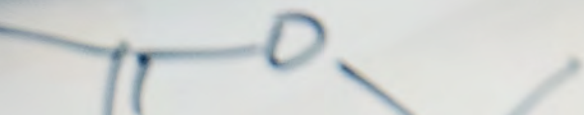
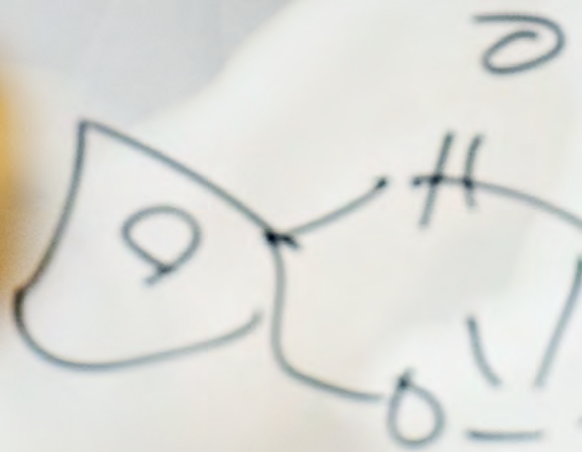
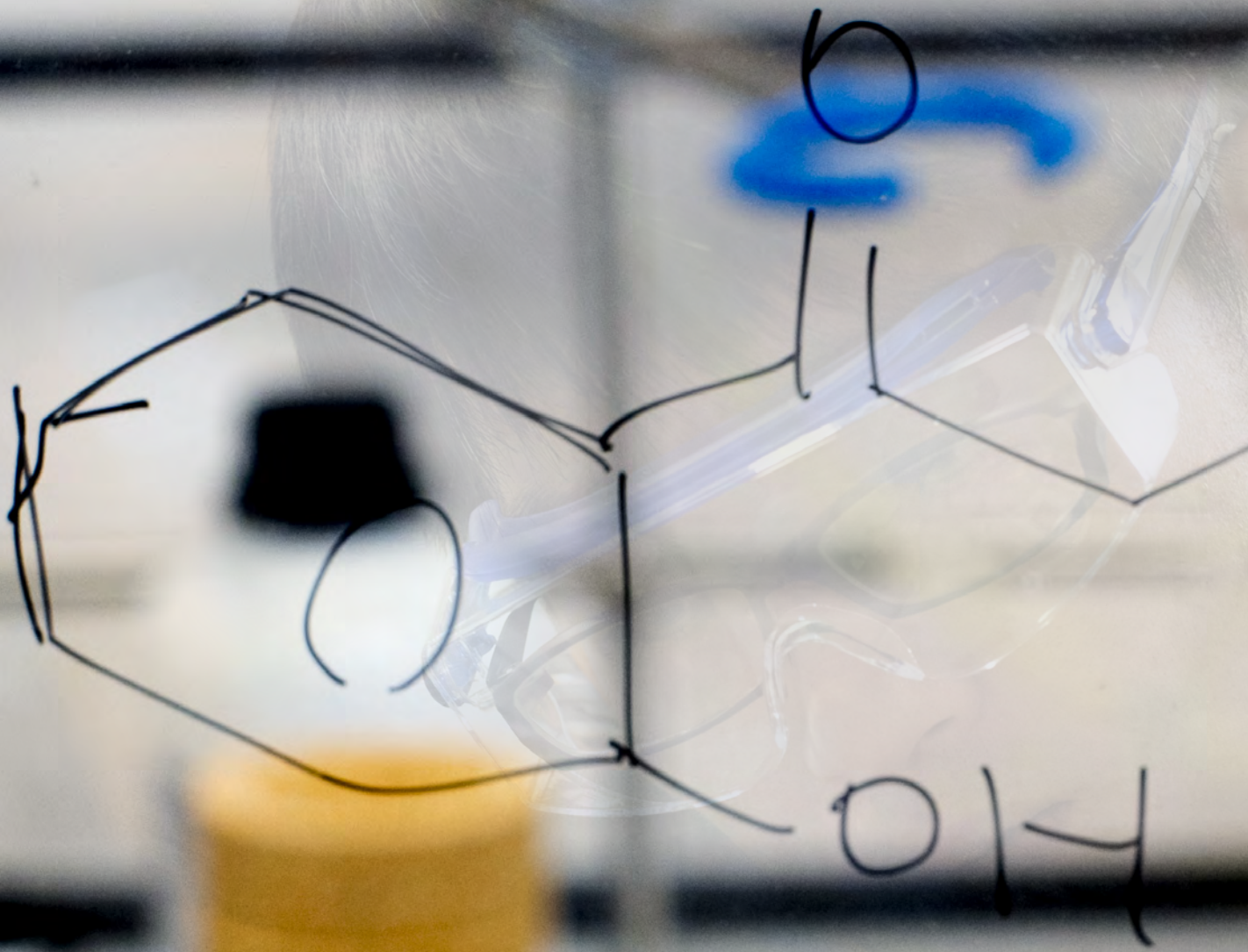




TRI-INSTITUTIONAL
THERAPEUTICS DISCOVERY INSTITUTE

Progress in Spite of Adversity

TDI ANNUAL REPORT 2020



The mission of the Tri-Institutional Therapeutics Discovery Institute (TDI) is to **encourage** our community to advance their groundbreaking biological discoveries to in vivo proof-of-concept studies. TDI provides industrial-scale technical support for academic projects, making it possible to rapidly assess the utility of specific therapeutic targets in disease-relevant contexts.

TDI **empowers** the community to translate research discoveries from bench to bedside by offering a menu of services that is unprecedented in both scale and scope within an academic environment. This is accomplished through a series of highly favorable academic-industry partnerships established through TDI, as well as our Innovation & Education Initiative, which provides community-wide training and support in order to maximize the impact of these partnerships on academic drug discovery.

We achieve our mission by **leveraging** the infrastructure, staff and intellectual capital of our academic and industry partners, as well as the generous support of philanthropists.

With the launch of key initiatives, TDI has established the first fully-funded, fully-staffed **bridge** from basic academic research discovery to human proof-of-concept demonstration.





Basic Academic Research Discovery

Tri-I Investigator identifies a new protein target implicated in human disease

TDI Early Project Initiative

Working in close association with the Investigator, TDI uses outside contractors and internal expertise to quickly assess viability of the protein as a new drug target

TDI-Takeda Drug Discovery Initiative

Tri-I Investigator collaborates with TDI and Takeda to develop a lead small molecule or antibody for in vivo proof-of-concept studies

Bridge Medicines/ Takeda Pharmaceuticals

Upon demonstration of in vivo efficacy, the project may advance to Bridge Medicines or Takeda as a preclinical candidate

New York Based NewCo

Bridge Medicines' venture capital partners may fund a NYC-based company with appropriate resources to execute human proof-of-concept clinical trials



Peter T. Meinke, PhD

Letter from the Director

Drug Accelerators: Guideposts for a Successful Mission

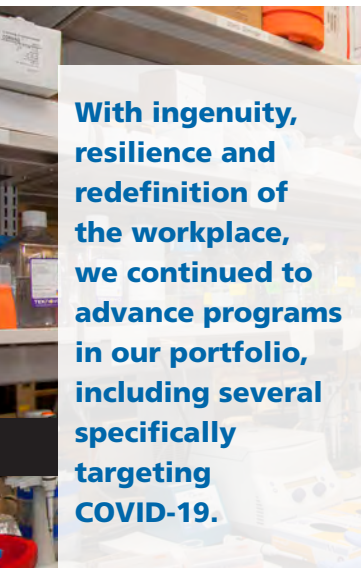
Drug discovery is an inherently high-risk endeavor, fraught with daunting challenges at every stage. While academic scientists excel at elucidating novel biology, these programs are routinely deemed too premature for industry partnerships despite the fact that pharmaceutical companies increasingly rely on licensed programs and products for economic success. As a result, promising innovations – those that have the power to meet unmet needs in medicine – often fail to reach the masses.

Seven years ago, Tri-Institutional (Tri-I) Therapeutics Discovery Institute (TDI) was born to bridge that gap. The idea was simple: tap into the plethora of brilliant researchers in the Tri-I community and mentor their projects on the journey to licensing and, ultimately, to patients. Embedded within the academic community of three powerhouse institutions – Weill Cornell Medicine, Memorial Sloan Kettering Cancer Center and The Rockefeller University – TDI is an independent entity that serves as a drug accelerator, harnessing the nascent power of scientists and pairing these innovators with pharma professionals. Under TDI's guidance, our parent institutions have been empowered to translate pioneering findings from bench to bedside. TDI accomplishes this by offering industry-quality drug discovery capabilities that break down barriers for researchers.

