

IBRI Values



COLLABORATIVE

We can't do research alone - the IBRI exists to enhance the robust life sciences ecosystem by bridging industry and academic research.



TEAMWORK

We work together as one team, both within and across our operations, and externally with our partners and stakeholders.



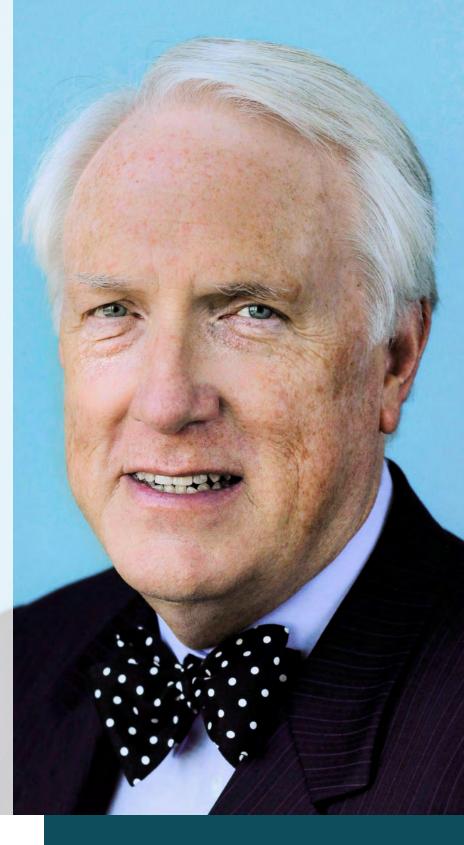
We are focused on game-changing research to help solve the most persistent health problems and challenges.



We do the right thing by adhering to the highest ethical standards and being honest, respectful, transparent, responsible and accountable.



We operate in a diverse ecosystem of colleagues, partners, stakeholders and patients where we respect diversity in people and in ideas.



Daniel Evans, former CEO of Indiana University Health, leads the IBRI Board of Directors as they set the strategic direction for the organization and guide us toward our vision to become a world-class research institute.

Executive Chairman's Letter

Dear IBRI Stakeholders:

The Indiana Biosciences Research Institute (IBRI) is becoming talent rich with the infusion of both seasoned and rising star researchers to the organization. These innovative new scientists, combined with the strong expertise that already thrives here, are driving advances in diabetes care, research into substance use disorders and creation of new technologies that improve patient health.

In my unique position as a native of Indiana and as a leader deeply rooted in the evolution of the Indiana life sciences economy, I am witness to the infinite potential that exists in our ecosystem and the ways that the IBRI is capitalizing and contributing:

Catalyst - The IBRI and its Applied Data Sciences Center (ADSC) figured prominently in a major real-world data study of type 2 diabetes that was published January 2019 in *Nature Medicine*. The IBRI was the catalyst that brought together Roche Diabetes Care BmBH, IBM and Eli Lilly and Company on this multi-year study.

Collaborator - The Mastracci Lab of the IBRI Diabetes Center assisted in the discovery of a new genetic disease named DHPS Deficiency with researchers from Columbia University.

Convener - The IBRI Pharmaceutical Biotechnology Center (PBC) became fully operational to aid in addressing some of the most pressing health issues in Indiana (i.e., opioid crisis) through the development of biotherapeutics.

Complementor - The IBRI was instrumental in creating an environment that shifted our Single Cell Analytics Center into a shared resource to benefit all scientists at the IBRI. The former center is now known as Bioanalytical Technologies.

Connector - The team watched in anticipation at the topping-off ceremony for Building 1, the new home of the IBRI and many of its partners in the 16 Tech Innovation District.

You will read more about these achievements and many others throughout this report. And, you'll learn about a group of other new researchers who are already innovating at the IBRI through the Lilly Diabetes Center for Excellence, a collaboration with the Indiana University School of Medicine and Eli Lilly and Company.

