

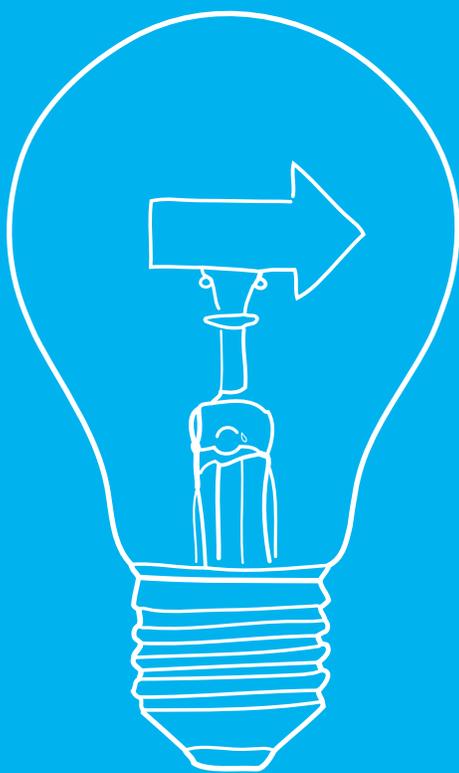


INNOVATION REPORT

Partnering to Change the Outcome



INNOVATION REPORT



About Cincinnati Children's

Cincinnati Children's Hospital Medical Center is a world-leading pediatric institution with a powerful research engine that is on the forefront of innovation. With nearly 900 faculty in over one million square feet of research space, Cincinnati Children's investigators have active research across more than 50 academic divisions. The output of this extensive research is a constantly evolving, robust pipeline and portfolio of novel therapeutics, diagnostics, medical devices, software/HIT and research tools.

Cincinnati Children's Center for Technology Commercialization (CTC) is actively forming partnerships with industry to bring its research discoveries to the market where they can have the greatest impact. Whether it's a traditional licensing deal, sponsored research agreement, or a more creatively structured deal, the CTC is flexible in how it collaborates with industry.

Our Team

Leadership

Niki Robinson, PhD Assistant Vice President

Technology Management

Korie Counts, PhD Director of Technology Management
Jon Brophy, MSE Senior Technology Manager
David Friedmann, PhD Technology Manager
Chalonda Handy, PhD Technology Manager
Justin Levy, JD Technology Manager
Tiffany Zerby, JD Technology Manager
Olivia Ballard, JD Technology Associate
Mel Biddulph Technology Coordinator

Project Management

Abbie Chandler, MHA Project Manager

Marketing

Michael Pistone Marketing Manager
Danielle Gray, MHSA* Market Analyst

Business Development

Hilary Hehman, MS, JD* Business Development Manager
Chris Stahl, MHSA Business Development Manager

Operations

Sonya Bridgeman, MBA Business Manager
Karen Boghossian Technology Data Analyst
Denise Clift Senior Administrative Assistant
Donna Phillips Administrative Assistant

*not pictured below



Contents

3	Innovations Report
4	Research & Discovery
8	Disclosures
10	Incubating Technologies
12	Protecting our Intellectual Property
16	Research Advancement
24	Available Technologies
20	Collaborations & Successes

INNOVATIONS REPORT

“pipeline offers promise...potential” – “smart collaborations are key”

Pipelines have a way of transforming things. From an infrastructure standpoint, pipelines have transformed the way we live by bringing resources to people and communities. In business, a pipeline can cause an organization to transform strategies based on “what’s to come.” At Cincinnati Children’s, our pipeline of new technologies—an array of therapeutics, diagnostics, medical devices, healthcare IT and research tools—offers promise

and potential to transform patient lives and the healthcare industry.

This year, we’ve seen a lot of encouraging changes in both the healthcare landscape as well as within our institution, and specifically our pipeline of innovations.

While securing traditional funding for early stage research has become more and more difficult, it’s caused research institutions and pharma and biotech companies to work together to ensure innovative research has the resources it needs to be commercially viable. This trend has caused us to create internal funding programs like our Innovation Fund; as well as, pursue risk-sharing models of collaboration with our industry partners, like our rare disease collaboration with Alexion Pharmaceuticals.

We’ve also seen—and are embracing—the future of gene therapy and its game-changing potential. We’re excited about Dr. Punam Malik’s corrective gene therapy for Sickle Cell Disease, which has entered its Phase I/II clinical trial and the many other gene therapy technologies currently under development in our labs.

We continue to see promising therapeutics and diagnostics enter our pipeline as well as innovative software and healthcare IT solutions. We’re developing commercialization strategies around these technologies individually as well as by therapeutic area.

We believe smart collaborations are key to advancing our technologies from the bench to the bedside, and together, with our partners, we continue to strive to be the leader in pediatric healthcare innovations.



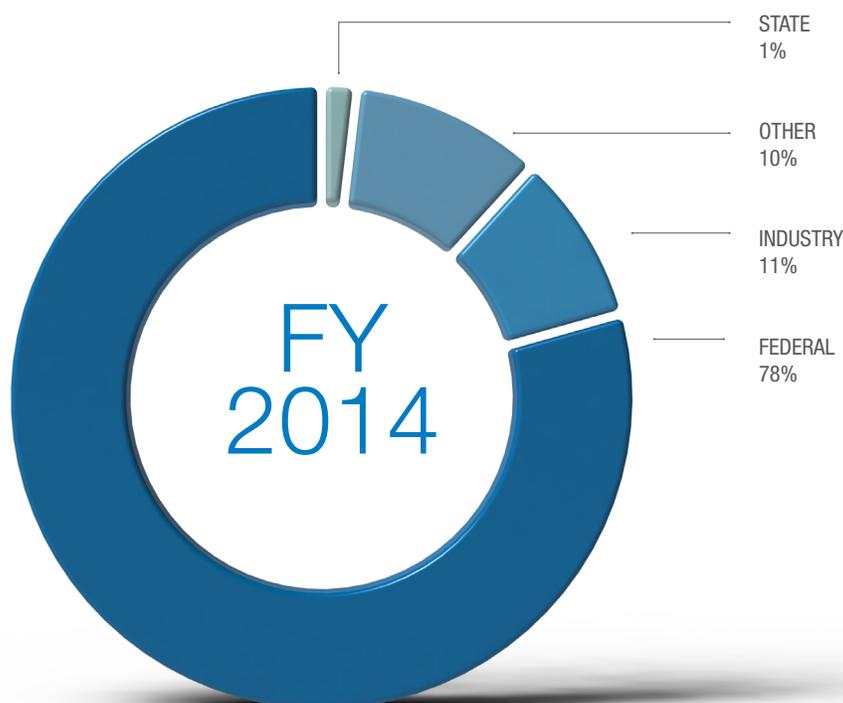
A handwritten signature in black ink, appearing to read 'Niki Robinson'.

Niki Robinson, PhD
Assistant Vice President

Research & Discovery

We are very fortunate at Cincinnati Children's to have some of the world's most innovative researchers and clinicians, focused on nearly every area of life science. Here is a snapshot of

just a few of our faculty members that are filling our pipeline with novel technologies capable of changing the outcome for patients in Cincinnati and around the world.



Distribution of Funding FY2014

SINGH PLANS TO ESTABLISH A CENTER FOR SYSTEMS IMMUNOLOGY

Our new Director of Immunobiology brings a strong dose of private sector experience to Cincinnati Children's as we transform the research methods that support new drug development.

Harinder Singh, PhD, joined us this fall after working since 2009 in the Department of Discovery Immunology at Genentech in San Francisco, where his roles included overseeing drug discovery and development projects. Before that, he worked for six years at the University of Chicago, where he was the Louis Block Professor of Molecular Genetics and Cell Biology, an investigator with the Howard Hughes Medical Institute, and Chair of the Committee on Immunology.

Our reconstituted Division of Immunobiology includes 15 faculty members who study the complex molecular mechanisms at work in the body's immune system. Their work is advancing our understanding of allergic asthma, type 1 diabetes, non-alcoholic fatty liver disease, and how the immune system responds to many other diseases.

Singh is an expert on regulatory molecules that enable pluripotent hematopoietic stem cells to generate various cells of the immune system. His group has identified key regulatory proteins that control cell generation in the immune system. Now his group is looking for candidate compounds that can influence how these proteins function, which could lead to improved treatments for a number of immune-related diseases.

Singh also is working to bring an important new element to the division: a Center for Systems Immunology. This growing area of research, fueled by recent leaps in computing power, explores how large networks of genes interact as systems rather than studying the functions of one gene at a time. By applying this approach, Singh and colleagues hope to identify entirely new targets for drug development.

Singh earned his PhD in Biochemistry and Molecular Biology in 1984 from Northwestern University and completed a post-doctoral fellowship in cancer research at the Massachusetts Institute of Technology in 1988.

He has authored more than 50 research papers, articles and book chapters and served as editor of *Molecular and Cel-*

lular Biology from 1997-2007. He has presented at scientific meetings throughout the United States, Europe, and Asia and was a member of the Board of Scientific Counselors for the National Cancer Institute. Singh also currently serves as an advisor to the California Institute for Regenerative Medicine.



WARE LEADS GLOBAL CLINICAL TRIALS TO HELP PEOPLE WITH SICKLE CELL DISEASE

Cincinnati Children's has added more firepower to its already extensive team of experts in sickle cell disease.

Russell Ware, MD, PhD, joined us in 2013 as our Director of Hematology and Executive Co-Director of the Cancer and Blood Diseases Institute. He also serves as Associate Director of our Center for Child Global Health.

