

INDIANA
BIOSCIENCES
RESEARCH
INSTITUTE

2020 ANNUAL REPORT

SHAPING THE
FUTURE of
TRANSLATIONAL
SCIENCE for
HOOSIERS and the
WORLD

A New Journey Begins

Cover image: An expression of beta-3-tubulin in ectodermal cells generated from the IBRI's iPSC Core Lab.

Dear IBRI Stakeholders,

It has been an honor to step into the role of president and CEO at this time in the history of the Indiana Biosciences Research Institute (IBRI). In addition to moving into Innovation Building 1 in the 16 Tech Innovation District, this is a very exciting time for the life sciences in Central Indiana.

While 2020 wasn't the year any of us had planned, the commitment of the IBRI team to scientific advancement amid COVID-19 restrictions was truly commendable. We:

- **Discovered two classes of compounds that pave the way for future clinical trials of potential treatments for type 1 diabetes (T1D).**
- **Used electronic health records to predict health outcomes in persons with T1D.**
- **Identified a new approach to studying autoimmune diseases that includes researching the immune system and target tissues.**

Since arriving, I have been working with the Board of Directors and our leadership team to map out a new strategic direction for the IBRI. Importantly, this must reflect the dynamic and evolving role of innovators in the biomedical field and optimize where the IBRI can be best positioned alongside industry and academia to advance science and deliver meaningful outcomes for patients.

Without a doubt, our strategic intent will continue on the ambitious path that was envisioned when the IBRI was first founded several years ago but updated for today's scientific opportunities and environment.

Fundamentally, we will focus on enhancing our integrated capabilities and adding depth to how we approach patient-informed translational science, both independently and through valued collaborations.

To enable our strategy, we will focus on four general scientific areas:

- **The IBRI Diabetes Center will remain the primary focus of our disease research, but over time we will extend to other diseases that share common systems and pathways.**
- **We'll develop new capabilities for molecular innovation and drug discovery to investigate disease processes and pursue new therapeutic approaches.**
- **We'll reimagine data sciences and create novel end-user inspired solutions that address complex analysis, simulation and prediction across the translational sciences.**
- **We'll create an expanded platform of enabling technologies to bring the best tools to bear on complex scientific problems.**



I believe the IBRI has an opportunity to emerge as a key strategic partner with industry and regional academic centers to find innovative solutions to some of the most challenging biomedical problems.

I appreciate your support, partnership and commitment to our collective success as we move forward on this journey.

