Published in final edited form as:

Biochem Mol Biol Educ. 2017 January 02; 45(1): 13–24. doi:10.1002/bmb.20978.

The Translational Science Training Program at NIH: Introducing Early Career Researchers to the Science and Operation of Translation of Basic Research to Medical Interventions

C. Taylor Gilliland¹, G. Sitta Sittampalam¹, Philip Y. Wang², and Philip E. Ryan^{2,*}

¹National Center for Advancing Translational Sciences, National Institutes of Health, Bethesda, MD

²Office of Intramural Training and Education, National Institutes of Health, Bethesda, MD

Abstract

Translational science is an emerging field that holds great promise to accelerate the development of novel medical interventions. As the field grows, so does the demand for highly trained biomedical scientists to fill the positions that are being created. Many graduate and postdoctorate training programs do not provide their trainees with sufficient education to take advantage of this growing employment sector. To help better prepare the trainees at the National Institutes of Health for possible careers in translation, we have created the Translational Science Training Program (TSTP)¹. The TSTP is an intensive 2–3 day training program that introduces NIH postdoctoral trainees and graduate students to the science and operation of turning basic research discoveries into a medical therapeutic, device or diagnostic, and also exposes them to the variety of career options in translational science. Through a combination of classroom teaching from practicing experts in the various disciplines of translation and small group interactions with pre-clinical development teams, participants in the TSTP gain knowledge that will aid them in obtaining a career in translational science and building a network to make the transition to the field.

Keywords

translation; translational science; education and training; pre-clinical development

Introduction

Translation is the process of turning observations in the laboratory, clinic and community into interventions that improve the health of individuals and the public – from diagnostics and therapeutics to medical procedures and behavioral changes. The central challenge is to

¹Abbreviations: NIH, National Institutes of Health; TSTP, Translational Science Training Program; OITE, Office of Intramural Training and Education; NCATS, National Center for Advancing Translational Sciences; DPI, Division of Pre-Clinical Innovation; IND, investigational new drug; GLP, good laboratory practice; CTSA, Clinical and Translational Science Awards Program; NDA, new drug application; FDA, Food and Drug Administration; RNAi, RNA interference; PK, pharmacokinetic; PD, pharmacodynamic; ADME, absorption, distribution, metabolism and excretion; Tox, toxicity; NME, new molecular entity; HTS, high-throughput screening; GMP, good manufacturing process.

*Corresponding author, ryanp@od.nih.gov; address: NIH Office of Intramural Training and Education, 2 Center Dr. MC 0234, Bethesda, MD, 20814.

advance the translation of basic discoveries into tangible health benefits. Thus, translational science is defined as the field of investigation focused on understanding the scientific and operational principles underlying each step of the translational process. This is a burgeoning discipline that, as it progresses, has the promise to catalyze the development and dissemination of novel medical innovations and bring more treatments to more patients more quickly. As the discipline gains recognition and more resources are dedicated to the study of translation, there will be an increase in the number of jobs within the field leading to a variety of interesting and worthwhile career opportunities to graduate-level biomedical scientists. These jobs will need to be filled by well-trained scientific personnel who understand translational science and how it is conducted. However, many graduate education curricula do not include information on the various career opportunities within translational science or provide sufficient training to prepare students to enter the field. To help expose graduate students and postdoctoral trainees conducting research at the National Institutes of Health (NIH) to the field of translational science and associated careers, the Office of Intramural Training and Education (OITE), in collaboration with the National Center for Advancing Translational Sciences (NCATS) and the Office of Translational Research at the National Institute of Neurological Disorders and Stroke (NINDS), created a Translational Science Training Program (TSTP) with the following goals for its participants:

1. Gain insights into the therapeutic, diagnostic and device discovery and development process from translational science experts
2. Become familiar with the broad career options in translational science for someone with a Ph.D. in biomedical research, both in the public and private sectors
3. Develop a network of professionals and mentors across the functional areas in translational science