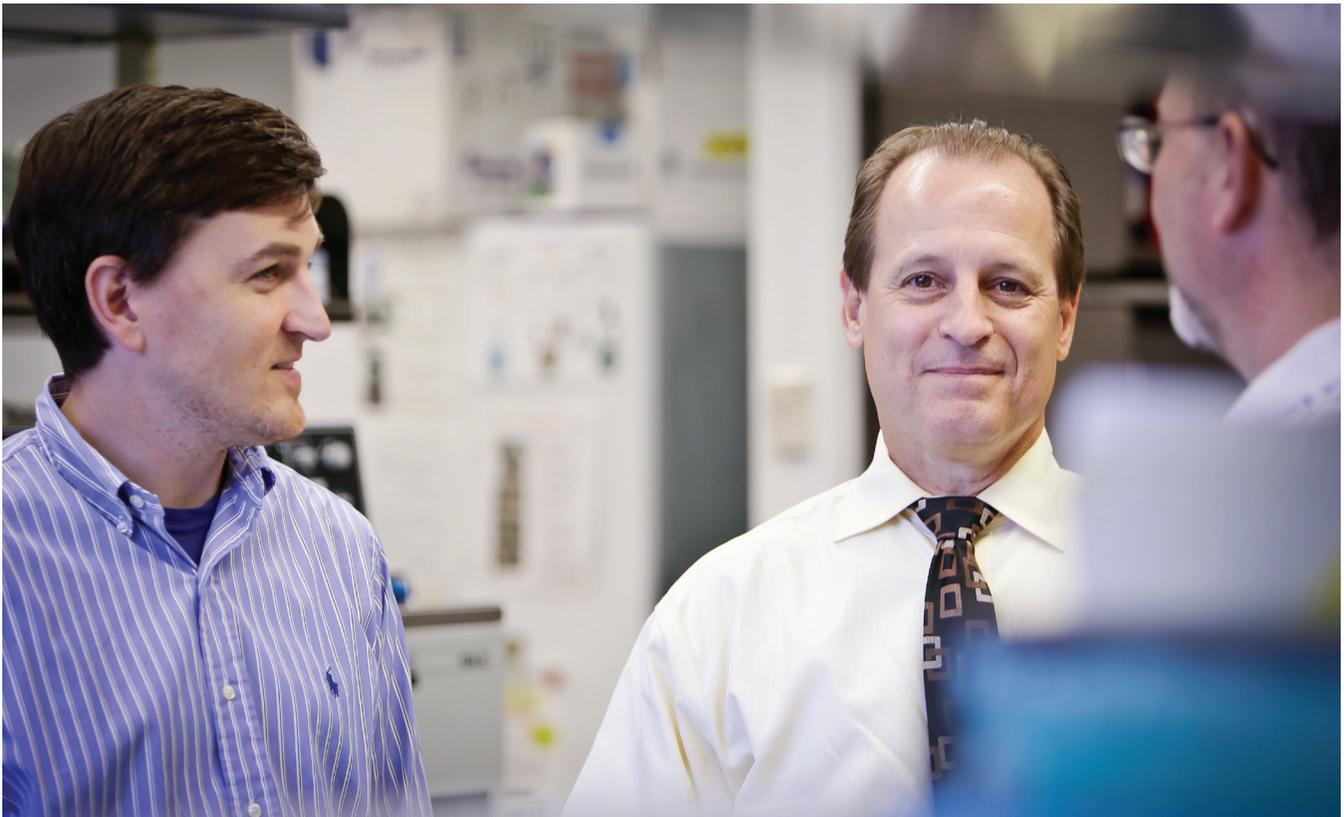
Ware is an expert in sickle cell disease who has published more than 225 peer-reviewed articles and has personally trained dozens of students and fellows. Ware's research interests focus on expanded use of hydroxyurea among children with sickle cell to manage iron overloads, prevent strokes, and improve quality of life, especially in Africa where more than 75 percent of children with sickle cell are born.

"If we really want to make an impact on this disease, we need to go outside the United States," Ware says.

In 2014, Ware will launch three research projects in Africa to improve outcomes for children with sickle cell: a disease mapping study in Uganda; a hydroxyurea clinical trial in Uganda; and another hydroxyurea study to involve up to 450 children in Angola, Kenya and the Democratic Republic of Congo.

At Cincinnati Children's, Ware's plans include expanding the Division of Hematology's research portfolio and building upon the national and international prominence of its clinicians.

Ware received his medical degree from Duke University and completed his pediatric residency at Baylor College of Medicine and Texas Children's Hospital. He completed a fellowship in pediatric hematology and oncology and a PhD in Immunology at Duke University. Russell began his academic career at Duke before moving to St. Jude Children's Hospital, then Baylor, where he served as chief of hematology.



RESEARCH PRODUCES BREAKTHROUGHS IN TREATING NEUROLOGIC CONDITIONS

Be it the nation's largest study of pediatric migraines, evaluating the best drugs to treat epilepsy, or groundbreaking advances against tuberous sclerosis and Duchenne muscular dystrophy, Cincinnati Children's is a global leader in developing better treatments for pediatric neurologic conditions.

Andrew Hershey, MD, PhD, FAHS, leads a division that has grown from five faculty members in 1997 to 38 in 2014. Since 2008, annual research funding for the division has doubled to nearly \$10 million and the results of this work have had significant impact.

A continuing large-scale study of children with absence epilepsy, led by Tracy Glauser, MD, has changed how physicians nationwide prescribe medications for this condition. Life expectancy for young men with Duchenne muscular dystrophy is growing thanks to innovative multi-disciplinary care approaches led by Brenda Wong, MBBS, MRCP.

Researchers Darcy Krueger, MD, PhD, and David Neal Franz, MD, have led studies establishing the critical role played by the mTOR molecular pathway in tuberous sclerosis (TS). This work has led to breakthrough clinical trials that demonstrate the ability of the drugs everolimus and rapamycin to shrink TS tumors in the brain and throughout the body. Previously, these tumors could be treated only with surgery.

Now a \$12 million study involving 40 medical centers is tackling the long-overlooked problems caused by pediatric migraine headaches. This research – led by Hershey and Scott Powers, PhD -- will compare the effectiveness of two commonly prescribed treatments -- topiramate and amitriptyline.

"Pediatric migraine is one of the five most prevalent childhood disorders in the United States," Hershey says. "Yet so far, there are no FDA-approved medications to prevent childhood migraines."

REDUCING THE RISK OF 'SUPERBUGS'

Cincinnati Children's is working to ensure that kids with bacterial infections receive the safest, most effective treatment thanks to infectious disease expert David Haslam, MD.

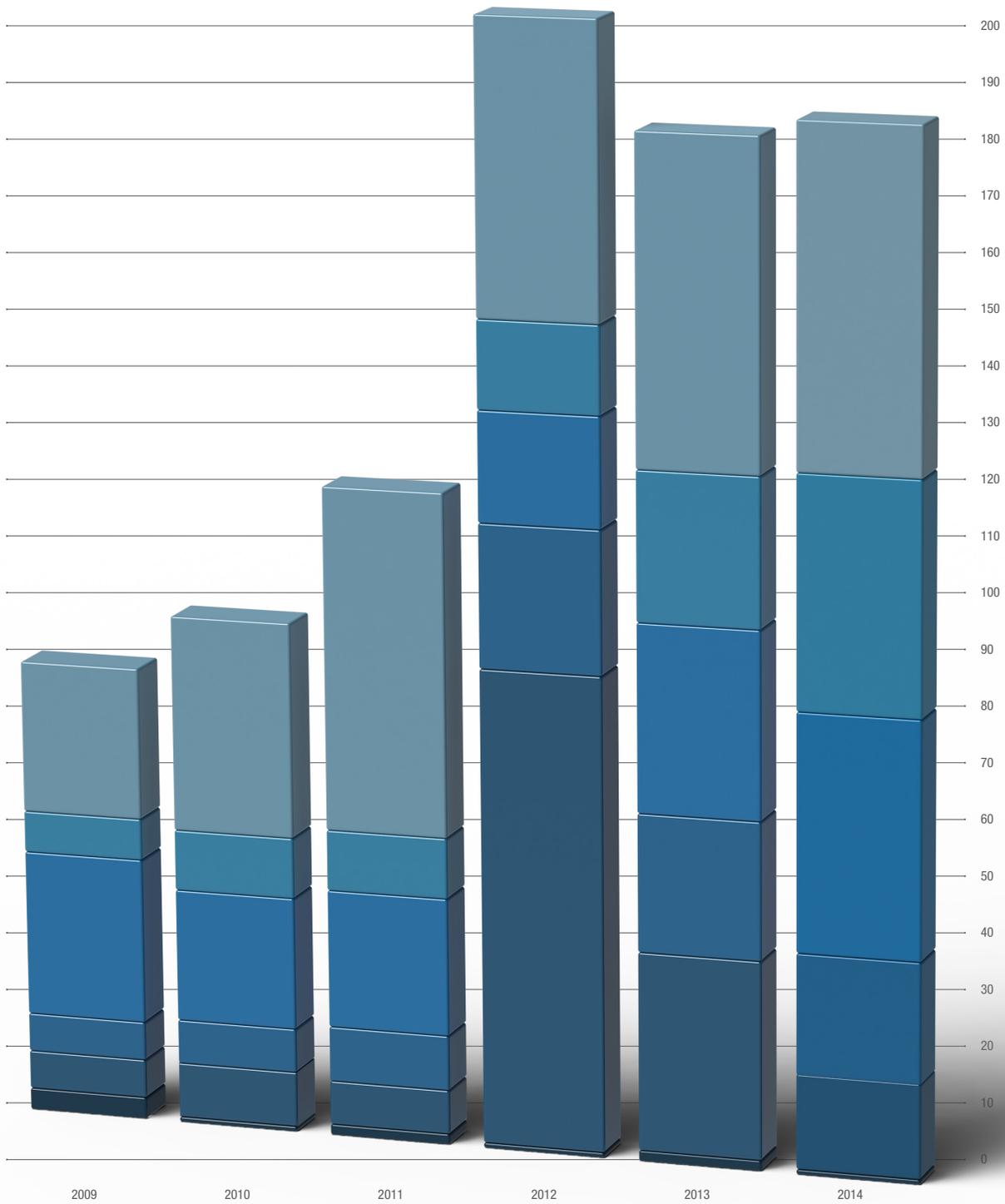
Haslam, who joined Cincinnati Children's Division of Infectious Diseases last year, heads our Antimicrobial Stewardship program. The program's goal is to lessen the use of broad-spectrum antibiotics by encouraging doctors to prescribe better-targeted antibiotic therapies.