TDI's success proves it is possible to establish a fully funded link from basic academic research discovery to human proof-of-concept demonstration. Our model increases not only the probability of licensing success, but also the economic value of these partnerships. Since inception, TDI has facilitated two new company spinouts and the licensing of eight technology assets. Many more commercialization opportunities are on the way.

Our engine of discovery is rendered feasible via several treasured partnerships. Leveraging the infrastructure, staff and intellectual capital of both academic and industry players – with generous philanthropic support – allows us to collaborate broadly to accelerate the translation of innovative biology. We are grateful for the continuing support of our Board of Directors as well as the transformative gifts made by Mr. Lewis Sanders, who first conceived of the TDI concept. This critical support nurtured our company throughout its infancy and continues to aid us as we grow into maturity.

The past year has brought formidable challenges. In the midst of an unprecedented global pandemic, we remained steadfast in our mission. At a time when many organizations were shuttering, our team developed creative solutions to thrive under the constraints of



a lockdown. For example, our relationships with more than one hundred Contract Research Organizations (CROs) across the globe allowed us to continue research activities unabated when our own labs were closed.

We gained, and never lost, momentum. With ingenuity, resilience and redefinition of the workplace, we continued to advance programs in our portfolio, including several specifically targeting COVID-19. TDI scientists also volunteered their expertise on external Scientific Advisory Boards dedicated to combating this deadly virus. You can read more about our work during the pandemic and contributions to drug discovery in the pages that follow.

The framework of TDI has proven stronger than ever. We are proud to share our blueprint for success with other entities that wish to invest in research institutions across the country. Here are the key guideposts that light our mission.

Technology Development Offices (TDOs).

To facilitate program partnering, TDI provides confidential technical support as needed to the TDOs of our parent institutions. Since its launch in 2013, TDI has supported over 110 programs from academic researchers in the Tri-I community in either small molecule or biologics modalities. TDI's scientific contributions have facilitated the launch of two NYC-based companies – Quentis Therapeutics and Sparian Bioscience – plus the licensing of four small molecule and four biologics programs to biopharmaceutical partners. In addition, these new partnerships included multiple sponsored research agreements that help defray the institutional costs of TDI.

TDI and Institutional Leadership. Highly trained former pharmaceutical scientists who joined our leadership ranks are integral to TDI's success and impart their experience to junior personnel via mentoring. Critically, support from the highest levels of leadership in the Tri-I academic community enables us to break down research silos and funnel the most promising programs into our pipeline.

Research Activities. The growth of CROs has contributed greatly to TDI's successful model. Due to our partnerships with diverse CROs worldwide, technologies that were once the sole province of pharma are now available to us, essentially à la carte. To advance valuable assets, our team utilizes these suites of cutting-edge discovery tools.

Funding. It takes years, or even decades, before a drug accelerator can yield significant financial returns. TDI is made possible by its parent institutions, generous philanthropic support, an industry collaborator and government grants. As successful partnerships begin generating returns, it is clear that TDI has taken important initial steps towards its goal of financial self-sufficiency.

Reproducibility. Preclinical research at academic institutions has long been plagued by a reproducibility gap. To identify flaws in experiments or treatments sooner and create more robust data sets, TDI developed a reproducibility protocol. Key elements of all programs must be independently replicated within TDI labs, at CROs or by deploying TDI staff to academic labs before TDI will deem the asset ready for partnering. TDI's commitment to generating validated data sets has been clearly

corroborated by recent development partners, who note that results validated at the TDI do, indeed, translate to external labs.

Program Selection. TDI is unique in the research setting because it remains agnostic to the therapeutic area or modality, focusing solely on innovation and unmet medical needs. In multiple projects, where biological pathways were poorly elucidated, Tri-I scientists have used TDI-generated, pharma-quality tools to identify entirely novel drug discovery programs.

Scientific Advisory Boards (SABs). TDI's independent SABs serve an essential function, supporting program intake, closure and completion, as well as providing technical guidance. Their independence and deep experience ensures that only the most innovative programs are selected for support.

Collaboration. TDI scientists and academic investigators work together to leverage the strength of both teams, a collaborative model facilitated by our proximity to all three campuses. Our innovative design couples unparalleled insights into foundational biology from academic scientists with TDI's deep drug discovery expertise, yielding the accelerated drug discovery pipeline that is our mission.

Education. For many Tri-I scientists, the drug discovery process is largely mystifying. One of TDI's goals is to educate the scientific community and empower them to recognize the translational potential of their basic discoveries while also addressing reproducibility concerns. Creating an entrepreneurial mindset also prepares researchers for new opportunities that emerge from translational research.

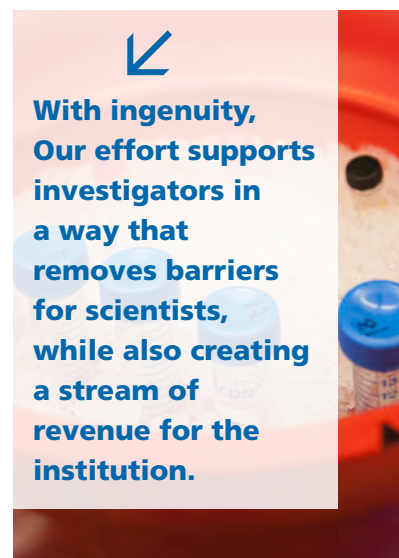
The Path Forward

There is a pressing need for drug accelerator services to cultivate the pipeline of tomorrow. This past year, despite having to surmount unprecedented obstacles, our scientists again proved that the TDI model works. We know where the gaps are between academia and industry, and have laid the foundation to bridge these previously siloed entities.

As we emerge from the pandemic and forge ahead towards a safer tomorrow, success demands infrastructure and processes that allow scientists and pharma to join together. At TDI, we have created viable and efficient mechanisms to convert innovative basic biology insights into therapeutics. Our effort supports investigators in a way that removes barriers for scientists, while also creating a stream of revenue for the institution. Together, we can achieve the common goal we all share: developing better therapies for patients.

The pages that follow open a window into the hallowed halls of innovation at TDI. We hope you enjoy diving into the remarkable projects we had the privilege of accelerating this year. Stay healthy, be well and enjoy the wonder of science.

Peter T. Meinke, PhD
Sanders Director



Science in the Time of COVID-19

Nearly a year and a half has passed since the COVID-19 pandemic changed life, and research, as we know it. All around the world, scientists and drug discovery experts have adjusted to a new virtual normal. TDI was no exception – our organization faced formidable challenges. Yet we persevered, continuing to advance science under unimaginable circumstances in creative ways that we never would have thought possible.



While hard-fought, the journey has been equally rewarding and inspiring. It all began in early January 2020 when the World Health Organization (WHO) reported that a disturbing new pneumonia had been identified in Wuhan, China. Nearly two weeks later, the first case of what become known as coronavirus disease 2019 (COVID-19) was confirmed in the United States. By the second week of March, the WHO had declared COVID-19 a pandemic. One by one, TDI's academic institutions – Weill Cornell Medicine, Memorial Sloan Kettering, and The Rockefeller University – began to close down. TDI soon found its research laboratories, along with those of its closest collaborators, completely shuttered. Until further notice, all TDI personnel – including those who spend more than 90 percent of their time in the lab – would be sheltering in place in their homes throughout the tri-state area.

With the virus rapidly spreading throughout Manhattan that spring, TDI's first priority was to protect our employees and help our collaborators. As a research organization owned by several teaching hospitals, we knew our colleagues and friends across the Tri-Institutional Community would be the ones on the frontlines fighting against this new disease. To assist these brave frontline workers, TDI identified and packaged all of the disposable gloves, masks and lab coats available in our Small Molecule and Antibody Discovery Labs and donated them to our colleagues at New York Presbyterian Hospital. We watched with pride and admiration as our parent institutions cared for floods of critically-ill New Yorkers. Our fellow scientists, some of whom are family members of TDI staff, were among the first to develop new protocols and insights to treat this mysterious virus.

Determined to rise up and get back to the science, the TDI organization quickly pivoted. Realizing the importance of continuing to advance our projects and engage our staff, we swiftly moved to a virtual format. Zoom meetings replaced in-person meetings. We drew heavily upon our extensive network of Contract Research Organizations (CROs) – particularly those in Asia where the pandemic had already eased – to run the experiments that TDI, and our academic collaborators, could no longer execute. We continued to meet, in virtual conference rooms, with principal investigators and their staffs across our community. We read papers, attended virtual seminars, designed

experiments for CROs to execute and analyzed results.

To support the larger community, we expanded our annual training offerings. We partnered with Schrödinger to sponsor a graduate-level, self-paced Computer Aided Drug Design course. In addition, we offered the TDI-developed course on Accelerating Academic Drug Discovery to a broadly expanded online audience.