Growing a vibrant research organization is challenging yet invigorating. It can be an emotional rollercoaster to build an organization that must deliver on the high expectations of its founders and realize their vision of a world-class research organization. True to that vision, the IBRI continues to make strides in catalyzing activities across Indiana's life sciences to deliver value to the people of Indiana and the world. Weighty aspirations indeed, but those that our founders, board of directors and IBRI leadership are poised to achieve.

The generosity of our friends and IBRI founders was also realized in 2019 with a \$5 million challenge gift from an anonymous donor and an initial \$2.5 million gift toward the challenge from John and Sarah Lechleiter of Indianapolis.

The IBRI remains steadfast in its mission and has already delivered on its commitment to Indiana and beyond to be a catalyst, connector, convener and collaborator to complement the burgeoning academic and industrial life sciences research ecosystem in Indiana and beyond.

As we move deeper into 2020...the progress of the redesigned strategic plan shows tremendous promise... an experienced search organization and committee will no doubt announce a new CEO in the coming months...and preparations are underway for the move to 16 Tech.

We are ready to leverage all the future holds and are grateful you are with us on this journey!

Regards,

Daniel F. Evans

Executive Chairperson IBRI Board of Directors



LAUNCHED CTOX, A
SHARED TOXICOGENOMIC
PLATFORM



COLLABORATED WITH CARDINAL HEALTH ON ITS SIMULATED HEALTH DATA



WORKED ON AN ALIGNED STRATEGY CALLED THE INDIANA HEALTH DATA TRUST





PUBLISHED TWO PAPERS - NATURE MEDICINE AND TOXICOLOGICAL SCIENCES

Leading the Applied Data Sciences Center is Daniel Robertson, PhD. He and his team are focusing on the creation of tools and the development of applications that will enable deep computer learning to assist researchers, clinicians and patients.

Applied Data Sciences Center

Today's world is increasingly driven by data. Just consider the little data collectors many of us have on our wrists (e.g., FitBits, Apple Watches, Garmins). Every day massive amounts of data are captured, and the rate of data generation continues to accelerate. In the life sciences, the convergence of information technology and biology presents an opportunity for innovations in how we apply data to solve big problems.

CTox: Helps Accelerate Drug Development

When the IBRI or other organizations are in the drug discovery process there is a need to know how the molecule being created will affect human health and the environment. This is often time consuming. The launch of CTox, a new early risk assessment tool using toxicogenomics, aims to shorten that time.

Eli Lilly and Company, Corteva Agriscience (formerly Dow AgroSciences) and the IBRI partnered to develop this open data analytics platform that is designed to facilitate sharing both private and public sector expertise and processes to enhance the reproducibility of results and catalyze advances in toxicogenomics.

We believe by making CTox widely available to the broader scientific research community that it will ultimately help accelerate drug development by enabling timely decisions on the safety of compounds early in the discovery process. CTox can help do this based on shared data sets, development of new toxicogenomic tools and the collective understanding of molecular structure.

This platform was featured in the August 2019 edition of *Toxicological Sciences*, "A Novel Open Access Web Portal for Integrating Mechanistic and Toxicogenomic Study Results." In the paper, the team highlighted CTox's capabilities by analyzing the effects of several toxicants on liver gene expression to predict toxicity study outcomes upon chronic treatment from expression changes in acute-duration studies.

Based on this publication and coordinated communication efforts including exhibiting the platform at the annual Society of Toxicology conference, numerous organizations are in the process of evaluating this platform. Some have even used internal project molecules with known toxicology as a test case. To the team's knowledge, these assessments derived from the CTox platform are concordant with the internal proprietary data.

Focused on Understanding Type 2 Diabetes from Electronic Health Records (EHR)

The Center has continued to drive the use of EHR from Regenstrief Institute with various industrial partners. This builds on the success and visibility from the publication in early 2019 of the article in *Nature Medicine* that showed how real-world patient data can better predict diabetes-related kidney disease in patients with the chronic disease. The team completed extracting, cleaning and processing a new type 2 diabetes (T2D) dataset from the Regenstrief Data Core. This data was cleaned and has supported multiple projects by Roche Diabetes Care GmbH to evaluate machine learning models with their partners.