Haslam will work with the hospital's clinical pharmacists, using an innovative software tool, Vigilanz. Cincinnati Children's is the only pediatric hospital currently employing the program. The tool allows them to identify in real time patients with bacterial infections, which medications they are receiving and whether those medications are the most effective. In cases where there might be a better alternative, the team will recommend alternatives.

"The point is to reduce the use of the 'big gun' broad-spectrum antibiotics that we know are not effective and might be more harmful in the long-term," Haslam says. Widespread use of broad-spectrum antibiotics has proven to be less effective and is giving rise to "superbugs," bacteria that don't respond to treatment.

Haslam says it's easy to understand why doctors want to knock out infections as quickly as possible, but newer studies are showing that better targeted therapies are just as effective without the "superbug" effect.



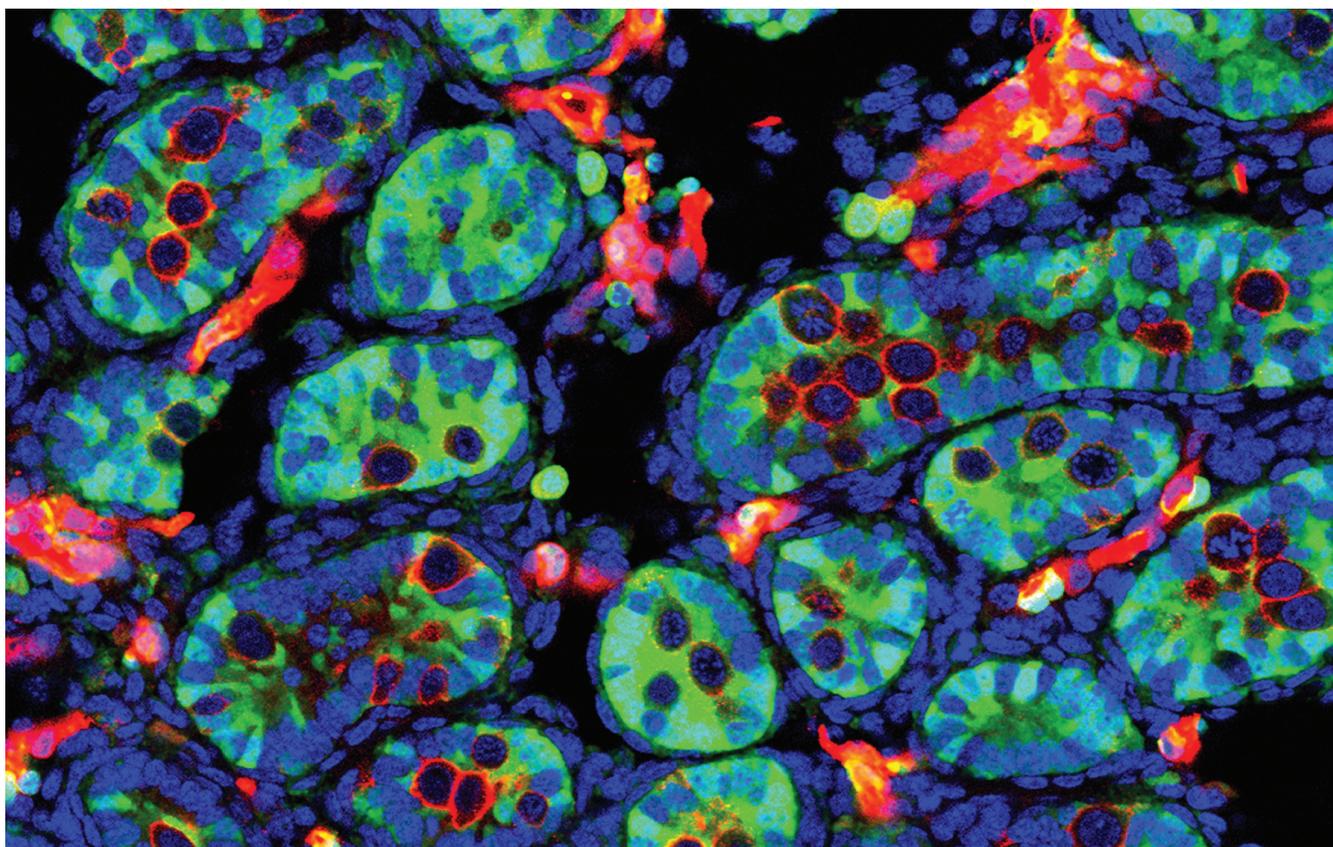


CTC disclosures from 2009-2014

Incubating Technologies

Just like a business incubator, a technology in our pipeline moves to an Incubating phase after it has been disclosed and assessed to further develop and mature. There are currently more than 180 technologies in Incubating and we have technologies moving in and out of this phase daily.

Technologies in Incubating represent what's coming next in terms of available technologies – here is a highlight of a few promising new technologies that we expect to be available in the coming year:



Therapeutics

Lee Grimes, PhD	Therapeutic for Cyclic Neutropenia (CN) and Severe Congenital Neutropenia (SCN)
Ian Lewkowich, PhD	Therapeutic for Treating Severe Allergic Asthma
Brian Varisco, PhD	Biologics that Restore Lung Function
Yi Zheng, PhD	Small Molecule Targeting NADPH Activation to Treat Inflammatory Conditions
Nicholas Nassar, PhD	Small Molecule Inhibitors for Novel Cancer Therapies
David Haslam, MD	Defining Probiotic Treatment for <i>C. difficile</i> Infection

Diagnostics

Michael Helmraath, MD	Biomarker for Intestinal Stem Cell Expansion
Patrick Winter, PhD	Targeting Tumors for Non-Invasive Mapping of a Cancer Biomarker
Stavra Xanthakos, MD	Biomarker for Fatty Liver Disease
Neeru Hershey, MD, PhD	Assessing Steroid Responsiveness in Asthma Patient

Medical Devices

Nancy Daraiseh, PhD	Infrared Motion-Based Suicide Risk Monitor
Thomas Inge, MD, PhD	Floating Jaw Clamp for Gastrectomy

Software/HIT

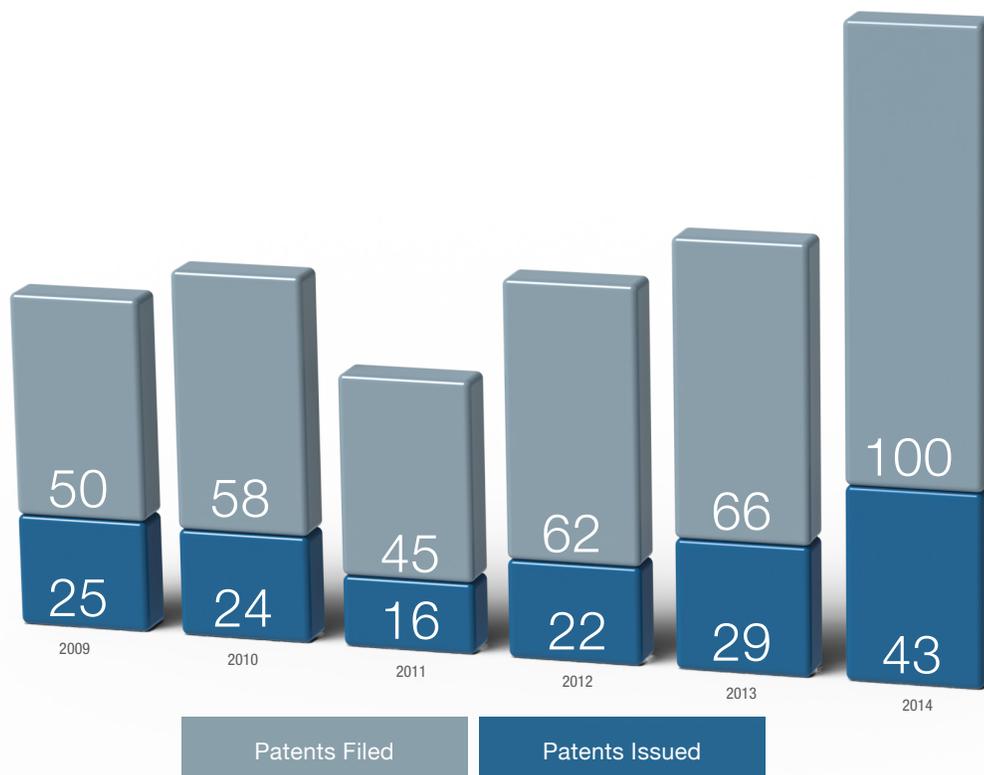
John Pestian, PhD	Natural Language Processing Methods for Clinical Diagnosis and Monitoring
Stuart Goldstein, MD	Curbing Acute Kidney Injury in High Risk Patients
Alexander (Sander) Vinks, PharmD, PhD & Tsuyoshi Fukuda, PhD	Dosing Algorithm to Prevent Patient Variability Response to Morphine

Protecting Our Intellectual Property

As technologies advance through our pipeline, a critical decision point comes when our Technology Management team must decide whether or not to file a patent on the intellectual property. These decisions are made strategically and are

based on a variety of factors including the technology itself, its novelty, and market need and size.

This past year, our office filed a total of 100 patents and 43 patents were issued.



