

INDIANA
BIOSCIENCES
RESEARCH
INSTITUTE

Science
creates

HOPE



2022 ANNUAL REPORT



Science
creates

HOPE

Dear IBRI stakeholders,

**Hope is something we all need, especially when facing life's biggest health challenges.
"Science Creates Hope."**

It is only three words. Yet, to the scientists at the Indiana Biosciences Research Institute (IBRI), it is a powerful statement that embodies our lifelong commitment to advancing innovative solutions for complex diseases.

We proudly share this message at the Indianapolis International Airport as an award-winning campaign welcoming guests and residents to find out more about the IBRI's translational research that is leading to novel therapeutics.

Throughout the past year, we have enhanced our science and patient impact by focusing our efforts to accelerate research in Alzheimer's disease ("Alzheimer's research — accelerated") and pediatric rare diseases, including osteosarcoma ("Battling a rare children's bone cancer") and neurofibromatosis 2 ("Using patient-centered science against NF2").

We also expanded our intern program to instill our passion for science in 10 students from our neighborhood high schools ("Future STEM leaders"), as well as six undergraduate and graduate students from the IU School of Medicine, Indiana University-Purdue University Indianapolis and Hanover College.

Our work to grow the biomedical community continued in 2022 through the expanded use of our lab space to a total of 13 resident start-ups ("Entrepreneurial ecosystem expansion").

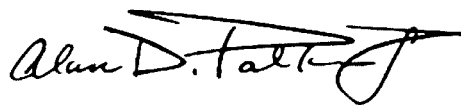
Additionally, we made significant steps toward achieving our vision of being a world-class collaborative research institution through our partnership with INSERM Paris ("INSERM Paris satellite lab opens at the IBRI").

In 2022, we renewed our strategy to enable innovation in the life sciences ecosystem, improve the efficiency of therapeutic discovery, and more quickly translate disease hypotheses into potential therapies that improve patient health outcomes here in Indiana and around the world.

That evolution has led us to an inflection point of growth in 2023 when we plan to add up to 20 new employees as part of our enhanced scientific capabilities in drug discovery ("The Dr. August M. Watanabe Drug Discovery Laboratory launched"), bioinformatics and enabling technologies.

To each of you, I want to say thank you. You helped us get here. You enabled us to expand our facilities, hire top talent, enhance our diabetes research footprint and move into new disease research areas. You help us create hope for patients through science. Hope that they will see better treatment — or even a cure — in their lifetime. I am grateful for your support in our shared mission to improve human health.

I also want to thank our team members, our collaborators and our member companies for your commitment and passion. Together we will make powerful discoveries to defeat disease.



Alan D. Palkowitz, PhD
President & CEO
Indiana Biosciences Research Institute

Two researchers
working with
the Bruker
HD Fourier
80 MHz NMR
spectrometer



Colorful pie blocks in the Watanabe
Drug Discovery Lab

The Indiana Biosciences Research Institute (IBRI) has leveraged more than 35,000 square feet of its biology lab space since the new headquarters opened in September 2020.

In 2022, the IBRI added the 5,000-square-foot Dr. August M. Watanabe Drug Discovery Laboratory that expands the organization's chemistry capabilities for molecular design and synthesis in support of its strategy to accelerate research in pursuit of novel therapeutics.

The Dr. August M. Watanabe Drug Discovery Laboratory LAUNCHED

Over the past two years, IBRI has invested in new capabilities to enable a broader platform in translational research that will connect basic disease science to new therapeutic hypotheses.

The Watanabe Drug Discovery Lab significantly enhances the Institute's molecular innovation area by expanding the types of applied research IBRI scientists can perform. This will, in turn, increase the variety of research funding IBRI scientists can qualify and apply for through federal grants and sponsored research. The capabilities offered by the new Watanabe Drug Discovery Lab also provide a path to valuable intellectual property that can become the foundation of technology licenses and new company formation.

Collectively, this will drive the growth of the IBRI and create new opportunities internally or with collaborators that otherwise would not be possible.