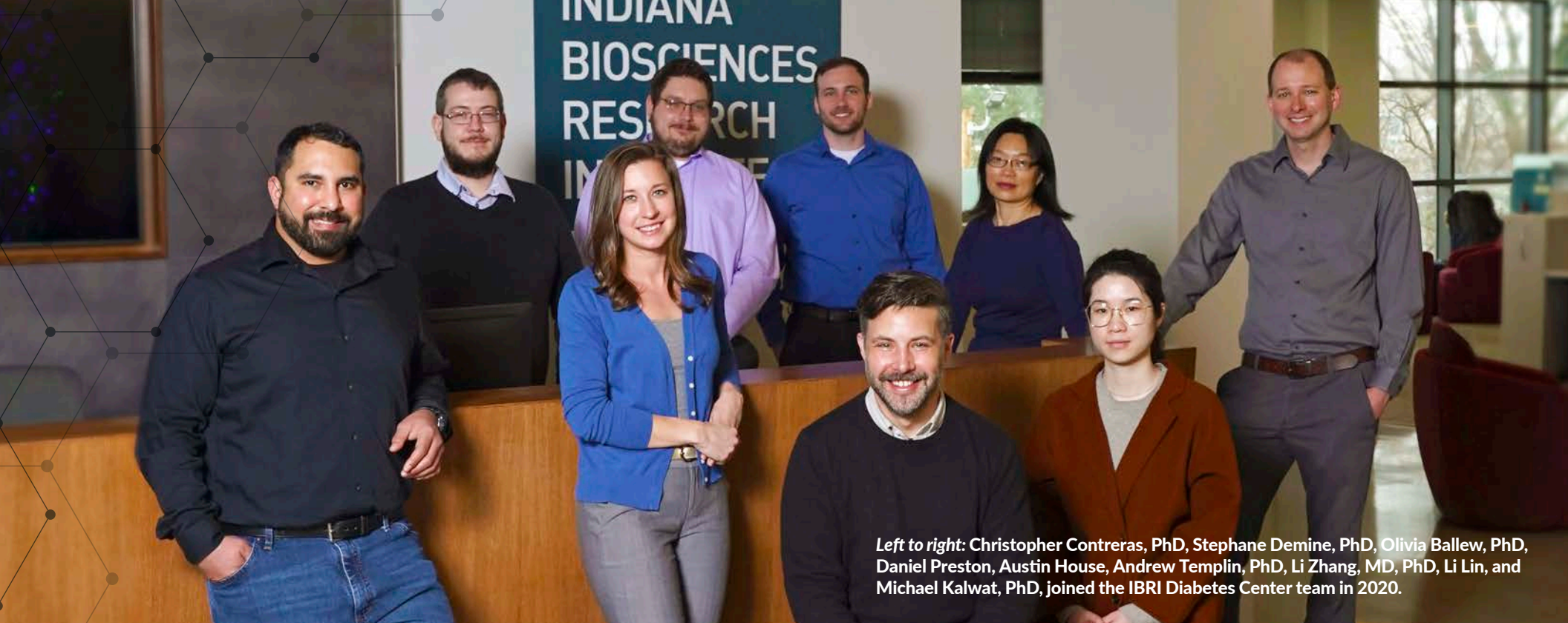
Very best regards,

A handwritten signature in black ink that reads "Alan Palkowitz". The signature is fluid and stylized, with a large, sweeping 'A' and a distinct 'P'.

Alan Palkowitz, PhD,
CEO & President, IBRI

A Nexus Point for Innovative Science

Innovation Building 1
in 16 Tech serves as the
new home of the IBRI.

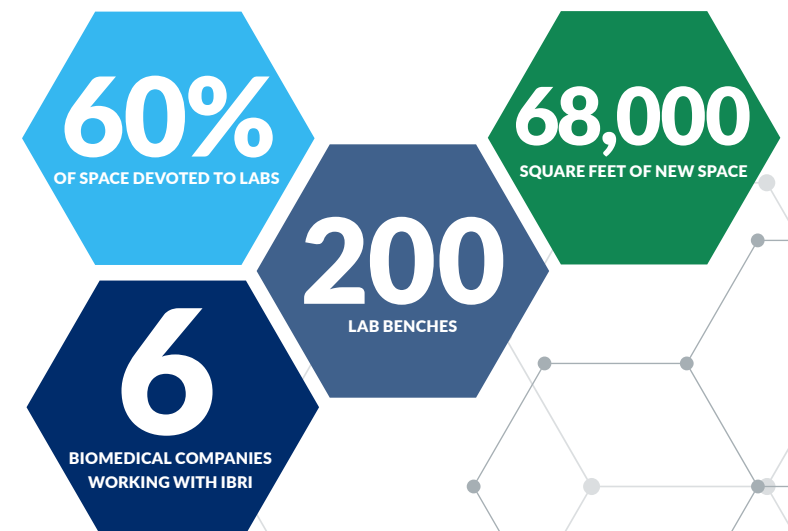


Left to right: Christopher Contreras, PhD, Stephane Demine, PhD, Olivia Ballew, PhD, Daniel Preston, Austin House, Andrew Templin, PhD, Li Zhang, MD, PhD, Li Lin, and Michael Kalwat, PhD, joined the IBRI Diabetes Center team in 2020.

In August 2020, 16 Tech formally cut the ribbon on its 50-acre mixed-use innovation district. In this new downtown community, 16 Tech seeks to support and foster cross-sector collaboration, promote innovation and boost economic growth and prosperity.

We at the Indiana Biosciences Research Institute (IBRI), were eager to move into the space we created that supports life sciences entrepreneurship, convenes diverse research teams and complements innovation in the ecosystem while remaining thoughtful about the impact on our neighborhood.

We see this new headquarters as a nexus point for academic institutions, industry, community and government. We envision the IBRI bringing these groups together to plan the future direction for life sciences in the Midwest. It all comes down to enabling innovation to translate research into improved health outcomes for Hoosiers and beyond.



One way to promote innovative science is to create an environment for new businesses to grow. To do this we partnered with 16 Tech and 1776, the nation's largest network of entrepreneurial incubators, to offer life sciences startups the opportunity to work in our space and use our equipment.