CTC patents from 2009-2014

Jeffrey Whitsett	5/14/2014	1995315AT	Austria	<i>Surfactant Protein D for the Prevention and Diagnosis of Pulmonary Emphysema</i>
	5/14/2014	1995315CH	Switzerland	
	5/14/2014	1995315DK	Denmark	
	5/14/2014	1995315NL	Netherlands	
	5/14/2014	1995315SE	Sweden	
	5/14/2014	1995315DE	Germany	
	5/14/2014	1995315ES	Spain	
	5/14/2014	1995315FR	France	
	5/14/2014	1995315UK	UK	
	5/14/2014	1995315IT	Italy	
	5/14/2014	1995315	EPO	
Donita Bylski-Austrow Eric Wall	2/19/2014	1370183FR	France	<i>Spinal Correction System</i>
	2/19/2014	1370183DE	Germany	
	2/19/2014	1370183GB	UK	
	2/19/2014	1370183IT	Italy	
	2/19/2014	1370183	EPO	
	7/16/2013	2,607,921	Canada	
Richard Wenstrup Alexander (Sander) Vinks Tracy Glauser John Pestian	11/19/2013	8,589,175	US	<i>Optimization and Individualization of Medication Selection and Dosing</i>
	6/27/2013	5567107	Japan	
Kenneth Setchell Victor Sorokin	5/7/2014	200680036577.1	China	<i>Method for Enantioselective Hydrogenation of Chromenes</i>
	3/28/2014	5507081	Japan	
	5/6/2014	8,716,497	US	
Prasad Devarajan Jonathan Barasch	10/25/2013	5392980	Japan	<i>A Method and Kit for Detecting the Early Onset of Renal Tubular Cell Injury</i>
	4/16/2014	ZL201110032921.2	China	
Prasad Devarajan Jonathan Barasch	1/30/2014	2011253624	Australia	<i>Method for Early Detection of Renal Disease and Injury</i>
Mark Halsted Neil Johnson Craig Froehle	7/9/2013	8,484,048	US	<i>Automated System and Method for Prioritization of Waiting Patients</i>
	9/3/2013	8,524,862	US	<i>Muteins of the C5a Anaphylatoxin, Nucleic Acid Molecules Encoding Such Muteins, and Pharmaceutical Uses of Muteins of the C5a Anaphylatoxin</i>

INTELLECTUAL PROPERTY

Prasad Devarajan Joerg (Jörg) Koehl (Köhl)	12/31/2013	8,617,802	US	<i>Organ Transplant Solutions and Method for Transplanting Organs</i>
Pirooz Eghtesady Christopher Lam	9/10/2013	8,529,514	US	<i>Cannula with Removable Sleeve</i>
Ardythe Morrow David Newburg Guillermo Ruiz-Palacios	7/10/2013 7/10/2013 7/10/2013 11/5/2013 5/14/2014 7/10/2013	602008025947.1 2185931FR 2185931GB 8,574,850 ZL200880112257.9 2185931	Germany France UK US China EPO	<i>Use of Secretor, lewis and Sialyl Antigen Levels in Clinical Samples in Predictors of Risk for Disease</i>
Kenneth Setchell Trent Lund Edwin Lephart Robert Handa	11/12/2013	8,580,846	US	<i>Use of Equol for Ameliorating or Preventing Neuropsychiatric and Neurodegenerative Diseases or Disorders</i>
Rashmi Hegde	7/16/2013	8,486,651	US	<i>Method for Identifying Agents for Inhibiting Cell Motility and Invasiveness</i>
Xi (Jason) Jiang Ming Tan	7/16/2013	8,486,421	US	<i>Antigen-Norovirus P-Domain Monomers and Dimers, Antigen-Norovirus P-Particle Molecules, and Methods for Their Making and Use</i>
Richard Lang Jeremy Duffield	4/22/2014	8,703,708	US	<i>Agents and Methods for Tissue Repair and Regeneration</i>
Paul Yelton Frederick Ryckman	1/21/2014	8,635,088	US	<i>Medical Facility Bed Availability</i>
Christopher Karp Senad Divanovic Jessica Allen	5/27/2014	8,735,347	US	<i>Regulation of energy metabolism and obesity by modulationg B cell activating factor (BAFF, BLYS) or BAFF signaling</i>
Ardythe Morrow David Newburg Guillermo Ruiz-Palacios	3/21/2014 3/4/2014	1689348EP 596099	EPO New Zealand	<i>Milk Oligosaccharide Compositions and Use Thereof in Treating Infection in Animals</i>
David Repaske	5/22/2013	1575916	European Patent Office	<i>Phosphodiesterase Activity and Regulation of Phosphodiesterase 1B-Mediated Signaling in Brain</i>
Yi Zheng	10/2/2012	2546727	Canada	<i>GTPase Inhibitors and Methods of Use</i>
Ardythe Morrow	4/5/2013 5/15/2013	5236189 1689348	Japan EPO	<i>Oligosaccharide Compositions and Use Thereof in the Treatment of Infection</i>
Kenneth Setchell	3/15/2013	5220406	Japan	<i>Use of Equol for Treating Skin Diseases</i>
Prasad Devarajan	3/13/2013 8/3/2012	ZL200580026786.3 5,054,525	China Japan	<i>Method for Early Detection of Renal Disease and Injury</i>
Donita Bylski-Austrow	5/31/2013	10-1272242	S. Korea	<i>Spinal Correction System</i>
Jason Jiang	10/2/2012	8,277,819	US	<i>Norovirus Particle for Use as an Antiviral or Vaccine</i>

Kenneth Setchell	1/3/2013	2006275587	Australia	<i>Method of Enantioselective Hydrogenation of Chromenes</i>
David Repaske	12/25/2012	160307	Israel	<i>Phosphodiesterase Activity and Regulation of Phosphodiesterase 1B-Mediated Signaling in Brain</i>
Jeffrey Whitsett	7/27/2012	5048678	Japan	<i>Surfactant Protein-D for Prevention and Treatment of Lung Infections and Sepsis</i>
Ardythe Morrow	11/20/2012	8,314,061	US	<i>Adiponectin for Treatment of Various Disorders</i>
Kenneth Setchell	3/14/2013	2006347276	Australia	<i>Use of Equol for Ameliorating or Preventing Neuropsychiatric and Neurodegenerative Diseases or Disorders</i>
Xiaoyang Qi	4/26/2013	5253402	Japan	<i>Spontaneously Forming Ellipsoidal Phospholipid Unilamellar Vesicles</i>
David Repaske	1/22/2013	1575916JP	Japan	<i>Phosphodiesterase Activity and Regulation of Phosphodiesterase 1B-Mediated Signaling in Brain</i>
Ardythe Morrow	12/7/2012	305964	Mexico	<i>Use of Secretor, lewis and Sialyl Antigen Levels in Clinical Samples in Predictors of Risk for Disease</i>
Christopher Karp	3/26/2013	8,404,656	US	<i>Methods of Treatment and Prevention of Diet-Induced Obesity and Sequelae Thereof</i>
Xiaoyang Qi	5/30/2013	2010200264	Australia	<i>Sapoin C-DOPS: A Novel Anti-Tumor Agent</i>
Prasad Devarajan	8/21/2012	8,247,376	US	<i>NGAL for Reduction and Amelioration of Ischemic and Nephrotoxic Injuries</i>
Yi Zheng	2/26/2013	8,383,124	US	<i>Mobilization of Hematopoietic Stem Cells</i>
David Williams	8/14/2012	8242246	US	<i>CHIMERIC PEPTIDES FOR THE REGULATION OF GTPASES</i>
Kenneth Setchell	9/11/2012	8,263,790	US	<i>Method for Enantioselective Hydrogenation of Chromenes</i>
Kenneth Setchell	5/28/2013	8,450,364	US	<i>Use of Equol for Treating Androgen-Mediated Diseases</i>
Kenneth Setchell	5/24/2013	5277221	Japan	<i>Sulfate Conjugates Of UDCA And Their Beneficial Use In Inflammatory Disorders And Other Applications</i>
David Repaske	5/22/2013	1575916DE	Germany	<i>Phosphodiesterase Activity and Regulation of Phosphodiesterase 1B-Mediated Signaling in Brain</i>
	5/22/2013	1575916ES	Spain	
	5/22/2013	1575916FR	France	
	5/22/2013	1575916GB	UK	
	5/22/2013	1575916IT	Italy	

Research Advancement

Innovative Funding Programs Drive Discoveries Towards Commercialization

As an institution, Cincinnati Children's takes a hands-on approach to ensuring its most promising research projects have the resources they need to advance to a point where they're ready for commercialization. Cincinnati Children's realizes the critical nature of funding for each step in the commercialization pathway, from idea incep-

tion to licensing or venture investment. To that end, Cincinnati Children's created many internal funding programs, detailed below, that aim to advance commercially-promising early stage ideas to the point where they may be licensed or the basis of a start-up company.

CINCINNATI CHILDREN'S INNOVATION FUND

Our Innovation Fund is a highly competitive program that provides critical early stage funding to commercially viable projects. Innovation Fund projects can receive up to \$200,000 over two years and must meet commercially relevant milestones. Projects can be therapeutics, diagnostics, medical devices, or software/IT.



Cincinnati Children's Innovation Fund

Margaret K Hostetter, MD

***Development of Peptide Vaccines and Antibodies
to Prevent Central Line Infections***

The goal of this project is to advance development of an antibody shown to prevent biofilm formation and Central Line Associated Blood Stream Infections (CLABSIs). The current antibody is effective against *Candida* and current research is underway to test against *Staphylococcus Epidermidis* and *Aureus*. This project is being evaluated for licensing and start-up opportunities.

Peter Margolis, MD, PhD & Michael Seid, PhD

The C3N Portal for Personalized Collaborative Care

Peter Margolis, MD, PhD and Michael Seid, PhD have built a personalized care portal. This technology is a collaborative learning system for patients, clinicians and researchers to support personalized care by integrating patient reported data with clinical data and using the data to drive decision making. This technology has been licensed to a company in California.

