TUTORIAL

Teaching Targeted Drug Discovery and Development to Healthcare Professionals

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INTRODUCTION

Drug discovery and development (DDD) is an interdisciplinary enterprise that spans the translational continuum. Despite DDD’s importance, formal training within medical and biomedical schools is lacking. In this tutorial, we outline the current educational landscape in DDD and the growing educational need in this area. Last, we describe the Health Innovations and Therapeutics concentration as an example of how to design and implement an educational program in DDD.

BACKGROUND: TRANSLATIONAL RESEARCH

Translational research, as defined by the National Institutes of Health (NIH), is the process of applying discoveries generated in the research laboratory and in preclinical studies to the development of trials and studies in humans to ultimately enhance adoption of best practices in the community.¹ Central to the movement from discovery to utility is the process of drug discovery and development (DDD), the primary means by which researchers and clinicians can develop effective treatments for disease. Despite its importance, rigorous training in DDD remains limited within most translational and biomedical science curricula, with the majority of training occurring informally and on an as-needed basis.²,³ As a result, physician involvement remains poor in the DDD sector.

The immense promise of translational research has led the NIH, which had previously supported mainly basic science and clinical researchers, to now support the training of clinicians and scientists in translational research and methodology. Today, this goal is overseen by the National Center for Advancing Translational Sciences division of the NIH, which was established in 2012.⁴ With the support of the NIH, the Translational Research Education and Careers core of our institution’s Clinical and Translational Science Institute (CTSI) implemented a Master’s of Science in Clinical Investigation (MSCI) program in 2006, followed by the development of an intensive certificate program in a portion of the curriculum.⁵,⁶ Today, all of the nation’s 62 CTSIs offer formal research training programs for postdoctoral scholars, with about half of these programs also offering programs to predoctoral scholars, such as medical and graduate students.⁴ By educating physicians and researchers in translational research methods, design, and analysis, the next generation of translational scientists will be well poised to lead translational research efforts.⁴–⁷

Although the primary aim of CTSI training programs is to equip graduates with skills to become independent investigators, many training programs are beginning to recognize the importance of fostering trainee collaboration with academia, industry, and government because such interactions are essential to advancement of medical research. In line with these aims, in 2010, a Clinical and Translational Science Award (CTSA) Industry Forum entitled “Promoting Efficient and Effective Collaborations Among Academia, Government, and Industry” was held in Bethesda, Maryland.⁸ A session on the topic of “Educational Curriculum in Translational Research: Opportunities among CTSAs, NIH, and Industry” outlined the current need to provide CTSI graduates with the preparation to collaborate with industry and government sectors.⁸

The workgroup espoused five steps needed to train the translational scientist: (i) academic-industry-government roundtables to facilitate dialogue; (ii) development of core competencies for education programs with the help of all stakeholders; (iii) availability and accessibility of established courses using repositories; (iv) development of new courses to address existing gaps in clinical and translational research curricula (including disease mechanisms and pharmacology to support DDD); and (v) opportunities for hands-on research and practical experience in DDD.⁸ The Health Innovations and Therapeutics (HIT) concentration within our institution’s MSCI program follows expansion of an R25-funded educational program in DDD (National Institute of Diabetes and Digestive and Kidney Diseases) and is designed to facilitate all of these aims. The DDD educational program was created in an effort to provide healthcare professionals with formal training in DDD in a multidisciplinary fashion. By introducing a coherent program of courses, seminars, and didactic sessions in DDD, as well as mentored research with access to academic, industry, economic, and government leaders, our trainees will be better equipped to translate research into useful innovation.

