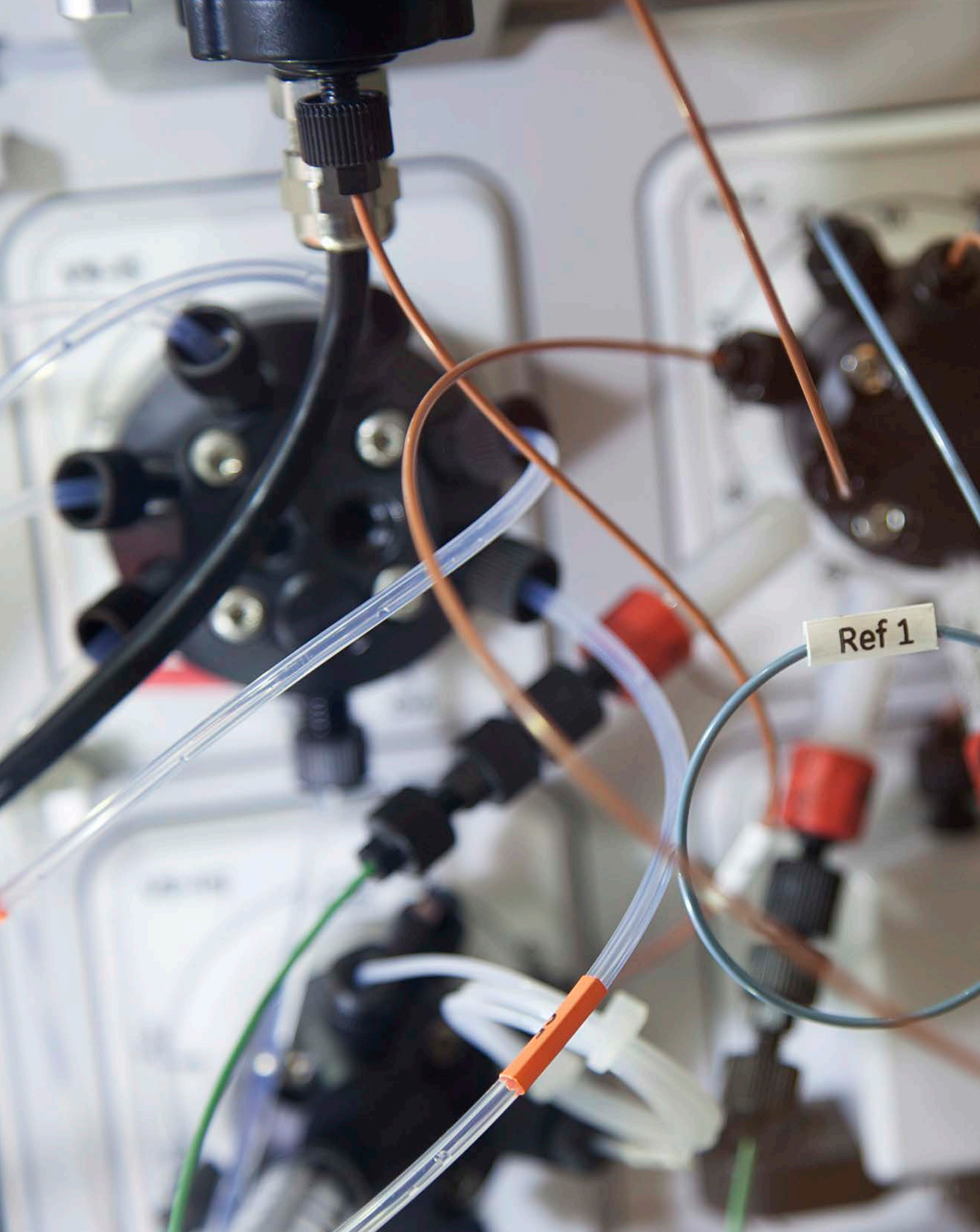
TRI-INSTITUTIONAL
THERAPEUTICS DISCOVERY INSTITUTE

TDI Annual Report
2017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The mission of 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 scale and scope in 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.

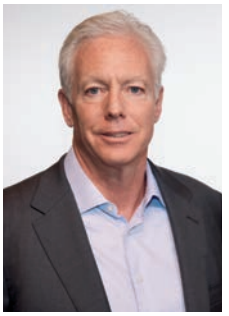
Tri-I Investigator identifies a new protein target implicated in human disease

TDI uses outside contractors and internal expertise to quickly assess viability of the protein as a new drug target

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

Upon demonstration of *in vivo* efficacy, project may graduate to Bridge Medicines for development as a pre-clinical candidate

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



Michael A. Foley, PhD

Letter from the Director

2017 capped a pivotal two-year period of growth for TDI, as we transformed from a small virtual organization, founded on the promise of accelerating academic-initiated drug development, to a robust brick-and-mortar operation with the proven ability to deliver results across a large and diverse project portfolio.

The past year has been a period of dramatic change for TDI. Our operation has grown in many ways since TDI was launched in 2014 with 3 full-time employees charged with overseeing 8 Small Molecule Drug Discovery projects. Today, our on-site staff of 30 effectively manages 30 projects across both the Therapeutic Small Molecule and Antibody Discovery portfolios. An additional 25 projects are executed under TDI's Early Stage Initiative, which offers targeted early-stage drug discovery support and delivers a high-quality pipeline of projects to the Therapeutic Small Molecule and Antibody Discovery programs. Our recently-formed partner company, Bridge Medicines Inc., has accepted its first project from the Small Molecule pipeline and is considering a second project. This expanded operational network represents the first uninterrupted path from basic academic research discovery to human clinical trials. Most importantly, TDI has demonstrated that this model achieves results: in 2017 we announced the successful completion of the first three projects from the Small Molecule Initiative.