John Perentesis, MD

Next-Generation Clinical Trials Management Software: Natural Language Processing to Identify Adverse Events in Clinical Trials

The costs and manpower required to test new drugs in clinical trials remains a major obstacle for getting new drugs to the bedside. This project is a revolutionary new approach addressing a significant unmet clinical need by developing a novel computer based approach to directly analyze medical records for patients enrolled on clinical trials.

John Pestian, PhD

Thought Markers as a Predictor of Repeated Suicide Attempts

This technology can identify suicidal patients with 90% accuracy using natural language processing and analysis, ultimately reducing suicide attempts and improving treatment. An additional grant of \$50,000 was awarded to this project through the Technology Validation and Start-Up Fund (TVSF) through the Ohio Development Services Agency. This technology has recently been successfully optioned by a personalized medicine company.

Hector Wong, MD

The Pediatric Sepsis Biomarker Risk Model

Hector Wong, MD has developed a technology that reliably identifies patients with septic shock at low/high risk for poor outcomes through effective stratification in septic shock, revolutionizing patient-centered decision support, clinical trials and quality assurance efforts. This technology has been spun out into a start-up company named Persepsys.

Yi Zheng, PhD

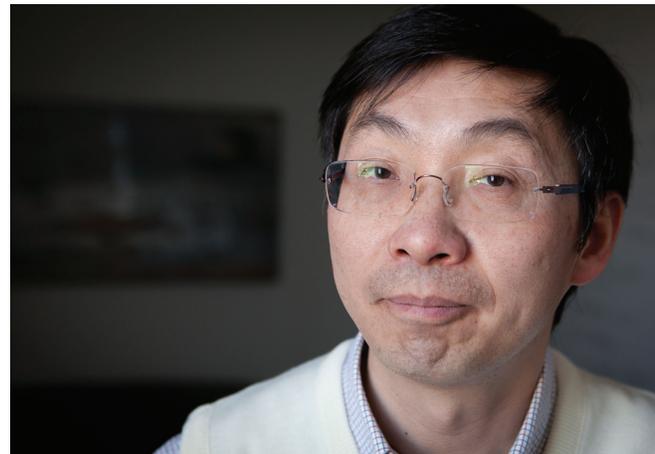
Novel Anti-inflammatory Drug Targeting NOX2 in Acute Lung Injury

The goal of this project is to develop a novel class of anti-inflammatory drugs that specifically target neutrophil NOX2 to ameliorate lung damage by Acute Lung Injury (ALI) and Acute Respiratory Distress Syndrome (ARDS). Optimization of lead NOX2-I inhibitors is complete and efficacy is being tested. This project has received additional commercialization funding through the NCAI project.

ROUND 1

PROJECT UPDATES

THE FOLLOWING PROJECTS WERE FUNDED DURING THE INAUGURAL INNOVATION FUND THAT TOOK PLACE IN 2012. HERE IS A SNAPSHOT OF WHERE THE PROJECTS CURRENTLY STAND IN YEAR 2 OF THE PROJECT.



ROUND 2
PROJECT UPDATES

THE FOLLOWING PROJECTS WERE FUNDED DURING THE SECOND ROUND OF THE INNOVATION FUND THAT TOOK PLACE IN 2013. THE GREATER CINCINNATI FOUNDATION SUPPORTED THIS ROUND WITH A \$100,000 GRANT. HERE IS A SNAPSHOT OF WHERE THE PROJECTS CURRENTLY STAND IN YEAR 1 OF THE PROJECT.

Lee Denson, MD

Ileal Transcriptome Analysis as a Diagnostic and Prognostic Tool in Inflammatory Bowel Disease

Lee Denson, MD is developing a diagnostic technology that uses genetic signatures and computer algorithms to delineate between the inflammatory bowel diseases (IBD), Crohn's disease and Ulcerative Colitis. The incidence of IBD in children has doubled over the last decade. This technology is designed to address a critical unmet need for a novel diagnostic and prognostic tool.

Charles Dumoulin, PhD

Magnetic Resonance Imaging in the Neonatal Intensive Care Unit

Charles Dumoulin, PhD has developed a novel neonatal MRI scanner to meet the diagnostic needs of fragile newborn babies at risk of injury during transport from the Neonatal Intensive Care Unit (NICU) to radiology for diagnostic scans. The smaller scanner, which can be housed right in the NICU and provide closer, quieter and improved imaging quality, is expected to have a major impact in improving care for premature babies. This technology is in start-up due diligence.

William Hardie, MD

Targeting the P70S6K in Pulmonary Fibrosis

William Hardie, MD is studying the 6 ribosomal protein kinase (p70S6K) as a potential pharmacological target in treating pulmonary fibrosis. In-vivo and in-vitro testing has been completed, and Hardie will soon be testing the efficacy of p70S6K inhibition in reversing established and progressive pulmonary fibrosis in mouse models.

Punam Malik, MD

An Improved Fetal Hemoglobin for Genetic Correction of Sickle Cell Disease

This project aims to build upon previous research that may offer the possibility of a one-time treatment for sickle cell disease resulting in a lifelong correction. Punam Malik, MD has since engineered an improved γ -globin gene that has a higher tendency to form HbF and has improved antisickling properties, resulting in superior correction of SCD. Malik is studying the mechanism of its improved antisickling activity and has recently initiated a Phase I clinical trial.

Senthil Sadhasivam, MD, MPH

Personalizing Pain Management with Opioids: Preemptive Risk Assessment, Personalized Decision Support and Point-of-Care Genotyping

This project is focused on the development of rapid-point-of care gene chip that allows physicians to precisely tailor the use of opioids for pain management in perioperative patients. Inadequate pain relief and side effects from perioperative opioids occur in up to 50 percent of patients. This technology has the potential to address a critical unmet medical need by using information on genetic variability in patients to prescribe precise, safe and effective pain medication.

Hector Wong, MD

Interleukin-27 as a Novel Diagnostic Biomarker for Sepsis

This project aims to further test and validate a novel diagnostic biomarker (IL-27) for rapid and early identification of sepsis in patients. Current diagnostic methods using microbiologic cultures can be imprecise and time consuming. Successful development of IL-27 as a novel diagnostic biomarker for sepsis would allow more prompt intervention with antibiotic therapy. A start-up company, Persepsys, has been created out of this technology.



ROUND 3**PROJECT UPDATES**

THE PROJECTS HERE WERE FUNDED AS PART OF THE FY14 FUNDING ROUND AND ARE CURRENTLY IN THEIR FIRST YEAR OF FUNDING.

Ming Tan, PhD***Multivalent vaccines against norovirus, rotavirus, hepatitis E virus and astrovirus***

Ming Tan, PhD is developing a vaccine to combat norovirus, rotavirus, hepatitis E virus and astrovirus, which cause epidemics of gastroenteritis and hepatitis that affect millions of people each year. Except for vaccines against rotavirus, there is no FDA proven vaccine or antiviral against these pathogens.

Lee Grimes, PhD***Inhibitors of STAT5***

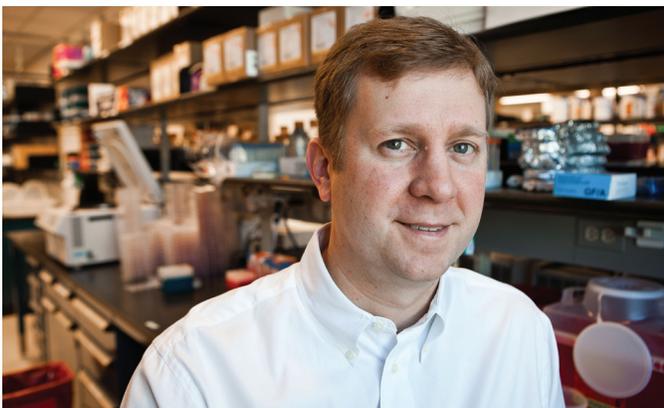
This project is working to develop new pharmaceutical compounds that target a molecule called STAT5, which plays a role in the progression of multiple cancers, including acute and chronic myeloid leukemia.

Michael Jordan, MD***Exploiting the DNA damage response to develop new therapies for immunologic diseases***

Michael Jordan, MD has developed a targeted method of suppressing harmful immune responses by taking advantage of how immune cells called lymphocytes respond to DNA damage. Jordan's team is working on a way to target activated immune cells so that undesirable immune responses are suppressed while helpful immune responses are allowed to proceed.

Prasad Devarajan, MD & Hermine Brunner, MD***Multiplex Lupus Nephritis Biomarker Panel***

Prasad Devarajan, MD and Hermine Brunner, MD have developed a blood test that detects the onset of kidney damaging lupus nephritis. This project aims to develop a practical clinical platform for the test to make the diagnosis faster and more accurate while improving quality of life and patient experience for the more than 1.5 million children and young adults with lupus nephritis