On-demand COVID-19 Tests

GenePace Laboratories is a biotech startup that acts as an on-demand service for organizations that need COVID-19 testing. Indiana Sports Corp. President Ryan Vaughn said, "GenePace Laboratories provided a holistic solution including testing and PPE procurement, quick turnaround times and a commitment to help us navigate unforeseen obstacles as they arose. They've allowed us to host sports events, when other cities have been unable to do so safely." GenePace Laboratories' goal is to offer a full suite of medical tests faster and with more accuracy.

Revolutionizing Heart Failure Treatment

FAST BioMedical is developing technology that has the potential to dramatically improve heart failure patient management by measuring – rather than estimating – both volume status and kidney function. Vice President of Product Development Dan Meier, PhD, explained, "The move to 16 Tech enables us to deploy more devices in more hospitals for multiple clinical trials. We'll be able to provide a rapid processing of samples using our plasma volume and kidney function measurement technologies to trial sites around the world."

Transformational Leadership

Cells (in red) from
the ventromedial
hypothalamus with neural
connections (in purple)
projected from another
area of the brain.



An institute built on a foundation of collaboration between industry and academia, as well as government and community, needs a leader that understands the unique needs of these groups. We were pleased to announce the arrival of just such a leader, Alan Palkowitz, PhD, in September 2020.



Alan Palkowitz, PhD

Chairman of the Board of Directors Daniel Evans, Jr., said, “Having spent time in industry and academia, Alan understands the many opportunities for collaboration to improve the lives of Hoosiers. He shares our passion for translational research and our vision to build a world-class organization that catalyzes activities across the life sciences ecosystem.”

Dr. Palkowitz maintains his role at the Indiana University School of Medicine as a senior research professor of medicine, where he directs the IUSM-Purdue TaRget Enablement to Accelerate Therapy

Development for Alzheimer’s Disease (TREAT-AD) Center. He also is a key contributor to the IU Precision Health Initiative.

Prior to joining the IU School of Medicine, Dr. Palkowitz served as the vice president of Discovery Chemistry Research and Technologies at Eli Lilly and Company. In his role, he was responsible for the global small molecule drug discovery strategy and delivery of clinical



← **Robert Bernhard, PhD**
Vice President for
Research, University of
Notre Dame



↑ **Jay Hess, MD, PhD**
Executive Vice
President for University
Clinical Affairs and
Dean of the IU School
of Medicine



↑ **Kenneth Custer, PhD**
Vice President, Portfolio
Strategy, Chief of Staff,
Lilly Research Labs, Eli Lilly
and Company



↑ **Tatiana Foroud, PhD**
Executive Associate Dean
for Research Affairs, IU
School of Medicine



← **Cris Johnston**
Director of the Indiana
Office of Management
and Budget



↑ **Hany Moselhi, MD**
Senior Vice President and
CMO, Roche Diagnostics
North America



→ **Theresa Mayer, PhD**
Executive Vice
President for Research
and Partnerships,
Purdue University



↓ **Aaron Schacht**
Executive Vice
President, Innovation,
Regulatory and Business
Development, Elanco



↑ **Wendy Srnicek, PhD**
Vice President, Integrated
Field Science, Corteva
Agriscience

candidates in disease areas including diabetes, oncology, immunology and neurodegenerative disorders.