The TSTP is an intensive program in which graduate students and postdoctoral trainees within the Intramural Research Program at one of the Institutes or Centers at NIH learn about the field of translational science and the scientific and operational processes by which therapeutics, diagnostics and medical devices are developed. The course is taught by a team of subject matter experts who are available to the participants for follow up communication and engagement, thereby providing participants with the opportunity to expand their network of professionals in the career paths available in translational science. The instructors have included a director and senior advisor of translational research units at NIH, a leader of a FDA drug evaluation division, individuals with many years of experience in the biopharmaceutical industry, life science business and marketing advisors, and clinician scientists, among others. The program has evolved through several iterations over the past few years to best meet the needs of the graduate student and postdoctoral trainee participants. We present here a brief history of the TSTP, the rationale for changes made to the program, and the current content and format. We hope that academic and other research institutions, as well as the biopharmaceutical industry, may find this report useful to expand their curricular offerings in this exciting and growing field. While the focus is on graduate and post-graduate level training, each of the modules and concepts covered in the TSTP

could be adapted to enhance undergraduate-level biochemistry and molecular biology curricula. The development of a novel therapeutic, medical device or diagnostic requires a firm understanding of foundational principles in biochemistry and molecular biology and could serve as a useful example of how these principles are applied to diagnose, treat and cure disease. Additionally, some universities and academic medical centers offer both masters and doctoral degree programs in clinical and translational science that qualified undergraduates can apply for. Awareness of the field of translational science early on in students' education should help them be competitive for such graduate programs and become members of the highly-skilled translational workforce.

Evolution of the Translational Science Training Program

Why the Bootcamp Format

The TSTP was first launched in the fall of 2010 as a 13-week, graduate level survey course with experts brought in to instruct on each stage of translation. Each class was two hours long and occurred during business hours. This format allowed for an in-depth study of each class topic and the use of many different case studies that covered a multitude of diseases and disorders. The class size was limited to allow the students to engage the presenters in meaningful discussions about the topics. However, attendance in the class was inconsistent from week to week and the overall attrition rate was high. Participants, all of whom were conducting research within the NIH Intramural Research Program, indicated that this schedule was too time-consuming given their rigorous research schedules and that a much more condensed version would be more effective. Students within a more traditional university setting may be more familiar with a standard class schedule and thus be amenable to the semester long format. A more condensed version was more appealing to the graduate student and postdoctoral trainees at the NIH and allowed us to offer the material to a higher number of trainees. In the fall of 2012, the course was re-launched as a two-day program held over consecutive days with a day-and-a-half long didactic component and a half-day long workshop focusing on preclinical development. The didactic component, referred to as the "bootcamp," covered the scientific, regulatory, economic and marketing knowledge of the translational process.

The second component included presentations, a tour, and small group discussions at the NCATS Division of Pre-clinical Innovation (DPI) research facilities for what is now referred to as the "workshop." This format proved to be more successful in providing the participants with critical information on translational science that met the outlined goals in a more accommodating time frame. Importantly, it also provided the participants an opportunity to visit a translational research facility for more in-depth presentations on pre-clinical development and to meet with NCATS scientists to discuss the course participants' research projects and how they might direct their research to a translational approach. Participation was initially limited to 35 students primarily to foster discussion in small groups during the workshop component and due to space and resource constraints.

Participant surveys also indicated that making the preclinical workshop and group discussions optional and extending the time dedicated to it would best address the majority of interests of the diverse array of graduate student and postdoctoral trainee attendees. Not

everyone found the workshop useful for advancing their particular career or research interests, while others desired more time to learn how therapeutic discovery and development is actually conducted.

In early 2015, the TSTP underwent a further re-design with the bootcamp material being expanded to two full days (see Figure 1 for a general overview and Table I for the agenda) and the workshop becoming an optional full-day program. With the two portions of the program separated by approximately one month, enrollment in the bootcamp was increased to 55 participants while the workshop was limited to 20 participants to facilitate small group discussions. A listing of the modules comprising the most recent version of the bootcamp component of the TSTP, as well as descriptions of the key concepts and terms for each module, is provided in Table II. Participants completing the bootcamp were then invited to specifically apply for the pre-clinical development workshop organized by NCATS. The description that follows reflects the most recent implementation of the TSTP in early 2015 and how the organizers anticipate the program will continue to be structured in the near future. However, TSTP organizers will continually utilize participant feedback to modify the curriculum and increase participant learning of the principles of translational science.