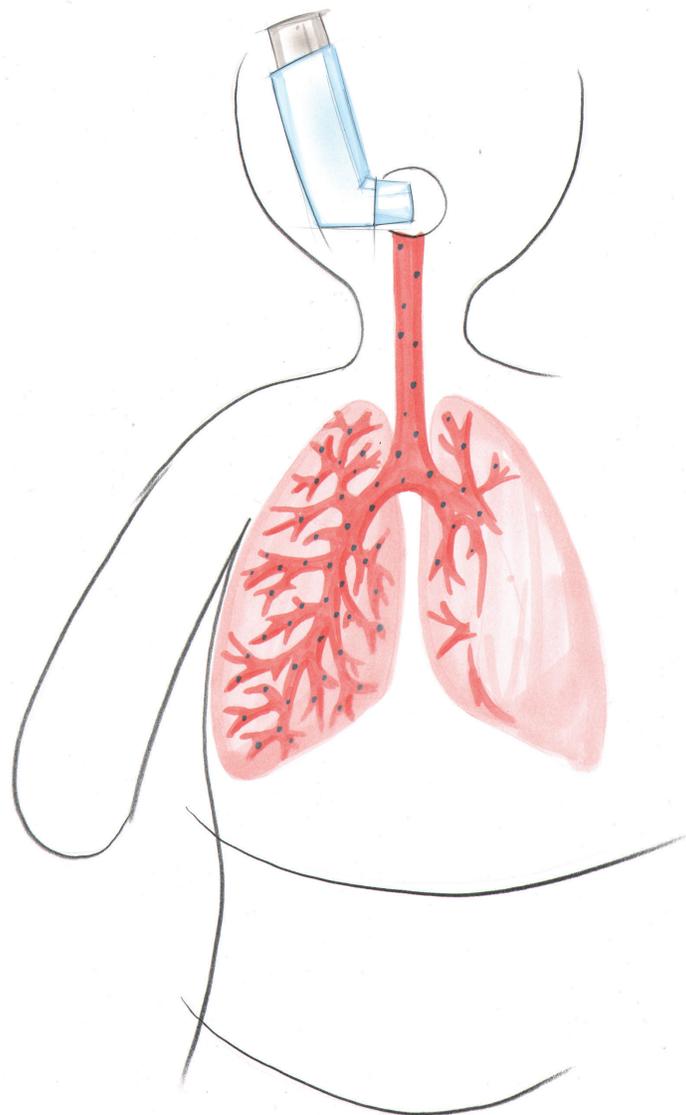
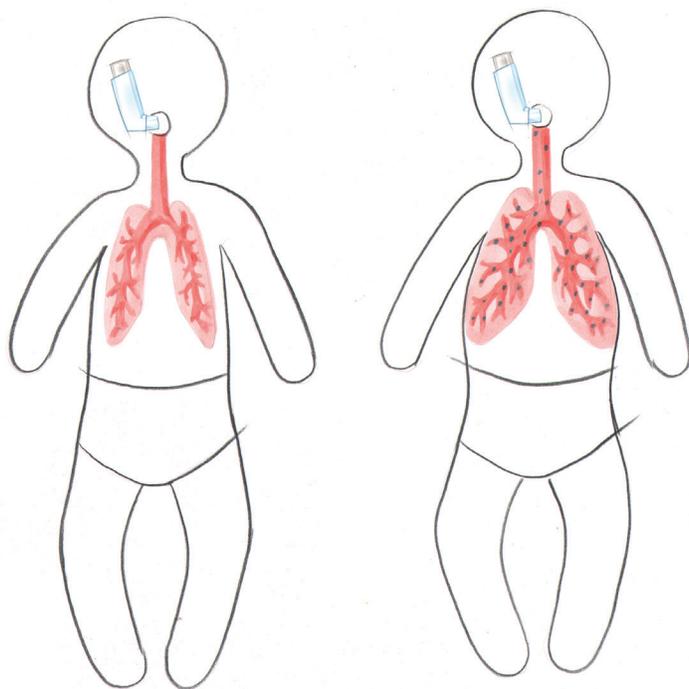


Ben-Gurion University Cincinnati Children's Collaborative (BG3C)

INTERNATIONAL PEDIATRIC MEDICAL DEVICE FUND

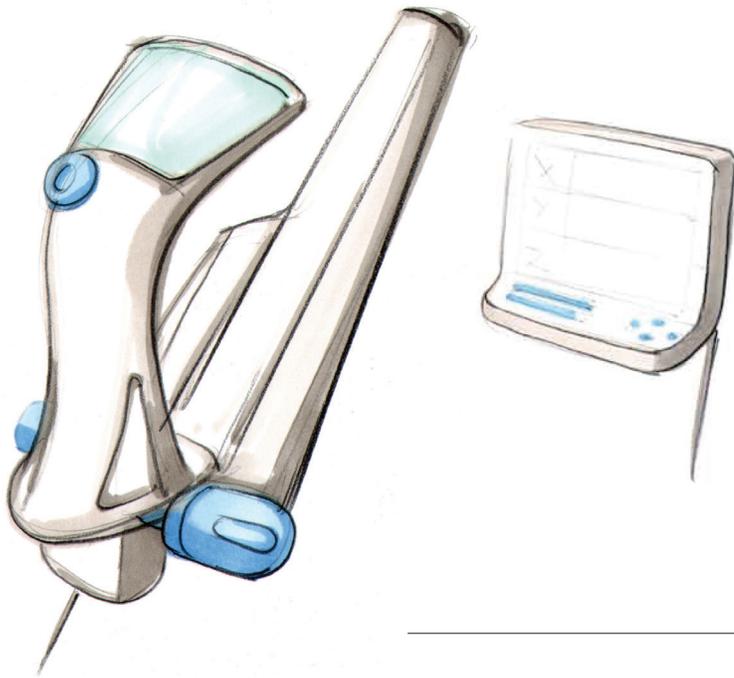
The Ben-Gurion Cincinnati Children's Collaborative (BG3C) is a collaborative between Ben-Gurion University of the Negev in Israel and Cincinnati Children's. The collaboration addresses the lack of medical devices designed specifically for children and identifies projects that need to be funded beyond design and development. The project combines the medical expertise of physicians at Cincinnati Children's with the extensive technical

and engineering capabilities of faculty at BGU. The goal is to improve health outcomes by ensuring device design is customized to meet the unique physiological differences and medical needs of children. The collaboration identifies and funds projects that meet a medical need and have a strong pathway to commercialization. Each project receives up to \$100,000 in funds.



**Jeffrey Whitsett, MD (CCHMC) &
Joseph Kost (BGU)**
Surfactant Delivery Device

The device consists of a delivery system for prolonged administration of surfactants to the lungs of premature babies using nanoparticles. Current procedures do not allow for the sustained release of proteins or other complex particles in the alveoli of infants or adults. This technology would do that, with the potential to deliver numerous therapies to the lower airway through a non-inflammatory delivery system.



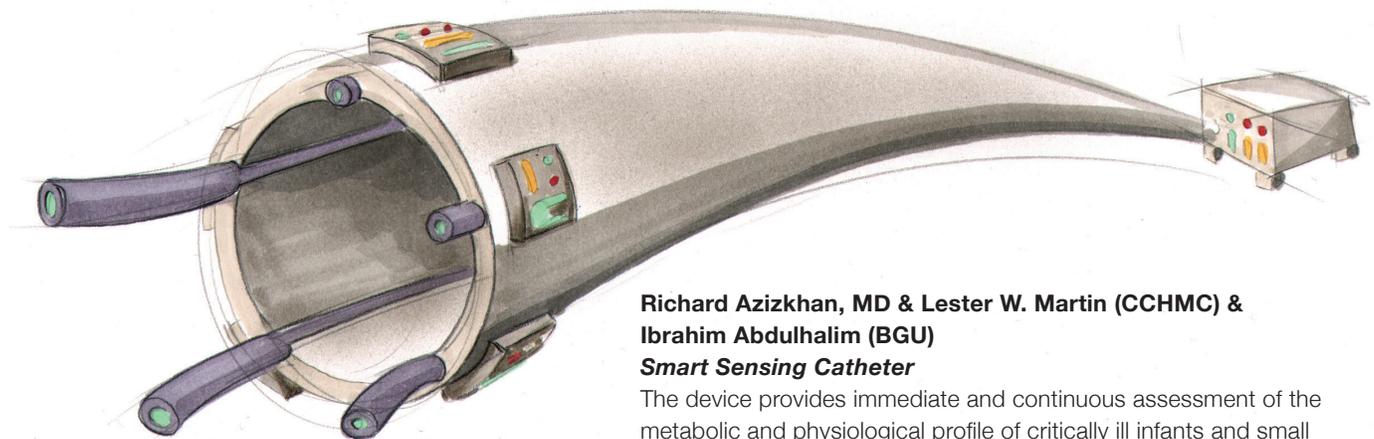
Daniel von Allmen, MD (CCHMC) & Hugo Guterman (BGU)

Image Guided Needle Insertion Device

The Human Assisted Needle Delivery System (HANDS) is a handheld medical device that links the sophistication of advanced imaging technology with the precision and accuracy of robotic guidance to provide targeted, accurate needle access to a particular site in the body. HANDS is designed to be a small and relatively inexpensive device that can reliably pinpoint a clinician's vascular target. A prototype of the device has been built and an additional grant of \$50,000 was awarded to this project through the Technology Validation and Start-Up Fund (TVSF) through the Ohio Development Services Agency.

Thomas Inge, MD (CCHMC) & Amir Shapiro (BGU)
Clamp for Stabilization/Uniformity of Traction of Stomach during Sleeve Gastrectomy

This project aims to build an improved clamp for use during sleeve gastrectomy surgery. This clamp will have innovative graspers with long jaws and a bending joint above the jaws, and a flexible plastic cover sleeve from the jaws tip up to the handle. This flexible sleeve will be disposable and sterile. This novel device will allow for uniform traction and exposure (visualization) of the stapler target region during this procedure.