Additionally, the Watanabe Drug Discovery Lab addresses a key deficit in the local biomedical community by providing innovators and early start-ups access to lab space and technology that supports drug discovery.

"One of our main objectives is to grow the biomedical community by being a catalyst for innovation," said Mary Mader, vice president of molecular innovation at the IBRI. "The new Watanabe Drug Discovery Lab will help us accelerate drug discovery, enhance our partnerships and create new opportunities."

The Watanabe Drug Discovery Lab features 13 ducted fume hoods dedicated to molecule synthesis. An additional 16 filtered fume hoods house chemistry equipment. The lab also incorporates a full chromatography suite, mass spectrometer, and a benchtop NMR (nuclear magnetic resonance), necessary for purification and characterization of compounds in advance of biological testing. ■



Dedicated to the life sciences

In 2023, the IBRI will officially dedicate its new drug discovery laboratory and conference center in honor of the late Dr. August M. Watanabe, who served as a champion of the life sciences through his work as a physician-scientist, chair of the Department of Medicine at the Indiana University School of Medicine, president of Lilly Research Laboratories and biotech entrepreneur.

POWERFUL DISCOVERIES

Defeat Disease

The Indiana Biosciences Research Institute (IBRI) has unparalleled expertise that is breaking boundaries to accelerate discoveries to defeat diseases.

In the past year, IBRI scientists have broadened their science and patient impact with efforts to accelerate research in Alzheimer's disease, as well as pediatric osteosarcoma and neurofibromatosis 2.

The Institute has new and expanded capabilities for therapeutic discovery, and it has advanced the achievement of its vision to be a world-class collaborative organization through an innovative partnership with researchers at INSERM (National Institute of Health and Medical Research) in Paris.



*IBRI Scientists
investigating diabetes*

INSERM Paris satellite lab opens at the IBRI

The vision of the IBRI is to build a world-class organization that accelerates innovative research across the life sciences community. The IBRI is turning that vision into reality by welcoming Roberto Mallone, MD, PhD, and Sylvaine You, PhD, to the Institute to open a satellite lab that will complement the work of their lab at INSERM Paris.



Roberto Mallone, MD, PhD, senior investigator at the IBRI



Sylvaine You, PhD, associate investigator at the IBRI

The Mallone-You Lab focuses on type 1 diabetes (T1D) research. T1D is an autoimmune disease resulting from the destruction of insulin-producing pancreatic beta cells by the immune system, specifically by autoreactive T lymphocytes, a type of white blood cell, that we all harbor. Mallone and You want to understand why autoreactive T lymphocytes turn aggressive and cause diabetes in some people.

To answer that question, they are exploring the mechanisms that make the beta cells more vulnerable to an attack by T lymphocytes. You said, “We hope our work at the IBRI will help us identify molecules that might protect beta cells and lead us to novel therapeutics that will better treat — or even prevent — T1D.”

Prevention of T1D is the primary focus of Mallone’s and You’s work at INSERM Paris. “While there will be an ocean between us, we

view these two labs as connected entities with regular meetings via video and visits for the scientists to both labs,” said Mallone.

“Launching a satellite lab at the IBRI provides us access to expertise we don’t have in Paris. We will be able to use the iPSC (induced pluripotent stem cell) Lab to generate beta cells. We will have access to experts who can help us model genes that may be involved in making individuals more susceptible to T1D. And we can further strengthen our relationship with the Indiana University School of Medicine.”

IBRI President and CEO Alan Palkowitz said, “We are excited to welcome the Mallone-You Lab to the IBRI. This is the start of a unique collaboration, and we are eager to see our partnership grow and to welcome other satellite labs to the IBRI in the future. ■

ADVANCES IN NEUROSCIENCE



Alzheimer's
researchers
Bruce Lamb and
Alan Palkowitz



Alzheimer's research — accelerated

The Indiana Biosciences Research Institute (IBRI) has been growing its footprint in Alzheimer's disease research over the past three years. This research is being led by Alan Palkowitz, PhD, president and CEO of the IBRI, and Bruce Lamb, PhD, executive director of the Stark Neurosciences Research Institute at the Indiana University (IU) School of Medicine. The team also includes Timothy Richardson, PhD, scientific director of molecular innovation at the IBRI, and Jeff Dage, PhD, senior research professor of neurology at the IU School of Medicine.