The Application and Applicants

Much like the course itself, the application process has evolved over time. An application process was and continues to be necessary because NIH intramural graduate student and postdoctoral trainee demand for the TSTP consistently outnumbered the maximum attendance level set by the program organizers. Currently, the TSTP is limited to students and trainees conducting research at the NIH itself through one of its Institutes or Centers; however, this report is aimed at enabling others outside of NIH, such as academic institutions and other translational research organizations, to adapt the TSTP to their own local context and offer it to their students and trainees. To participate in the previous iterations of the TSTP, applicants were required to submit a one-page proposal detailing how their research projects could be applied to the development of a therapeutic, diagnostic or device. Those applicants who demonstrated an interest in learning more about translational science and developed a thoughtful approach to translating their own research were selected. However, many applicants had difficulty in completing this task prior to completing the course and learning about translational science and what constitutes a translational research project. This emphasized the important role the TSTP and other programs like it play in increasing the awareness and understanding of translational science amongst the general biomedical research community. The application process for the bootcamp was subsequently simplified in order to elucidate prior knowledge and uncover any misconceptions of the field, while a separate application for the optional workshop was instituted. Those applying to bootcamp were required to submit two 100 word statements: 1) detailing their interest in the course; and 2) explaining their current understanding of translational science. Those participants who completed the bootcamp and were interested in participating in the workshop were asked to complete a separate translational science exercise, which will be discussed in detail below.

The First Stage: TSTP Bootcamp

The bootcamp is currently composed of modules taught by knowledgeable individuals with many years of experience in relevant areas of translation. The key terms and concepts covered in each module are provided (Table II). Critical to the success of the bootcamp is finding instructors that can convey information in an effective and engaging manner and facilitate participant discussion. The therapeutic development of imatinib (Gleevec®) is used as a case study in some of the bootcamp modules so the participants can see how a particular therapeutic moved through the translational process to an actual therapeutic.

Bench-to-Bedside Overview

The opening module sets the tone for the bootcamp. The instructor begins by asking the participants what they hope to learn over the course of the two days and how they define “translation.” The instructor then uses the answers to tailor discussion of the key definitions, history and principles of therapeutic discovery. It is important that the participants understand each step in the translational process and the resources required to complete each step. For example, participants should understand where in the translational process there is a strong need to develop new technologies to screen out compounds as early as possible that would ultimately be ineffective or unsafe. Depending on the expertise of the instructor, the discussion could be extended beyond therapeutics to include the unique development challenges for diagnostics and devices.

Target Validation

New molecular targets for therapeutic action are continually being identified in basic science laboratories; however, only a small percentage of these targets are considered as candidates for drug development (termed “druggable”). The instructor in this module walks the participants through the process of choosing a “valid” target, focusing on understanding signaling pathways and on “nodes” where multiple pathways intersect. In addition, it is emphasized that target validation also depends on other aspects of the disease biology, such as intra-cellular vs extra-cellular targets, information about molecules modulating the target in publications, in the clinic or on the market, availability of animal models, etc. The identification and validation of the BCR-Abl tyrosine kinase as a target for the treatment of chronic myelogenous leukemia, and the development of imatinib as an effective inhibitor of the target, is provided as a case study.

Intellectual Property and Patenting

In this module, participants are introduced to the purpose and the uses of patents. Through a discussion of the different types of patents the instructor demonstrates how inventors can protect their invention and its usage. Extra attention is paid to the “claims” portion of the patent as this is where the scope of the patent is determined. While patents are the main focus, other intellectual property documents such as material transfer agreements, non-disclosure agreements, and cooperative research and development agreements are briefly discussed. Using the patent for the cardboard insulator sleeve that can be found in just about every coffee shop in America as an example, the instructor walks through each part of an

actual patent application. This example is effective at demonstrating the complexity of the patent document for such a seemingly simple invention.

Pre-Clinical Development and IND-Enabling Studies

The FDA requires specific studies before a potential therapeutic or diagnostic is allowed to progress into first-in-human clinical trials. In this module, the instructor walks the participants through preparations for a phase I trial by looking at the timing of filing an investigational new drug (IND) application and the cost of moving through the IND submission process. In 2015, a short segment was added in this session on Good Laboratory Practices (GLP) and what those are, why they were started and what purpose they serve.