As the restrictions slowly eased, in May, our Antibody Discovery team was the first group to go back into the lab. Safety was of the utmost importance. The TDI team flexed, improvised, de-risked and innovated. For example, we implemented a system that allowed our scientists to sign out specific portions of the lab, so that they could work in a safe and socially distanced manner. We also supported our staff in their extraordinary commuting costs to decrease the risk of using public transportation.

The results of these creative solutions were pipelines of programs that continued to advance. Early in 2020, long before the impending global pandemic hit the U.S., TDI engaged in its annual goal-setting exercise. Remarkably, despite the year's unforeseen challenges, we successfully achieved the majority of the goals our leadership team set for the organization. An example of the number of projects planned for initiation and completion is illustrated below.



Pipeline	Launched Projects		Completed Projects	
	Goal	Achieved	Goal	Achieved
Early Stage SM	7	2	10	8
Early Stage Ab	6	4	11	8
Therapeutic SM	9	8	7	7
Therapeutic Ab	5	7	4	3

As we look back on 2020, the pain and hardship still feel very palpable. We join the rest of the country in grieving lives lost and irrevocably changed. But at the same time, we are uplifted by the power of what can be accomplished by a small team of people dedicated to a common goal. Even though we were forced to work physically apart, we banded together more strongly as a team – supporting each other both scientifically and personally. No matter what the circumstances, at TDI, our mission never falters. And together, we will continue to develop new cures for patients who need them most.

2020 Highlights TDI Outputs

The promise of TDI is being realized. As the table below illustrates, TDI has licensed many innovative technologies to industry and helped to launch two new companies. It is truly extraordinary for such a young and dynamic organization to have successfully completed and licensed eight programs in such a compressed timeframe. TDI is fortunate to have access to such rich and diverse foundational science and the opportunity to collaborate with leading experts in the Tri-Institutional community. **Projects of particular interest are highlighted throughout the following pages.**

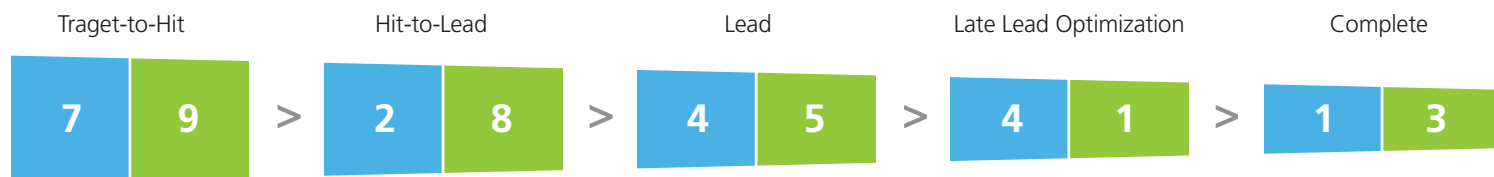
Year	Institute	Disease Area	Modality	Status
2016	WCM MSK	Oncology Pain	Small molecule Small molecule	NewCo: Sparian Bioscience NewCo: Quantis, Inc.
2017	MSK MSK RU	Oncology Oncology Oncology	Small molecule Small molecule Small molecule	STARR grant received by PI Available for licensing Licensed to Bridge Medicines
2018	MSK RU WCM WCM WCM	Oncology Infectious Disease Inflammation Stroke, Sepsis Oncology	Biologics Biologics Small molecule Small molecule Small molecule	Licensed to pharma Available for licensing Licensed to Bridge Medicines Available for licensing Licensed to pharma
2019	RU RU WCM	Autoimmune disease Hearing regeneration Malaria	Small molecule Small molecule Small molecule	Licensed to pharma Licensed to Decibel Therapeutics Available for licensing
2020	RU MSK MSK MSK WCM	Oncology Oncology Oncology Oncology Contraception	Small molecule Biologics Biologics Biologics Small molecule	Licensed to Bridge Medicines Licensed to pharma Available for licensing Licensed to Caribou Biosci. Available for licensing

As a junior physician-scientist, it can be a daunting task to translate work in the lab into therapeutic opportunities. Over the past 10 years we have developed multiple cellular and mouse models to understand the role of cAMP signaling in skin diseases. Our collaboration with TDI has led to multiple lead compounds capable of blocking inflammation in the skin and restoring pigment defects in the skin and eyes. This collaboration has allowed me to marry my knowledge of skin disease and drug formulation with exceptional medical chemistry and pharmaceutical ingenuity. Our work has supported new NIH awards and is sure to drive the development of new therapeutics. I am truly grateful for the contributions of TDI.



Jonathan Zippin, MD
Associate Professor of Dermatology
Weill Cornell Medicine

2020 TDI Pipeline: Early & Late Stage Projects



■ Small Molecules ■ Antibodies

Oncology	Autoimmune Disease	Infectious Disease	...and more
Breast cancer Colorectal cancer Hematologic tumors Homologous recombination-deficient cancers Leukemia Lung Cancer Lymphoma Myelodysplastic Syndrome Pancreatic cancer Prostate cancer Resistant ovarian cancer Resistance to immunotherapy Sarcoma Squamous cell carcinomas ... and more	Psoriasis	Tuberculosis	Diabetic Retinopathy Fibrosis Hypereosinophilic Syndromes Inflammatory Vascular Diseases Mosquito biting Obesity Peanut allergy Retinal Regeneration

Sparian Biosciences spun out of MSK with the worldwide rights to SBS1000- a novel analgesic for acute and chronic pain. SBS1000 was, in fact, the very first compound on which TDI engaged in 2014. The confirmatory efficacy, PK, and exploratory toxicology data that was generated by TDI ultimately allowed Sparian to secure \$20M in NIH/ NIDA HEAL grant funding. We are now anticipating filing an IND by Fall 2021 with plans to enter human trials in January 2022. We are grateful to TDI for initially championing the project and sheparding the compound through the very early stages of development and allowing us to hit the ground running on our way to the clinic. Because of the work initiated by TDI, Sparian now has four drugs under development and is the recipient of two NIH-sponsored grants totaling \$23M in funding.




Jeffrey B. Reich, MD
 CEO and Co Founder
 Sparian Biosciences

Innovative Small Molecule Techniques Open More Doors in Breast Cancer Research



Developing a more individualized approach to cancer treatments has the potential to improve efficacy and reduce adverse effects.



Genetic research has shown that mutations are common in many different types of cancer. Over the last decade, this new understanding led to an important shift in cancer therapeutics. Physicians are increasingly moving away from organ-based treatments to a more personalized approach that is tailored to the specific patient and tumor. Developing a more individualized approach to cancer treatments has the potential to improve efficacy and reduce adverse effects. In 2017, the Xiaojing Ma Lab at Weill Cornell Medicine (WCM) identified a promising new drug target. They discovered a protein associated with the development of either breast or ovarian cancer in some 25 to 35 percent of patients. High expression levels of this protein were found to increase tumor growth, encourage metastasis, or spread, and reduce the body's immune response to the tumor.

With this key target identified, the next step was to develop a small molecule that could be used as a potential therapeutic. The team of Principal Investigators (PIs) – several of whom had worked with TDI in the past – reached out to collaborate on this new project. The PIs had studied this new protein target carefully and developed an exquisite understanding of its functions. Due to this, they decided that rather than simply inhibiting the protein, the project team's objective should be to reduce its abundance by selective degradation, essentially sending the offending protein into the cell's "waste management" system. They posited that this approach had a higher probability of success.

The use of PROTAC (Proteolysis Targeting Chimera) to degrade highly expressed proteins is an exciting new approach in the field of small molecule drug discovery. The technology is unique because it allows scientists to target proteins that were previously deemed undruggable. A PROTAC consists of two small molecules tethered together. One of these molecules binds to the protein of interest while the other binds to a different cellular protein that tags the entire complex for recycling via the cell's "garbage disposal" system, thus reducing the amount of the target protein in the cell.

Across the pharmaceutical industry, the first examples of these new PROTAC molecules are just beginning to enter into clinical trials. The revolutionary potential that this novel technology unlocks in the treatment of previously untreatable diseases ensures

that many other new PROTAC therapeutics, already on the cusp of clinical evaluation, will likely advance rapidly to patients in need.

Due to the infancy of the field, most PROTAC compounds are designed based on a previously known molecule that binds to the target of interest. In this project, not only were there no known inhibitors of this newly discovered protein, but there were no definitive molecular models of this protein to help guide discovery efforts. TDI's approach, therefore, was to first identify compounds that bound to the protein and then to convert them, via chemical elaboration, into PROTAC molecules. Due to challenges associated with this particular target, many traditional screening methods were deemed impractical. The team worked with the PIs at WCM to develop suitable reagents for this target, and established a fragment library screen to search for the most molecules that bound to the protein of interest.

