand the genetic regulation of thoracic aortic aneurysm progression and examine the role of genetic pathways in the initiation and progression of aortopathy in mouse and human. Dr. Jegga assists with the functional genomic analyses of the data generated from the aortopathy model systems. (Anil Goud Jegga, DVM, MRes)

**Heart Institute** » Robert Hinton, MD

Dr. Marsolo and his team created the first version of an i2b2-based web portal that will allow external users to browse phenotypic and genotypic information on patients with pulmonary arterial hypertension (PAH). After a cohort has been identified, users can send a request for data and samples to the PAH biorepository, which will then service the request. (Keith Marsolo, PhD)

**Human Genetics** » William C. Nichols, PhD

Dr. Aronow is a leading expert in the design and analysis of DNA microarrays, including Incyte and Affymetrix technologies. His collaboration efforts with Dr. Prows include microarray design, oversight in all aspects of microarray analysis, including data sorting and data analysis. Additionally, Dr. Aronow oversees the in-depth in silico analyses and generates appropriate figures, tables and the related text for manuscript preparation. (Bruce J. Aronow, PhD)

**Human Genetics** » Daniel R. Prows, PhD

Dr. Marsolo and the i2b2 team have worked with colleagues in Emergency Medicine to identify and extract data from the electronic health record so that it can be uploaded into the expanded version of the Pediatric Emergency Care Applied Research Network (PECARN) registry. The i2b2 team has successfully transmitted a full year's worth of Emergency Department data to the coordinating center and is working to pilot test a de-identification process for full-text data elements. (Keith Marsolo, PhD)

**James M. Anderson Center for Health Systems Excellence** » Evaline Alessandrini, MD, MSCE

**Emergency Medicine** » Evaline Alessandrini, MD, MSCE

Dr. Marsolo and his team developed data collection forms and reports for new projects of the quality improvement networks that are part of the State of Ohio's BEACON initiative (Best Evidence for Advancing Childhealth in Ohio Now), including the Ohio Perinatal Quality Collaborative (OPQC), where Dr. Lannon is co-PI. In the case of OPQC, this includes a new to improve outcomes of children with Neonatal Abstinence Syndrome, a growing concern among newborns in Ohio. (Keith Marsolo, PhD)

**James M. Anderson Center of Excellence** » Carole Lannon, MD, MPH

Dr. Marsolo and his team are developing a more modular data collection and reporting infrastructure for the Solutions for Patient Safety collaborative, a network that is focused on reducing serious safety events. These new modifications will make it easier for the network to pilot new measures within the collaborative, speeding the time to implementation. (Keith Marsolo, PhD)

**James M. Anderson Center of Excellence** » Stephen E. Muething, MD

Dr. Marsolo and his team continue to support the quality improvement and research efforts of the ImproveCareNow

Network, which focuses on improving the outcomes of children with Inflammatory Bowel Disease (IBD). They are extending the registry of ImproveCareNow to allow more data to be uploaded directly from the electronic health record (EHR), reducing the amount of data that must be entered via double data entry. They are also working to increase the number of centers that are collecting registry data in the EHR, with over a dozen centers now actively transferring data. Dr. Marsolo and his team have also created several new versions of the pre-visit planning and population management reports that are used for care management, which have been well-received by the network.

This group is also participating in three projects that are part of the Patient Centered Outcomes Research Institute's (PCORI) National Patient-Centered Clinical Research Network (PCORnet). The informatics team is participating in two Clinical Data Research Network (CDRN) awards, as well as a Patient-Powered Research Network (PPRN). Dr. Margolis is co-PI of one of the CDRNs and the PPRN. Among the various required tasks of these awards, Dr. Marsolo and his team will create standardized extracts of EHR data for CCHMC 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. (Keith Marsolo, PhD)

**Gastroenterology, Hepatology and Nutrition** » Shehzad Saeed, MD, FAAP, AGAF.

**James M. Anderson Center for Health Systems Excellence** » Peter Margolis, MD, PhD

**Pulmonary Medicine** » Michael Seid, PhD

Dr. Salomonis is collaborating with Dr. Rindler in the analysis of restrictive cardiomyopathy disease RNA-Seq profiles. (Nathan Salomonis, PhD)