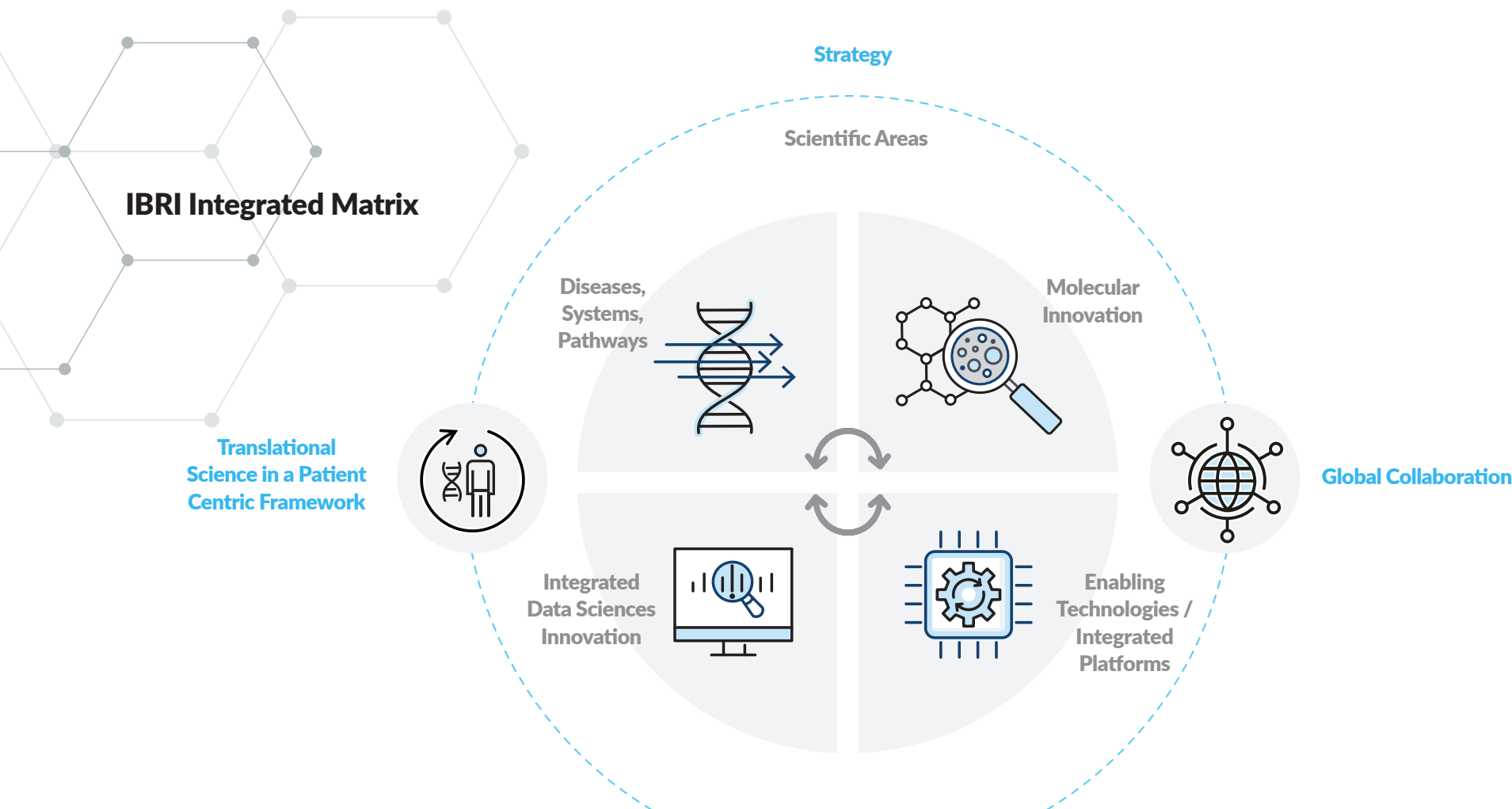
Dr. Palkowitz has worked with the Board of Directors and leadership team to design a new strategic direction for the IBRI. He knows that to truly shape the future of translational science we must transform to achieve ambitious goals.

Catalysts for Collaboration

We had the honor of welcoming eight life sciences leaders to our Board of Directors in 2020. They joined current board members Wayne Burris, Daniel Evans, Jr., John Lechleiter, PhD, Patricia Martin, Dan Peterson and Bill Stephan, and began working to help us achieve our goal to emerge as a key leader of innovative translational science that focuses on improving health outcomes in Indiana and the world.

Shaping *the* Future of Translational Science

Assistant Investigator
Andrew Templin provides
direction to Assistant
Research Associate Li Lin
about her project.

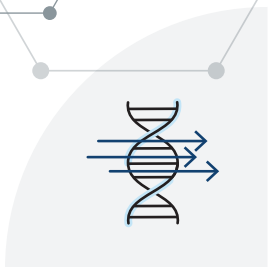


We are entering an exciting era driven by significant advancements in our abilities to study complex disease processes and propose new ways to intervene toward improving patients' lives. Much of this has been inspired by what we can now study and learn directly from patients in the form of novel genetic and genomic analyses of disease tissues along with human-derived models for preclinical experimental work. These approaches have led to a better molecular understanding of disease and patient heterogeneity, in addition to new therapeutic hypotheses to explore. It is ultimately our goal to return these findings to patients in the form of novel therapies and diagnostics that improve disease outcomes.

We therefore envision translational science as a cyclical process of continual learning and applied research that begins and ends with the patient. Through the lens of a research institute, there are multiple entry points from diverse scientific disciplines for insights, hypothesis generation and medical innovation leading to potential breakthroughs. The four foundational areas of scientific focus at the IBRI will provide us the core talent and capability to pursue translational science in this new patient-centric framework.