At the beginning of the pandemic, these compounds had not been developed into full PROTAC molecules. But by harnessing both internal and external resources, the team was able to overcome the obstacles of lockdown. When laboratories closed in the U.S., TDI identified Contract Research Organizations (CROs) in China and Germany who were available to carefully profile the compounds. This enabled the team to quickly identify and evaluate new structures to drive this project forward.

TDI's efforts successfully led to identification of the first known PROTAC molecules for this specific target. When these PROTAC molecules were examined in breast cancer cells, the target protein indeed was degraded. With additional chemical modifications, the team improved the molecule's potency and is currently focused on the enhancement of other physical/chemical properties of the PROTAC molecules, so they can be advanced to evaluation in disease-relevant models.

The team established that PROTAC molecules can be designed based on a fragment screen despite not having any definitive knowledge of the protein target's structure. In the future, TDI will likely utilize this approach to degrade other undruggable targets.

New and innovative approaches are desperately needed in many solid tumor cancers of the breast, ovaries and prostate. Exploring the compelling biology of this protein of interest will hopefully lead to more specific treatments for cancers in patients with currently unmet medical needs.



Cancer Therapeutics: Identifying New Molecular Targets to Treat Late-Stage Prostate Cancer

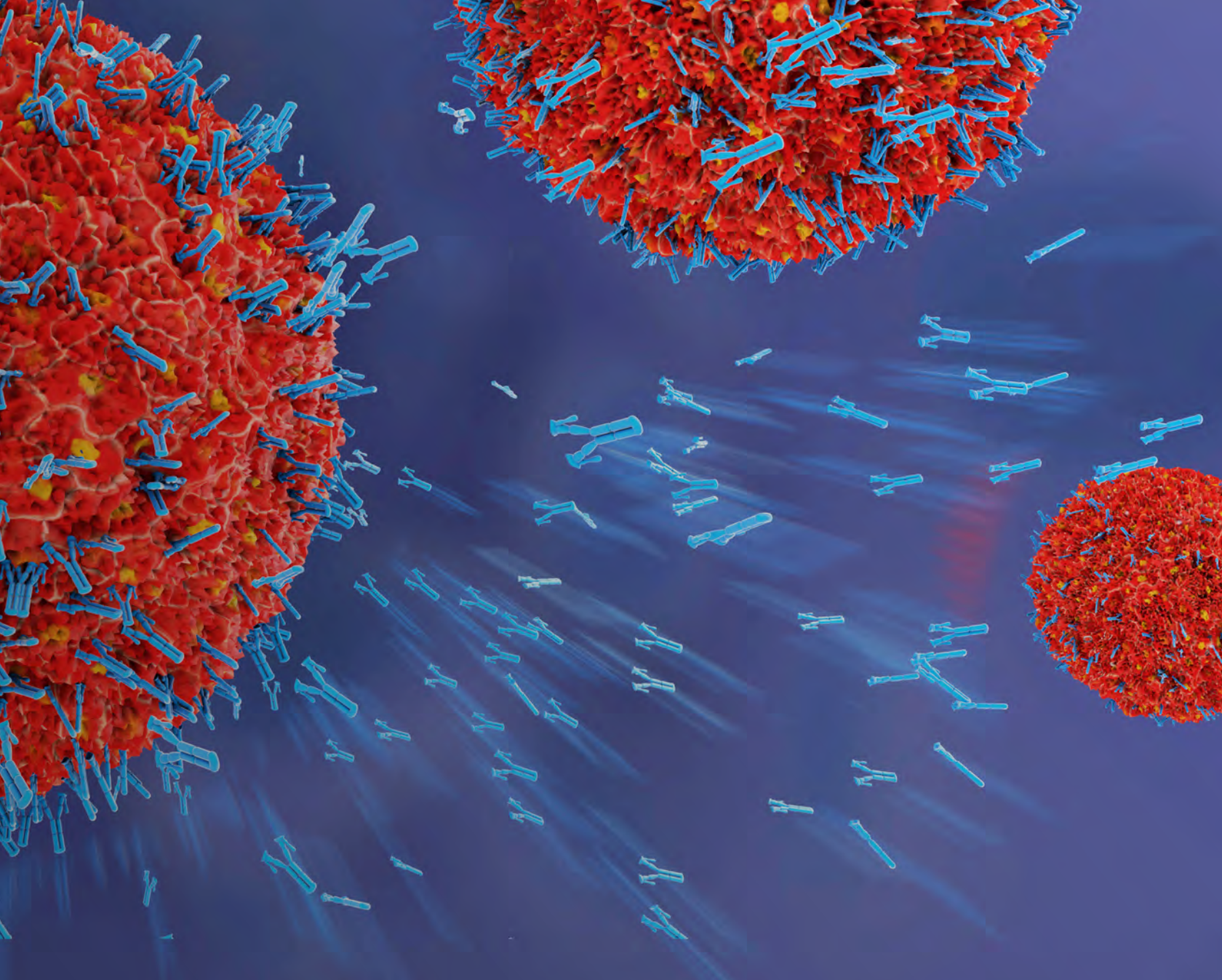
The outlook for patients with metastatic–castration-resistant prostate cancer (mCRPC) has long been bleak. Patients diagnosed with this advanced form of prostate cancer rarely survive more than two years.

Hormone therapy, which stops the body from producing the testosterone that feeds the cancer, is one of the mainstays of treatment. However, in mCRPC, the disease becomes ‘castration-resistant’ – meaning it no longer responds to these therapies and spreads beyond the prostate to the rest of the body. Between 10 and 20 percent of prostate cancers are castration-resistant.

Patients with mCRPC are, unfortunately, left with few therapeutic alternatives. For decades, Dr. Philip Kantoff, Chair of Medicine at Memorial Sloan Kettering Cancer Center (MSK), has known that finding a new way to tackle this late-stage cancer is critical.

A few years ago, he discovered an important clue. Dr. Kantoff identified a particular enzyme, known as a kinase, which shows increased expression in specific prostate cancer cell lines relevant to late-stage disease. Kinases control cellular signaling by turning other proteins “on” or “off” with the addition of specific modifications. They therefore serve as a signaling hub, showing changes in many cancers. This particular kinase of interest is known to be involved in several key cancer signaling pathways and could provide a new therapeutic approach to develop treatments for mCRPC.

One of the senior members of the Kantoff Lab, Dr. Goutam Chakraborty, was the lead scientist who identified these kinase expression changes in prostate cancer cell lines isolated from patients with mCRPC. Dr. Chakraborty worked collaboratively with TDI to translate his findings and take the first steps toward developing new therapeutics.



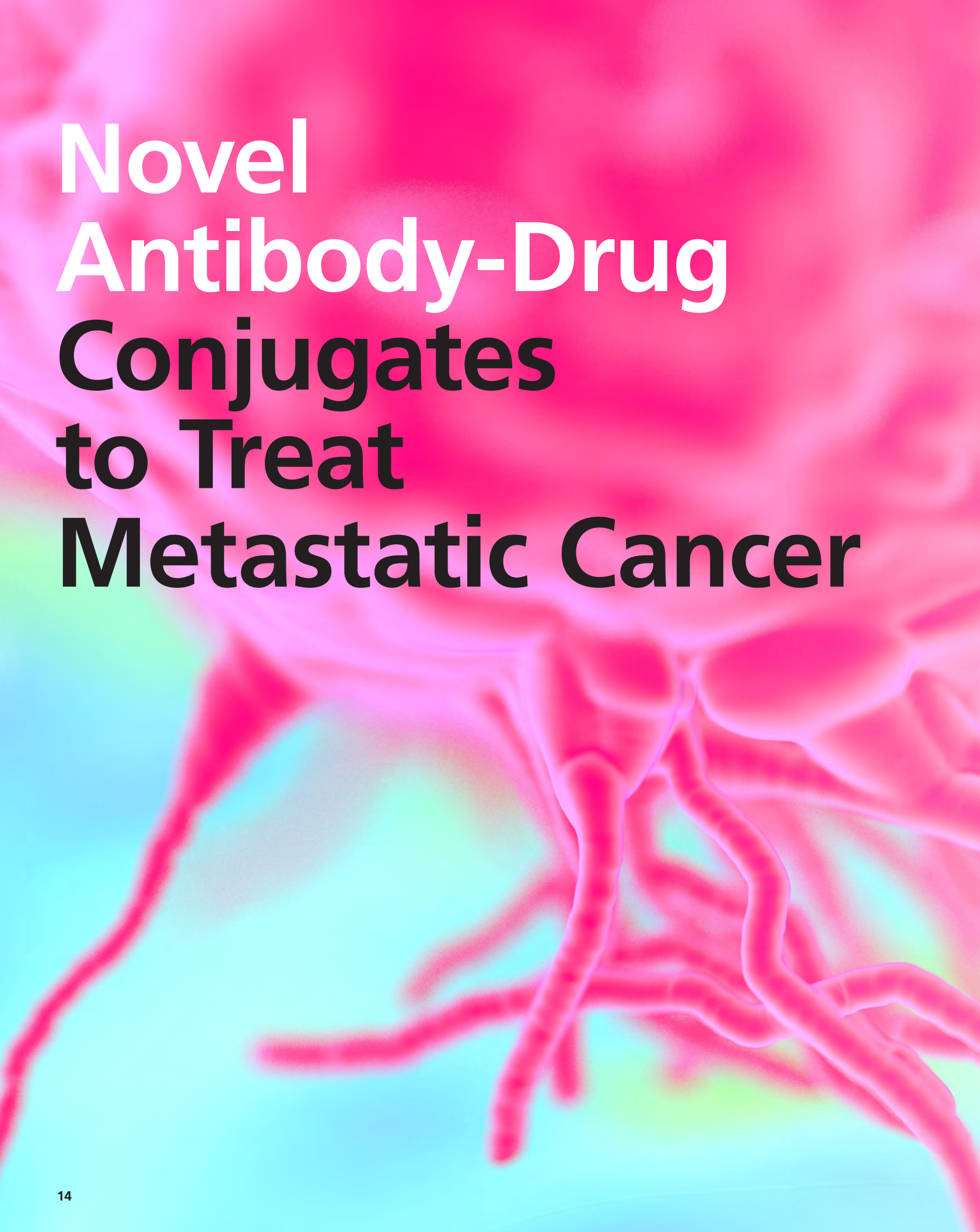
TDI's Small Molecule (SM) Biology Team helped to design genetic experiments to further validate this target. The next step was to determine which small molecule inhibitors, if any, already existed that targeted this protein. TDI's Chemistry team scoured the scientific literature and identified an existing inhibitor to test. TDI's SM Biology team used this existing inhibitor to run cell-based combination studies to evaluate the utility of targeting this kinase in conjunction with a current standard-of-care treatment for mCRPC.