Additionally, the IBRI team played a critical role in supporting prework that led to another collaboration by Regenstrief with a multi-national company. The IBRI team delivered the data toward the end of the year that helped drive efforts to build a diabetes medication recommendation system. This collaboration is anticipating a publication in 2020 where the results and partnership will be revealed.

Health Data Trains the Next Generation

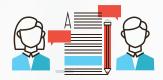
In 2019, we collaborated with the innovation arm of Cardinal Health – FUSE – on its simulated health data. This led to joining Cardinal Health on multiple webinars and meetings to explore the value of this type of simulated data. It also allowed us to be the first to utilize this data for training purposes in an IUPUI biostatistics course.

Helping Drive Indiana's Diabetes Strategy

In part influenced by a collaborative project in 2016 between the IBRI, the Indiana State Department of Health (ISDH), the Indiana State Management and Performance Hub (MPH), the Indiana Health Information Exchange (IHIE) and IU Health, the state legislature generated a mandate (HEA1175) in 2018 for ISDH to deliver a state-wide diabetes strategy leveraging local data sources rather than national patient-reported data. We had the opportunity to work with key partners (e.g., MPH, IHIE and Regenstrief Institute) on an aligned strategy called the Indiana Health Data Trust that assisted ISDH to meet the deadline to deliver its diabetes strategy.



SINGLE CELL ANALYTICS CENTER OBJECTIVE MET



ONE SIERRA PAPER
PUBLISHED BY TWO STAFF
MEMBERS



TWO COMPLETED
TECHNOLOGIES – BIOMEMS
POC ANALYZER AND SIERRA
REAGENT – IN RECORD TIME





FOUR STUDENTS
COMPLETED THEIR WORK
HERE, GRADUATED AND
FOUND JOBS!

Michael Pugia, PhD, is leading the Bioanalytical Technologies group in the development of state-of-the-art technology platforms and methods to support the IBRI's development of new standards of patient care and therapeutics.

Bioanalytical Technologies

For years we have been analyzing bulk populations of cells. While this is still critical work, we're now in an age of single cell analysis. Single cell technologies, such as microfluidics and mass spectrometry, are more sophisticated and provide a more comprehensive picture of a cell. Why is this important to Hoosiers? It means diagnosing diseases faster and more accurately, moving to treatment quicker and improving health outcomes.

Technologies Complete in Record Time

In 2016, when the Single Cell Analytics Center was organized, its mission was to develop technologies that would diagnose diseases efficiently, quickly and accurately. The center set a goal to accomplish this in five years, which at that point was ambitious.

Fast forward to 2019: The center achieved its goal two years ahead of schedule. Under the leadership of Director Michael Pugia, PhD, the center completed BioMEMs and SIERRA.

SIERRA Reagent

SIERRA is the Signal Ion Emission Reactive Release Amplification platform that helps diagnose infections and other diseases from a single cell. The research to show SIERRA's effectiveness for identifying rare cells in whole blood was published in *Analytical Chemistry* by team members Zane Baird, PhD, and Zehui Cao, PhD, with assistance from Anna Geisinger. This project also had support from Indiana University-Purdue University Indianapolis, Indiana University School of Medicine and the State of Indiana.

BioMEMs Point of Care (POC) Analyzer

BioMEMs is a biological microelectromechanical system that uses micro-sized components to reduce cost and improve sensitivity of diagnostic tests. For this project, we collaborated with Steven Wereley, PhD, at Purdue University and submitted research to Lab on a Chip about this new POC system. We also partnered with Frédérique T. Deiss, PhD, at Indiana University-Purdue University Indianapolis to submit an electrochemistry paper to Analytical Chemistry that demonstrated culture-free bacterial detection in clinical samples.

Now that SIERRA and BioMEMs are complete, we evolved the Single Cell Analytics Center into the Bioanalytical Technologies group that is still being led by Pugia and his team that includes Geisinger and Dylan Frabutt, PhD.

