

**INDIANA
BIOSCIENCES
RESEARCH
INSTITUTE**

2016 ANNUAL REPORT



**DISCOVERY
WITH PURPOSE**



**A NEW MODEL
FOR INNOVATION**



2016: A YEAR OF GROWTH

The Indiana Biosciences Research Institute (IBRI) was founded on the principle of “Discovery with Purpose.” The Institute’s goal is to deliver research that has a meaningful impact on the lives of people, beginning with those affected by diabetes, metabolic disease, and poor nutrition.

From its inception in 2013, the IBRI has steadily developed partnerships, acquired funding and built the systems to create an environment where research can be done and then translated into innovation and new technologies. With the help of its Scientific Advisory Board, composed of top scientists from the IBRI’s industry partners—Lilly, Roche Diagnostics, Cook Medical, and Dow AgroSciences—the IBRI has identified key research areas including metabolic discovery and translation, applied data sciences, and single cell bioanalytics.

With this foundation in place, in 2016 the Institute began to acquire world-class scientific talent, develop a unique set of research capabilities, and initiate collaborative projects that will ultimately drive the IBRI’s success.

THE INDIANA LIFE SCIENCES ECOSYSTEM

INSTITUTES, INFO EXCHANGES

MHIN
INDIANA HEALTH INFORMATION EXCHANGE
REGENSTRIEF INSTITUTE

DIAGNOSTICS
ROCHE
SIEMENS

GOVERNMENT
STATE OF INDIANA
CITY OF INDIANAPOLIS

RESEARCH UNIVERSITIES

PURDUE UNIVERSITY
INDIANA UNIVERSITY
UNIVERSITY OF NOTRE DAME
INDIANA CTSI

DEVICES, CELLULAR

COOK MEDICAL
ZIMMER BIOMET
DEPUY SYNTHES

LIFE SCIENCES ENTREPRENEURS

ANAGIN, INC
XYLOGENICS
DIAGNOTES
APEXIAN
ZORION MEDICAL

TECHNOLOGY

HCL.COM
TECHPOINT
MOSER CONSULTING
BIG DATA
SALESFORCE

PAYERS

ANTHEM
MD WISE

LAB TESTING, DEVELOPMENT

COVANCE
LABCORP
ENVIGO

PROVIDERS

COMMUNITY HEALTH NETWORK
ESKENAZI HEALTH
IU HEALTH
ST. FRANCIS HEALTH

NUTRITION
DOW AGROSCIENCES
ELANCO
MEAD JOHNSON

THERAPEUTICS
ELI LILLY AND COMPANY

ELI LILLY AND COMPANY



ENVIRONMENT FOR SUCCESS

The state of Indiana has a large life sciences industry: 265,000 Hoosiers whose employment tracks directly to the life sciences industry; \$62 billion in annual economic impact; and \$9.9 billion annually in product exports (more than automobile manufacturing). Further, the impact of the life sciences industry is statewide. Eli Lilly and Company alone spends \$1 billion with suppliers in the state across 62 of 92 counties.

The state's unique life sciences sector represents varied, yet complementary and shared, areas of expertise including pharmaceuticals, medical devices and diagnostics, medical delivery systems, and nutrition. Only one other state in the country matches Indiana's life science sector's size and diversity.

The IBRI is bringing together—for the first time—Indiana's life sciences industries and research universities to more effectively pursue innovation and applied research to improve human health in Indiana and around the world. The Institute's model and applied orientation are uniquely suited to bridging the gap between industry and academia. This model is particularly powerful as an approach to foster collaboration and leverage resources in an era of financial constraint and challenging science. The IBRI “bridges the space in between” to connect Indiana's life sciences sector and is an effective vehicle for driving innovation and economic development.

¹BioCrossroads Annual Report. 2015.

²Eli Lilly and Company, 2013.

³TEconomy/Bio. The Value of Biosciences Innovation in Growing Jobs and Improving Quality of Life. 2016.



ATTRACTING
WORLD-CLASS
TALENT

This year the IBRI made great strides in attracting top scientific talent, including its Chief Scientific and Innovation Officer and its first two Research Fellows. The Institute also added a Senior Scientist and a Visiting Research Fellow in the Applied Data Science Center and filled key administrative positions.