**Molecular Cardiovascular Biology** » Tara Rindler, PhD

Dr. Lu and his team work closely with Dr. Xu in developing statistical models to analyze gene expression during the development of mouse models with the goal of understanding the role of SREBP network in surfactant lipid homeostasis and lung maturation. (Long (Jason) Lu, PhD)

**Section of Neonatology, Perinatal and Pulmonary Biology** » Yan Xu, PhD

Dr. Lu works with Dr. Morrow's on a program project "The Role of Human Milk in Infant Nutrition and Health." The research is designed to transform the fundamental understanding of human milk glycans and infant glycans in relation to disease risk and translate our discoveries into novel therapeutics, dietary interventions, and diagnostic tools that improve infant and child health. (Long (Jason) Lu, PhD)

**Section of Neonatology, Perinatal and Pulmonary Biology** » Ardythe L. Morrow, PhD

Drs. Aronow and Wagner serve as Co-Investigators on Dr. Prasad Devarajan's Pediatric Center Excellence in Nephrology grant entitled "Critical Translational Studies in Pediatric Nephrology", where the goal is to support basic, translational, and clinical research on critical pediatric kidney diseases that have major unmet needs. The overarching theme of the Cincinnati Children's PCEN is to conduct innovative and high-impact bench-to-bedside studies on three critical but underserved pediatric kidney diseases. The three areas of focus at Cincinnati Children's include acute kidney injury, focal segmental glomerulosclerosis, and lupus nephritis. Dr. Aronow serves as the Bioinformatics Core lead and Dr. Wagner is part of the proteomics core led by Dr. Ken Greis. (Bruce J. Aronow, PhD, Michael Wagner, PhD)

**Nephrology** » Prasad Devarajan, MD

Dr. Wagner, in his role of informatics lead on an NICHD contract ("Cincinnati MRI Imaging Neuronal

Development", Dr. Holland, PI), collaborates with the PI and Dr. VanNest (Division. of Neurology) to build and disseminate a database of fMRI images of normally developing brains. (Michael Wagner, PhD)

**Imaging Research Center** » Scott Holland, PhD

**Neurology** » Jennifer VanNest, PhD

Dr. Pestian and his team are collaborating with Dr. Byars on innovations in neuropsychology research. (John P. Pestian, PhD, MBA)

**Neurology** » Anna Weber Byars, PhD, ABPP-Cn

Dr. Pestian and his team are collaborating with the Neurology team for the on-going development of CHRISTINE, a clinical decision support system for identifying optimal drug therapy for patients with epilepsy, and ADHD. (John P. Pestian, PhD, MBA)

**Neurology** » Hansel Greiner, MD, Katherine D. Holland, MD, PhD, and Shannon M. Standridge, MPH, DO

Dr. Pestian and his team are collaborating with the Neurosurgery department to develop novel NLP algorithms related to epilepsy neurosurgery. (John P. Pestian, PhD, MBA)

**Neurosurgery** » Francesco T. Mangano, DO, FACS, FACOS

Dr. Salomonis collaborates with Dr. Kamath on unbiased identification of cell free RNAs and their cell of origin from term, preterm and prenatal amniotic fluid. This will be used to identify novel biomarkers for distinct neonatal morbidities (respiratory, feeding, neurological, infection) as well as novel informatics tools for cell of origin. (Nathan Salomonis, PhD)

**Perinatal Institute** » Beena B. Kamath-Rayne, MD, MPH

Dr. Salomonis collaborates with Dr. Muglia to identify glucocorticoid receptor target splicing and gene expression changes that may contribute to early life stress. (Nathan Salomonis, PhD)

**Perinatal Institute** » Louis J. Muglia, MD, PhD

Dr. Salomonis is collaborating with Dr. Kallapur with the analysis and functional interpretation of distinct Rhesus Macaque placental viral inflammation associated preterm labor initiating events using RNA-Seq. (Nathan Salomonis, PhD)