Assistant Investigators
Andrew Templin, PhD,
Michael Kalwat, PhD, and
Li Zhang, MD, PhD, from
the IBRI's Lilly Diabetes
Center of Excellence.



Translating Disease Research into Novel Therapies

Diabetes will remain our primary disease focus as we seek to increase our understanding of the pathogenesis of the two most common forms of the disease – type 1 and type 2 diabetes. Our goal is to translate this knowledge into novel therapies, while also looking to expand into other autoimmune and degenerative diseases over time.

Our diabetes researchers have always sought to be catalysts for local collaborations between academia and industry. As we look to the future, we seek to expand connections with other research centers and businesses in Indiana, throughout the US and around the world. These relationships will help us to create new tools to better understand disease, develop novel therapies and continue building a strong scientific network. Even amid the challenges brought forth by the COVID-19 pandemic, we reached key milestones that have prepared us for this next leg of our journey.

Diabetes Trailblazers

In 2020, we established three new labs that are led by assistant investigators Andrew Templin, PhD, Michael Kalwat, PhD, and Li Zhang, MD, PhD. These labs are part of the IBRI Diabetes Center, which is led by Decio Eizirik, MD, PhD, and Robert Considine, PhD, and are in addition to the Flak Lab.

The Templin Lab focuses on understanding molecular mechanisms that underlie the relationship between islet immune responses and beta cell dysfunction and death in the setting of diabetes. Dr. Templin and his team place emphasis on the concept that beta cell intrinsic properties are central drivers of islet inflammation and immune responses, and together these promote the progressive beta cell dysfunction and loss that lead to diabetes.

The Kalwat Lab is investigating the molecular mechanisms underlying pancreatic islet beta cell function in health and in type 1 and type 2 diabetes. Dr. Kalwat's team uses a combination of approaches including

small molecule and genetic high-throughput screening, as well as genetically-encoded biosensors to gain knowledge about beta cell function. Identifying new pathways and targets is necessary to develop therapeutics that protect and restore the function of these cells in diabetes.

The Zhang Lab is researching the pathogenesis of islet autoimmunity and antigen-specific immune interventions for treating type 1 diabetes (T1D). Over the last decade, Dr. Zhang and her collaborators have worked to understand the pathogenesis of T1D and explored an effective immune intervention to halt or postpone the development of the disease using spontaneous diabetic mouse models. The Zhang Lab will continue to identify more advanced antibody and cell therapies to benefit T1D patients and high-risk individuals.

Indianapolis' First iPSC Core

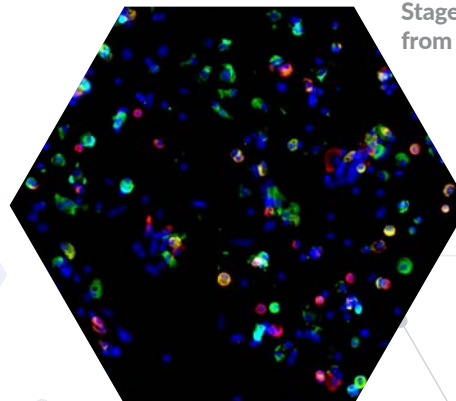
We marked the opening of Indianapolis' first induced Pluripotent Stem Cell (iPSC) Core in 2020. The stem cells we work with are adult cells that are modified and are derived from skin or blood cells and then reprogrammed into other human cells. We are using the iPSC Core to better understand the pathogenesis of T1D

by generating human beta cells and neurons. For example, the iPSCs we generate can synthesize and secrete insulin and be used to screen for new drugs that may protect beta cells early in the disease and therefore slow the progression of diabetes.

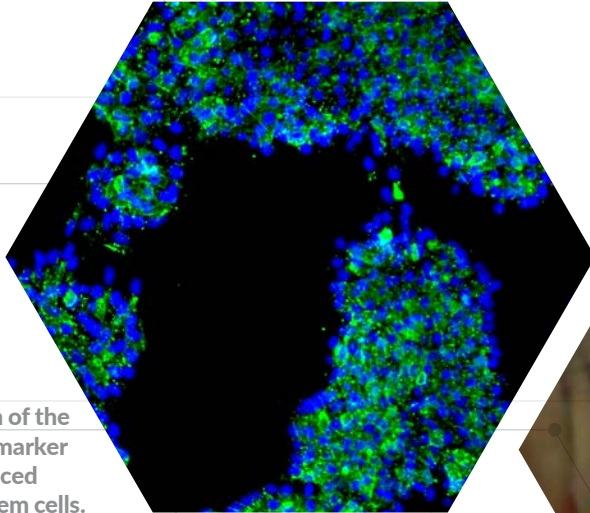
We also can complete CRISPR-Cas9 screening based on iPSC-derived beta cells and immortalized beta cell lines and are working to generate co-cultures of iPSC-derived beta cells with specific genetic modifications and immune cells. The capabilities of the iPSC Core allows us to work with researchers around the world – and right here at home – to create the cells needed to identify novel drugs and other treatments.