Richard Azizkhan, MD & Lester W. Martin (CCHMC) & Ibrahim Abdulhalim (BGU)

Smart Sensing Catheter

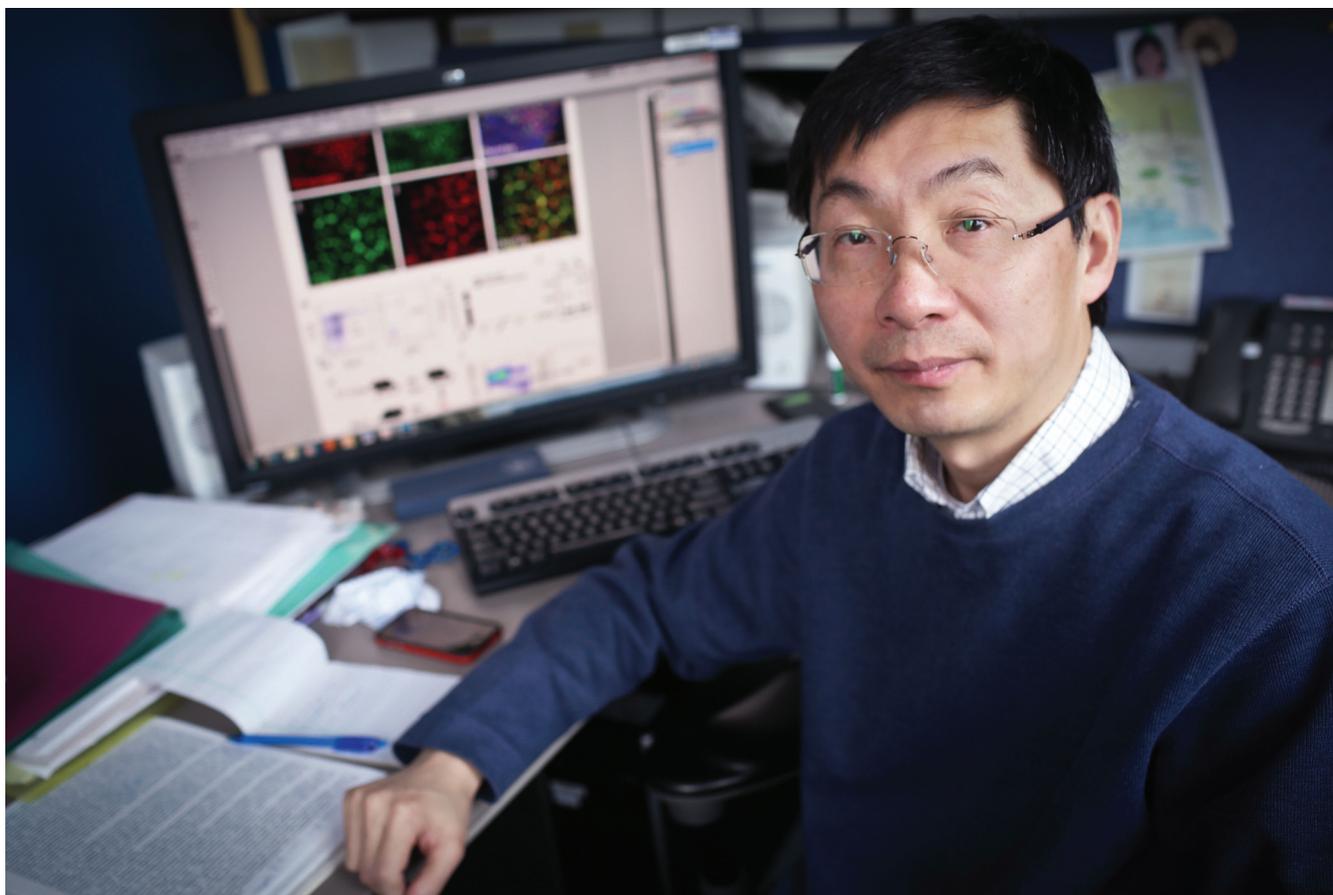
The device provides immediate and continuous assessment of the metabolic and physiological profile of critically ill infants and small children. Secondly, this technology will reduce the need for repeated tests, thus reducing costs for the health system and society. Catheter utilization is widespread; therefore, this technology has the potential for broader application in the adult market.

The NIH Centers for Accelerated Innovation (NCAI)

COLLABORATIVE COMMERCIALIZATION GRANT

The NIH Centers for Accelerated Innovation (NCAIs) is aimed at identifying technologies and moving them through the commercialization pathway. The NCAI is an award that was granted to the Cleveland Clinic Innovation Accelerator and partnering institutions: Cincinnati Children's, The Cleveland Clinic Lerner College of Medicine; Case Western Reserve University, The Ohio State University, and University of Cincinnati. The NCAI, funded by the NIH's National Heart, Lung, and Blood Institute (NHLBI), targets technologies to improve the diagnosis, treatment, management, and prevention of heart, lung, blood, and sleep disorders and diseases. The effort is part of a major initiative to improve how

basic science advances and discoveries are translated into commercially viable products that improve patient care and advance public health. Funding for projects is used for product discovery or development-related activities, high throughput screening, product definition studies, preclinical studies, feasibility studies, prototype development, proof-of-concept or validation studies. NCAI funds awarded to projects at Cincinnati Children's receive matching funds from the institution. From the first round of awards Yi Zheng, PhD, received a grant for his Novel Anti-inflammatory Drug Targeting NOX2 in Acute Lung Injury project.



InnovIG Grants

Collaboration between CincyTech and the Cincinnati Children's Innovation Fund

InnovIG is a synergistic collaboration between CincyTech's Imagining Fund and Cincinnati Children's Hospital Medical Center's Innovation Fund. Through the InnovIG program CincyTech works with Cincinnati Children's Innovation Fund awarded projects that are not yet licensed, and provides them each with a CincyTech Imagining Grant of up to \$45,000. The funding is used to assess the critical needs and proof points that will lead to commercialization or a start-up recommendation for the technologies. Activities conducted using this funding include market analysis, value proposition, regulatory pathway analysis, operational requirements, IP review, and Remaining R&D/IP proof points needed to engender start-up phase. To be considered for this funding a project must have an Innovation Fund.



Tomorrow Fund

Ohio Third Frontier Pre-Seed Program

The Tomorrow Fund is a program through the Ohio Third Frontier with matching funds from Cincinnati Children's for pre-seed funding for Ohio based start-up companies. The Tomorrow Fund continues the pipeline of funding for early stage innovations by investing in a select number of commercially viable technologies that meet specified criteria for company formation by Cincinnati Children's. With input by experienced investment professionals in the SW Ohio region, funds are invested in companies spun out of Cincinnati Children's innovations. To date, with Tomorrow Fund I and II, \$6.4 million has been invested in 7 start-up companies. Funds I/II have successfully attracted investments of over \$70 million while creating over 200 jobs with an average annual wage of \$109,546. In June, 2014, Cincinnati Children's received funding from the Ohio Third Frontier to initiate Tomorrow Fund III, a \$6 million fund. Tomorrow Fund III builds on the accomplishments of Tomorrow Funds I/II and provides greater resources to capitalize on Cincinnati Children's growing pipeline of qualified opportunities and increased financial commitment to pre-company development.

Technology Validation & Start-up Fund Grant

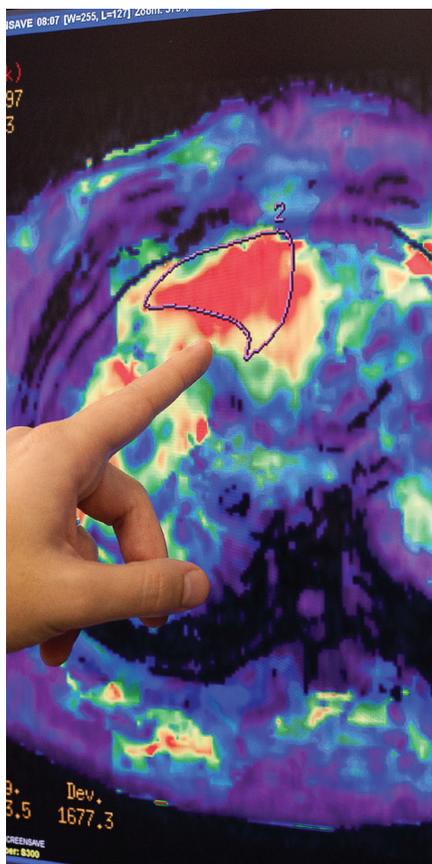
Ohio Development Services Agency Grants

Through the CTC, Cincinnati Children's has received three Ohio Third Frontier Technology Validation and Start-up Fund (TVSF) grants. The TVSF grants are in support of protected technologies developed at Cincinnati Children's that need known validation that will directly impact and enhance both their commercial viability and ability to support a start-up company. The three Cincinnati Children's projects are the Suicide Risk Index, NICU MRI, and the HANDS project. Each project receives \$100,000 in total funded, matched 1:1 from Cincinnati Children's and the Ohio Third Frontier. These funds provide crucial support in validating innovations and pushing them to commercialization.

Available Technologies

Our portfolio of available technologies is comprised of more than 50 therapeutics, diagnostics, medical devices, and software products. It is constantly evolving as technologies are licensed and new ones enter. To the right is a sampling of technologies currently available for licensing.

If you would like to learn more about any of these technologies, please contact the CTC's Business Development group at: partnering@cchmc.org or 513-636-4285.



Diagnostics

Simultaneous ASL/BOLD Functional MRI

Imaging acquisition using arterial spin labeling with blood-oxygen-level dependence functional magnetic resonance.

Scott Holland, PhD
Division of Radiology

Diagnostic & Prognostic Biomarker for Crohn's Disease

An antibody-based diagnostic that optimizes treatment strategy at time of diagnosis and every 6 months thereafter.

Lee A. Denson, MD
Division of Gastroenterology, Hepatology and
Nutrition

Biomarker Panel for Genome Instability

A method of using a biomarker panel to predictively diagnose gene instability and cancer susceptibility, based on metabolites in patient fluids.

Susanne Wells, PhD
Division of Oncology

Software

Correlation Imaging for High Speed MRI

The new technology provides a framework to accelerate MR image acquisition.

Yu Li, PhD
Department of Radiology

Patient Services Operational Dashboard (PSOD)

The dashboard is a system for tracking, evaluating, predicting, and suggesting staffing solutions based on patient census and acuity formulas.

William Vidonish, Project Manager, Department
of Patient Services

Therapeutics

Genetic Correction of Hemoglobinopathy Including Sickle Cell Disease

A gene therapy method for treating sickle cell disease (SCD) using a modified stem cell that produces corrective antisickling hemoglobin.

Punam Malik, MD
Division of Experimental Hematology
& Cancer Biology

Lung Cancer Therapeutic

This technology is a small molecule inhibitor of Midkine for the treatment of currently untreatable lung cancers.