RAINER FISCHER, PHD, accepted the position as Chief Scientific and Innovation Officer in October. Dr. Fischer has built and led the Fraunhofer Institute for Molecular Biology and Applied Ecology (IME) in Aachen, Schmallenberg, Muenster, Giessen, Frankfurt and Hamburg in Germany, and its subsidiaries in Newark, Delaware, and Santiago, Chile for the past 19 years. The Fraunhofer-Gesellschaft is the largest applied science research organization in Europe, with research aimed at addressing issues of health, security, production technology, energy, materials, and the environment.

During his time at the Fraunhofer, Dr. Fischer grew the IME Institute from 40 to 680 employees, raised almost one billion euro in extramural research funding, and established international collaborations with academia and industry in more than 25 countries. Those collaborations include many of the leading global companies in the biotechnology, pharmaceuticals, agriculture, food, and chemical industries.

In addition to his leadership experience, Dr. Fischer also serves as Department Head of the Institute for Molecular Biotechnology at RWTH Aachen University where he was recently awarded a Distinguished Professorship. Dr. Fischer created the department, co-establishing both undergraduate and graduate programs that have matriculated more than 300 students. He is a prolific presenter and has published more than 330 peer-reviewed scientific papers which have been cited almost 15,000 times. Dr. Fischer also co-founded five biotechnology startups, holds 40 patents and has 64 patent applications pending. He will join the Institute in early 2017.

As the Chief Scientific and Innovation Officer for the IBRI, Dr. Fischer will set the scientific focus for the Institute and will work alongside President and CEO David Broecker to recruit top talent, grow the institute's endowment, and develop collaborative projects.

MICHAEL PUGIA, PHD, joined the IBRI in late October as a Research Fellow and Director of the new Single Cell Bioanalytics Center. Dr. Pugia comes to the IBRI following a successful 30-year career in the biomedical in-vitro diagnostic industry. There he contributed to more than 20 new product launches for Bayer and Siemens and spent 15 years as a director of research and development working on next generation analytical and diagnostic technologies in collaboration with leading institutions and companies. Dr. Pugia's primary research interest is the development of single-cell bioanalytical technology for proteomic biomarkers discovery in the fields of endocrinology and oncology.

In 2009 Dr. Pugia was awarded the Siemens Inventor of the Year for his work on a miniaturized "lab-on-a-chip" diagnostic tool. He also was recognized with nine Bayer

Science and Technology Awards including the Outstanding Bayer Technology Award, the Bayer Corp Quality Excellence Award, and the Near Patient Testing Segment, General Manager Award for Exceptional Leadership. The American Association of Chemistry honored Dr. Pugia as the Samuel Natelson Senior Investigator in recognition of outstanding service for the advancement of clinical chemistry, and as the winner of the 1st Annual AI Free Memorial Lectureship.

Dr. Pugia holds 367 U.S. and foreign patents, has 72 pending patents, and has 55 manuscripts, 13 book chapters and hundreds of conference papers and lectures in a wide variety of chemistry disciplines to his name. He earned his PhD in chemistry from Texas Tech University and his bachelor's degree in chemistry from Clarkson University. While working in industry, he has held adjunct positions as a Visiting Scholar at the University of Notre Dame and as a Clinical Research Professor at the University of Louisville Medical School.



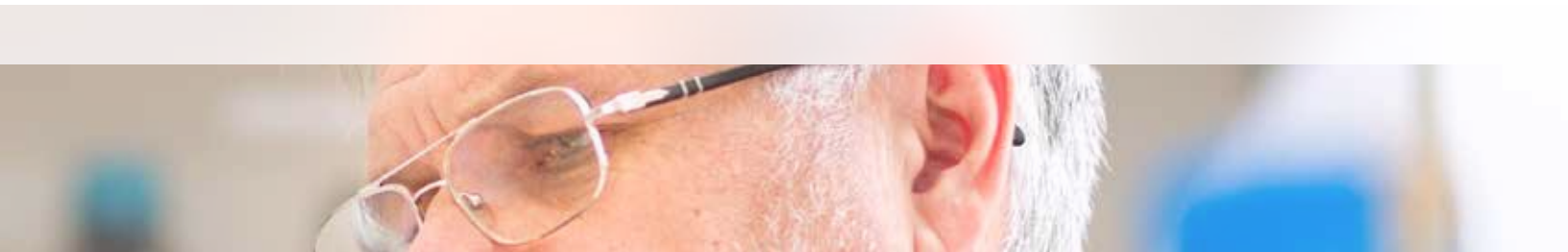
The IBRI's first independent investigator, **TERESA MASTRACCI, PHD**, started in April. She is an emerging talent from Indiana University School of Medicine with expertise in developmental biology applied to metabolic function. Her research focuses on finding ways to provoke regeneration of the insulin-producing beta cells that are dysfunctional or destroyed in people with diabetes. This research is designed to produce new diabetes treatment options that identify ways to slow or even halt progression of the disease.