The IBRI is complementing and expanding on the IU School of Medicine's Alzheimer's disease pre-clinical research programs by

bringing additional capabilities to the IUSM-Purdue TREAT-AD (Target Enablement to Accelerate Therapy Development for Alzheimer's Disease) Drug Discovery Center.

The TREAT-AD Drug Discovery Center is one of only two centers in the entire U.S. Scientists at the TREAT-AD center and the IBRI are focused on neuroinflammation, a key driver and initiator of Alzheimer's. IBRI scientists are targeting microglia, the immune cells of the brain. They are currently developing therapies to test hypotheses for regulating microglia that may cause neuroinflammation. The goal of TREAT-AD and its IBRI



TREAT-AD
TaRget Enablement to Accelerate
Therapy Development for AD

collaborators is to create molecules and generate data to share with the broader Alzheimer's research community for further study.

"Our hope is that we can create assets that could have a path to the clinic and could potentially be new medicines," said Palkowitz. "Ideally, we'd create successful therapeutics that help to arrest development of Alzheimer's earlier in the disease process, instead of later stages where it is difficult to alter the course of the disease."

Lamb added, "It is a thrilling time to be part of the Alzheimer's research community. For the first time in decades, we have two FDA-approved Alzheimer's medications. While they may not be perfect, we can say we've moved into the treatment phase." ■

Battling a rare children's bone cancer

As the Indiana Biosciences Research Institute (IBRI) expands its disease research into pediatric rare diseases, it has had the opportunity to collaborate with Karen Pollok, PhD, associate professor of pediatrics and director of the Preclinical Modeling and Therapeutics Core for the IU Simon Cancer Center.

Pollok focuses her research on osteosarcoma, an aggressive form of bone cancer most often diagnosed in patients younger than 40 years old, working with tumor cells donated by Tyler Trent and other patients. Trent was a Purdue University student and cancer research advocate who died in 2019, after a long battle with osteosarcoma.

From Trent's tumor tissue, Pollok created the TT2 cell line, which is one of several patient cell lines Mary Mader, vice president of molecular innovation, and Anna Geisinger, senior research associate, both at the IBRI, are working with to identify novel combination therapies to target osteosarcoma.

"What makes this project different than some of our other research is the access we have to clinicians and patients," said Mader. "Big pharma doesn't have the kind of direct access we do through our collaboration with researchers at the IU School of Medicine."

Geisinger added, "Sometimes we get feedback directly from parents of patients about how much this research is needed to improve treatment for their kids. It makes me feel like I'm doing something truly life-changing to hear that kind of feedback directly from parents."

Mader and Geisinger are using the IBRI's molecular biology tools to screen combination therapies that inhibit CDK4/6, enzymes that are important to cancer cell division. The data generated by the IBRI will provide the needed rationale to proceed with a future clinical trial, based on what is learned, and to determine if the treatments can be well-tolerated by patients. ■

