The mission of TDI is to encourage our community to advance their groundbreaking biological discoveries to animal 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 are 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 discoveries.

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.
Discover
All TDI projects begin with a groundbreaking research discovery by a member of the Tri-I community.

Apply
At TDI, we apply the best modern medicinal chemistry techniques and technologies to our partnered projects.

Support
By providing industry-level support for each academic project, we rapidly assess the therapeutic potential of the research discovery.

Control
Academic investigators and their host institutions retain control over all intellectual property generated in execution of a project.
Letter From The Director

Tri-I TDI brings together researchers from Memorial Sloan Kettering Cancer Center (MSKCC), The Rockefeller University (RU), and Weill Cornell Medicine (WCM) with collaborators across the globe to remove the barriers that impede drug discovery in academic settings. Together with our partner, Takeda, we are enabling the discovery of next-generation drugs by empowering our faculty with the tools, technology, and expertise to meet this extraordinary challenge.

The power of Tri-I TDI resides in its access to leading edge biological insights. The key ingredient in drug discovery is deep knowledge of the biological target or pathway under investigation and its role in disease initiation and progression. The knowledge and experience resident in our community of the most promising and innovative new approaches to preventing and treating disease could never be matched by any pharmaceutical company in the world. This is the reason that the pharmaceutical industry is slowly and steadily ceding responsibility for early-stage drug discovery to leading academic institutions, such as MSKCC, RU and WCM.

The chasm between biological insights and impact on patients can seem overwhelming. Creating drugs requires that we access the roads and bridges that connect technologies, skills and expertise with biological insights and talent. A well-placed bridge can make crossing an expansive chasm both manageable and safe.

Tri-I TDI’s primary role in the community is to access the technologies and tools to cross the chasm from insight to impact as needed and only for the task they are required to perform. Our lean approach allows Tri-I TDI to remain nimble and greatly reduces its investment in infrastructure while leveraging the best tools, technologies and talent that the world has to offer.

Tri-I TDI’s culture of collaboration has resulted in a very interesting social experiment. Takeda has seconded fifteen scientists to our community to help accelerate our drug discovery efforts. Integrating Japanese industrial chemists into an American academic environment has been a challenging yet rewarding experience for all parties.

As we complete our first full year of research I could not be more pleased with the results that we have obtained to date. We have one program that has met a key milestone and is in license negotiations. We anticipate that we will select compounds for animal proof-of-concept experiments for four other programs in the first half of 2016.

The report that follows underscores the vital role of philanthropy in creating and enabling Tri-I TDI to perform its role in the community. We are especially grateful to Mr. Lew Sanders whose generous gift created Tri-I TDI. We are indebted to several philanthropists, our partner institutions, and several foundations for generous support of our work.

We would also like to acknowledge the visionary leadership of Dr. Laurie Glimcher, Dr. Marc Tessier-Lavigne, and Dr. Craig Thompson that created the novel, innovative and collaborative model that is Tri-I TDI. We draw additional strength from the other members of our board: Dr. Barry Coller, Mr. Juan Harrison, Dr. Carl Nathan and Dr. David Scheinberg.

Michael A. Foley, PhD
Sanders Director
Connecting Communities:
Building a Culture of Scientific Collaboration

TDI functions as an important social experiment, the success of which will have great impact on the future of drug discovery and development. One year into this experiment, we are witnessing the enormous benefits that accrue from breaking down traditional institutional and cultural boundaries.
Forging **Connections**
Across the TRI-I.

Each of TDI’s three governing bodies – the Board of Directors, the Scientific Advisory Board, and the Intellectual Property Committee – is composed of representatives from the three institutions. While working toward the shared mission of supporting TDI’s success, the members of these three groups have forged productive and respectful relationships with one another. As a unique entity with the mandate to deliver value to all three institutions, TDI is building relationships with scientists across the Tri-I. We frequently have the opportunity to connect individuals at different institutions whose interests and expertise are aligned.

“Seven months ago we simply had an idea, and today we have small molecules that inhibit our most exciting biological target. We never could have anticipated being able to translate our **exciting biological findings** into our own small molecule inhibitors. This relationship will be invaluable for academic labs looking to take their research to the next level.”

Dr. Sarah Bettigole, WCM
Partnering Chemists with Biologists.