As I reported last year, 2016 saw a major expansion of TDI's scientific mission, as the Therapeutic Small Molecule project portfolio expanded from 8 to 20 projects and we launched three major initiatives: the Antibody Discovery program, the Early Project Initiative, and Bridge Medicines. In 2017, we began a significant expansion of our on-site scientific team in order to accommodate these enhanced activities and responsibilities. These growth campaigns, both in portfolio scope and in staffing, are a direct result of the scientific successes that TDI realized in its early years of operation.

Our key accomplishments over the past year include:

- Assembling a stellar team of 17 industry-experienced scientists to support Small Molecule discovery. Prior to joining TDI, these chemists held leadership roles on the discovery of 11 approved drugs and 18 clinical stage compounds.
- Launching a hiring campaign to onboard 9 scientists to staff the Antibody Initiative.
- Establishing an excellent working relationship with our partner, Bridge Medicines. Key members of the Scientific Leadership Team are co-appointed at both TDI and Bridge Medicines, providing transparency and fluidity for projects that transition from TDI to Bridge Medicines.
- Successfully executing projects within the Early Project Initiative. In 2017, 5 of these pipeline projects were advanced to the Antibody or Small Molecule initiative, where they receive full drug discovery support. Moreover, Quentis Therapeutics, a Series A company, was launched with $48M on the basis of work performed under TDI's Early Project Initiative.
- Completing 3 projects in the Therapeutic Small Molecule Portfolio; 1 of these is licensed to Bridge Medicines, and discussions are underway for Bridge Medicines to accept a second project.
- Launching two exciting new Education initiatives: the Tri-Institutional Drug Discovery Course and a Postdoctoral Research Fellowship, both of which were undertaken in partnership with Roche.

Over the next year, we look forward to onboarding additional new Therapeutic Small Molecule and Antibody Discovery projects and advancing 6 more projects to Bridge Medicines. We will continue to scale our team and portfolio to meet the needs of the Tri-Institutional community.

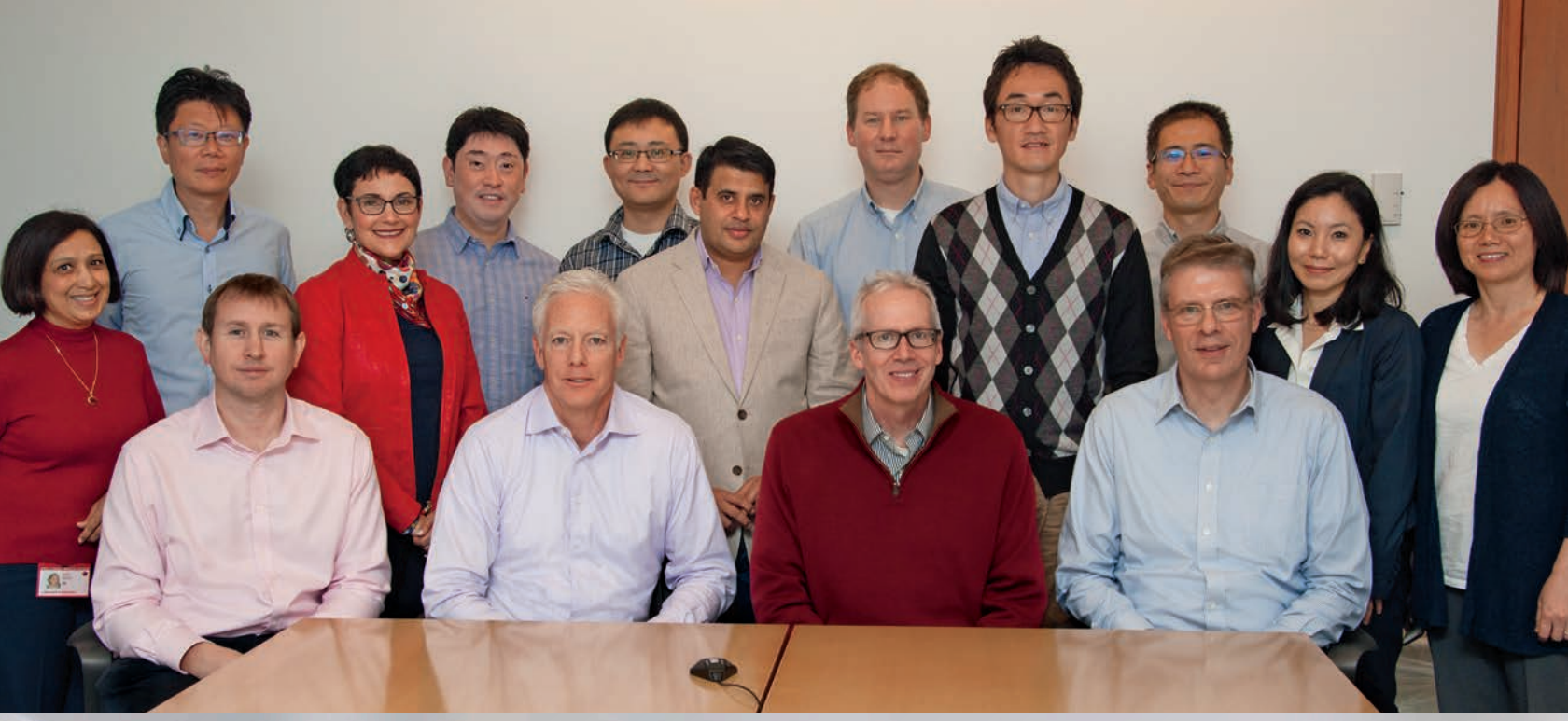
As we look forward to the challenges and opportunities of 2018, we gratefully acknowledge the support of Mr. Lewis Sanders, whose generous gifts made possible the establishment and continued growth of TDI. Our partner, Takeda plays a critical role in our success by bringing its knowledge of drug discovery and development to every project. We appreciate the leadership provided by our Board of Directors, whose unfailing support and vision have been crucial to our success. Finally, we are deeply fortunate to have the opportunity to partner with world-class scientists at The Rockefeller University, Weill Cornell Medicine, and Memorial Sloan Kettering Cancer Center on a range of incredibly exciting, potentially groundbreaking drug discovery projects.