Based on this data, a proof-of-concept (POC) study was conducted at MSK's Antitumor Assessment Core Facility. Consistent with the cell-based results, this *in vivo* study showed robust inhibition of tumor growth when the inhibitor for the kinase of interest was used alone, as well as when it was combined with the current standard-of-care drug. Both options demonstrated superior efficacy to the existing standard of care. The team is now focusing

their efforts on developing a proprietary molecule that inhibits the kinase for further therapeutic development. The final step for this project will be to conduct a more comprehensive POC study using this novel compound.

Remarkably, all of this science continued to advance despite the unforeseen challenges of the pandemic. While meetings moved to a virtual format, the team continued to drive the project forward by working with external Contract Research Organizations and a Core facility at MSK that was considered essential and remained open.

The goal for this project is to eventually develop a proprietary inhibitor of the kinase that would become an effective new treatment for late-stage mCRPC. Success in this program may also have ramifications for other oncology applications and, as a consequence, the team is currently evaluating the inhibition of the kinase of interest in blood cancers.



Novel Antibody-Drug Conjugates to Treat Metastatic Cancer

The vast majority of cancer deaths are caused when the disease spreads beyond the primary tumor. Finding a way to limit or prevent the formation and spread of cancer, also known as metastatic disease, would have a major impact on the overall survival rate of cancer patients.

A few years ago, Drs. Joan Massagué and Karuna Ganesh, researchers from Memorial Sloan Kettering (MSK), discovered why an adhesion protein on the cell surface, originally found to be involved in brain development, was required for the growth of cancer cells and the formation of metastases. Since this protein is essential for the spread of tumors, and largely absent from other adult tissues, it represents an attractive target for cancer therapy.

The next step was to discover an antibody that could selectively bind to this adhesion protein. The investigators at MSK collaborated with TDI's Biologics team to achieve this goal. Together, they generated and characterized a panel of antibodies that could strongly bind to the cell adhesion protein. The scientists then linked a small, toxic drug to the antibodies. These antibody-drug conjugates (ADCs) selectively bind to cancer cells with the cell adhesion protein on their surface to deliver their toxic "payload," thus killing the cells and shrinking, or even removing, the tumor.

The program's biggest challenge was to ensure the toxic drug remained stably attached to the antibody. If it prematurely detached from the antibody prior to reaching the cancer cells, the toxic drug could cause adverse side effects for the patient. TDI helped solve the problem of premature detachment by testing several novel types of stable "linkers" between the antibody and the toxic drug, identifying ADCs suitable for further evaluation.

The researchers showed that the ADCs potently eliminate tumors in multiple disease-relevant assays, as well as confirmed that the ADCs were safe for use in preclinical models. The next step will be to produce the ADCs on a larger scale and advance them to clinical trials.

The TDI Biologics team's expertise in antibody discovery was instrumental throughout this project, from generating and screening the antibodies to engineering and optimizing the ADCs, as well as assessing the manufacturability of ADCs to be produced in large quantities for clinical trials. The novel linker technology that was used to stabilize the ADCs may also have broader applications and may be used in future drug discovery programs at TDI.

Finding a way to limit or prevent the formation and spread of cancer, also known as metastatic disease, would have a major impact on the overall survival rate of cancer patients.

We came to TDI as a cancer genetics lab with an idea, but no experience in drug development. The biologists, computational and medicinal chemists, and advisory team have brought this idea to life. We set out to develop selective inhibitors against a very challenging target and TDI worked with us to design various diverse and paralleled strategies to meet this goal. It has been a thoughtful and tailored approach, and one of the most fruitful collaborations I have been involved in. In addition to the generation of multiple new lead compounds that we are actively pursuing, the biggest and most welcome surprise is the time and energy that the team has put forth to understand the biological rationale behind our project and make sure we understand the chemistry and strategy underlying drug development. I'll tell anyone that will listen: Work with TDI if you have the chance.



Lukas Dow, PhD
Associate Professor of Biochemistry in Medicine
Weill Cornell Medicine



Our collaboration with TDI on small molecule inhibitors of a key mycobacterial enzyme was truly an exceptional and a highly rewarding experience. TDI took our small molecule, which had no antibacterial activity due to limited intracellular accumulation, and developed analogs that were able to permeate the waxy mycobacterial cell wall and engage our target. Further optimization led to analogs with the extended residence time on the bacterial but not on the human enzyme, building *in vivo* selectivity. Improvements in metabolic stability afforded superior bioavailability for the efficacy proof-of-concept testing in a mouse model of tuberculosis. We owe this remarkable progress to the talented team of experts assembled by TDI.

Ruslana Bryk, PhD

Associate Professor of Research in Microbiology and Immunology
Weill Cornell Medicine

Redirecting the Immune System to Fight Tumors

Acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS) are blood cancers that affect over a quarter million people each year. Despite being the most common leukemias in adults, the overall survival rate remains poor with limited treatment options.

The primary function of our immune system is to keep any unusual activity in check. Certain tumors, however, escape this surveillance. Over the last decade, the scientific community has increasingly found innovative ways to instruct the immune system to attack and eliminate cancer cells.

In CAR T-cell therapy, for example, T-cells use special proteins called chimeric antigen receptors (CARs) that guide them to recognize vulnerable targets to attack on tumor cells. In this treatment, T-cells are taken from the patient and genetically engineered in the lab to follow special instructions. CAR T-cells have shown tremendous promise in treating patients with refractory or relapsed lymphoid malignancies like acute lymphoblastic leukemia (ALL).

Drs. Anthony Daniyan and Renier Brentjens from Memorial Sloan Kettering (MSK) played a critical role in developing a successful CAR T-cell treatment known as CD19 CAR therapy. Building on this promising foundation, they are exploring ways to tackle various blood cancers and solid tumors with novel CAR therapy approaches.

These MSK researchers identified a protein of interest that is present on cancer cells in over 85 percent of AML patients. Their goal was then to identify novel antibodies that could effectively target this tumor antigen and increase CAR T-cell activity. However, unlike other cancers, AML and MDS cells have a unique problem. They lack a single suitable antigen that would help a cancer victim's body appropriately identify them as leukemic cells. As a result, complementary approaches needed to be employed. Recent data suggested that targeting two antigens simultaneously was the best approach against AML.

When these investigators approached TDI, they were working with an existing sub-optimal molecule to combat this problem, but the TDI Biologics team designed new and effective strategies to discover better candidates. The MSK researchers tested a combination of two antibodies discovered by TDI against two common AML antigens. The results showed complete eradication of the tumor in an *in vivo* model.

The next step is to take these lead CAR candidates into human trials. Based on these promising results, the antibodies should eliminate most, if not all, malignant cells in pediatric and adult AML patients. TDI has played an important role in helping improve therapies for this challenging group of cancers with very limited treatment options.

Over the last decade, the scientific community has increasingly found innovative ways to instruct the immune system to attack and eliminate cancer cells.