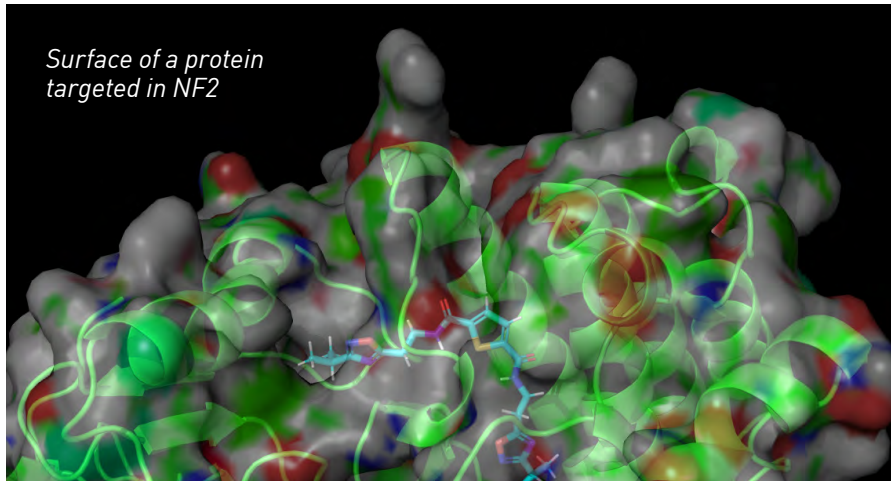


VP of molecular innovation Mary Mader working in the Watanabe Drug Discovery Lab.

Scientist Anna Geisinger working with cells in her investigation of osteosarcoma.



THERAPIES TO TARGET OSTEOSARCOMA



Surface of a protein targeted in NF2

Using patient-centered science against NF2

Olivia (name changed to protect her identity) was a high school track star. Her season started out strong, but as it progressed, things started to change. First, she started to occasionally feel dizzy. Then, she started to lose her balance. Within a few short months, Olivia could no longer walk straight.

What she and her parents didn't know was that within her ears, small vestibular schwannomas — benign nerve tumors — were forming. These tiny tumors were causing Olivia's dizziness, balance issues and walking difficulty.

As Olivia's parents sought treatment for her, they found Dr. Steven Rhodes, pediatric oncologist at Riley Children's Health, who diagnosed Olivia with neurofibromatosis 2 (NF2).

It is a rare neurologic disorder that causes tumors (derived from malignant Schwann cells) to form on nerves that support balance and hearing. In 2021, Dr. Rhodes and Dr. D. Wade Clapp, chair of the Department of Pediatrics at the Indiana University (IU) School of Medicine, began working with scientists at the Indiana Biosciences Research Institute (IBRI) to research treatments for NF2

patients. Together the scientists pinpointed drug combinations that could immediately proceed to clinical trials. Dr. Clapp noted, "We have identified one drug that informally is showing progress by reducing the number of surgeries, while also ensuring that the tumors in NF2 patients are stable or shrinking a little."

As the year turned to 2022, Dr. Rhodes, Dr. Clapp and the IBRI team worked to accelerate their research. They did so with the help of Olivia, who agreed to provide blood samples that were transferred to the IBRI. Now in the experienced hands of Bill Carter, senior research associate at the IBRI, Olivia's blood cells are being reprogrammed into induced pluripotent stem cells (iPSCs) and then differentiated into Schwann cells that are uniquely representative of her disease. Once Carter has created a bank of Schwann cells, he will be able to test drug combinations in the lab, rather than having Olivia try different medications.

"We hope the iPSCs will help us personalize the therapy for each individual child going forward," said Dr. Clapp. "And, as we look toward 2023 and beyond, we are collaborating with the IBRI to learn more about the underlying disease and identify new chemical matter that will shrink NF2 tumors." ■

Science and nature ignite passion

Bill Carter has always had a curiosity about nature. It started growing up on his family's farm in Muncie, Ind., and only grew stronger as he studied biology at Ball State University. However, it was IU School of Medicine Distinguished Professor Loren Field, PhD, who truly ignited Carter's passion, which is generating induced pluripotent stem cells (iPSCs).

The science behind iPSCs involves taking naturally occurring adult skin and blood cells and re-programming them to generate a specific type of cell. Field also introduced Carter to the IBRI and today Carter is using his more than two decades of experience to improve the health of young Hoosiers.

"We recently learned about two young women who had been diagnosed with NF2," said Carter. "As a parent of four, it was difficult to hear from their doctor about the health struggles they face at such a young age."

In addition to the work Carter is doing with blood samples, explained in the previous story, "Patient-centered

science," he is using CRISPR, which is a system that can target specific stretches of genetic code and edit DNA at precise locations. He knows that when the NF2 gene is impaired, it creates a greater risk of developing certain tumors.