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NEED FOR PHYSICIAN AND MEDICAL STUDENT INVOLVEMENT IN DRUG AND DEVICE DEVELOPMENT

Despite increases in efforts and funding for drug development, the US Food and Drug Administration (FDA) approval of new molecular entities (NMEs) has been slow to progress. Between 2007 and 2010, the average number of NMEs and biologics approved was 21, a level typical for the 1970s. Simultaneously, the number of new drugs approved per billion US dollars spent on research and development has nearly halved every 9 years since 1950. Notably, the physician's role in drug development has traditionally been limited to carrying out phase III clinical trials, with little involvement in preclinical and early clinical design phases. We argue that physician awareness, training, and involvement in all stages of DDD may lead to more collaborative science that may result in future NMEs.

Surveys from pharmaceutical medical associations indicate a dearth of continuing professional development programs in pharmaceutical medicine, and physicians who do work in pharmaceutical companies typically lack formal training in DDD. In addition, physician involvement in DDD is typically limited to the role of a consultant, rather than truly leading the development of the device or drug. Recognizing this deficit, four countries in Europe (Switzerland, United Kingdom, Belgium, and Ireland) as well as Mexico and Argentina, have accepted Pharmaceutical Medicine as a distinct medical specialty, providing formal didactic training to physicians and postgraduates opting to enter into this specialty. Device design, which is fraught with slow processing times, high costs, and regulatory obstacles, has also shown historically low physician involvement. Physicians continue to demonstrate a poor understanding of the process of device design, and it has been suggested that greater involvement of physicians in this field could help to streamline design of novel devices.

A number of training programs have been developed to teach DDD to healthcare professionals, including PharmaTrain, a public-private partnership of international universities, societies, and pharmaceutical companies, and AstraZeneca in partnership with the Leicester Medical School. Additionally, the Merck Research Laboratories pioneered a course at Columbia University on pharmaceutical research that also focused on the key skills needed for a career in industry. A number of CTSA institutions in the United States as well have begun offering courses in DDD for students. The University of Iowa and Mayo clinic's CTSA, for example, have developed courses on innovation and collaboration with industry. Although such courses provide an overview of DDD, including the property and contracting components, they provide limited firsthand exposure to industry. To our knowledge, the HIT concentration represents the first dedicated training program, including both master's programs and certificate programs, in DDD among currently existing CTSAs in the United States. Special interest competencies for academia-industry drug development were outlined by the CTSA Working Groups and Key Function Committees in 2011, as shown in Table 1.

Table 1 Clinical and Translational Science Award Core Competencies for Academia-Industry Drug Development

| Core CTSA competencies for teaching drug development |
|------------------------------------------------------|
| I. Science of drug development |
| II. Regulatory issues |
| III. Recruiting investigators |
| IV. Designing clinical trials |
| V. IRB and data safety monitoring |
| VI. Budgets and contracts |
| VII. Clinical trial management |
| VIII. Conflict of interest |
| IX. Developing new areas of collaboration |

CTSA, Clinical and Translational Science Award; IRB, institutional review board.

Core competencies for teaching drug development as outlined by the CTSA Working Groups and Key Function Committees on November 15, 2011. Adapted from referenced document below.

Competencies for Academia-Industry Drug Development, Competencies for Medical Device Innovation and Technology. 2009. https://ctsacentral.org/wp-content/documents/SpecialInterestCompetencies.pdf.

MSCI CORE PROGRAM

Our institution’s MSCI is a 2-year formal training program that aims to provide healthcare professionals with the skills to become independent investigators in translational research. The MSCI program is open to clinical and translational investigators at doctoral levels in all health disciplines, and has enrolled professionals as diverse as surgeons, psychologists, dentists, and nurses. There is also the opportunity for predoctoral students, such as medical students and dental students, to participate in the MSCI and obtain an MD/MSCI dual degree. Matriculated medical students at our institution have the opportunity to apply for the program during their third year of medical school, beginning the program in June following completion of their core clerkships. Medical students are expected to dedicate 1 full year between their third and fourth years, as well as 3 months during their fourth year, to the MSCI program. The MD/MSCI program successfully trained 20 medical students over the first 4 years of the program, producing upward of 38 peer-reviewed publications in a variety of diverse scientific journals.