Michael A. Foley, PhD
Sanders Director

2017

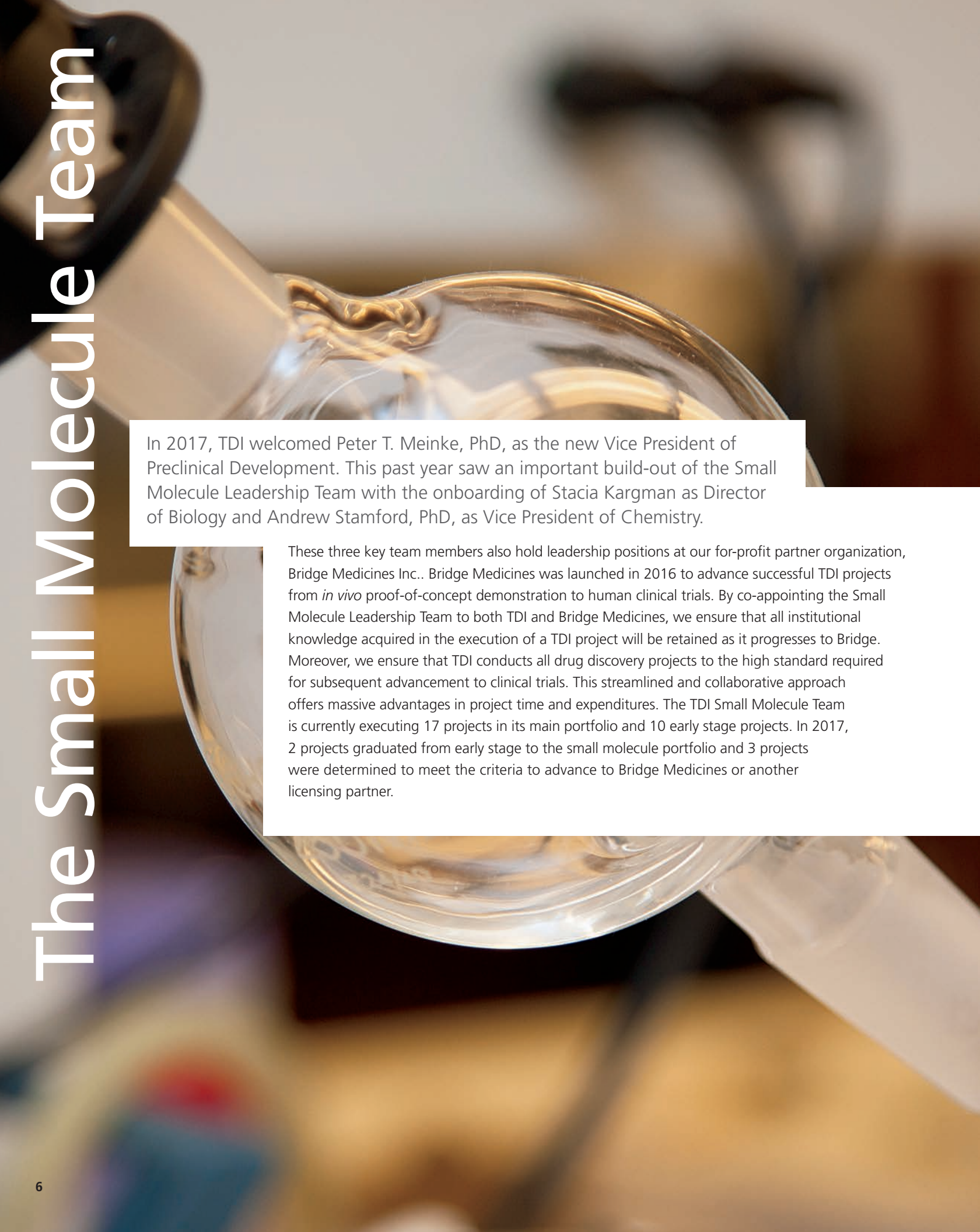
A Year of Growth

TDI was originally structured as a largely **virtual organization**, in which the majority of scientific activities were either outsourced or **performed** by Takeda employees embedded in on-site laboratories. From its inception in 2013, and for its first several years of operation, TDI operated with a team of fewer than five full-time employees.



Over the past year, TDI has experienced significant growth, as the organization has taken on many more drug development projects and significantly expanded its mission to encompass antibody drug discovery, early stage project support, and – with the establishment of our for-profit partner, Bridge Medicines, Inc. – late preclinical drug development. These expansions of scope and responsibility, coupled with a growing portfolio and a demonstrated ability to catalyze translational research across the Tri-Institutional community, have led us to reconsider the original vision of a small, lean organization with few permanent employees and significant outsource activity. In order to best serve our communities, the TDI Board of Directors has made the strategic decision to build up a more robust on-site presence through the hiring of a larger permanent staff in both the small molecule and antibody programs. Thus, 2017 saw major changes in the TDI organizational structure as we began the process of hiring a world-class team of skilled and highly experienced scientific leadership and staff.

The Small Molecule Team



In 2017, TDI welcomed Peter T. Meinke, PhD, as the new Vice President of Preclinical Development. This past year saw an important build-out of the Small Molecule Leadership Team with the onboarding of Stacia Kargman as Director of Biology and Andrew Stamford, PhD, as Vice President of Chemistry.