The Small Molecule Biology Team: Partnering with Principal Investigators to Accelerate Drug Discovery

Upon its founding in 2013, TDI was structured as a single-modality organization focused on small molecule drug discovery, with medicinal chemists from Takeda Pharmaceuticals embedded in the organization. At this juncture, all biological discovery and small molecule activity analysis occurred in the labs of the collaborating principal investigators (PIs) across the Tri-Institutional (Tri-I) Community. As TDI worked in close concert with these PIs over the years, it became apparent that, while they were certainly world-leading experts in their fields of biological study, they lacked the time or resources to also become experts in every assay (a type of analytical test) required to advance their small molecule drug discovery programs.

While the assays employed to support drug discovery range from simple to highly complex, the construction of highly robust and reproducible assays often requires deep expertise in enzymology (the study of how enzymes work), cell biology and genetics.

To fill this gap, TDI built a Small Molecule (SM) Biology team. This is an innovative group of scientists who collaborate with PI laboratories, performing independent program-specific biology experiments and guiding efforts at Contract Research Organizations (CROs) in order to propel academic projects to *in vivo* proof-of-concept, a key milestone in drug discovery. This team ensures that when TDI completes a program, the science is robust and reproducible, and the lead molecule(s) is ready for the next stage of development.

TDI's Biology team completes a strategic framework for a successful early drug discovery program. Each program is designed to be a productive collaboration between the

PI and TDI's SM Biology, Computational Chemistry and Medicinal Chemistry teams with the overall goal being the development and evaluation of small molecule modulators of target proteins that regulate disease processes. Once these molecules are identified, they are tested in disease-relevant models. If they demonstrate success, they are then made available for licensing to industry or spun out into a new company.

The key to the SM Biology team's success is a rich history of experience and collaboration. Every program in TDI's small molecule portfolio has a lead biologist that oversees the project from the validation and selection of the target through the development and execution of key assays, including reagent confirmation and study design.

TDI's biology experts have a broad base of academic and industry experience that perfectly complements the PI's focus in the lab. The team specializes in designing genetic studies and molecular biology approaches to validate targets. They also develop robust, industry-quality assays to test compounds synthesized by TDI's Medicinal Chemistry team. The SM Biology team provides critical aid in the development of biochemical and cell-based assays to drive these programs.

TDI's SM Biology team has supported many successful projects related to the most pressing human health conditions, including malaria, tuberculosis, hearing and vision loss, COVID-19, fertility and many types of cancer. They are a vital element to the success of TDI's mission to accelerate academic drug discovery.



Members of TDI's SM Biology Team

Stacia Kargman - Vice President, Biology

Ms. Kargman has over 30 years of experience in the pharmaceutical industry. After earning her BS in biology from Columbia University and completing graduate studies at the Weizmann Institute of Science in Israel, she joined the Department of Pharmacology at Merck



Frosst Centre for Therapeutic Research, Canada. After 25 years in Montreal, she accepted a transfer to Merck, New Jersey, where she served as External In Vitro Pharmacology Lead across the Merck network. In this role, she oversaw scientists in China and Europe generating pharmacological data for early

drug discovery. Over the course of her career, Ms. Kargman has been involved in bringing eight novel medicines to market, including treatments for asthma, pain and hepatitis C virus. Ms. Kargman joined TDI in 2017 to build and lead the SM Biology team.

Leigh A. Baxt, PhD - Associate Director, Biology

Dr. Baxt earned her PhD at Stanford University School of Medicine studying intramembrane proteases (enzymes that degrade proteins) in the human intestinal parasite *Entamoeba histolytica*. She did her postdoctoral research in the lab of Dr. Marcia Goldberg at Massachusetts General Hospital & Harvard Medical School focusing on host and bacterial determinants that control antibacterial autophagy during *Shigella* infections. She worked briefly at a small startup company, Coronado Biosciences, aiming to develop helminth eggs into therapeutics for Inflammatory Bowel Disease. She then joined the lab of Dr. Ramnik Xavier of the Broad Institute as a Research Associate/Staff Scientist where she performed genome-wide screening to elucidate new host factors involved in antibacterial autophagy and directed development of high-content imaging assays for the group. Dr. Baxt brought her deep expertise in genetic target validation, cell biology and assay development to TDI in January of 2018.



Efrat Finkin-Groner, PhD - Associate Director, Biology



Dr. Finkin-Groner earned her PhD in Pharmacology under the direction of Dr. Marta Weinstock-Rosin at The Hebrew University of Jerusalem investigating "multi-functional drugs for the treatment of neurodegenerative diseases." Her postdoctoral studies were conducted at Memorial Sloan Kettering Cancer Center in the

lab of Dr. Yael David where she explored the functionality of site-specific modified histones – proteins that play a major role in DNA packaging and gene expression. Before joining TDI as a full-time team member, Dr. Finkin-Groner was also a postdoctoral scholar at TDI, where she acquired deep expertise in enzymology and biochemical assay development.

John Pichardo, Research Specialist, Biology

Mr. Pichardo has over 25 years of drug discovery and development experience in the pharmaceutical sector. He spent time at numerous organizations including Schering Plough, Bristol-Myers Squibb and PCT Therapeutics where he developed expertise in assay development and laboratory automation. Mr. Pichardo has been an important player in establishing key assay capabilities at TDI by leading the acquisition and installation of several new tools in the SM Biology Lab.



Daleum (Daniel) Kim, Research Associate, Biology

Mr. Kim joined TDI in 2020 after studying Biochemistry at the University of Wisconsin, Madison and spending several subsequent years in academic research. Directly prior to joining TDI, he worked in the lab of Dr. Ari Melnick, at Weill Cornell Medicine, where he worked on a team that was focused on developing new immunotherapies for cancer patients. Mr. Kim brought expertise with *in vivo* studies to TDI and was instrumental in advancing at least one small molecule program to date.



TDI has grown and transformed to meet the changing needs of the scientific community since it was first founded in 2013. One of the most significant changes that occurred over those seven years was the evolution of TDI from an organization focused solely on the discovery of small molecule compounds to one that also supports the discovery and development of biologics.

With this shift, scientists at TDI opened the door to a myriad of new possibilities – uncovering novel therapeutic antibodies, proteins and other large molecules. These are also the building blocks for antibody-drug conjugates and multi-specific antibodies, as well as cell and gene therapies. As innovative and highly effective treatments for patients with a variety of diseases have expanded over the last two decades, identifying these novel large molecules has become increasingly important. TDI is proud to have a strong presence in this arena.

TDI's Biologics Group was launched in 2015 with the arrival of Dr. Ivo Lorenz, Vice President of Biologics. Charged with building and leading this essential part of the organization, Dr. Lorenz successfully grew his team from six to 18 members in only four years. This rapid expansion required that a robust organizational structure be established.

Mr. Paul Balderes was hired in October of 2017 to establish the **Lead Optimization** team and **Dr. David Andrew** joined TDI in September of 2018 as the head of **Lead Identification**. Both scientists bring deep expertise in biologics drug discovery, each with significant technical accomplishments in their areas of specialization. They then carefully recruited young and dynamic leaders to manage specific aspects of the therapeutic biologics discovery process. TDI is fortunate to have these talented scientists on staff.

TDI Biologics Leadership Team: Advancing Innovative Immunotherapies

Lead Identification Team Leaders

Yang Zhang, PhD – Associate Director, Antibody Generation

Dr. Zhang earned his PhD with a concentration in Microbial Physiology from China Agricultural University. He engaged in postdoctoral studies at ShanghaiTech University in the lab of



Dr. Sachdev S. Sidhu, where he focused on antibody discovery and engineering using phage display technology. Dr. Zhang subsequently built expertise in other display technologies, such as yeast and mammalian cell display technologies. He has strong hands-on experience with antibody library construction, antibody selection and screening as well as antibody engineering.

His work led to the discovery of a number of promising antibodies and fusion proteins for therapeutics. It also resulted in several original research articles and book chapters.

At TDI, Dr. Zhang leads the Antibody Generation team, whose members use both hybridoma and phage display technologies as they search for novel protein binders that will modulate diseases.

Irina Lebedeva, PhD – Associate Director, Assay Development & Screening

Dr. Lebedeva is a cell and molecular biologist who received her PhD from Moscow State University and did her postdoctoral studies at the National Institutes of Allergy and Infectious Disease at the National Institutes of Health. She possesses a strong background in the study of signal transduction pathways, cell surface and cell membrane receptors, as well as biologics-based therapeutics.

As the leader of the Assay Development & Screening team at TDI, Dr. Lebedeva designs and



validates biochemical and cell-based assays for mechanistic and functional testing of antibodies. She also provides technical training on assay development and screening methodologies for the members of her team and other functional teams at TDI.