Research Associate Daniel Preston prepares induced pluripotent stem cells in the iPSC Core Lab.



Stage 7 beta-like cells from the iPSC Core Lab.



An expression of the pluripotency marker SSEA4 in induced pluripotent stem cells.



Drug Repurposing for Type 1 Diabetes

In partnership with Eli Lilly and Company/Lilly Research Laboratories and Dr. Carmella Evans-Molina's team at the Indiana University School of Medicine, we initiated a project aimed at evaluating immune modulators for their potential to protect pancreatic beta cells in models of T1D. We also are working with the Lilly team to decipher the potential role for the central nervous system in weight loss due to multi-incretin agonists.

Senior Research Associate Donalyn Scheuner, PhD, works with Postdoctoral Fellow Olivia Ballew, PhD in the iPSC Core Lab.



Reimagining Data Sciences

During the past year, the data sciences team continued its focus on the creation of tools and analyses to answer specific questions in health-related problems. For example, a multi-year collaboration with the IBRI, Eli Lilly and Company and the Indiana University School of Medicine culminated in a research study that highlights how electronic health records combined with biospecimens could predict possible comorbidities in persons living with diabetes. The team also delivered a new platform to host electronic health records and disease-specific cohort data and variants where Eli Lilly and Company has placed two specific diabetes and cardiovascular cohorts for access by their scientists.

Other collaborations include understanding the effects of a specific medication type on the prevention of a cardiovascular condition, determining whether metformin has beneficial effects in autoimmune diseases, and identifying the rate of diabetic ketoacidosis in the initial diagnosis of type 1 diabetes patients.

With this strong data, technology and collaboration foundation, we envision tremendous opportunities for data sciences in the context of our new approach to patient-informed translational science. Innovation in this area will empower our researchers through data integration, analytics and simulation to better understand disease mechanisms and accelerate novel biomarker and therapeutic discovery. Specific examples that will be critical components of our new data sciences platform include:

- **Expanded analysis of complex datasets from private and open sources to inform disease understanding and therapeutic hypotheses.**
- **Linked informatics and computational platforms to create innovative virtual drug discovery engines to accelerate and improve the translation of preclinical research to patients.**
- **Novel capabilities that focus the power of computation and simulation to solve specific problems across the translational spectrum.**

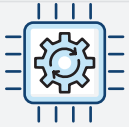


Expanding Molecular Innovation

Access to innovative molecules and experimental reagents are an essential part of translating disease hypotheses into potential therapies. We plan to expand our existing capabilities in biologics to

enable access to a wider range of molecules for studying diverse proteins and drug targets with the optimal chemical tools. Specifically, this new platform will position the IBRI to:

- **Pursue strategic drug discovery opportunities within and external to the IBRI that represent compelling opportunities to impact underserved diseases.**
- **Address limitations of emerging molecular therapeutic modalities to improve scope and effectiveness in targeting disease.**
- **Integrate molecular capabilities into innovative discovery platforms to expand therapeutic possibilities and value creation.**