Dr. Mastracci completed her post-secondary education in Canada, earning her bachelor's degree from the University of Guelph, and her PhD from the University of Toronto at the Lunenfeld-Tanenbaum Research Institute. She moved on to postdoctoral studies at Columbia University and the Naomi Berrie Center for Diabetes Research in New York. Here Dr. Mastracci merged her interests in developmental biology and human disease by studying how the pancreatic insulin-producing beta cell develops and functions in the normal

and diabetic contexts. In 2007, Dr. Mastracci was named the Naomi Berrie Fellow in Diabetes Research and was granted research support by the Russell Berrie Foundation. Subsequently in 2010, she was awarded a prestigious Postdoctoral Fellowship from the Juvenile Diabetes Research Foundation, which continued to support her career development and research.

RAGHU MIRMIRA, MD, PHD, accepted a 10 percent appointment as the first Indiana Research Fellow and Interim Scientific Director for IBRI in January. Dr. Mirmira played a critical role in overseeing the establishment of facilities for functional areas of research.

Dr. Mirmira's appointment highlights the collaborative nature of the Institute. He is the Director of the IU Center for Diabetes and Metabolic Diseases, one of only 16 NIH-funded Centers across the nation. He is the primary investigator for a grant from the NIH Human Islet Research Network (HIRN),



the Eli Lilly and Company Chair in Pediatric Diabetes, the Director of the Pediatric Diabetes Research Group at the Indiana University School of Medicine's Herman B Wells Center for Pediatric Research, and the Director of the NIH-funded IU Medical Scientist Training Program for combined MD, PhD students. Dr. Mirmira is also the associate editor of several leading top tier journals in the field and a member of the editorial boards for several others, chairs the NIH NIDDK B study section, and has been a member of the American Society for Clinical Investigation since 2010.

a Research Career Award from the National Institutes of Health for his work. Dr. Mirmira was one of only nine medical researchers in the country—and the only diabetes researcher—to receive the Discovery Health Channel Medical Honors Award.

Dr. Mirmira serves as a member of the Diabetes, Endocrinology and Metabolic Diseases B Subcommittee of the Diabetes and Digestive and Kidney Diseases Initial Review Group, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health.



Dr. Mirmira received his bachelor's, MD, and PhD degrees from the University of Chicago. Dr. Mirmira served his medical residency and subspecialty training in diabetes and endocrinology at the University of California at San Francisco, where he studied how insulin-producing beta cells form during development in the embryo, and received the Physician Postdoctoral Fellowship Award from the Howard Hughes Medical Institute and

Furthering the collaborative efforts of the IBRI, Notre Dame Professor **NITESH CHAWLA, PHD**, joined the IBRI as a Visiting Fellow of the Institute at 10 percent time. He will help build the IBRI's capacity in applied data science.


Dr. Chawla's innovative research on data science, machine learning, and network science has led to transformative

interdisciplinary applications in healthcare, life sciences, environmental and climate sciences, education, business, and national security.

The Frank M. Freimann Professor of Computer Science and Engineering, Dr. Chawla also serves as director of both the iCeNSA research center on network and data sciences and the Data Inference Analytics and Learning Lab (DIAL) at the University of Notre Dame. He has brought more than \$19.5 million dollars in research funding, published more than 185 papers with over 10,800 citations, and was twice awarded Notre Dame Computer Science and Engineering's

Applied data science capabilities that will integrate multiple so-called sources of "big data" with biological information is a key area of investment for the IBRI. This convergence of information technology and life sciences is an exciting area for future innovation. The Applied Data Science Center will help the IBRI create tools and develop applications that will enable deep computer learning to assist researchers, clinicians, and patients.

To support the continued growth of the organization, the IBRI hired key administrative staff in 2016, including Mark Andersen as the Chief Financial Officer and Vice President for Administration, Christy Denault as the Director of



Outstanding Teaching Award. He is the recipient of the IBM Watson Faculty Award, the IBM Big Data and Analytics Faculty Award, IEEE Computational Intelligence Society Outstanding Early Career Award, and the National Academy of Engineering New Faculty Fellowship. Dr. Chawla also founded his own data science software company, Aanalytics, which helps others harness the power of data to fuel their economic engines.