Required MSCI core courses include: Clinical Research Methods, Clinical Trial Design, Integrative Seminar, and Introduction to Biostatistics, as well as dedicated research time with a faculty mentor (Table 2). The Clinical Research Methods course provides an overview of principles of clinical research and protocol development through lectures and small group exercises; Clinical Trials Design showcases various approaches in varying sized clinical trials; and Introduction to Biostatistics provides basic biostatistical knowledge. Finally, Integrative Seminar provides a forum for students to come together in small groups to discuss and troubleshoot their research projects.

During the first year of the MSCI, trainees are expected to submit a human subject research protocol to the Institutional Review Board (IRB), obtain IRB approval, write a literature review, and submit an abstract to a regional or national meeting. In the second year of the program, trainees are required to submit a first author abstract to a regional or national meeting, submit an original manuscript
Table 2  Masters of science in clinical investigation core curriculum

| Term       | Course title                                      | Credits |
|------------|--------------------------------------------------|---------|
| Year 1     |                                                  |         |
| Summer     | Clinical Research Methods                        | 3       |
| Fall       | Introduction to Biostatistical Analysis           | 3       |
|            | One of:                                          | 3       |
|            | ◦ Advanced Epidemiology                          |         |
|            | ◦ Drug Development in a New Era                  |         |
|            | Integrative Seminar                              | 1       |
| Spring     | Scientific Integrity and the Responsible Conduct of Research | 0       |
|            | Clinical Trial Design                            | 4       |
|            | Biomolecular Medicine                            | 4       |
|            | Health Services Research Methods (elective)      | 4       |
|            | Integrative Seminar                              | 1       |
|            | Independent Research                             | 1       |
|            | Advanced Biostatistics – II (elective)           | 3       |
| Year 2     |                                                  |         |
| Fall       | Medical Informatics                               | 3       |
|            | Grant Writing                                     | 0       |
|            | Integrative Seminar                              | 1       |
|            | Independent Research                             | 1       |
|            | Advanced Biostatistics – II (elective)           | 3       |
| Spring     | Integrative Seminar                              | 1       |
|            | Independent Research                             | 5       |

Table 3  Masters of science in clinical investigation milestones

Milestones

- Submit an abstract to a regional or national meeting (as first or middle author).
- Submit a manuscript for a review paper (as first or last author).
- Be a lead author on an abstract submitted to a regional or national meeting.
- Prepare and submit a manuscript for publication (as first author).
- Prepare (and submit to the Executive Committee) a grant application for federal or other national funding.
- Prepare and submit an academic portfolio.
- Prepare and submit a master’s thesis to faculty and fellow trainees.

for publication, identify a suitable grant, prepare and submit a grant application for federal funding, and defend their research in an oral presentation (Table 3). In addition, at the conclusion of the program, trainees are required to assemble all scholarly materials (including posters, abstracts, publications, and grants), as well as an updated curriculum vitae and/or NIH-style biosketch into an academic portfolio that is submitted to the program for review.

The MSCI currently offers three tracks of study: Translational Research, Health Innovations and Therapeutics (MSc-HIT), and Comparative Effectiveness Research. Below, we will describe key components of the MSc-HIT curriculum, while also providing pilot data demonstrating trainee satisfaction with individual courses that were offered by our CTSI prior to the proposed launch of the formal MSc curriculum, scheduled for Fall 2017. These courses were piloted to over 210 graduate students during the 5 years over which they were offered.

MSC-HIT CURRICULUM

The HIT concentration was approved by the Department of Education of the State of New York and will be offered to all students entering the MSCI program beginning in Fall 2017. The program director has been the principal...
investigator for the past 5 years for an educational grant in DDD, which was used to conduct a number of successful DDD courses available to MSCI students and outlined below. The success of these courses has allowed the program director to expand these courses into a concentration within the MSCI program. Other faculty members involved in the HIT program are experts in the field of innovations, therapeutics, and DDD and are dedicated to teaching the next generation of translational researchers.