Bright Future Ahead

As we look to the horizon things look bright for the Bioanalytical Technologies group.

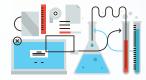
We already are members of and partners with the Center for Bioanalytic Metrology (CBM), which is a partnership between Indiana University, Purdue University and Notre Dame University that is funded by the National Science Foundation. The CBM seeks to solve current, emerging, and industry-relevant problems and create new capabilities in measurement science.

While we are working on other bioanalytical technologies, like what we did with SIERRA and BioMEMs, we also continue to support the work of IBRI diabetes research. For example:

We published research that showed whether mice developed diabetes.

We've submitted a paper featuring research that shows the ability to predict the risk of death from cardiovascular or kidney disease in individuals with type 2 diabetes.

We published a novel new lipodomic bioanalytic method for detecting resistant bacteria with Professor Graham Cooks of Purdue University in Analytical Chemistry and have been applying this to diabetic wound analysis with Professor Chandan Sen of the Indiana University School of Medicine.



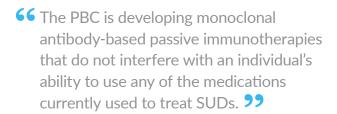
ESTABLISHED CAPABILITIES
FOR ANTIBODIES,
LEAD DISCOVERY AND
OPTIMIZATION



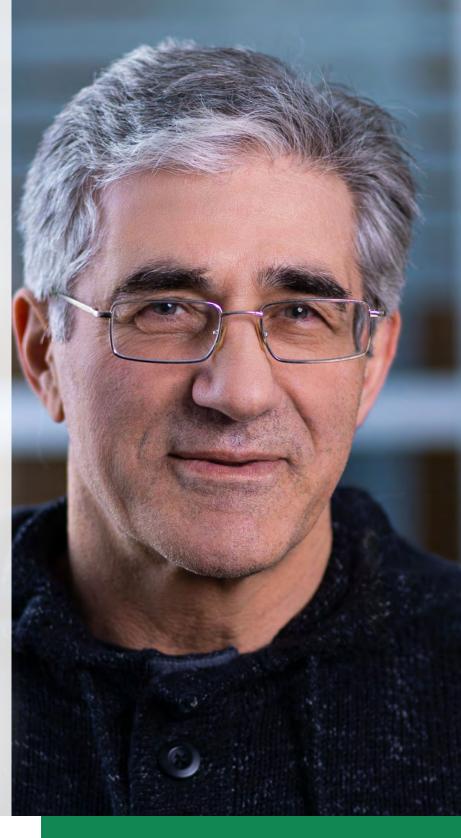
INITIATED MULTIPLE COLLABORATIONS
AND PROGRAMS FOR TREATMENT OF
SUBSTANCE USE DISORDERS



IDENTIFIED ANTIBODY HITS
WITH POTENTIAL THERAPEUTIC
EFFECTS



Vidadi Yusibov, PhD, research program director of the PBC



Vidadi Yusibov, PhD, is leading the Pharmaceutical Biotechnology Center as it focuses on translational research and the development of antibodies, proteins and vaccines for public health and biopreparedness.

Pharmaceutical Biotechnology Center

The prevalence and societal impact of substance use disorders (SUDs) is an acknowledged public health crisis. While an imperfect measure of its impact on society, opioid overdose deaths can be viewed as the leading edge of this crisis. In a 12-month period, ending April 2019, it was estimated that 67,123 Americans died from an opioid overdose. While multiple medications are now available to treat opioid use disorders, given the prevalence and societal burden, additional well tolerated and effective therapies are needed.

The PBC is developing monoclonal antibody (mAb)-based passive immunotherapies. This approach is based on complexing a drug of abuse in the periphery, thereby preventing it from reaching the central nervous system. This approach offers a high degree of specificity to drug abuse, can be administered in quantities to sustain amounts required for clinical efficacy in all patients and does not interfere with an individual's ability to use any of the medications currently used to treat SUDs.