External Affairs and Communications, and Jacob Smith as the Director of Information Technology. Former CEO of Indiana University Health, Daniel Evans, Jr., was named as chairman of the IBRI Board of Directors.



BUILDING STRENGTHS

The IBRI is building a unique set of capabilities designed to support the work of our researchers and enhance other capabilities that are available through partnerships with academia and industry. As we launch the Institute, we have developed the following:

METABOLIC MOUSE CORE

The IBRI has a Metabolic Mouse Phenotyping Core designed to provide an array of sophisticated research techniques for the purpose of investigating mouse models of human disease. The core advances medical and biological research by providing researchers with comprehensive, standardized, and high quality metabolic phenotyping services for mouse models of diabetes, diabetic complications, obesity and related disorders.

The core utilizes the TSE System metabolic caging for up to 16 mice that includes indirect calorimetry, food and water intake and activity measurements. The core also offers services that include EcoMRI, GTT, ITT, islet isolation, GSIS, and tissue procurement. The core also offers extended time food and water intake measurements by utilizing the BioDaq caging system.

ZEBRAFISH CORE

The IBRI Zebrafish Core Facility is a shared resource that provides researchers with the ability to utilize the zebrafish model organism in their studies. Zebrafish have several advantages over other model organisms including ease of genetic manipulation, a sequenced genome, rapid external development, high fecundity, extensive regenerative capabilities, and straightforward husbandry requirements. Our facility has the capacity for 120 tanks, with an expanding complement of transgenic models. This facility will assist our researchers and collaborators as they work to better understand human development and diseases by providing access to a unique tool by which molecular mechanisms can be explored in vivo.

MICROSCOPY CORE

The Microscopy Core houses state-of-the-art microscopy equipment with related imaging acquisition software for use by IBRI researchers and collaborative projects. Currently the Core contains a Zeiss LSM 710 confocal microscope with capacity for high resolution imaging, a Leica M205 fluorescent dissecting microscope with a camera for wholemount imaging, and two Leica M80 dissecting microscopes outfitted with cameras and video monitors to provide teaching and interactive learning capabilities.

CELL CULTURE CORE

The IBRI Cell Culture Facility supports research studies that require the culture of human and/or animal-derived primary and immortalized cells. The facility contains all necessary equipment to facilitate this in vitro culture work including, but not limited to, cellular analysis, manipulation, and microscopy.

FAIRBANKS INSTITUTE TISSUE CORE

Originally funded with a \$10 million gift from the Indianapolis-based Richard M. Fairbanks Foundation in 2006, the Fairbanks Institute created a next generation biorepository as a resource for research on chronic diseases of aging. INBank™ enrolled participants in what was at the time a unique long-term health study that linked biological samples with participants' real-time medical histories, allowing tracking of the progression and complications of the disease over time. The IBRI now houses a replica of that biorepository of roughly 17,000 samples with the ability to connect those samples to longitudinal medical data for purposes of research.

COLLABORATION TO ACHIEVE CHANGE

The IBRI has a proven ability to overcome organizational barriers to facilitate complex, multi-organizational projects. Institute researchers have ongoing projects with a variety of partners, including:

REGENERATION OF BETA CELLS IN TYPE 1 DIABETICS

Teresa Mastracci, PhD, is performing research in the area of type 1 diabetes with a specific focus on beta cell regeneration. The progressive loss of insulin-producing beta cells in the pancreas characterizes all forms of diabetes. The daily administration of exogenous insulin is a viable and long-standing therapy. However, research efforts are now aimed at generating therapeutics that can ultimately fix, not just treat, the beta cell loss. Mastracci is studying specific molecules that can be targeted by drugs to preserve or regenerate the insulin-producing beta cells in the pancreas of individuals suffering from type 1 diabetes. This research is funded through a Career Development Award from the Juvenile Diabetes Research Foundation (JDRF), recognizing Mastracci as a promising early career scientist.

BIOMARKER IDENTIFICATION

In partnership with external collaborators from various universities, and utilizing resources from the Network of Pancreatic Organ Donors with Diabetes (nPOD), the Integrated Islet Distribution Program (IIDP), and ongoing

clinical trials at Indiana University School of Medicine, Dr. Mastracci is working to identify biomarkers of beta cell preservation and growth in humans.