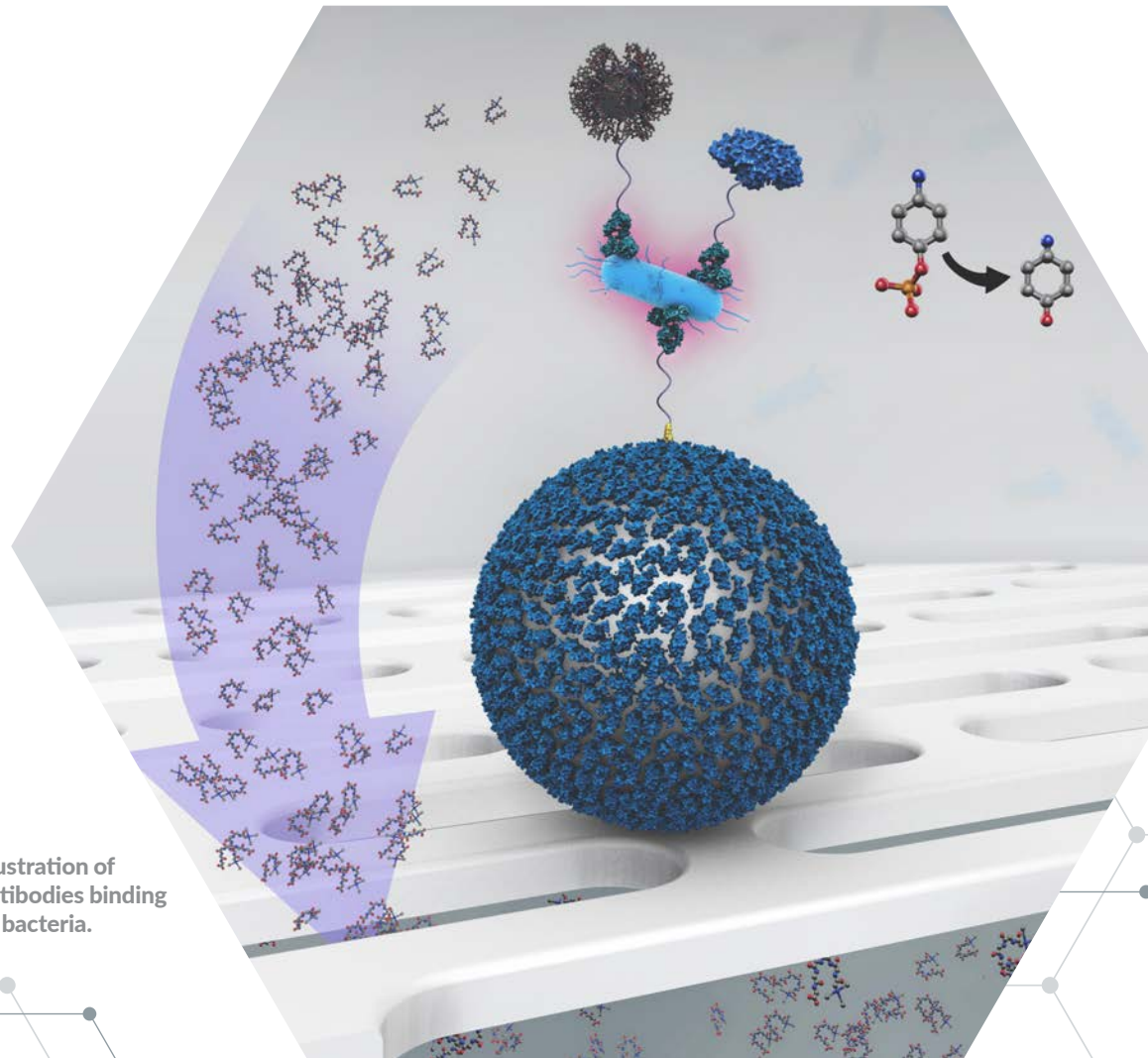
Developing New Technologies to Solve Complex Scientific Problems

Technological advances continually transform biomedical science. The IBRI will require a dynamic and diverse assembly of cutting-edge tools to pursue our innovative research strategy. We will enable the IBRI and our collaborators with the best scientific tools to carry out our work, either constructed internally or accessed through innovative partnerships. We envision our technologies platform to be a leading example of how to integrate human derived data and experimental models to improve translation to patients. Additionally, the IBRI's unique technology footprint will enable local innovators to translate novel hypotheses into attractive opportunities through creative discovery and business models.

IBRI Technology Update: Diseases Diagnosed Faster and Better

In 2020, the IBRI outlicensed one of the technologies developed by IBRI researchers to BioMEMS Analytics, LLC, a startup company based in Indiana. The technology licensed is a biological electromechanical system that uses micro-sized components to reduce cost and improve sensitivity of diagnostic tests. This technology shows our focus on the future of translational science in a patient-centric framework. Indeed, at the heart of this technology is an innovative approach to diagnose diseases faster and with more precision, allowing a quicker translation from patient diagnosis to effective treatment.

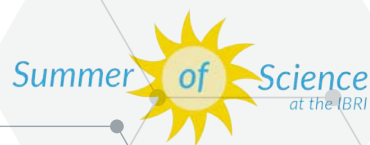
Illustration of antibodies binding to bacteria.