"Our goal with this work," notes Carter, "is to use CRISPR to study the Schwann cells in the

disease state in vitro, meaning in a controlled environment, and look for ways to prevent tumors from ever forming."

Carter knows there is still work to do. "I am confident that the platform we are creating will help accelerate research into new, more efficient therapies for patients." ■



Scientist Bill Carter works with Schwann cells in the iPSC Lab

The Indiana Biosciences Research Institute (IBRI) is proud to promote innovative science. In 2022, the IBRI welcomed four life sciences start-ups, two of which are highlighted here, to work in its space and use its equipment.

The IBRI supports entrepreneurship in the life sciences, convenes diverse research teams and complements innovation in the ecosystem. The number of IBRI resident start-ups now totals 13 that are working to create hope for patients through science.



*Dr. Anne Rietz
working in
the Kovina
Therapeutics lab*

Entrepreneurial Ecosystem EXPANSION

Treatment HPV premalignant infections and cancers

Kovina Therapeutics is focused on two objectives — stop Human papillomavirus (HPV) premalignant infections before cancer develops and treat HPV cancers after detection.

Kovina CEO Kristin Sherman and Vice President of Finance Colleen Beeler are dedicated to this work in part due to the potential impact on women's health. Today, women diagnosed with premalignant cervical infections caused by

HPV undergo surgery to treat the infection, which may result in side effects and impact fertility.

“We believe Kovina’s research will lead to a topical medication to treat HPV premalignant infections before cancer forms,” Sherman said. “Kovina also is developing an oral therapeutic for use after HPV progresses and cancer is diagnosed, to provide much-needed treatment options for patients.”

Kovina moved its operations to the IBRI in June 2022. Beeler noted the benefits the IBRI offers the start-up life science community, “In a previous start-up, Kristin and I needed to create a new facility for the company but found few options available. Ultimately, establishing a standalone lab was the best option, which is certainly capital-intensive. The fact that the IBRI offers shared equipment, and the necessary support structure provides a significant benefit for life science start-ups.” ■

Moving from Charlottesville to Indianapolis

In 2022, the IBRI was pleased to welcome Ourobio to its Indianapolis, Ind., labs from Charlottesville, Vir. Co-founder Alec Brewer said, “Moving to the IBRI has enabled us to start expanding our team, allowed us to accelerate our progress in developing engineered microorganisms, and provided us with access to higher throughput fermentation equipment we haven’t been able to use since moving out of our university lab.”

This pre-revenue company started as an academic research project

called Transfoam in early 2019 and was spun out into a company in March 2020, and rebranded to Ourobio in 2022. The company’s goal is to reduce the creation of microplastic pollution and the barriers to biodegradable plastic adoption. Co-founders Brewer and Kobe Rogers met in a synthetic biology class at the University of Virginia, where the team bonded over their shared passion for sustainability, synthetic biology and biochemistry.

“I’ve witnessed the beauty of the ocean, but also how it’s being treated,” said Rogers. “I realized I could use my knowledge and passion to make a big change in the world.”

This past year, in addition to moving to Indianapolis, Ourobio has conducted



Alec Brewer and Kobe Rogers, co-founders of Ourobio

a significant amount of market research that showed they have an opportunity to solve an unmet need in the biomaterials/plastics industry. ■

Future STEM LEADERS

One of the primary goals of the Indiana Biosciences Research Institute (IBRI) is to grow the biomedical community by being a catalyst for innovation and supporting STEM education.

By focusing on high school and undergraduate students in the IBRI neighborhood, the organization hopes to create a pipeline for young Hoosiers to gain the knowledge and skills needed to stay in Indiana and pursue scientific careers. In 2023, the IBRI will also launch its own college internship program.

Providence Cristo Ray High School (PCRHS) Corporate Work Study

The IBRI was introduced to the PCRHS Corporate Work Study program in 2021 by its IT partner, BlackInk IT. This is when the IBRI first met freshman PCRHS student Kaleel Mumford.