The chemists and the biologists have established healthy and productive working relationships on all project teams. Over the past year, the chemists and biologists have built a comfortable and mutually respectful rapport, and team members meet frequently to discuss research progress and troubleshoot challenges. Regularly scheduled monthly meetings of the full project teams ensure that projects are on track and that all required resources are available to the groups.
Our 12-member Small Molecule Scientific Advisory Board (SAB) provides guidance on the selection and execution of projects in our portfolio. The external members are leaders and innovators in the pharmaceutical and biotech industries, and the internal members are established biological researchers selected from across the Tri-I. Together, our SAB represents a diverse and highly accomplished cross-section of esteemed academic scientists and industry experts, with invaluable insights into drug development and the biotech landscape. Over the past year, the external and internal SAB members have bridged cultural differences and developed a common language to assess TDI projects. Ongoing project-based guidance from members of the SAB has been critical to the successful advancement of the projects within the TDI portfolio.
The Takeda scientists from Japan have done an impressive job of acclimating to life in NYC. The secondees quickly learn to adapt to the unique demands of working within a fast-based American research environment with a “start-up” mentality. During their time here, they take an unprecedented level of responsibility for the execution and management of their projects. Takeda scientists are bringing home with them valuable new leadership skills and unique insight into the American work culture and drug development process.

“The Takeda Experiment.”

“In 2009, we reported two classes of inhibitors that selectively inhibit the Mtb proteasome. However, the first class of inhibitors was unstable in aqueous solution and the second class was unstable on incubation with microsomes. We tried to improve the pharmaceutical properties of the inhibitors by developing peptidomimetic classes, but our studies progressed slowly until we began to consult with TDI.”

Dr. Gang Lin, WCM
Accomplishments: Accelerating Drug Discovery Across the Tri-I

The central mission of TDI is to link Tri-Institutional researchers in the biomedical sciences with industry experts in drug discovery in order to accelerate the translation of groundbreaking academic discoveries into clinical therapeutics. Our first year of small molecule drug discovery has been very productive. We have clearly demonstrated the ability to execute on the projects in our portfolio: One of our projects is in biological due diligence with Takeda and three others should have chemical matter suitable for in vivo proof-of-concept by early 2016. Most importantly, we have established the foundation of a highly efficient, scalable model for academic-initiated drug discovery. Our current small-molecule drug discovery portfolio, led by PIs from across the three institutions, represents a diverse range of target classes and potential therapeutic indications. Each of our projects features a highly innovative approach and each seeks to address a significant medical need facing the medical community.

“Academic research laboratories are well positioned to generate new discoveries and therapies, but not for many aspects of development. TDI has provided extraordinary expertise and advice on how to commercialize a new discovery. For my project, that has entailed pharmacokinetic and safety studies, as well as synthetic efforts in drug optimization. Their help has been essential to taking our project forward.”

Professor Gav Pasternak, MSKCC
“The collaboration with the TDI has been extremely important for our lab. We have received superb advice about chemical strategies to modify a lead compound for treatment of Alzheimer’s disease, and the chemistry has been executed by the TDI staff with great skill. We could never have attempted these studies on our own. **The TDI scientists and administrators are extraordinarily knowledgeable**, effective, and collegial, and have made our collaboration productive and a pleasure.”

Professor Sid Strickland, RU
Education and Outreach: Bringing Drug Discovery Expertise to The Tri-I

A central element of TDI's mandate is the Sanders Innovation and Education initiative. This initiative directly impacts all members the Tri-Institutional research community. In an effort to educate the community in the process of drug discovery and development, we sponsor Schrödinger trainings, an entrepreneurship course, a medicinal chemistry course, and the Sanders seminar series.

Schrödinger Software Training.
Since October of 2014, TDI has hosted over 20 Schrödinger training sessions, both onsite and via webinar. In addition to live classes, which are offered on a regular basis, all members of the Tri-I community can download course materials or watch webinar recordings of available classes at any time.

Sanders Seminar Series.
Our monthly Sanders Seminar Series brings accomplished academic and industry researchers in the biomedical sciences to the Tri-Institutional community. Recently, the Sanders seminar series formally merged with the Tri-Institutional Chemical Biology Program and the Hunter College Chemical Biology seminar series. This merger has allowed us to attract the most influential practitioners of chemical biology and drug discovery in the world to speak in the Sanders seminar series.

Drew University ResMed Course.
The Drew University Residential School on Medicinal Chemistry and Biology in Drug Discovery is a week-long graduate level, accelerated program on the fundamentals of drug discovery, from initial target validation through clinical development. Class sessions are led by leaders in the field from major pharmaceutical companies. In June, 2015, TDI provided access to this course, via live-streaming, to the Tri-Institutional community. The class was a great success and we anticipate offering this course to the community on an annual basis.