The instructor reiterates how the cost of development of a drug increases dramatically as the entity moves into clinical trials, and that failures during this phase are more costly than earlier in the pipeline. This emphasizes the importance of having highly predictive assays and technologies for determining efficacy and toxicity early in the pre-clinical development stages in order to reduce the chance of costly late-stage failure. While pre-clinical development is often described as a pipeline, the instructor emphasizes that the process does not happen in a linear fashion. Each stage in translation generates information that can loop back and feed into any other stage to inform therapeutic development (for a graphic representation of the translational science spectrum go to <https://ncats.nih.gov/translation/spectrum>). It should also be emphasized that translation requires a team science approach with researchers spanning multiple disciplines (such as medicinal chemistry, protein chemistry, pharmacology, toxicology, metabolism, bioinformatics, pharmaceuticals, regulatory sciences and clinical trial design) all working collaboratively to achieve the shared goal of bringing a new treatment to patients.

NCATS Clinical and Translational Science Award (CTSA) Program

The purpose of this module is to provide participants with an overview of the NCATS CTSA Program and the opportunities the hubs provide for further training in translational science. Under NCATS' leadership, the Clinical and Translational Science Awards (CTSA) Program supports a national network of medical research institutions — called hubs — that work together to improve the translational research process to get more treatments to more patients more quickly. CTSA Program hubs collaborate locally, regionally and nationally, fostering innovation in training and research methodologies. All CTSA Program hubs offer programs in clinical and translational research training at the pre- and post-doctoral level, which can include KL2 Mentored Clinical Research Scholar Awards and TL1 Clinical Research Training Awards. KL2 awards support mentored research career development for clinical investigators who have recently completed professional training and who are commencing basic, translational and/or clinical research. TL1 awards support students seeking a practical introduction to clinical and translational research. Training is also provided by many CTSA Program hubs in non-traditional skills such as regulatory science, entrepreneurship and team science.

Clinical Trial and Drug Development Planning

The purpose of this module is not only to convey information about what the different phases of the clinical trial process entail, but to also highlight the amount of preparation that goes into taking a product through the clinical process. The instructor spends time describing all four phases of clinical trials, including the number of patients enrolled, the purpose, and estimated costs of each phase. After focusing on the actual clinical trials, the instructor discusses the development plan to get a therapeutic through the process and how the plan may differ between small and large biopharmaceutical companies. Regardless of those details, the plan is developed to compile the essential therapeutic safety and efficacy information to be able to submit a New Drug Application (NDA) to and receive marketing approval from the FDA. The clinical development of imatinib is again used as a case study to describe each trial phase, with attention paid to the fact that this was not a typical case for clinical trials.

FDA - New Drug Evaluation and Review

The FDA relies upon a multidisciplinary team of diverse experts across the translational spectrum to review the NDA and make a final recommendation regarding approval of the therapeutic. The instructor discusses the seven person review team assigned to each application and the role each person plays in the process. The instructor also explains each step of the process and the timing of a review that generally takes 10–12 months. Companies looking to submit an NDA to the FDA for approval can participate in a “Pre-NDA meeting” with an FDA reviewer to discuss the process in detail. The instructor then focuses on a few case studies where there were concerns raised during the review and how they are addressed. Also, expedited programs (Fast Track, Breakthrough Therapy, Priority Review, Accelerated approval) are discussed and when using these programs is appropriate. To explain how the expedited programs work, the instructor gives examples of drugs currently on the market that have been approved through each of the expedited programs.

Marketing and Product Launch

This module covers material that is entirely new to most of the participants. The main goals of the module are for scientists to learn the basic characteristics of marketing and how marketing can affect product development. The session starts with a general overview of marketing followed by an interactive product launch again using imatinib as a case study. The instructor explains why marketing is important to product development and then leads the participants through an active learning activity in which they design a mock product launch. For this activity, the instructor asks the participants questions to guide them through a strengths, weaknesses, opportunities, and threats (SWOT) analysis that may impact launch success. Participants then propose strategies designed to maximize strengths and opportunities, and minimize weaknesses and threats. These proposed strategies are then compared to the actual plan executed for the launch of imatinib.