These three key team members also hold leadership positions at our for-profit partner organization, Bridge Medicines Inc.. Bridge Medicines was launched in 2016 to advance successful TDI projects from *in vivo* proof-of-concept demonstration to human clinical trials. By co-appointing the Small Molecule Leadership Team to both TDI and Bridge Medicines, we ensure that all institutional knowledge acquired in the execution of a TDI project will be retained as it progresses to Bridge. Moreover, we ensure that TDI conducts all drug discovery projects to the high standard required for subsequent advancement to clinical trials. This streamlined and collaborative approach offers massive advantages in project time and expenditures. The TDI Small Molecule Team is currently executing 17 projects in its main portfolio and 10 early stage projects. In 2017, 2 projects graduated from early stage to the small molecule portfolio and 3 projects were determined to meet the criteria to advance to Bridge Medicines or another licensing partner.

My collaboration with TDI has been vital to helping develop novel strategies for the treatment of stroke and other vascular disorders. The experts in medicinal chemistry and therapeutic antibody development at TDI and Bridge Medicines have helped my laboratory and facilitated the path forward for pre-clinical development of novel therapeutics.

The team at TDI has also helped us to establish key collaborations within the Tri-Institutional community. It is only by doing this multidisciplinary collaborative research with a team of basic scientists, drug discovery experts and clinicians that ground-breaking basic science discoveries can be translated to the clinical realm. We are very thankful to Dr. Foley for his vision and for building this unique and unprecedented initiative in the Tri-Institutional community.

Teresa Sanchez Garcia Vao
Assistant Professor of Pathology and Laboratory Medicine,
Weill Cornell Medicine

TDI Licenses first program to Bridge Medicines, Inc.

Topical Treatment of Superficial, Cutaneous Basal Cell Carcinoma

Dysregulation of the Hedgehog signaling pathway has been linked to a number of common cancers, including basal cell carcinoma (the most common human cancer), meningioma (the most common human brain neoplasm), and medulloblastoma (the most common pediatric brain malignancy). Transport of the hedgehog-activated transcription factor from the cilium to the nucleus by the motor protein dynein 2 is a key step in the Hedgehog pathway. Professor Tarun Kapoor's Lab at The Rockefeller University has shown that inhibition of dynein 2 can disrupt the Hedgehog pathway and eradicate tumor cells. Although the Kapoor group had demonstrated proof-of-principle in their studies, an improved lead compound was needed in order to test the viability of dynein 2 inhibition as a therapeutic strategy. A medicinal chemistry effort undertaken at TDI led to the identification of a promising new dynein 2 inhibitor with potent, mechanism-based activity and physical properties that render it amenable for use as a topical agent. TDI's extensive preclinical characterization of this lead compound suggests that it is suitable for more extensive development with our partner, Bridge Medicines, who have licensed this technology as the first program to enter their portfolio from the TDI.

Under Mike Foley's leadership, TDI has assembled a truly impressive array of talented professionals, technologic tools, and cutting-edge projects. **The Tri-Institutional campus provides innovative brilliance for new ideas, and the TDI team provides a powerful path forward towards generation of new drugs.** Mike and his TDI team operate with passion, determination, and the highest levels of personal integrity. It is exciting for Bridge Medicines to have an opportunity to advance such promising, novel programs and to interact so closely with the TDI team in their mission to develop new, important medical treatments.

Bill Polvino, MD
CEO, Bridge Medicines, Inc.

"Working with TDI has been a highly productive and constructive part of our research program. The TDI team has truly catalyzed the development and now selection of last-stage components for **a complex multi-part therapeutic strategy that we believe will add measurably to the impact of immunotherapy.** On a specific note, the attention to updates and scientific collaboration provided by Ivo Lorenz and his colleagues has been a highlight. We eagerly look forward to the next steps."

Jedd D Wolchok, MD, PhD
Chief, Melanoma and Immunotherapeutics Service
Lloyd J Old/Ludwig Chair in Clinical Investigation
Director, Parker Institute, MSKCC
Associate Director, Ludwig Center, MSKCC

The Antibody Team

In 2017, the TDI Antibody Drug Discovery Initiative significantly expanded its on-site capabilities, while also continuing to work with CROs for specific tasks.

This hybrid onsite-offsite solution provides a high degree of flexibility, allowing the team to handle an expanding number of projects with efficiency and rigor. A hiring campaign is currently underway, and by the time of its completion in 2018, we anticipate having 18 full time employees in the Antibody division. Under the leadership of Ivo Lorenz, PhD, Vice President of Biologics, 9 scientists with extensive industry experience have been hired to date, including Paul Balderes, TDI's new Director of Biologics Lead Optimization. In addition to executing 9 Antibody Discovery Projects and 24 Early Stage Projects, the Antibody Team has been working to bring high-level scientific capabilities to the Tri-Institutional community. In 2017, the team established a proprietary Phage Display Library that has already yielded valuable antibodies against novel targets. The Antibody Team currently operates from the 19th floor of the Zuckerman Research Building at Memorial Sloan Kettering Cancer Center.

Accomplishments

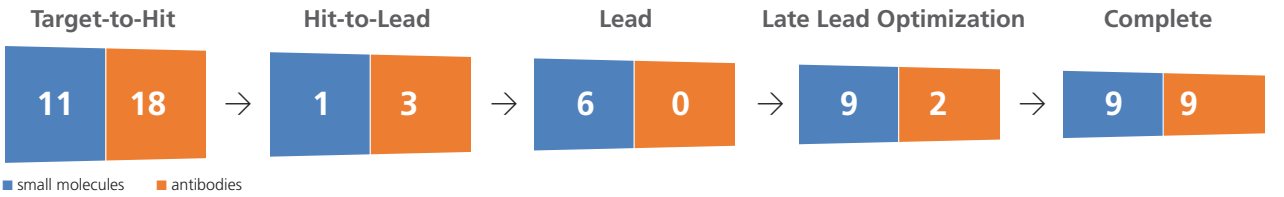
Development of eIF4A RNA Helicase Inhibitors for Cancer Therapy.