Profile and Growth

In 2019, the Pharmaceutical Biotechnology Center (PBC) finished building laboratory infrastructure, established critical workflows, assembled a talented team of scientists and initiated core program activities. As a translational research organization, the PBC is organized into two well-equipped functional groups:

Target and Therapeutic Discovery – focused on molecular biology, including all aspects of gene design and vector construction.

Protein Optimization and Developability Assessment – focused on the characterization and optimization of the target molecule as it matures into a clinical product.





LAUNCHED THREE NEW INVESTIGATOR LABS



ESTABLISHED AN IPSC (INDUCED PLURIPOTENT STEM CELLS) CORE LABORATORY



PUBLISHED RESEARCH IN FOUR JOURNALS INCLUDING NATURE GENETICS AND DIABETES CARE



66 I'm eager to be part of the IBRI and to work with my new colleagues to help create breakthroughs in the diagnosis, treatment and management of diabetes in Indiana and beyond. 99

Investigator Decio Eizirik, MD, PhD

Robert Considine, PhD, is leading the IBRI Diabetes Center with tremendous support from Decio Eizirik, MD, PhD. Together with their team, they are focused on the molecular basis of diabetes and its complications, including mechanisms for beta cell regeneration.

IBRI Diabetes Center

Many of the innovations in diabetes care have happened here in Indiana. The IBRI is poised to inspire the next generation of innovations in diabetes care through its research into skeletal muscles and glucose intake, how the brain effects energy expenditure, and the relationship between beta cells and the immune system. The goal of these integrated research lines, tackling the different pathways that lead to obesity and diabetes, is to improve the lives of individuals with diabetes and ultimately lead to diabetes prevention.

World-Renown Investigator Joins IBRI

In July 2019, at our first-ever Diabetes Seminar, we announced that Decio Eizirik, MD, PhD, had joined our team. Eizirik arrived at the IBRI from Université Libre de Bruxelles (ULB) Center for Diabetes Research in Brussels, Belgium.

As Eizirik established his lab, he added Donalyn Scheuner, PhD, Stephane Demine, PhD, and William Carter. Eizirik and his team have already made strides on:

Beta cells and the immune system – published in *Nature Genetics*. While this research helped us understand why some people get diabetes and others get arthritis despite having several risk genes in common, it also showed us that only targeting the immune system for type 1 diabetes (T1D) therapies is not enough. We must also boost beta cell survival. With this knowledge we can focus on developing novel therapies to treat T1D.

Establishing an induced pluripotent stem cells (iPSCs) core at the IBRI and validating an iPSC-based model to develop pancreatic beta cells to better understand the pathogenesis of T1D. The stem cells we work with are adult cells that are modified. This core allows us to screen for new drugs that may protect beta cells early in the disease and therefore slow the progression of T1D. This research was published in Stem Cell Research & Therapy.

Testing a new treatment for a human monogenic form of diabetes – Friedreich ataxia – published in *JCI Insight*. This is the first time a treatment has shown interesting perspectives to slow the progression of this devastating disease. Importantly, it also validates the use of iPSC in screening for new drugs for rare and difficult-to-treat diseases.

Two New Labs Approach Diabetes in Different Ways

The fourth quarter of 2019 brought the launch of two new labs in the Diabetes Center – Flak Lab and Witczak Lab. First, we welcomed Jonathan Flak, PhD, and his expertise in the central nervous system's regulation of glucose metabolism. Dr. Flak added David Johnson to his team and together they are focused on investigating the neurocircuits that are critical to obesity and diabetes. Then, we introduced Carol Witczak, PhD, who is an expert in the molecular and cellular factors that regulate muscle metabolism. Her research with Parker Evans is centered around understanding the molecular and cellular factors that regulate skeletal muscle glucose uptake and metabolism in response to type 2 diabetes and exercise.