Jeffrey Whitsett, MD
Director, Perinatal Institute

Polyvalent Complexes for Vaccine Development

A method of preparing very large protein complexes for use as multivalent vaccines against infections of multiple types.

Ming Tan, PhD
Division of Infectious Diseases

Targeted Oncology/Retinopathy Therapeutic & Discovery Platform

Analogous compounds of benzbromarone that inhibit pathological angiogenesis, specifically in ophthalmic- and oncology-related diseases.

Rashmi S. Hegde, PhD
Division of Developmental Biology

Therapeutic Protein Delivery Across the Blood-Brain Barrier

A delivery mechanism which allows large-molecule therapeutics to transcytose the blood-brain barrier for treatment of neurological disorders.

Dao Pan, PhD
Division of Experimental Hematology

Small Molecule Inhibitors of Norovirus

This technology provides a novel approach to inhibiting norovirus infection through blocking the histo-blood group antigen binding interface.

Jason (Xi) Jiang, PhD
Division of Infectious Diseases

Compound to Promote Stem Cell Mobilization and Engraftment

Y16 and its analogs inhibit G protein-coupled RhoGEFs, slowing cancer cell growth, migration, and invasion.

Yi Zheng, PhD
Division of Experimental Hematology
& Cancer Biology

Collaborations & Successes

The CTC understands the important role that our industry partners play in moving innovative research from the bench to the bedside – whether that’s through a license, sponsored research, strategic alliance, or creative partnership. The

CTC is actively pursuing industry collaborations across all therapeutic areas and is open to risk-sharing models. Here are a sampling of some of our recent industry collaborations and commercialization successes:



ALEXION AND CINCINNATI CHILDREN'S LAUNCH RARE DISEASE INNOVATION FUND

Alexion Pharmaceuticals and Cincinnati Children's recently announced a research collaboration that will leverage the early stage research and clinical expertise of a leading pediatric institution with the drug development experience and capabilities of an industry leader.

Under the terms of the agreement, Alexion will have the opportunity to fund selected research programs through the Alexion Rare Disease Innovation Fund. Following completion of the funded research programs, Alexion will have an exclusive option to enter into a licensing agreement for these programs.

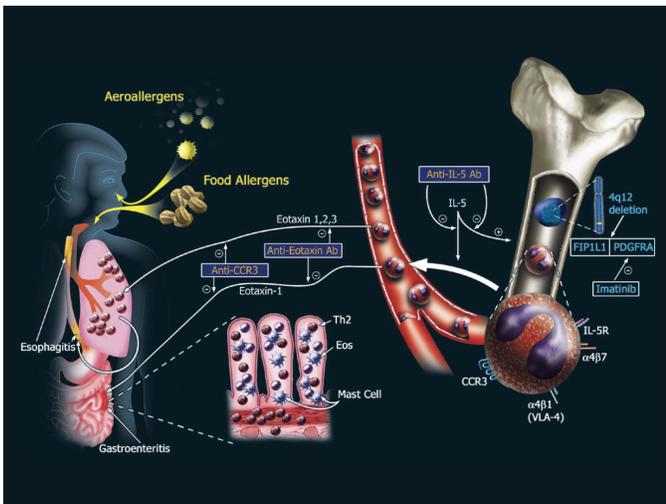
The Alexion fund is a focused opportunity within Cincinnati Children's broader Innovation Fund, which covers all therapeutic areas and technology types. Alexion will focus its selections based on the company's specialty of developing new treatments for complex and rare diseases.

CINCINNATI CHILDREN'S CO-HOSTS RARE DISEASE PARTNERING RECEPTION AT BIO 2014

The second annual Rare Disease Partnering Summit was held at the Biotechnology Industry Organization's (BIO) convention that took place in June of 2014 in San Diego. The event, a collaboration between Cincinnati Children's and Children's Hospital Los Angeles, brought together leading companies and research institutions working in the rare disease space to form meaningful collaborations focused on discovering and advancing life-saving therapies.

The success of this event highlighted the important need for collaboration between industry and academia, particularly in the rare disease space. The event was sponsored by Rare Disease Therapeutics, REDI Cincinnati, NPS Pharma and Nixon Peabody.

DIAGNOSTIC TEST FOR EOSINOPHILIC ESOPHAGITIS (EOE) LICENSED TO DIAGNOVUS



Cincinnati Children's has entered into an Exclusive License Agreement with Diagnovus for its technology shown to diagnose eosinophilic esophagitis (EoE), a chronic upper gastrointestinal disorder. The technology, developed by Marc Rothenberg, MD, PhD, looks at the expression levels of a focused panel of genes to identify patients with EoE.

The currently available test, ENGAUGE® GI-EoE, is a gene expression based assay that can quickly and accurately diagnose patients with EoE, independent of eosinophil count. ENGAUGE® GI-EoE can also aid in the identification of patients who are negative for EoE due to steroid-induced remission, which can assist physicians in developing treatment strategies. ENGAUGE® GI-EoE is highly sensitive, specific, cost effective and is accurate in both children and adults. This test uses routine FFPE biopsy material and does not require an additional endoscopy and biopsy procedure.

CTC LICENSES CUSTOMER RELATIONSHIP MANAGER (CRM) SOLUTION FILE FOR TECHNOLOGY TRANSFER, WINS MICROSOFT INNOVATION AWARD

What started as a simple project to implement CRM software to improve the business development and marketing efforts of the CTC, turned into a CRM Solution File that has the potential to change the way research institutions market their available technologies to industry.

The CRM Solution File, licensed to Aspect, allows an institution to capture the Areas of Interest of a company and run a report against its portfolio of available technologies that are categorized based on the same Areas of Interest, thus providing

a “Matching Report” that shows exactly what technologies the institution should share with the company.

“We needed to be very targeted in what technologies we put in front of a potential partner,” said Chris Stahl, Business Development Manager for the CTC and one of the primary inventors on this project. “In order to do that, we needed to be using the same language when we talked about a company’s Areas of Interest and our available technologies.”

As the CTC continued to refine the platform, it was apparent that there was value in other technology transfer offices having access to a solution like this. “We knew that if other institutions started interacting with pharma and biotech companies with this level of efficiency, it would improve the industry as a whole,” Stahl added. “And that’s what ultimately led us to license the technology back to Aspect, who has the infrastructure in place to be able to offer the tailored solution to tech transfer offices anywhere in the world.”

The CTC was honored to be nominated for and win a Microsoft Health Users Group Innovation Award in the category of Innovation in Infrastructure Optimization for the Solution File.

Microsoft
Health Users Group

Innovation Awards 2014
WINNER

SYNTHETIC VERNIX TECHNOLOGY LICENSED TO SIRONA BIOCHEM

Cincinnati Children’s and Sirona Biochem signed a Letter of Intent and subsequently a License Agreement to create an anti-aging skin care treatment that combines Cincinnati Children’s patented synthetic vernix technology created by Marty Visscher, PhD and Sirona Biochem’s patented cell preservation glycoprotein.

Sirona will lead the development, with support from Cincinnati Children’s, of the anti-aging cream incorporating the proprietary technologies of each organization. The resulting new anti-aging product will be patented with the goal of licensing the new technology to a global leader in the cosmetic and consumer packaged good marketplaces.

Right: An infant is shown shortly after birth with some vernix still intact – vernix provides incredible protection to the skin while a baby is in utero.



ASSUREX HEALTH: FROM ZERO TO 200

Cincinnati Children's spinout Assurex Health sees unprecedented growth and doesn't plan on slowing down anytime soon

In 2006, Assurex Health was founded based on technology from Cincinnati Children's and Mayo Clinic with the hopes of changing the outcome for patients suffering from behavioral health conditions. Assurex Health's proprietary technology, with six issued worldwide patents and eight more in process, helps clinicians determine the right drug for individual patients through pharmacogenomics, evidence-based medicine, and clinical pharmacology.

Assurex Health is experiencing growth on many fronts; here are a few areas of key growth and impact:

- Grew from zero employees in 2006 to 200+ today
- Launched with approximately \$500,000 in seed stage funding and have currently brought more than \$45MM in equity and debt investments into the region
- Expanded its GeneSight® product portfolio from one to four:



GeneSight® Psychotropic

This test analyzes genes that may affect a patient's response to antidepressant and antipsychotic medications. The test includes pharmacokinetic genes from the Cytochrome P450 family and pharmacodynamic genes related specifically to the serotonin system are genotyped.

GeneSight® ADHD

This test analyzes genes that can affect a patient's response to ADHD medications, including stimulant and non-stimulant medications. The test includes pharmacokinetic genes from the Cytochrome P450 family and pharmacodynamic genes related to the regulation of neurotransmitters. every day now."

GeneSight® Analgesic

This test analyzes genes that can affect a patient's response to pain medications. The test includes pharmacokinetic genes from the Cytochrome P450 family and pharmacodynamic genes that mediate the analgesic effects of commonly prescribed opioid, NSAID and muscle relaxant medications. In addition, the report can help clinicians find the right medication for patients with opioid dependency.

GeneSight® MTHFR

This test can help clinicians determine if additional folic acid supplementation is necessary.

- Opened Toronto Lab in 2013 as its first international expansion and is now currently selling in Canada and South America
- Over 8,000 healthcare providers have used GeneSight technology to help more than 75,000 patients to date and Assurex Health has processed more than 150,000 GeneSight tests.

While the employee growth and economic impact is great, what the leadership and employees of Assurex Health care about most is the positive impact they're having on patients. "What's most important," says Don Wright, executive vice president and COO, "is that our technology works and it saves lives every day – hundreds of lives every day now."



CENTER FOR TECHNOLOGY COMMERCIALIZATION (CTC)

Cincinnati Children's Hospital Medical Center
3333 Burnet Ave, MLC 7032
Cincinnati Ohio 45229
513.636.4285
www.cincinnatichildrens.org/ctc