UNDERSTANDING PUBLIC HEALTH IN INDIANA

IBRI Visiting Fellow Dan Robertson, PhD, worked with several government and non-profit health organizations to drive a rapid collaborative project to explore the available information for improved understanding of public health in Indiana. This project provided insights into available regional data and facilitates planning ways to better access and integrate data in the future to drive evidence-based programs and measure success within the state. A follow-on collaboration that uses the results and insights from this completed project is being planned.

DIGITAL DEVICE DATA COLLECTION

With the rapid emergence of digital devices and associated toolkits such as Apple's ResearchKit for iOS, personal devices are expected to be a key factor in understanding non-biological factors as it relates to disease. To generate experience in how to best drive research and innovation with these devices, Dr. Robertson initiated a collaboration with IBRI and a small entrepreneurial company with experience in health-based applications to generate a platform that will allow research of clinical application of these devices and securely capture this data for analysis

BETTER UNDERSTANDING TYPE 2 DIABETES

As shown by other research, type 2 diabetes is a complex, multi-symptomatic metabolic disease with variability in the patient population related to disease progression, therapeutic response, or related complications. Working in partnership with Eli Lilly and Company, Roche Diagnostics, the Regenstrief Institute and Indiana University, Dr. Robertson is working to better understand how type 2 diabetes varies in different patients, the first step to identifying new targets for the development of novel patient treatments and improved diagnostic tools. The first-of-its-kind partnership will have access to information on more than 800,000 type 2 diabetics in the State of Indiana. The project advances IBRI's research focus on "big data," and the convergence between life science research, informatics and technology.

COLLABORATIVE TOXICOGENOMICS PLATFORM

As new data in genomics, transcriptomics, proteomics, and metabolomics is becoming available to the research community, there is a lack of standard capabilities to analyze, collaborate, and reproduce the emerging methods for early risk assessment across organs, tissues, and species. Specifically, there is a lack of transparency across academic agencies regarding what is being done in the industry research programs. This lack of transparency may result in delays in adoption of new approaches to risk assessment and

inconsistent interpretation of results if methods cannot be reproduced by academic scientists. A network-based approach may help address that by, for example, improving the ability to make quantitative assessments by extrapolating data to human or other species regarding new agrochemicals or pharmaceutical projects.

Dr. Robertson is working with Dow AgroSciences and Eli Lilly and Company to generate a shared platform for early risk assessment using toxicogenomics that can accelerate the development of the supporting science and increase adoption of new risk assessment tools by the broader research community.

INNOVATORS' ENGAGEMENT PROGRAM

Part of the mission of the IBRI is to serve as a catalyst for entrepreneurial activity. There is a shortage of both lab and office space for life sciences startups in central Indiana. The IBRI has created an Innovators' Engagement Program that enables small and semi-virtual organizations to tap IBRI resources at market rates, but on a "pay as you go" basis, which enables these organizations to access underutilized but essential resources that otherwise are not available or are unaffordable.

LILLY ENDOWMENT GRANT

In February, Lilly Endowment Inc. and the Eli Lilly and Company Foundation donated \$85 million to support the IBRI's vision to build a world-class research institute that will serve as a catalyst for accelerating research and innovation.

"IBRI holds great promise to enhance Indiana's position as a global leader in life sciences innovation with its novel model that will forge deep and synergistic collaborations among Indiana's life sciences companies and research institutions," said N. Clay Robbins, chairman, president and CEO of Lilly Endowment.

"Indiana must continue to expand and enhance its intellectual capital and strengthen its economy, and we believe IBRI will further both of these imperatives while at the same time fostering research designed to improve health outcomes throughout the world."

In October, Cook Medical made a \$1 million research grant to support the next phase of growth for the Institute dedicated to discovery science and applied research leading to innovation targeting cardio-metabolic disease, diabetes, and poor nutrition. The donation was matched through a grant from the Lilly Endowment.

"We're proud to support the IBRI and their pursuit to attract the best and brightest to Indiana to develop and discover the next

generation of medical breakthroughs," said Steve Ferguson, chairman of the board of Cook Group. "The partnership with IBRI provides opportunities to improve patient care while stimulating Indiana's economy through the life sciences industry."

The Lilly Endowment and the Cook Grant have now pushed the IBRI over the \$100 million mark in total capital raised.