Exploration of Neurodevelopmental Delay and Seizures

Teresa Mastracci, PhD, and her lab team continued their work on the polyamine and hypusine biosynthesis pathway. In 2019, Mastracci published a significant paper in the *American Journal of Human Genetics* identifying rare recessive gene variants in deoxyhypusine synthase that result in neurodevelopmental delay and seizures in humans. This previously unknown monogenic disease is now known as "DHPS Deficiency." She presented this work at the Gordon Research Conference. Mastracci also received a grant from the DHPS Foundation entitled, "The role of human DHPS mutations in development and disease," to continue her work in this area.

Sweet Response

In 2019, Robert Considine, PhD, continued his research into how the brain responds to sweet tastes. He presented data to the American Diabetes Association and the Obesity Society that showed women with obesity have greater activation of brain areas in response to oral sucrose than normal weight women, even though there is no difference in their preferred sweet taste. Food choice, determined to a large extent by our brain, is crucial in maintaining normal body weight, and understanding these complex processes will help to clarify the ongoing obesity epidemic.



Building 1 Topping Off Ceremony

Under a beautiful blue Midwestern sky, our new home – Building 1 of the 16 Tech Innovation District – reached its maximum height July 11. For the first time, it felt real. For all the talk about the 16 Tech Innovation District and what it aspired to embody, we finally saw the structure of our new office and the first building in 16 Tech complete.

The IBRI team had the opportunity in June 2019 to sign one of the 10-foot-long ceremonial steel beams that was placed atop the five-story building July 11. Our names joined those of our partners, our community members and the men and women who designed and are building our new home.

We watched in awe as crane operators hoisted and construction workers welded the beams in place. It was

a momentous occasion celebrated by our soon-to-be neighbors in Building 1 including the Central Indiana Corporate Partnership and IU School of Medicine, as well as leaders from 16 Tech, Browning Davis and other contractors.

We eagerly await the day in May 2020 when we will receive the keys and look forward to being fully settled in by fall 2020.



The IBRI in the Community

We are guided by five core values – teamwork, integrity, innovation, inclusion and collaboration. It's our commitment to collaboration that leads us to work with our local community to help neighbors in need, improve Hoosier health and educate STEM leaders.

Our mission is to improve health by targeting diabetes, cardiometabolic diseases and poor nutrition. While we do this through discovery and research in our labs, we also live our mission in the community through service.



Improving Health with Food Security

Each year on World Diabetes Day, which is Nov. 14, we partner with employees from Browning Investments to volunteer at Gleaners Food Bank of Indiana. Gleaners fights hunger by distributing food to hungry Hoosiers throughout the state. In 2019, our combined teams sorted 12,772 pounds of food for 10,643 meals.

Helping Neighbors in Need

We accepted a challenge from the Browning Investments team to see who could bring in the most donations to Goodwill of Central & Southern Indiana. The real winners of this challenge were Goodwill and Flanner House.

Together, Browning and the IBRI donated 108 13-gallon bags of clothing and household items, which led to more than \$500 in Goodwill vouchers we could share with clients at the Flanner House.

Educating the Next Generation of STEM Leaders

In the summer of 2019, we hosted five interns from neighboring high schools who were interested in pursuing college careers in STEM. We also welcomed several college students who shadowed our scientists for a day. We feel it is vital to cultivate the next generation of STEM-focused researchers. By giving them this opportunity to work alongside our research teams, we fuel their passion and live out our mission.



Supporting the Juvenile Diabetes Research Foundation (JDRF)

In addition to receiving grant funding from the JDRF, Teresa Mastracci, PhD, serves on the JDRF Medical Advisory Board, gave the keynote address at the Type One Nation Summit in March 2019 and champions JDRF fundraising at the IBRI. She joined other members of the JDRF Ride Team from Indiana in a 100-mile bike ride in LaCrosse, Wis., that raised money for JDRF-sponsored type 1 diabetes research. She also co-led the JDRF One Walk Team, which includes team members from the IBRI, IU Health, IU School of Medicine and the IU Center for Diabetes and Metabolic Diseases.

Discovery with Purpose

Our mission is to become the leading independent, industry inspired applied research institute focusing on the discovery and development of innovative solutions to improve health, targeting diabetes, cardiometabolic disease and poor nutrition.