Students are selected for the MSCI program through a competitive application process, which requires a personal statement, recommendation letters, and curriculum vitae. Applicants also identify a mentor and submit a research proposal. Applications are reviewed by the MSCI executive committee.

The MSc-HIT will require students to complete specific HIT courses (Table 4) in addition to the required MSCI core courses (see above and Table 2). The Integrative Seminar will focus on health innovations. The HIT-specific core courses include: Biotechnology Industry, Structure, and Strategy; Drug Development in a New Era; and Molecular Signaling in the Discovery and Development of Therapeutics. Students will be required to take at least one selective: Medical Informatics or Biomolecular Medicine. Additional electives are also offered and include: Advanced Epidemiology; Advanced Biostatistics; Health Services Research Methods; and Trending Topics Seminar. Finally, there will be a required research component dispersed among three of the four semesters. The requirements for the research component of this concentration will be the same as that for the current translational research concentration; a thesis must be submitted at the end of the program, and the work presented in oral form to the students’ peers and mentors. Students will be required to complete at least 35 credits: 23 credits of MSCI core courses and independent research and 12 credits of core HIT courses (Table 2). Milestone expectations are the same as those for the MSCI (Table 3).

There is also the opportunity to obtain an abridged form of the MSc-HIT degree as a certificate in Health Innovations and Therapeutics. As part of the HIT certificate program, students are required to successfully complete the HIT core courses only: Biotechnology Industry, Structure, and Strategy; Drug Development in a New Era; and Molecular Signaling in the Discovery and Development of Therapeutics.

CORE HIT COURSES AND NEW ELECTIVES

Core HIT courses and selected new electives will be described below. Trainee satisfaction with courses that have been offered by our institution’s CTSI prior to the proposed launch of the formal MSc HIT curriculum will also be provided. These data are provided not to prove the effectiveness of these courses but to provide an idea of trainee-perceived course satisfaction.

As per grant administration, data collected in individual course evaluations do not constitute human subjects research and were, therefore, exempt from the IRB approval process.

Drug development in a new era

This course was piloted as a selective for graduate students at our institution, where it aimed to provide an overview of new drug development to interested students. Through a combination of lectures and discussions with invited lecturers from both the academic and private sector, students learned about the various steps involved in the drug development process. Lecturers included basic and translational science researchers, physicians who work in pharma, clinicians and personnel involved in DDD, an intellectual property and patent attorney, experts in regulations, policy, and marketing, as well as drug safety monitors, to name a few, making for a broad variety of perspectives. A dedicated lecture on emerging devices for diabetes management is also included in the curriculum to expose students to certain aspects of device development. The learning objectives were to:

1. Learn the vocabulary and principles of new drug development.
2. Assess the nonclinical background of the drug.
3. Learn practical skills for interacting with regulatory agencies during the course of new drug development.
4. Discuss the financial and marketing issues behind new drugs.

At the culmination of the course, students were required to complete a paper tracing the development of a drug from the basic science level to FDA approval.

Preliminary data from the first 2 years of the course showed good course efficacy and satisfaction. A total of 37 students enrolled, including 11 MD/MSCI dual degree students (30%), 11 PhD students (30%), 4 faculty (11%), 7 fellows (20%), and 3 MS students (9%). Pre-course and post-course surveys with knowledge questions related to the course were completed by 89.2% of students, and revealed significant increases in the knowledge of course domains. Additionally, the majority of the lecture ratings completed by 81.1% of students were 3 or greater, on a 5-point scale.16

These results, which demonstrate that students gained knowledge from the course and rated the lecturers highly, suggest that a dedicated program in DDD will be educational and well-received.