Community Connections

The sun rises over
Innovation Building 1 in
16 Tech as another day of
innovative science begins.

At the Indiana Biosciences Research Institute, we are guided by five core values – teamwork, integrity, innovation, inclusion and collaboration. It's our commitment to collaboration that leads us to work within our community to help improve Hoosier health, foster entrepreneurship and educate STEM leaders.



Connecting Science to a Global Community

As leaders at the IBRI saw that the COVID-19 pandemic would keep us quarantined through the summer, they felt it vital to keep scientific collaborations going. This led to the launch of the "Summer of Science" at the IBRI seminar series. At the direction of Decio Eizirik, MD, PhD, scientific director of the IBRI Diabetes Center, our goal was to introduce our scientists to 12 researchers from around the world and to inspire ideas to improve the health of Indiana residents and those beyond our borders.

Researching – and Walking – for a Diabetes Cure


As with so many events this year, the JDRF One Walk went virtual. We joined Team BETA Watch Out, which is made up of families, scientists and health care workers from the Indiana University (IU) School of Medicine, IU Health and Riley Hospital for Children, to walk at least 1,600 miles. By Nov. 1, the IBRI team had walked 380 miles and raised just over \$3,000 toward the \$10,000 goal.

Fostering Entrepreneurship

Our commitment to being a catalyst for innovation also extends beyond research and to entrepreneurship through AXIS, a mentoring program focused on developing Indiana's life sciences entrepreneurial talent. We are proud to be a founding partner of this program that launched last year and is currently nurturing 10 burgeoning innovators.



Frameworkx
An Idea Exchange for Indiana Life Sciences



InnovationDigi

Life Sciences Go Virtual

When the COVID-19 pandemic sent everyone safely behind computer screens, so, too, did many life sciences events. We worked with our colleagues at BioCrossroads to coordinate two virtual Frameworkx events featuring Michael Pugia, PhD, director of bioanalytical technologies, and Daniel Robertson, PhD, vice president of digital technology. Our leaders shared their expertise on the topics of digital transformation in healthcare and disruption in point-of-care diagnostics. Robertson also served as a moderator for a discussion at InnovationDigi about innovating organizational culture to embrace digital transformation.



Mentoring STEM Leaders

Last summer, members of our team helped mentor students from our neighborhood. Brad Mills and Dan Robertson, PhD, worked with students from TechPoint's SOS (Summer Opportunities for Students) Challenge. Mills and Robertson guided students who developed an app, Go-VID U, for colleges and universities to track COVID-19 hotspots on campus. And seven of our scientists participated in the five-week Indiana CTSI (Clinical and Translational Sciences Institute) K-12 Virtual Summer STEM program. They worked with five rising seniors, who come from families that are economically disadvantaged.

Gifts Support Real Solutions

The success of the IBRI is in large part due to the generosity of our founders, stakeholders and private donors who are committed to the goal of accelerating research to find solutions faster than ever before for the people of Indiana and beyond. We greatly appreciate our donors, who in 2020 made signature philanthropic gifts enabling the IBRI to meet the necessary requirements to achieve the final \$10 million milestone from the State of Indiana.

As we move through 2021, philanthropy from donors and foundations will continue to be a key pillar of our financial strategy. In parallel, we also will work to further diversify funding of our work through competitive research grants, sponsored research with key stakeholders, collaborations and through other special initiatives.

Financial Strength (as of 12/31/2020)

Operating expenses: **\$11.6 million**

Capital expenditures: **\$9.9 million**

Endowment balance: **\$141.9 million**

Team members: **43**

Thank You

Thank you to authors and editors Alan Palkowitz, Jay McGill, Mark Andersen, Robert Considine, Decio Eizirik, Andrew Templin, Michael Kalwat, Li Zhang, Stephane Demine, Dan Robertson and Lisa Soard. We also are grateful for design from Settimi Creative, photography by Jennifer Driscoll and web design by TBH Creative.



Top left: Assistant Investigator Li Zhang, MD, PhD, discusses next steps with Research Associate Doreen Eastes.



Bottom left: Assistant Investigator Jonathan Flak, PhD, enters cells into the plate reader with Assistant Research Associate Andrew Elmendorf.



Top right: Assistant Research Associate Fiona Armoo works with Michael Kalwat, PhD, in his lab.



Bottom right: Members of the Templin Lab: Assistant Research Associate Li Lin and Postdoctoral Fellow Chris Contreras, PhD.