JDRF CAREER DEVELOPMENT AWARD

Teresa Mastracci, PhD, a Senior Scientist at the IBRI, received a 2016 Career Development Award from JDRF, the leading global organization funding type 1 diabetes research, in September. It was one of only two Career Development Awards issued in 2016.

Dr. Mastracci will use the \$750,000 award to continue her work in the area of beta cell regeneration. Her study will look at how polyamine and hypusine biosynthesis can be harnessed to reverse the progression of type 1 diabetes. Her goal is to identify new drugs that preserve or regenerate healthy beta cells, which will help to slow or even halt the progression of type 1 diabetes. Beta cells are the only cell type in the body that produces insulin, a hormone that is lacking in people with type 1 diabetes.

According to the Centers for Disease Control and Prevention, type 1 diabetes currently affects nearly 1 in 11 Americans. The World Health Organization estimates that worldwide 422 million adults have diabetes. Type 1 diabetes is sometimes referred to as “juvenile onset” because it is diagnosed in early childhood and requires lifelong insulin therapy.

The JDRF Career Development Award is designed to assist exceptionally promising researchers early in their careers. Past recipients of the award include Maike Sander, Director of the Pediatric Diabetes Research Center at the University of California San Diego; Mehboob Ali Hussain, Director of the Diabetes Center at Johns Hopkins University; and Matthias Hebrok, Director of the Diabetes Center at the University of California San Francisco. JDRF previously funded Mastracci’s research in 2010 with a prestigious JDRF Postdoctoral Fellowship.

PLACE MAKING AND 16TECH

The Institute is advancing plans to occupy approximately 75,000 square feet of open office and research space in the Indianapolis 16 Tech innovation community just north of the IUPUI campus. The 16 Tech innovation community is purpose-built to attract the best talent to collaborate, create and commercialize new ideas across a spectrum of advanced industries, including life sciences, technology, advanced manufacturing and the arts. The 60-acre innovation community stresses proximity of people and places to encourage collaboration and innovation, and will include flexible research space, ample public space, a mix of housing opportunities and retail and office space. As the anchor tenant, IBRI is stimulating the future development of the community for researchers, entrepreneurs, innovators and businesses. Groundbreaking is expected in early 2017.

BOARD OF DIRECTORS

The members of the IBRI Board of Directors represent the life sciences industry, academia, and government. They are committed to realizing the vision of the IBRI as a global leader in applied research to improve human health.

David Broecker

President & CEO, Indiana Biosciences
Research Institute

Wayne Burris

Senior Vice President & Chief Financial Officer,
Roche Diagnostics Corporation

Darren Carroll

Senior Vice President of Corporate Business
Development, Eli Lilly and Company

Daniel Evans, Jr.

Former Chief Executive Officer, Indiana
University Health

David Johnson

President & CEO, BioCrossroads and President
& CEO, Central Indiana Corporate Partnership

Dan Peterson

Vice President, Industry & Government Affairs,
Cook Group, Inc.

Jon Serbousek

Mid-Tech Industry Advisor, Board Advisor

Bill Stephan

Vice President for Engagement,
Indiana University

Micah Vincent

Director of Office Management and Budget,
State of Indiana

Steve Webb

External Technology & Intellectual Property
Development Leader, Dow AgroSciences

SCIENTIFIC ADVISORY BOARD

The members of the IBRI Scientific Advisory Board represent the deep, diverse talent pool across the life sciences industry and academia. They are committed to identifying new collaborations and areas of scientific commonality where the IBRI can facilitate breakthrough research.

Suresh Garimella, PhD

Executive Vice President for Research &
Partnerships, Purdue University

Brian Heald

Head of Diabetes Care Global Research &
Development, Roche Diagnostics

Michael Hiles, MSEE, PhD

Vice President for Research & Development,
Chief Scientific Officer, Cook Biotech, Inc.

Gary Krishnan, MSc, PhD

Global Lead for External Innovation,
Endocrine, Eli Lilly and Company

Jay McGill, PhD

Senior Director, Eli Lilly and Company Lilly
Research Laboratories

Raghu Mirmira, MD, PhD

Indiana Research Fellow, Scientific Director,
and Core Laboratories Director

Alan Wright, MD, PhD

Chief Medical Officer, Roche Diagnostics
Corporation

Steve Webb

External Technology & Intellectual Property
Development Leader, Dow AgroSciences

FOUNDERS

The IBRI Institute Founders are public,
private, and corporate donors who have led
the way in building the Institute.

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Indiana University Health

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