Bench To Bedside Initiative.
Under the Sanders Initiative, TDI hosts an entrepreneurship class that is open to all members the Tri-I community. This class, “From Bench to Bedside: Business Fundamentals for Entrepreneurial Scientists,” teaches basic financial analysis and the principles of entrepreneurship. Lectures cover the process of evaluating the market potential of a technology, building basic financial models, funding mechanisms, and writing and presenting a business plan to potential investors. The mission of this class is to equip scientists in our community with the fundamental skills needed to translate their ideas into commercially accessible products that will ultimately benefit patients. The class culminates in an end-of-semester “Shark Tank” event, where students pitch business plan presentations to a panel of VC investors. The Bench to Bedside initiative has proven very popular, and resulted in the creation of several seed-funded biotech startups.

Project Consultation • Project Management • Grant Writing.
Outreach across the community is a central element of our mission. Over the past year, our small team has helped numerous researchers across the Tri-I to navigate the early stages of the drug discovery process. In one-on-one consulting sessions, the Director provides concrete advice to Tri-I faculty on strategies for rapidly advancing their research projects into the drug discovery pipeline. TDI’s VP of Operations and Portfolio Management works with Tri-I faculty to establish and manage relationships with key academic and industry partners. TDI’s Science Writer has written, edited, or provided constructive feedback on over a dozen grant proposals from across the Tri-I. As we expand, we anticipate that our impact on the community will continue to grow as well.
Tools & Technologies: Bringing Drug Discovery Capabilities to The TRI-I

Takeda Pharmaceuticals.

Key to TDI’s success is our unique relationship with Takeda Pharmaceuticals. Under this partnership, a team of sixteen Takeda-employed Medicinal Chemists has relocated from Japan to New York City to lead drug development activities for the small molecule projects in the TDI portfolio. Takeda is an incredibly valuable partner for TDI, and their investment in the TDI vision has allowed us to leverage their global resources to perform key drug discovery and development activities. Both parties are beneficiaries of this unique partnership. In exposing Takeda chemists to a fast-paced American academic research environment, TDI is bringing value to Takeda by training their next generation of leaders. At the end of their tenure, these secondees are bringing home new insights and perspectives in drug discovery research.

As part of our partnership, Takeda also provides TDI access to a wide variety of highly valuable supporting technologies. These additional resources enable TDI to advance projects quickly and efficiently.

Our Partners.

One of TDI’s main goals is to make powerful drug discovery technologies available to all researchers in the Tri-I community. A key accomplishment has been the formation of a close relationship with Schrödinger, Inc, a leader in in silico chemical simulations for drug discovery research that is used by nearly every major pharmaceutical and biotech company. Through the Sanders Innovation and Education Initiative, we have established a one-of-a-kind relationship with Schrödinger, in which practically all of their tools are freely available to all researchers in the Tri-I community. Training sessions, hosted by TDI, ensure that researchers are able to use this software to maximal benefit.

The Schrödinger relationship serves as a template for similarly productive partnerships with a range of cutting-edge technology-based organizations, including Horizon, Cyclofluidic, WuXi, and the New York Structural Biology Consortium. We continue to develop strategic relationships with world-class providers of tools and technologies in both the small molecule and antibody realms.
“Working with TDI has been enormously helpful to our project since it has made it possible for us to **test our hypothesis by analyzing many compounds in our functional assay**. It has also been a great pleasure to work as a multidisciplinary team comprised of medicinal chemists, computational structural biologists, and experimentalists. We especially appreciate Dr. Foley’s leadership and guidance.”

Professor Barry Coller, RU
An Integrated Vision for Academic Drug Discovery

As we enter our second full year of operation, we are poised to further expand the ability of TDI to bring drug discovery capabilities to the Tri-I community. In addition to increasing the number of small molecule projects supported through the Takeda partnership, we are on the verge of launching two new initiatives: The Antibody Drug Discovery Initiative, which is modeled after the small molecule program, and The Early Project Initiative, which provides targeted support for early-stage small molecule and antibody drug discovery projects.

The Early Project Initiative.
In order to cultivate a rich pipeline of drug discovery projects for the TDI portfolio, we bring key services to the Tri-Institutional community to support promising early-stage projects in the small molecule and antibody realms. These services include medicinal chemistry, computational chemistry and biology, assay development consultation, high throughput screening, in vivo testing, and project management support. Through outreach activities within the community, we aim to identify ~24 high-quality projects per year for early-stage support.

The Antibody Initiative.
Biologics, including antibodies, are rapidly emerging as one of the most important areas of drug discovery. Antibody-based therapeutic development represents a key area of opportunity that aligns particularly well with the research interests of the Tri-Institutional community. As is the case with the small molecule landscape, there is a high demand among Tri-Institutional researchers to leverage TDI’s scientific and organizational expertise for the generation of high-quality antibodies that can serve as either biological tools or potential therapeutics. Toward this end, we recently entered an agreement with Takeda, who will provide pharma-level support for antibody drug discovery projects. Dr. Ivo Lorenz recently joined TDI as our new VP of Biologics. In 2016, we aim to onboard six antibody drug discovery projects from across the Tri-I.