Vision

Build a world-class organization of researchers, engineers and business professionals that catalyze activities across the Indiana (and beyond) life sciences community.

Goals

Catalyze opportunities through the industryinspired design of solutions for health problems associated with diabetes, cardiovascular disease and nutrition.

Complement and enhance the Indiana life sciences ecosystem by linking life science expertise to Hoosier health.

Connect industry, academia and the public sector to expedite solutions for the most pressing health issues related to cardio-metabolic diseases, including diabetes and poor nutrition.



Rong Qi, PhD, hosted high school senior Lindsay Lawlor to help Lindsay explore her interest in biochemistry. Rong gave her a tour of the labs and talked with her about data analysis.

66 The IBRI is connecting academic discovery from across the globe to industry development and public and private enterprise to improve human health. It is truly Discovery with Purpose. 99

Indiana State Health Commissioner Kristina Box, MD, FACOG

Board of Directors

Kristina Box, MD, FACOG

Indiana State Health Commissioner

Wavne Burris

Former Senior Vice President and Chief Financial Officer at Roche Diagnostics Corporation

Dan Evans, Board Chair

Former Chief Executive Officer of Indiana University Health

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Former Chief Executive Officer at Eli Lilly and Company

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Vice President of Industry and Government Affairs at Cook Group Inc.

Jon Serbousek

Managing General Partner at Pinnacle Advisory Partners

Bill Stephan

Vice President for Engagement at Indiana University

Donor Spotlight

Board of Directors Executive Chairperson Daniel Evans mentioned in his letter at the beginning of this report that the IBRI was the beneficiary of tremendous generosity from our friends and IBRI founders last year. In recognition of these gifts, we asked John and Sarah Lechleiter of Indianapolis, who donated \$2.5 million toward a \$5 million challenge gift, why they give to the IBRI.

Why is it important to you to donate to the IBRI?

There are many worthy causes Sarah and I could support. We choose to contribute to the IBRI because it represents a unique opportunity for Indiana to differentiate itself by building on our formidable strengths in the life sciences. Plus, it's fun to be part of a start-up and to help nurture its growth!

John, you've been called the inspirational leader for the IBRI. As you inspire others, how would you describe the personal satisfaction of giving to the IBRI that you have experienced?

I was pleased to play a part at the inception of the IBRI, along with many organizations and individuals, including other corporate leaders, the Lilly Endowment and our governor. Since that time, it's been energizing to get people excited about the IBRI and its promise. It's also been heartening to see the IBRI grow to a mid-sized nonprofit on the verge of moving to new state-of-the art facilities in the 16 Tech Innovation District later this year. Speaking personally, as someone trained as a scientist, it gives me great pleasure to know that our support goes directly to funding important scientific research.

What excites you and Sarah the most about the work the IBRI is doing?

We're most excited about the cutting-edge work IBRI scientists are doing in diabetes, population health and addiction — things that matter to the health of Hoosiers and all our fellow citizens. The IBRI will always be more than a research institute; We believe it will be a force for good.

What is your vision for the IBRI in 2020 and beyond?

Our vision for the IBRI is grounded in what has already been accomplished. In a relatively short time, the IBRI has been instrumental in building and strengthening connections between the corporate life sciences community and our major research universities. It has gained the support of major benefactors, including the Lilly Endowment and the State of Indiana. Our vision is that the IBRI continue to play the role of convener, catalyst and champion for the life sciences in our state. We hope that in 10 years, we can point to a number of important accomplishments in the life sciences sector and say, "This would not have happened if not for the IBRI."



Thank You

Thank you to authors and editors Robert Considine, Decio Eizirik, Jonathan Flak, Stephanie Grinage, Teresa Mastracci, Michael Pugia, Dan Robertson, Lisa Soard, Carol Witczak and Vidadi Yusibov. We also are grateful for design from Settimi Creative, photography by Fred Walls, web design by TBH Creative and printing by Miles Press.

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