Cancer cells often harbor genetic mutations that cause abnormal increases in the translation of proteins. This enhanced translation activity is thought to be crucial for the tumor cell's survival and proliferation. Therefore, small molecule drugs that can shut down the cancer cell's translation machinery are of significant interest to cancer researchers. The Wendel lab at MSKCC has been exploring the effects of inhibiting one key enzyme in the oncogenic translation pathway: eukaryotic initiation factor 4A (eIF4A) helicase. The eIF4A helicase is responsible for unwinding mRNA to allow translation to begin. Moreover, eIF4A is a protein that is overexpressed in a number of cancers, including acute lymphoblastic leukemia (ALL), B-cell lymphoma, and small-cell lung cancer. When this project was accepted into the TDI portfolio, Dr. Wendel and his team had already identified a promising eIF4A inhibitor; however key efficacy and safety studies had not yet been conducted. The TDI Small Molecule Discovery Team worked with the Wendel group to prove the efficacy and safety of the lead candidate in a relevant preclinical model. The results of these studies were very encouraging, and this exciting project is now ready for a new partner to complete the key studies required for an Investigational New Drug application with the FDA.

Nanoformulated PI3K Inhibitors for Oncologic Applications.

Mutation of the PI3K protein and subsequent activation of the PI3K signaling pathway is implicated in a number of human cancers, including head and neck squamous cell cancer (HNSCC). Many groups have attempted to develop inhibitors of the PI3K protein, and while several have been identified, all carry serious toxicity issues that limit their clinical potential. To address this challenge, MSKCC Professors Daniel Heller, Maurizio Scaltriti and José Baselga teamed up to design a PI3K inhibitor with substantially enhanced activity and decreased toxicity. In order to minimize systemic toxicity, the researchers encapsulated the PI3K inhibitor inside nanoparticles. These nanoparticles are designed to localize to the tumor site by targeting a molecule, P-selectin, that is abundantly produced in the tumor environment. Upon reaching the tumor microenvironment, the nanoparticle releases the encapsulated molecule, where it selectively inhibits the oncogenic PI3K protein, disrupting the signaling pathway and suppressing tumor growth. In animal models, the team confirmed that the nanoparticle-encapsulated PI3K inhibitor does, in fact, accumulate specifically in the tumor microenvironment, where it exerts the desired anti-tumor effects while sparing healthy tissues from deleterious exposure and related toxicities. In 2017, the team entered into a partnership with TDI with the goal of identifying more potent small molecule PI3K inhibitors for inclusion in the nanoparticle. A medicinal chemistry campaign undertaken at TDI led to the discovery of several new PI3K inhibitors. A promising lead compound was generated that demonstrates the desired increased potency and decreased toxicity to mammalian cells. The MSKCC team is now in the process of identifying an external licensing partner to advance this exciting program to human clinical trials.

2017 TDI Pipeline: Early & Late Stage Projects



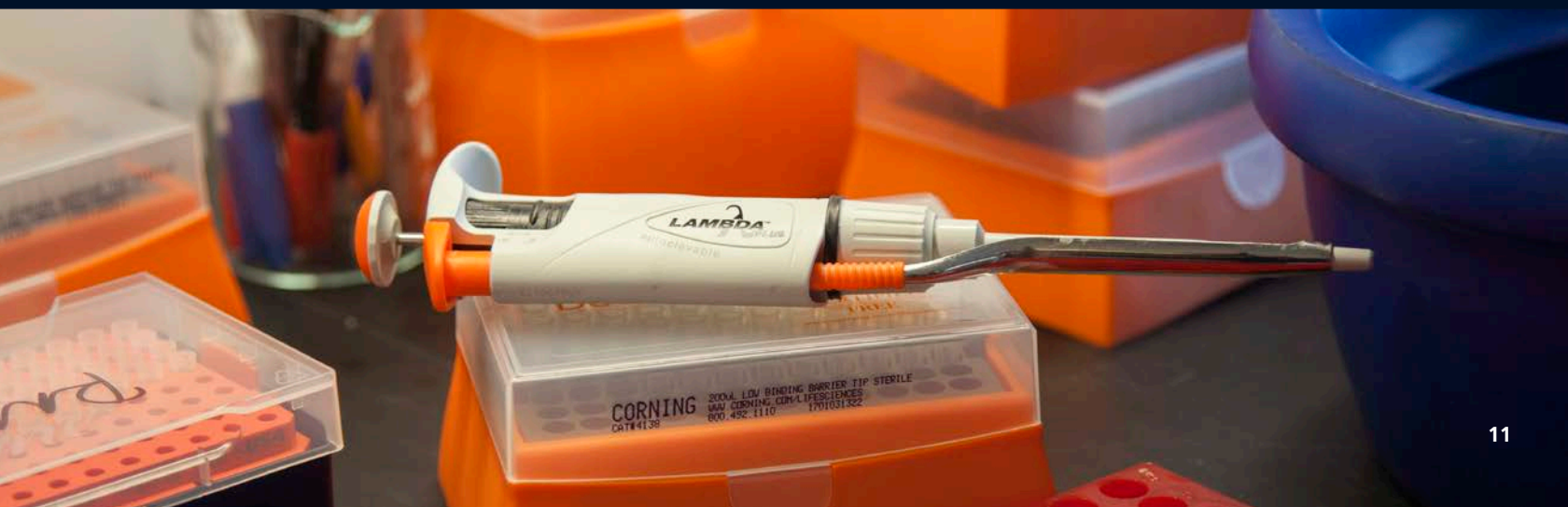
Oncology	Neuroscience	Infectious Disease	…and more
Basal cell carcinoma	Alzheimer's disease	Bacterial infection	Addiction
Brain cancer	Niemann Pick's disease	Fungal infections	Auto-immune disease
Breast cancer	Parkinson's disease	HIV	Imaging
Colorectal cancer		Malaria	Lupus
HPV-induced cancers		Tuberculosis	Non-alcoholic fatty-liver disease
Leukemia		Zika virus	Osteoporosis
Liver cancer			Psoriasis
Lung cancer			Stroke
Lymphoma			Sickle cell anemia
Melanoma			Type II Diabetes
Neuroendocrine Cancers			Vascular malformation
Ovarian cancer			
Pancreatic cancer			
Prostate cancer			
Solid tumors			
Squamous cell carcinoma			