**Perinatal Institute** » Suhas Kallapur, MD

Dr. Lu serves as a Co-Investigator on Dr. Clancy's R01 grant entitled "MR Predictors of Infection, Inflammation and Structural Lung Damage in CF", where the goal is to develop new tools needed to monitor early lung disease, and to bring new therapies to infants and toddlers with Cystic Fibrosis. On this grant project, the team uses new imaging and blood-based technologies to improve our ability to monitor lung status in young children with CF. (Long (Jason) Lu, PhD)

**Pulmonary Medicine** » John P. Clancy, MD

Dr. Pestian and his team are collaborating with Dr. Sorter in the development of decision support tools to measure the likelihood of repeated suicide attempts. (John P. Pestian, PhD, MBA)

**Psychiatry** » Michael T. Sorter, MD

Dr. Jegga collaborates with the Dey Lab and Das Lab in their mission to understand the signaling networks that influence uterine biology in the context of embryo-uterine interactions during pregnancy and delivery. He is

specifically focusing on the miRNA-based regulation of implantation, labor, and pre-term birth. (Anil Goud Jegga, DVM, MRes)

**Reproductive Sciences** » Sudhansu K. Dey, PhD and Sanjoy K. Das, PhD

Dr. Wagner, as Director of the Informatics Core of the NIAMS-sponsored Cincinnati Core Center for Rheumatic Diseases (Dr. Thompson, PI), collaborates closely with Investigators Drs. Thompson and Harley on genome-wide analyses of variants contributing to juvenile rheumatic disease. (Michael Wagner, PhD)

**Rheumatology** » Susan Thompson, PhD

**Center for Autoimmune Genomics and Etiology (CAGE)** » John B. Harley, MD, PhD

Dr. Pestian and his team are collaborating with the surgery department to develop novel NLP algorithms. (John P. Pestian, PhD, MBA)

**Pediatric General and Thoracic Surgery** » Richard G. Azizkhan, MD

## Grants, Contracts, and Industry Agreements

Grant and Contract Awards	Annual Direct
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### ARONOW, B

**A Genitourinary Development Molecular Anatomy Project - Database and Website**

National Institutes of Health(Western General Hospital)

R01 DK 092983	09/30/11-08/31/16	\$34,640
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**Generating Molecular Markers that Subjectively Label Urothelial Sub-Populations**

National Institutes of Health(Columbia University Medical Center)

U01 DK 094530	09/30/11-08/31/16	\$6,000
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**NHLBI Progenitor Cell Biology Consortium Bioinformatics Core**

National Institutes of Health(University of Maryland)

U01 HL 099997	05/01/13-04/30/16	\$150,701
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**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)

	07/01/13-06/30/16	\$13,072
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**Digestive Health Center: Bench to Bedside Research in Pediatric Digestive Disease - Bioinformatics Core**

National Institutes of Health

P30 DK 078392	06/01/12-05/31/17	\$98,924
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**Molecular and Spacial Mapping of Bladder Nociceptors During Development and Maturation**

National Institutes of Health(University of Melbourne)

U01 DK 101029	09/23/13-08/31/14	\$47,326
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### HUTTON, J

**Cincinnati Center for Clinical and Translational Sciences and Training - Informatics Core**

National Institutes of Health(University of Cincinnati)

UL1 RR 026314	04/03/09-03/31/15	\$145,054
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### LU, L

**A Network-Based Approach to Associate HDL Subspeciation with Function**

National Institutes of Health

R01 HL 111829 08/01/12-06/30/17 \$403,691

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**MA, J****Regulation and Scaling of a Morphogen Gradient**

National Institutes of Health

R01 GM 101373 08/15/12-06/30/17 \$183,350

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**MARSOLO, K****Implementation of the BEACON Quality Improvement Data Infrastructure - Federal**

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

09/23/11-06/30/16 \$238,907

**Implementation of the BEACON Quality Improvement Data Infrastructure - State**

Ohio Department of Health(Ohio State University)