During his first year at the IBRI, he helped enter data into the back end of the IBRI website, making the new site possible. He worked with the projection systems in the IBRI conference rooms and learned how to keep data and networks secure.

Back at the IBRI as a sophomore, Mumford has explored the Institute's advertising campaigns,



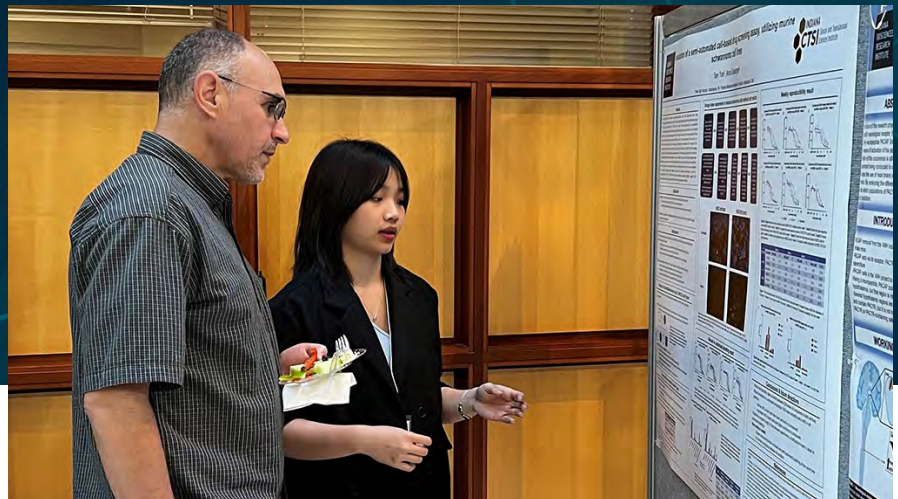
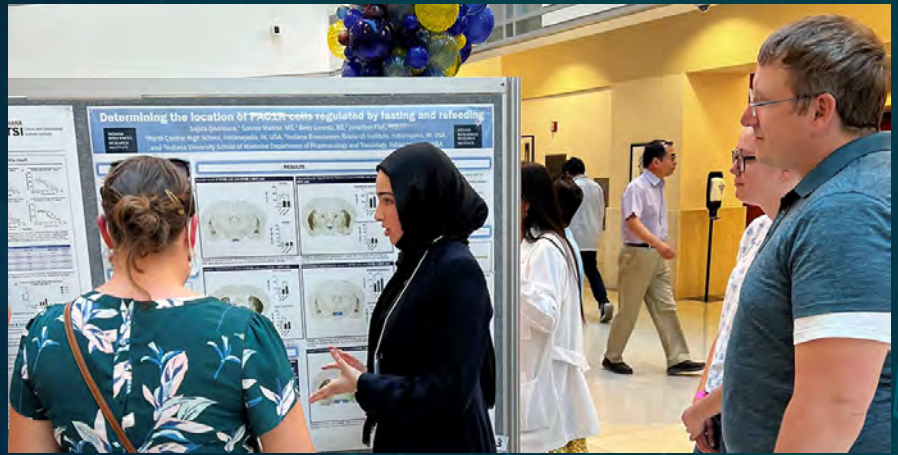
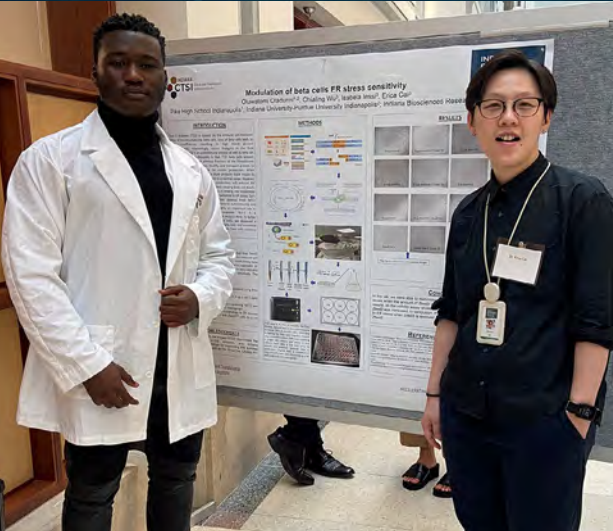
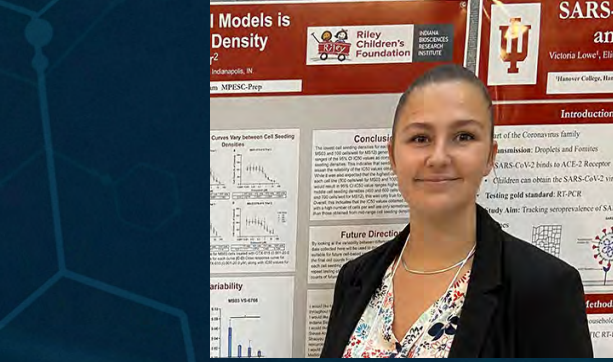
Providence Cristo Rey High School Sophomore Kaleel Mumford and his mentor, Lisa Soard.