Advancing programs from the Early Stage pipeline to therapeutic development

TDI launched the Early Stage Project Initiative in 2016. This program was established with the goal of generating a robust pipeline of small molecule and antibody drug discovery projects for TDI. Under this initiative, meritorious projects lacking sufficient preliminary data to join the TDI-Takeda partnership are offered project management support along with a focused menu of services, including medicinal chemistry, computational chemistry and biology, assay development consultation, high-throughput screening and antibody generation. The aim is to leverage TDI expertise and outside services to help PIs rapidly address key questions regarding the viability of the project; those that meet predefined criteria for success are invited to enter into the Small Molecule or Antibody Initiatives.

In 2017, two small molecule projects successfully completed the Early Stage Project Initiative. The first, which focuses on development of new therapies that cross the blood-brain barrier to treat primary and metastatic brain tumors, has now advanced to the TDI Small Molecule Pipeline. The second project uses a nanoparticle formulation for targeted delivery of a potent inhibitor of a protein that is over-expressed in a number of human cancers, including head and neck squamous cell cancer. The robust Early Stage support provided by TDI enabled this project to advance quite rapidly, and the PIs are now exploring external partnering opportunities.

The recently-established Antibody Initiative also advanced its first project from the Early Stage Initiative to the Therapeutic Discovery Pipeline in 2017. This program is aimed at developing antibodies to attack tumor re-initiating cells derived from therapy-resistant metastases. In addition, seven early-stage antibody programs were successfully completed by generating antibodies for target validation experiments in the laboratories of the academic investigators.



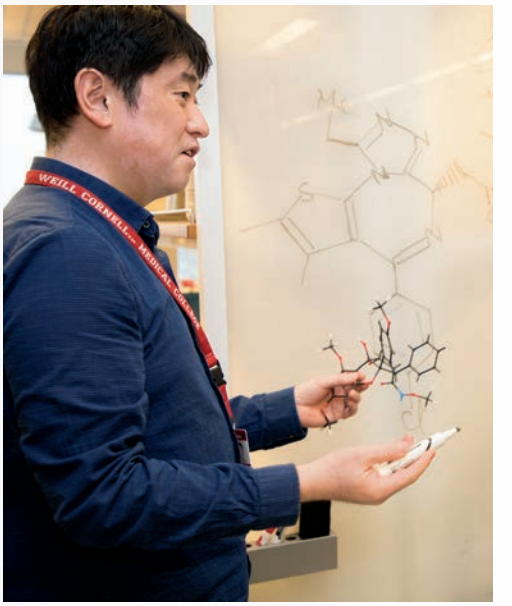
Profiles

Peter Meinke, Vice President of Preclinical Development

TDI is pleased to welcome Dr. Peter T. Meinke as Vice President of Preclinical Development. Peter is an industry veteran with extensive experience across all stages of drug discovery, from target validation through early clinical development. After completing his PhD at Syracuse University with Professor GA Krafft and conducting postdoctoral research at Columbia University with Professor W. Clark Still, Peter joined Merck Research Laboratories, where he remained from 1989 until 2016. Programs under Peter's direct supervision have produced one drug – the NS5A inhibitor, elbasvir, for the treatment of chronic hepatitis C – along with 13 development compounds that have advanced into the clinic in seven distinct therapeutic areas. In 2017, Peter received the prestigious ACS Heroes of Chemistry Award in recognition of his contributions to the invention of elbasvir. He is co-author of over 90 peer-reviewed publications and co-inventor on more than 35 patents. Peter also has significant international leadership experience: from 2008 to 2016, he worked and lived overseas in Shanghai, China, where he directed and mentored global drug discovery research teams while managing attendant business issues. In 2016, Peter retired from Merck as Executive Director of Discovery Chemistry and joined TDI as Vice President of Preclinical Development.

Yoshiyuki Fukase, Director of Medicinal Chemistry

Dr. Yoshi Fukase, TDI's Director of Medicinal Chemistry, is a native of Osaka, Japan, and a graduate of Osaka University. After completing his undergraduate studies, he remained at Osaka University, earning his PhD in Chemistry under the supervision of Professor Shoichi Kusumoto, working on the synthesis of the complex glycoconjugate, lipid A, and analogues thereof in order to clarify its role in the innate immune system. Yoshi continued his training at Harvard University, where he conducted postdoctoral research with Professor Stuart Schreiber and Dr. Jared Shaw. In 2004, Yoshi returned to Japan to join Takeda Pharmaceuticals as a Medicinal Chemist. At Takeda, he has worked across multiple therapeutic areas, including cardiovascular disease, immunology, oncology, and pain, and contributed to two drug candidates that are currently under clinical evaluation. In 2014, Yoshi was among the first cohort of Takeda scientists to be seconded to TDI as embedded medicinal chemists. As the leader of a medicinal chemistry team, Yoshi worked closely with the Tri-Institutional PIs and the Takeda scientists to advance early stage projects. In 2017, Yoshi was asked to extend his tenure at TDI due to his enthusiastic embrace of this new drug development paradigm. In his current role as Director of Medicinal Chemistry, Yoshi leads drug discovery research projects and is responsible for the design, synthesis, and evaluation of target molecules to test program-specific hypotheses. He works in close collaboration with TDI's academic and industrial partners, including contract research organizations and his home organization, Takeda. He takes particular pride in supporting and mentoring younger scientists from Takeda and from our collaborating labs.