08/01/13-06/30/16 \$119,274

**MEDTAPP Neonatal Abstinence Syndrome (NAS) - Federal**

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

01/14/14-06/30/15 \$19,145

**MEDTAPP Neonatal Abstinence Syndrome (NAS) - State**

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

01/14/14-06/30/15 \$8,088

**Scalable Collaboration Infrastructure for a Learning Healthcare System**

Patient-Centered Outcome Research Institute(Harvard University)

CDRN-1306-04608 04/01/14-09/30/15 \$27,085

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**PESTIAN, J****Multi-Institutional Pediatric Epilepsy Decision Support**

National Library of Medicine

R01 LM 011124 07/22/11-06/30/14 \$241,590

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**SALOMONIS, N****NHLBI Progenitor Cell Biology Consortium Bioinformatics Core**

National Institutes of Health(University of Maryland)

U01 HL 099997 07/01/13-04/30/16 \$41,332

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**SOLTI, I****EHR-Based Patient Safety: Automated Error Detection in Neonatal Intensive Care**

National Institutes of Health

R21 HD 072883 08/01/12-07/31/14 \$166,075

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**WAGNER, M****Cincinnati Rheumatic Disease Core - Core 4**

National Institutes of Health

P30 AR 047464	08/25/11-06/30/16	\$56,957
<b>Gene Expression in Pediatric Arthritis - Core B</b>		
National Institutes of Health		
P01 AR 048929	09/01/11-08/31/16	\$180,911
		<b>Current Year Direct</b>
		<b>\$2,182,122</b>

#### Industry Contracts

##### MARSOLO, K

Ohio Children's Hospital Association Foundation		\$414,547
		<b>Current Year Direct Receipts</b>
		<b>\$414,547</b>

#### Funded Collaborative Efforts

##### ARONOW, B

###### Global Gene Expression Atlas of Craniofacial Development

National Institutes of Health

Potter, S 09/21/09-04/30/14 5%

###### Critical Translational Studies in Pediatric Nephrology

National Institutes of Health

Devarajan, P 09/21/12-08/31/17 4%

###### Genetic Analysis of Murine Chronic Hypoxia-Induced Pulmonary Hypertension

National Institutes of Health

Nichols, W 04/01/10-03/31/14 5%

###### Genotype-Phenotype Associations in Pediatric Cardiomyopathy

National Institutes of Health

Ware, S 04/01/13-03/31/16 5%

###### Risk Stratification and Identification of Immunogenetic and Microbial Markers of Rapid Disease Progression in Children with Crohn's Disease