Lead Optimization Team Leaders

Abdul Khan, PhD – Sr. Associate Director, Protein and Cell Line Production



Dr. Khan earned his PhD in natural sciences from Max F. Perutz Laboratories at the University of Vienna, investigating virus-host interactions with a particular focus on rhinoviruses that cause the common cold. He then went on to pursue postdoctoral studies at the Center for Advanced Biotechnology and Medicine, Rutgers University, where his

main area of research was structural aspects of the hepatitis C virus (HCV) host interaction and vaccine design. In this work, he developed hundreds of antibodies for functional and structural studies. Dr. Khan solved the first high-resolution structure of the HCV surface envelope protein E2, which represented a major contribution to that field.

At TDI, Dr. Khan's team generates high-quality recombinant proteins and stable cell lines to support antibody discovery efforts. In the time since he established the team, they have instituted standard operating procedures for reagent generation, novel immunogen designs and high-throughput antibody production. These techniques play a vital role in the success of Biologics at TDI.

Elisabeth Nyakatura, PhD – Associate Director, Antibody Engineering

Dr. Nyakatura earned her PhD at the Free University in Berlin and went on to complete a Postdoctoral Fellowship at the Albert Einstein College of Medicine in New York. Prior to joining TDI, she was a Research Assistant Professor at Albert Einstein. Her work focused on the development of antiviral antibodies, working collaboratively with partners in academia and industry, as well as at the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID). This research led to a number of scientific publications in high-impact journals.



At TDI, Dr. Nyakatura leads the Antibody Engineering team. This team works on the design, formatting and engineering of antibody and antibody-based therapeutics. As part of this effort, she oversees sequence analysis and optimization, antibody affinity maturation, humanization and stabilization. These activities can substantially shorten the path to the clinic for a novel biologic drug.

Olivia Vergnolle, PhD – Associate Director, Bioanalytics

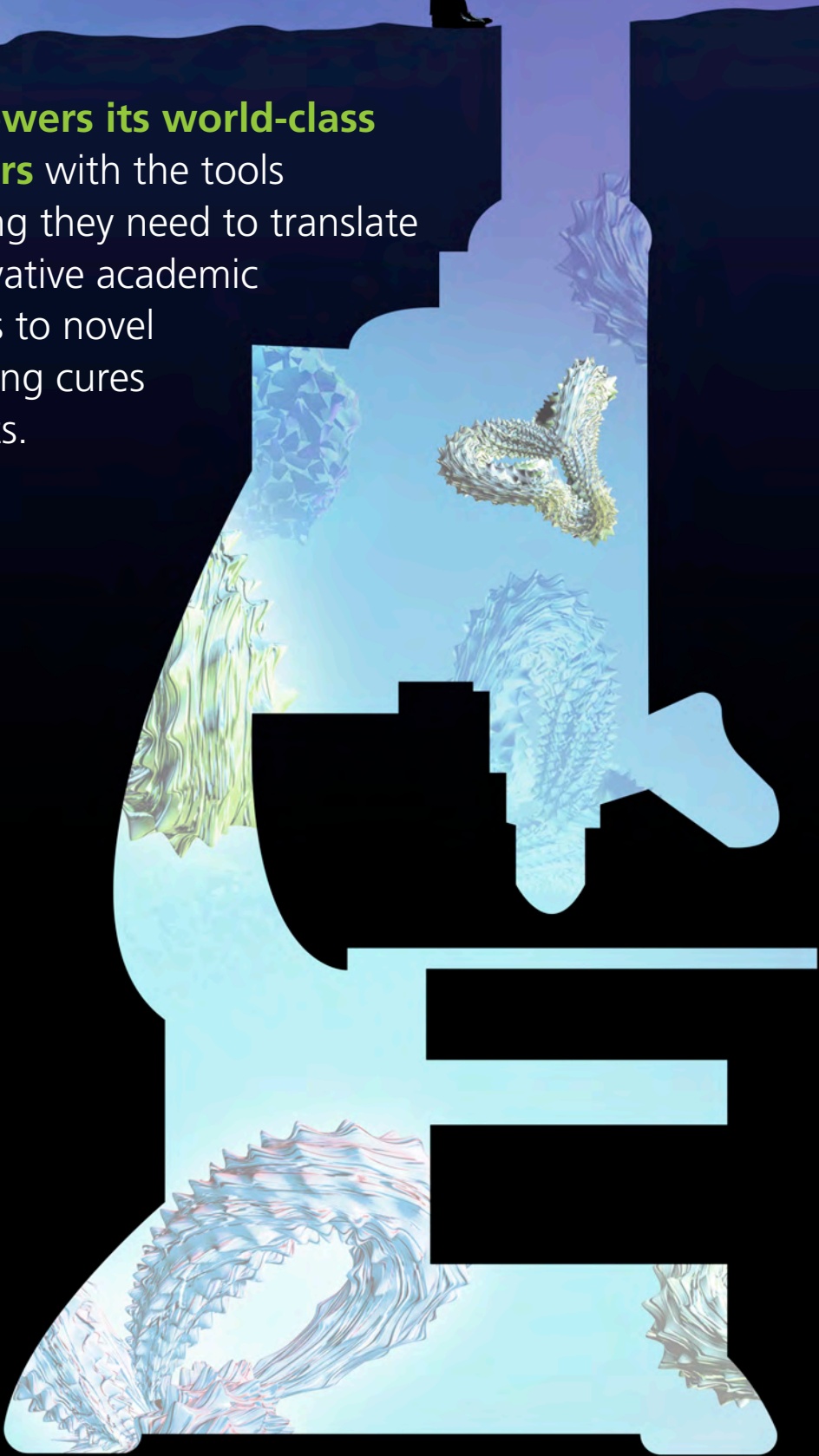
Dr. Vergnolle obtained her PhD in Biochemistry from Cambridge University. During her postdoctoral studies at Weill Cornell Medicine and the City University of New York, she focused on bacterial enzymes involved in *Mycobacterium tuberculosis* virulence. She then obtained an appointment as a Research Assistant Professor at the Albert Einstein College of Medicine where she expanded her protein engineering toolbox by developing immunogen- and antibody-based antiviral treatments in response to current and emerging viral threats.



At TDI, Dr. Vergnolle leads the Bioanalytics team. This group uses a broad range of biochemical and biophysical protein analytical techniques to characterize therapeutic antibodies and proteins. Dr. Vergnolle and her team also define, establish and execute developability testing, pre-formulation screening and manufacturability assessment efforts for antibodies. This process ensures a seamless transition of projects from the discovery to development phase, and ultimately advancement to clinical trials.



TDI empowers its world-class researchers with the tools and training they need to translate their innovative academic discoveries to novel life-changing cures for patients.



Education and Innovation

The Sanders Education and Innovation Initiative is a key component of TDI's offering to the Tri-I Community. Through this initiative, TDI empowers its world-class researchers with the tools and training they need to translate their innovative academic discoveries to novel, life-changing cures for patients. To fulfill this mission, TDI supports seminar series, workshops, for-credit courses and training opportunities. TDI's industry-seasoned professionals also provide in-person training on new drug discovery processes. These offerings are described in more detail below.

Schrödinger Software Access and Training

A key accomplishment of TDI's Sanders Innovation and Education Initiative has been the formation of a close relationship with Schrödinger, Inc., a leader in *in silico* chemical simulations for drug discovery research. Under our unique partnership arrangement, nearly all of Schrödinger's computational tools are *freely available* to all researchers in the Tri-I community. TDI hosts regular training sessions throughout the year in order to ensure that researchers are able to use this powerful software to maximal benefit.

"From Molecule to Prescription" Drug Development Class, Weill Cornell Graduate School

This course was designed in collaboration with drug development experts from Roche and provides a foundation of knowledge into the multi-disciplined process of developing a new medication. It includes real-world challenges encountered in the areas of discovery, development, manufacturing, global regulatory approval and commercialization of new medicines. It also addresses the impact of emerging technologies to healthcare and the development process.

Small Molecule and Antibody Drug Discovery – The Ins & Outs, Dos & Don'ts

This four-module course is offered by TDI leadership and staff scientists, typically once per year at each of the Tri-I parent institutions. In previous years, attendance was limited to approximately 20 students per section because the instructors felt that questions could be addressed more effectively in a small group setting. However, 2020 changed many paradigms and the nature of this offering was among them. In order to offer additional opportunities for engagement across the Tri-I Community, TDI moved this class to a virtual format and opened it to any and all from the three institutions. In the April 2020 offering, there were close to 200 students registered for this course.

The course covers some general information about TDI and how the community can access its resources and support, and then goes in-depth on both small molecule and antibody drug discovery, including illustrative case studies, to ensure that the students have a point of reference for their new knowledge.

TDI definitely provided substantial value-add to our research efforts. From their enthusiastic interest in our project at the outset, their organizational approach, frequent and seamless communication, the focused effort by Ivo and his team and their delivery of high-quality reagents that enabled our non-human primate studies, they really came through for us. They were the ideal collaborators, and I look forward to further joint projects in the future.