Paul Balderes, Director of Biologics Lead Optimization.

Paul Balderes came to TDI in October 2017 with over twenty-five years of biopharmaceutical industry experience, having contributed to the development of four commercially approved antibody cancer therapeutics. Prior to joining TDI, Paul was Director of Biologics Technology in Oncology Research for Eli Lilly and Co. In this capacity, he oversaw biologics development of the pre-clinical portfolio and successfully delivered numerous candidate antibodies to clinical development. In addition, he directed the research phase of an antibody-drug conjugate (ADC) program in partnership with Immunogen, successfully bringing Lilly's first ADC into clinical development. As Director of Biologics Lead Optimization at TDI, Paul is responsible for overseeing the late-stage biologics portfolio, including lead optimization, antibody engineering and bioanalytical assessment, and delivering candidate molecules to clinical development.

David Huggins, Senior Director of Computational Biomedicine.

Dr. David Huggins earned his PhD in Chemistry at Oxford University in 2005 under the supervision of Professor Grahame Richards and Dr. Guy Grant in the fields of molecular docking and algorithm design. He continued his scientific training at MIT, where he conducted postdoctoral research with Professor Bruce Tidor. Here, his research focused on the molecular design of HIV-1 protease inhibitors that avoid problems of resistance. In 2007, David joined the University of Cambridge, where he worked at the interface of physics, chemistry, and biology as part of a team developing methods to tackle difficult drug targets such as protein – protein interactions. In 2014, he received a Medical Research Council grant to fund his research group at the Cavendish Laboratory in Cambridge to develop novel software tools for drug discovery. In 2017, David joined TDI as the Senior Director of Computational Biomedicine, where he leads the computational modeling team. His special areas of interest are binding free-energy calculations and the thermodynamics of solvation.

Stacia Kargman, Director of Biology.

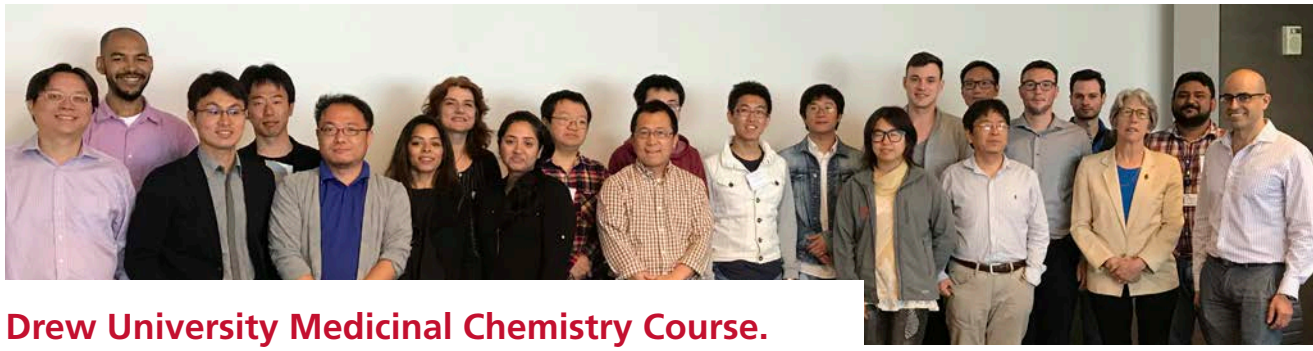
Stacia Kargman, TDI's Director of Biology, has over 30 years of experience in the pharmaceutical industry. After earning her BS in biology from Columbia University and completing graduate studies at the Weizmann Institute of Science in Israel, Stacia joined the Department of Pharmacology at Merck Frosst Centre for Therapeutic Research, Canada. After 25 years in Montreal, Stacia accepted a corporate transfer to Merck, New Jersey, where she would serve as External In Vitro Pharmacology Lead across the Merck network, overseeing scientists in China and Europe in generating pharmacological data for early drug discovery. Over the course of her career, Stacia has been involved in bringing eight novel medicines to market, including treatments for asthma, pain, and hepatitis C virus. In the summer of 2017, Stacia joined TDI as Director of Biology. In this role, she works with Principal Investigators and TDI Chemists, contributing biological and pharmacological expertise, and helping to develop and oversee biological assays with the goal of delivering proof-of-concepts experiments to TDI's many projects.

Andrew Stamford, Vice President, Chemistry.

Dr. Stamford is an accomplished medicinal chemist with expertise across all aspects of small molecule drug discovery from program inception to early clinical development. He earned his PhD in organic chemistry at the University of Sydney and conducted postdoctoral research in natural product synthesis at the University of Texas at Austin. Prior to joining TDI, Dr. Stamford was at Merck and Schering-Plough for 25 years where he led or contributed to multidisciplinary drug discovery teams targeting diseases in the CNS, anti-infective, cardiovascular and diabetes therapeutic areas, advancing more than 10 drug candidates into clinical development. A particular area of Dr. Stamford's focus is Neuroscience drug discovery. In this area, he has contributed to programs that delivered clinical candidates in Alzheimer's disease, Parkinson's disease, and neuropathic pain. Dr. Stamford is coauthor of over 70 peer-reviewed publications, and is a co-inventor on more than 100 issued United States patents. At TDI, Dr. Stamford provides scientific leadership across the portfolio of small molecule drug discovery projects.