learned how to use CSS (Cascading Style Sheets), a rule-based coding language, and continued to build upon his IT experience. Mumford said, "[Working at the IBRI has been] a good experience that has helped me to get ahead and learn how to program."

Herron Classical Schools Internship

For the second time, the IBRI partnered with Herron Classical Schools to host two high school seniors for the full school year in its labs. Mya Suber, who worked in the Flak Lab, arrived at the IBRI interested in environmental science, but open to exploring the biomedical field and the IBRI's diabetes research. As the internship came to a close, Suber said, "I loved assisting my lab team members. They are all so passionate about what they do. I want to go into research because of this experience."

Giovanna Wunaki worked with team members in the Kalwat Lab and the Cai Lab to learn foundational skills



like pipetting and to be introduced to scientific equipment that wasn't available at her school. Wunaki said, "The IBRI provided me with an advantage to learn that has prepared me to further my academic career at Purdue University."

IBRI Summer College Internship Program

The IBRI has designed an internship program for college students to obtain applied learning experience that will complement and extend their traditional education. This internship program will launch the summer of 2023. These experiences will help the students explore career opportunities and assist in clarifying personal and educational goals. Students conduct research in the

IBRI's state-of-the-art laboratories, learn innovative techniques and work with IBRI experts.

Students in the IBRI internship program can choose to explore medicinal chemistry, computational chemistry, bioinformatics, cellular pharmacology, induced pluripotent stem cell technologies, disease pathogenesis, as well as competitive intelligence and finance.

Indiana CTSI Project SEED/STEM

Each summer the IBRI hosts approximately five interns

from neighboring high schools who are interested in pursuing college careers in STEM.

For eight weeks they work in IBRI labs, learn from IBRI assistant investigators and become part of the IBRI team. 2022 was the first year, since the pandemic began, that students participating in the Indiana CTSI's (Clinical and Translational Sciences Institute) Indianapolis Project SEED/STEM at the IBRI were able to give poster presentations to their peers, mentors, family and friends. ■

Clockwise, from top left: Hannah Leffew, rising senior at Hanover College; Sajida Qaddoura, North Central High School student; Tam Tran, Pike High School student; Oluwatomi Oladunni, STEM summer intern

Financial STRENGTH

Research continues to grow as a source of hope and strength at the Indiana Biosciences Research Institute (IBRI).

In 2022, the IBRI increased its federal grant and sponsored research submissions by 52 percent leading to a total external funding growth increase of 9 percent.

As of December 31, 2022, IBRI investigators had more than three times the amount of funding opportunities planned and submitted compared to the prior year. This continued focus on diversified research funding will fuel future growth for the IBRI, ultimately benefiting the patients and community it serves.



Operating Expenses..... **\$12.7M**



Capital Expenditures..... **\$3.1M**



Team Members..... **46**







Member Companies..... **13**



Member Company Employees..... **36**

THANK YOU

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