Neil H. Bander, MD

Bernard & Josephine Chaus Professor of Urologic Oncology
Weill Cornell Medicine

Virtual Summer Internship Program Inspires Young Scientists

How do you run a summer program with the goal of getting young scientists into the lab safely during a global pandemic? The Tri-I Chemical Biology Summer Program (ChBSP) successfully bridged that gap last year by transforming its annual lab-based internship into a fully remote research experience.

In July 2020, five undergraduate students participated in an immersive, month-long virtual program organized by researchers at Memorial Sloan Kettering (MSK) and sponsored by TDI. These students, most of whom were entering their senior year, participated in a wide variety of scientific and career development training activities. For example, they joined the first-year Tri-Institutional PhD Program in Chemical Biology (TPCB) students in a semi-weekly journal club, attended a weekly chemical biology seminar series hosted by the Memorial Sloan Kettering (MSK) Chemical Biology Program and participated in lunchtime “Meet the Faculty” sessions to gain exposure to the wide variety of science across the Tri-I Chemical Biology Program.

Every student was assigned to a group and paired with a pre- or post-doctoral student advisor who was physically present in the lab. The teams were in constant communication over Zoom to discuss experiments. Although the interns could not touch the materials or use the tools, they were able to assist with other elements of the project. They participated in experimental planning by reading papers and researching topics, as well as brainstorming ways to organize and present data. The students also performed modeling and data analysis, developed their own hypotheses and drew conclusions. Moreover, the students attended both group and sub-group meetings with the Principal Investigators, thereby gaining expertise not only on their particular project but in the larger goals of the lab. At the end of the internship, the students presented their work alongside other summer interns at MSK as part of an online poster session.

One goal of this internship is to expose promising young students to the experience of being a graduate student at a biomedical research institution. To cultivate relationships and further expose them to our community, the teams also hosted online hang-out sessions. Even though they could not physically be in the lab, they were actively engaged with the TPCB students, as well as other members of the Tri-I community.

The summer program is an important part of TDI's educational mission. It is made possible with generous financial support from the Sanders Innovation and Education Initiative at TDI, and is run under the leadership of Daniel Bachovchin, PhD, and Ushma Neill, PhD, from MSK.

A few students became so engaged in their projects that they continued to attend group meetings after the program officially ended. At least one intern has decided to return to the Tri-I community for graduate school. The organizers at MSK and TDI were delighted to offer this invaluable experience that helped cultivate career development and accelerate science during an unprecedented time.



Fragment-Based Drug Discovery: A Novel Starting Point for Identifying Hit Compounds

New advances in research allow scientists to target proteins that were previously thought to be undruggable. For instance, traditional small molecule drugs can only target about 20 percent of all proteins found in humans. However, novel protein degradation strategies, which destabilize proteins for recycling in the cell, are an exciting and rapidly growing drug discovery technique with the potential to expand the number of druggable proteins. This technique, which includes molecular glues and proteolysis targeting chimera (PROTAC), is being widely explored in small molecule drug discovery and may have the ability to unlock the therapeutic potential of the remaining 80 percent of human proteins.

Several challenges still remain. Finding a good chemical starting point for these additional, largely unstudied protein targets is limited by a lack of key tools, including structural information or biochemical assay methods to evaluate binding ability and activity.

Since limited knowledge exists regarding these proteins, alternate approaches are sometimes required to identify a chemical starting point for a medicinal chemistry optimization effort, such as the use of a library of chemical fragments. Fragments are compounds of low molecular weight that can serve as a launching pad for the drug discovery process. Fragments are screened at high concentration because of their small size, which results in weak binding into pockets on their target protein. However, despite fragments binding weakly, their low molecular weight gives them a distinct advantage: the interaction between the fragment and the protein is highly efficient.

Fragments also form a smaller number of intermolecular interactions when compared with the larger compounds used in traditional screening modalities. Therefore, small collections of these fragments cover a broader chemical space. As a result, fragment-based drug discovery methods are becoming common fixtures for identifying lead compounds in laboratories today.

TDI employed a fragment-based approach on a recent project where the drug concept was compelling but there were no tools or assays available for the target protein. To maximize the opportunity to identify effective fragments, also known as hits, this project utilized two fragment libraries. The first was a fluorinated fragment library assembled by TDI for screening using nuclear magnetic resonance (NMR) spectroscopy. A second screen was carried out using a fragment library in The Rockefeller University Screening Core. Hits were identified from both screens. These hit compound fragments were then used to successfully build a PROTAC molecule by tethering the fragment that bound to the protein of interest to another fragment that acts as a signal to the cell that this complex should be degraded and disposed of in the cell's normal "garbage disposal" system (see full story on page 10). In this way, proteins that initiate and perpetuate disease can be eliminated from the cell.

When no chemical starting points exist, fragments can provide a vital foundation for research. Through exploration of structure-activity relationships, scientists can understand the chemical space and hit fragments can be elaborated to provide drug-like compounds. In this project, TDI was able to design a targeted protein-degrading compound from hits generated by screening fragment libraries. As a result, a novel chemical tool is now available for exploring the exciting biology associated with this target.

TDI Platinum Phage Library: Expansion Enhances Antibody Discovery Capabilities

Phage display is an important technology in therapeutic antibody development. Using this methodology, the binding regions of antibodies or other small protein fragments are packaged into a bacteriophage, a virus that infects only bacteria. These phage viruses express – or display – these antibody fragments on their exterior coat, allowing scientists in the lab to probe their ability to bind to specific target proteins. By creating large and highly diverse libraries of antibody fragments, researchers can greatly increase their ability to find antibody fragments that bind proteins of interest in the required locations and with the appropriate strength to modulate a protein's activity.

Using this technology, scientists can not only discover novel antibodies, but also optimize the biophysical properties of these antibodies. These findings may eventually be used in the development of therapeutics.

In 2017, TDI worked closely with Antibody Design Laboratories and Global Bio to generate a proprietary phage display library with more than 10 billion unique antibody sequences. Based on early successes using this

original library, TDI substantially expanded this phage library screening capability in 2020 – working again with the Antibody Design Laboratories and Global Bio – to generate what is known as an ALTHEA Platinum Library™. Upgrading to a platinum library means that TDI now has access to 160 billion human antibody genes. Over the past year, this library has dramatically accelerated the antibody discovery workflow at TDI.

There are many applications for phage display technology. For example, it has been used successfully on multiple chimeric antigen receptor (CAR) T-cell projects. In CAR T-cell therapy, T-cells from the patient's own immune system are extracted and engineered in the laboratory to express the single-chain antibody on the surface of the T-cell. When the T-cells are infused back into the patient, they target specific tumor cells. Using the newly expanded library accelerates the ability to discover antibody fragments that are used as building blocks for CARs.

This new technology has already yielded important results. In 2020, TDI used the ALTHEA phage library to identify a panel of antibodies, in collaboration with a research group at Memorial Sloan Kettering. These new molecules were so novel and showed such therapeutic potential that they were recently licensed to a biotech company who will continue to prepare them for clinical trials. TDI looks forward to additional programmatic successes using this powerful technology to help patients with unmet medical needs.



TDI Delivers more than Molecules

The collaborations that TDI engages in across the Tri-I Community are highly varied. TDI reaches across a broad range of therapeutic areas and offers assistance with very early stage projects, where the therapeutic target may



not be known, through to late stage programs where the molecule of interest may simply need additional optimization to be suitable for licensing, or to serve as the starting point for a new company.

The net benefit of these collaborations are not only molecular assets that are ready to move toward the clinic, but optimized molecules that are useful as new and powerful tools. These tools are typically not available to

academic researchers, lacking access to industrial-level discovery and optimization processes. However, they enable the investigators to dive deeper into their biology of interest and add significantly to the body of knowledge in their area of expertise. This is reflected by an increase in publications accepted by top-tier peer-reviewed journals, by the generation of patents and by increased success in raising additional research funding from grant institutions.



Over the last seven years, TDI staff, working with investigators across the Tri-I community, have contributed to approximately **20** publications in peer-reviewed journals and over **25** patents.

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Absorption Systems
Axelead
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Eurofins
Frontage Labs
Pharmaron
WuXi AppTec
Zyleris

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BPS Bioscience
EpiCypher
Reaction Biology
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Partner with Us

TDI brings together some of the finest minds in the world from Memorial Sloan Kettering Cancer Center, The Rockefeller University and Weill Cornell Medicine with collaborators across the globe to remove the barriers that impede drug discovery in academic settings. Together with our partner, Takeda Pharmaceutical Company, Ltd., we are enabling the discovery of next-generation drugs by empowering the Tri-Institutional faculty with tools, technology and expertise.

With the help of your investment, we will continue to meet this extraordinary challenge.



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