"Working with the Tri-I TDI has been incredibly rewarding. Ivo and his team's **meticulous and systematic efforts in protein-based therapeutic development have empowered us** to uncover unanticipated biological insights of relevance to human cancer."

Sohail Tavazoie, MD, PhD
HHMI Faculty Scholar & Leon Hess Associate Professor
Head, Laboratory of Systems Cancer Biology
The Rockefeller University



Drew University Medicinal Chemistry Course.

In June, TDI once again brought the Drew University Residential Course in Chemistry and Biology in Drug Discovery to NYC for the Tri-I Community. This week-long class, which is taught by leaders in drug discovery and development across industry and academia, was held at the Alexandria Center. The 2017 session was a particular success, as a record number of graduate students, postdoctoral researchers, and faculty members successfully completed the course.

"From Molecules to Prescription" – Drug Development Course Developed for the Tri-I Community

TDI is committed to educating the Tri-Institutional community on the leading edge of medicinal chemistry and translational research. Toward this goal, in 2017 TDI partnered with Roche to develop a Drug Development Course, titled "From Molecule to Prescription," to be offered to graduate students across the Tri-I who are interested in pursuing drug development and translational research in an academic or industry setting. The course provides a foundation of integrated knowledge of the multi-disciplined process of developing a new medication, incorporating real-world challenges encountered in the discovery, development, manufacture, approval, and commercialization of new medicines. TDI is pleased to offer this class in Spring, 2018.

Innovation & Education

Postdoctoral Fellowship Program

In 2017, TDI and the Roche Foundation worked together to establish a Postdoctoral Program, funded by Roche, that provides training for postdoctoral researchers who are planning to pursue careers in the biological sciences. Dr. Zoe Mbambo, an investigator in the laboratory of Dr. Kyu Rhee at Weill Cornell Medicine, was named the first Roche-TDI Postdoctoral Fellow in 2017.

A critical limitation of modern antibiotic development is the lack of technologies to track the fate of a drug candidate as it enters the bacterial cell. The activity of a drug depends on its ability to both reach and inhibit its intended targets. However, while technologies exist that enable researchers to determine whether the drug inhibits its target, it is quite difficult to monitor whether the drug actually reaches its target in the bacterial cell. The Rhee lab aims to fill this gap through the use of newly developed experimental technologies. By directly elucidating the levels and fates of drug candidates within bacteria, the lab has discovered bacterial metabolism of chemical compounds to be a major, and previously unstudied, determinant of compound activity. This newly-discovered knowledge will assist in the development of transformational new treatments for this devastating disease.

In 2018, two additional postdoctoral fellows will be named; these fellows will be embedded at TDI and will be conducting research in Computational Chemistry and Medicinal Chemistry.

2017 Community Service

In order to promote team unity and forge connections with the broader New York City community, TDI participates in service-oriented activities throughout the year.

On October 20, 2017, TDI participated in a rewarding day of service with the American Red Cross. Team members prepared 300 Shelter Administration relief kits and restocked 30 Daily Response Vehicles with direct service Mass Care supplies. In 2017, TDI also collected funds to support relief for Puerto Rico's hurricane victims and donated nearly 150 toys to the Pediatrics Department at Memorial Sloan Kettering.

TDI's Strategic Partners

Preclinical drug discovery and drug development services

Absorption Systems
Charles River Labs
Crystal Pharmatech
Eurofins
Frontage Labs
Ora
Particle Science
Pharmaron
Zyleris PharmaTech

Biochemical and cell-based assays

Charles River Labs
Eurofins
Evotec
Horizon
Reaction Biology

Structural biology, protein expression & purification

New York Structural Biology Consortium
Structural Genomics Consortium
TropIQ
XTAL Biostructures
R&D Systems

Antibody discovery & development

Ablexis
Antibody Design Labs
Cell Essentials
ChemPartner
DiscoverX
GenScript
LakePharma
Taconic
WuXi

Computational chemistry, biology & virtual screening

Schrödinger

Chemical synthesis

Robertson Microlit
Syngene
TGC Life Sciences
WuXi

Innovative screening technologies & unique libraries

HitGen
Torrey Pines
WuXi
XTAL

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Dedicated to Bringing Value to the TRI-I Community

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Program, Memorial Sloan Kettering Cancer Center

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Memorial Sloan Kettering Cancer Center

EMERITI

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Weill Cornell Medicine

Marc Tessier-Lavigne, PhD
Former President, The Rockefeller University

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Senior Lecturer, Department of Biological
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Kathleen Metters, PhD
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Sr. VP Pfizer Global R&D

Joseph Vacca, PhD
Head of Chemistry, Cyteir Therapeutics;
Acting Head of Chemistry, Quentis Therapeutics

Sean Brady, PhD
Investigator, Howard Hughes Medical Institute,
Evnin Associate Professor, Laboratory of Genetically
Encoded Small Molecules, The Rockefeller University

James Fagin, MD
Chief, Endocrinology Service,
Memorial Sloan Kettering Cancer Center

"We entered into the TDI collaboration with a low-potency chemical inhibitor that targets a pathway whose improper activity can cause certain types of cancer. **Our collaboration with the extraordinary team of chemists at TDI led to the development** of compounds that are not only orders of magnitude more potent than the initial hit but that also address several chemical liabilities that plagued the hit compound. Our current lead compound is active in preclinical models. Moreover, participating in this partnership has been an invaluable learning experience for me and my lab members."

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The Rockefeller University

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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 Pharmaceuticals, we are enabling the discovery of next-generation drugs by empowering our faculty with the most up-to-date tools, technology, and expertise.

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

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