Biotechnology industry, structure, and strategy

This one-semester course was piloted as an elective for students at our institution’s School of Business, where it provided an overview of the biotechnology industry and the key factors for success in this field, and will now be offered as part of the MSc-HIT program. Specific session topics included: strategy and business models, drug discovery, drug development, intellectual property, manufacturing, deals: financing in the capital markets, deals: partnerships, and financing, sales and marketing, personalized medicine, pricing: the interface of economic analysis, public policy, and bioethics, and biotechnology: nonhealthcare applications. Teaching was according to a case-based, business school model. At the end of the course, students were required to complete a short paper describing key challenges facing a real-life biotechnology company and
Molecular signaling in the discovery and development of therapeutics

This course has also been offered to graduate students as part of an NIH-funded drug development educational program, and gives an overview of modern approaches to drug design and development. The course covered various topics, such as virtual library screening, rational drug design, combinatorial chemistry, and molecular signaling pathways from the point of view of drug targeting, including gene and protein targets, and methods of drug design. Specific course topics included: drug development themes, computational drug discovery, glycosaminoglycan modulation of signaling pathways: implications for drug development, immunotherapy for tauopathies, gastrointestinal hormones, human immunodeficiency virus therapeutics, ras/cancer, akt signaling, drug addiction, adenosine receptors, receptor for advanced glycation end-products, and diabetic complications, aldose reductase and diabetes complications, diabetic neuropathy trials and choice of end points, molecular signatures of disease, and drug development (Supplementary Table S1). New and emerging technologies are emphasized in all the courses, with lectures on drug repurposing and disease networks and signatures as drug targets. Learning objectives were to:

1. Identify, categorize, and critique the diverse classes of drugs.
2. Learn the most important drug discovery tools.
3. Identify a suitable molecular target for drug development.
4. Choose an appropriate drug discovery technique to develop a drug for this target.
5. Design a system to evaluate this drug.
6. Explain the problems that are likely to affect the development potential of this drug.

At the end of the course, students were required to complete a paper on a method/approach to design a therapy targeting one of the disease processes described in the class meetings. This course has been designed to provide a background that will prepare trainees for translational research in clinical pharmacology and basic science, which are being increasingly recognized as key components in the translational research continuum. Preliminary data from the first 2 years of this course showed positive results. Over 2 years, a total of 23 students had enrolled. On pre-course and post-course surveys completed by 65.2% of students, respondents acknowledged significant increases in knowledge as a result of the course. Additionally, 69.6% students provided evaluations of the course’s lectures, which were generally rated highly. One hundred percent of students gave lecture rating of 3 or greater, on a 5-point scale.

Trending topics elective seminar

This novel course will focus on important issues in the area of HIT, allowing students to discuss these topics in an informal setting. The topics will change annually with the changing environment of healthcare; however, potential topics include new drugs, new health devices, revolutionary discoveries, journal reviews, and changes in intellectual property law.

Program assessment strategy

Relevant DDD training for interested scientists, and like-minded individuals in medical and biomedical science schools, is essential to increasing productivity in the field. The HIT program and the potential development of similar programs within the CTSI network may facilitate this goal. Program evaluation is a vital part of the development of any educational system and will be carried out on a semester-by-semester basis following the initiation of the program in Fall 2017. The Logic Model is one suitable system for evaluation of the MSc-HIT, and consists of careful review of program inputs (e.g., funding, facilities, and faculty), activities (e.g., courses and research projects), outputs (e.g., number of exercises or students), and outcomes (e.g., knowledge scores, publications, and/or grants). Qualitative data in the form of faculty and student quotes can also be useful in course evaluation. For the MSc-HIT program, students will complete pre-course and post-course surveys related to knowledge of course topics and course satisfaction that will be used as part of the program evaluation. Additionally,
CONCLUSIONS

The ability to translate basic science research into clinical practice has become essential in advancing medical research. As we described, there are now many training programs for healthcare professionals in translational research, yet formal training programs that focus on DDD are lacking. The HIT concentration represents a novel program that will address this gap in training and can serve as a model for other CTSI's.

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Conflict of Interest. The authors declare no conflicts of interest.

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