The Small Molecule Initiative.
Our first year of small molecule drug discovery was very productive. One of our projects graduated TDI and entered licensing discussions with Takeda, while three other projects should have chemical matter suitable for in vivo proof-of-concept by early 2016. We have begun to onboard a second cohort of small molecule drug discovery proposals from the Tri-Institutional community. Having demonstrated the feasibility of this model in the pilot stage, we are now planning to significantly expand the number of projects receiving TDI support.

The Sanders Education and Innovation Initiative.
As we grow, we also expand our educational and outreach activities with the goal of impacting a greater swath of the broader community. Initiatives under development include an Oxford-TDI Graduate Fellowship, which will connect scientists across disciplines and continents; an undergraduate research program which will introduce young scientists to the world of biomedical research; and new academic-industry partnerships that will make cutting-edge technologies available to the Tri-I community.

The graphic below highlights TDI’s vision for an integrated platform for academic-initiated drug discovery. Our ultimate objective is to remove the barriers that too often keep high-quality academic drug discovery projects from advancing from discovery through design, optimization, and development.
### Objectives
- Validate novel targets, MOAs
- Leverage Tri-I biology expertise
- Create first integrated academic drug discovery unit

### Enabling Technologies
- Computational Chemistry
  - FEP
  - Watermap
  - Live Design
  - Molecular Dynamics
- High Throughput Screen
- Microfluidic Chem Bio
- Combo screening
- Cell lines
- Medicinal Chemistry
- Pharmacology
- Antibodies: human, mouse, and other species

### Design
- Design tool compounds
- Demonstrate on-mechanism activity, *in vitro and in vivo*

### Optimize
- Hit-to-lead
- Lead optimization:
  - Potency
  - Selectivity
  - Pharmaceutical properties

### Develop
- Preclinical development
- Regulatory Affairs
- Clinical development

### Partners
- Cyclofluidic
- Charles River Laboratories
- NIH
- WuXi
- Structural Genomics Consortium
- Takeda
- New York Structural Biology Consortium

### Discover
- Takeda
- Schrödinger
- Charles River Laboratories
- Horizon / CombinatoRx
- New York Structural Biology Consortium
- Takeda

### Develop
- Takeda
- To be determined

### To be determined
- Microfluidic chemistry and assays
- Pharmacology
- FEP
- Watermap
- Live Design
- Structural Biology
“Through the TDI initiative we have assembled a dynamic team of biologists and chemists to study an extraordinarily difficult problem… The addition of Takeda and the leadership of Dr. Foley has been of tremendous benefit, and we have new tool compounds that far exceed our expectations … This has been a very satisfying collaboration as all parties are highly motivated to succeed and achieve a common goal.”

Professor Yariv Houvras, WCM
Leadership Team:
Dedicated to Bringing Value to The TRI-I

BOARD OF DIRECTORS

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Marc Tessier-Lavigne, PhD
President, The Rockefeller University

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President and CEO, Memorial Sloan Kettering Cancer Center

Juan Harrison
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Kazuyoshi Aso, PhD
Vice President, Medicinal Chemistry

Ivo Lorenz, PhD
Vice President, Biologics

Sandy Lorber
Vice President, Finance
Partner with Us

TDI is exceedingly fortunate to have some of the finest minds in the world collaborating to turn their research into next-generation drugs.

Tri-TDI brings together researchers from Memorial Sloan Kettering Cancer Center (MSKCC), The Rockefeller University (RU), and Weill Cornell Medicine (WCM) with collaborators across the globe to remove the barriers that impede drug discovery in academic settings. Together with our partner, Takeda, we are enabling the discovery of next-generation drugs by empowering our faculty with the tools, technology, and expertise.

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

“TDI leverages the strength of the pharmaceutical industry under a pure academic setting. With the aid of TDI scientists, we were able to evaluate hundreds of potential drug candidates in an extremely short period time and more importantly communicate the results and calibrate promising research avenues in a timely manner. The TDI sets up a new mode for collaboration between academic labs and pharmaceutical industry.”

Professor Minkui Luo, MSKCC

“This unique collaboration has enabled our basic research-focused, academic lab to achieve an end result that typically only occurs at the commercial/industrial level. The medicinal chemistry support from the TDI chemists and Directors has been invaluable in accelerating progress through the bench to bedside pathway.”

Professor Marilyn Resh, MSKCC