Crohn's and Colitis Foundation

Denson, L 07/01/13-06/30/17 5%

###### Molecular Genetic Analysis of Craniofacial Development

National Institutes of Health

Jiang, R 07/01/13-06/30/16 4%

###### Genetics, Mechanisms and Clinical Phenotypes of Arrhythmogenic Cardiomyopathy

National Institutes of Health

Towbin, J 08/23/13-06/30/18 5%

###### Molecular Patterning of Mammalian Dentition

National Institutes of Health

Jiang, R 09/12/13-06/30/18 5%

###### Lung MAP Atlas Research Center

National Institutes of Health

Whitsett, J Potter, S 06/15/14-04/30/19 5%

**Molecular Atlas of Lung Development**

National Institutes of Health

Whitsett, J 06/15/14-04/30/19 7%

**Single Cell/RNA-Seq Dessection of Human iPS Cell Development Into Intestine**

National Institutes of Health

Potter, S Wells, J 09/20/13-07/31/17 5%

**JEGGA, A****Biological Basis of Phenotypes and Clinical Outcomes of Biliary Atresia**

National Institutes of Health

Bezerra, J 09/01/09-08/31/14 5%

**Digestive Health Center: Bench to Bedside Research in Pediatric Digestive Diseases - Bioinformatics Core**

National Institutes of Health

Bezerra J 06/01/12-05/31/17 10%

**Molecular Genetic Analysis of Craniofacial Development**

National Institutes of Health

Jiang, R 07/01/13-06/30/15 5%

**NHLBI Progenitor Cell Biology Consortium Systems Biology Bioinformatics Core**

National Institutes of Health

Aronow, B 05/01/13-04/30/16 20%

**Role and Regulation of the Human DEK Proto-Oncogene**

National Institutes of Health

Wells, S 07/01/13-06/31/15 5%

**KOURIL, M****Abused and Non-abused Females' High-risk Online Behaviors: Impact on Development**

National Institutes of Health

Noll, J 07/01/12-06/30/17 25%

**Cincinnati Center for Clinical and Translational Sciences and Training**

National Institutes of Health

Heubi, J 04/03/09-03/31/15 15%

**LU, L****Role of SREBP Network in Surfactant Lipid Homeostasis and Lung Maturation**

National Institutes of Health

Xu, Y 07/01/11-06/30/16 10%

**MR Predictors of Infection, Inflammation and Structural Lung Damage in CF**

National Institutes of Health

Clancy, J 10/01/12-09/30/16 20%

**Balance of Th17 Cells and Tregs in Candida albicans Vaginal Colonization in Pregnant Macaques and Humans**

Gates Foundation

Hostetter, M 10/01/13-09/30/15 25%

**The Role of Human Milk in Infant Nutrition and Health**

National Institutes of Health		
Morrow, A	08/01/13-07/31/14	5%
<b>MARSOLO, K</b>		
<b>Cincinnati Center for Clinical and Translational Sciences and Training</b>		
National Institutes of Health		
Heubi, J	04/03/09-03/31/15	15%
<b>Better Outcomes for Children: GWAS and PheWAS in eMERGEII</b>		
National Institutes of Health		
Harley, J	05/01/12-04/30/15	11%
<b>National Biological Sample and Data Repository for Pulmonary Arterial Hypertension</b>		
National Institutes of Health		
Nichols, W	03/03/12-02/28/17	5%
<b>Open Source Science: Transforming Chronic Illness Care</b>		
National Institutes of Health		
Margolis, P	09/30/09-08/31/14	3%
<b>Enhancing the Sustainability of a Pediatric Learning Health System</b>		
National Institutes of Health		
Margolos, P	09/30/13-09/29/15	20%
<b>A National Pediatric Learning Health System</b>		
PCORI		
Margolis, P	01/01/14-06/30/15	12%
<b>ImproveCareNow: A Learning Health System for Children with Crohn's Disease and Ulcerative Colitis</b>		
PCORI		
Margolis, P	01/01/14-06/30/15	5%
<b>Improving the Quality of Pediatric Emergency Care Using an Electronic Medical Record Registry and Clinician Feedback</b>		
AHRQ		
Alessandrini, E	09/30/11-09/29/16	0%
<b>PESTIAN, J</b>		
<b>Impact of Initial Therapy and Response on Long Term Outcome in Children with CAE</b>		
National Institutes of Health		
Glauser, T	09/01/10-08/31/14	15%
<b>SOLTI, I</b>		
<b>Better Outcomes for Children: GWAS and PheWAS in eMERGEII</b>		
National Institutes of Health		
Harley, J	05/01/12-04/30/15	11%
<b>WAGNER, M</b>		
<b>Cincinnati Center for Clinical and Translational Sciences and Training</b>		
National Institutes of Health		
Heubi, J	04/03/09-03/31/14	15%

**The Genetic Linkage in Lupus**

National Institutes of Health

Harley, J 10/27/10-02/28/15 10%

**Pediatric Functional Neuroimaging Research Network**

National Institutes of Health

Holland, S 09/28/09-09/27/14 20%

**Critical Translational Studies in Pediatric Nephrology**

National Institutes of Health

Devarajan, P 09/21/12-08/31/17 5%

**Better Outcomes for Children: GWAS and PheWAS in eMERGEII**

National Institutes of Health

Harley, J 05/01/12-04/30/15 10%

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**Total \$2,596,669**