Panel Discussions on the Realities of the Biopharmaceutical Industry

The panel discussion was added to the bootcamp in the spring of 2015. The modules thus far are primarily focused on the translational development of small molecule drugs given the

broad familiarity with this class of therapeutic. However, participant feedback in previous years indicated a desire to learn more about biologics, medical devices and diagnostics and how bringing these products to the market might differ. There is insufficient time in a two-day course to discuss developing these products in addition to the current focus on small molecule development. To provide exposure to these fields we invite experts in developing biologics, medical devices and diagnostics to participate in a panel and describe how development of these products differs from small molecules and answer questions from the participants. This panel also provides the participants with an additional opportunity to network with experts representing diverse occupations in translation.

The Second Stage: Pre-clinical Development Workshop

The pre-clinical development workshop, organized by NCATS in collaboration with OITE, focuses on the methods and technologies employed in the translational research process from target validation to IND submission. The day-long workshop is divided into four modules: short scientific presentations on a range of pre-clinical development topics; a tour of high-throughput screening and compound management facilities; small group discussions with working translational scientists; and a Q&A and networking session with NCATS researchers (see Table III for an example agenda). Participation is available to those NIH intramural graduate students and postdoctoral trainees who completed the prior two-day bootcamp of the TSTP and who had been selected based upon completion and review of the translational science exercise described below.

The Translational Science Exercise

The translational science exercise asks TSTP bootcamp participants to think about how to develop and implement a translational science project based on their current research program or interests. The exercise provides participants with an opportunity to apply what they had learned in the bootcamp portion of the program and to develop their ideas in preparation for the small group discussions. The exercise requires participants to prepare a brief background and specific aims for a hypothetical project that would translate the applicant's area of basic research or research interest towards the development of a new drug, device, diagnostic or vaccine. Specifically, participants are asked to describe the disease relevance of a known or hypothetical biological target, a method of target identification and validation, and an assay that could be used to screen compounds against the target (additional details provided in Table IV). The exercise is provided to the participants immediately following the final presentation in the bootcamp with a submission deadline of one week later. A review committee consisting of an expert in the full spectrum of pre-clinical drug development, two translational scientists with expertise in assay design and development, and the workshop organizer is assembled to review the exercises. Each reviewer provides critical and constructive feedback, highlights excellent and innovative ideas, suggests areas for strengthening, asks clarifying questions, and includes references to helpful scientific literature.

To increase the efficacy of the group discussions and ensure a low participant-to-expert ratio, the exercise is also used by the review committee to limit the number of participants for the

workshop to 20 graduate students and postdoctoral trainees. The precise number of participants is dependent on the availability of sufficient meeting space, resources, and the number of expert volunteers, which will vary depending on the local resources available at each institution. In general, the exercises are evaluated by how well the applicant followed the guidelines, provided a thorough response, and created a logical plan for pre-clinical development. Reviews are completed within one week after the deadline for submission, and the top applicants are chosen by consensus following a meeting of the review committee. After providing the feedback from each reviewer to each applicant, the applicants are encouraged to address the comments and submit a revised exercise prior to the workshop. Many of the workshop participants have indicated the comments from the translational scientist reviewers aid in their understanding of the critical design components of an early-stage translational research project. The reviewers have noted some participant confusion on differentiating target validation and screening experiments, difficulty in identifying a “druggable” target, and a general lack of understanding of the need for counter screens and secondary assays to confirm hits from compound screens. These topics will be emphasized in future iterations of the workshop. The revised exercises are shared with the small group discussion leaders in advance of the workshop to provide them with sufficient time to read the exercises and prepare comments for the discussion.

The pre-clinical development workshop begins with a brief overview of the challenges in pre-clinical translational science as well as the programs, infrastructure and resources available at the institution implementing the workshop (NCATS in this case) to advance early-stage biomedical innovations to first-in-human studies. Subsequent presentations delve into the details of target identification and validation with RNA interference (RNAi) technology, assay design and development for screening chemical compounds, the methods to de-risk drug candidates and evaluate pharmacological efficacy, and the IND-enabling studies required to initiate clinical trials. Key concepts highlighted in each presentation are provided in Table V.

The workshop organizers are considering an alternative arrangement of these presentations with the goal of increasing the level understanding amongst the participants. It may be more effective to discuss each stage of pre-clinical development using a single case study of a therapeutic candidate developed by scientists at NCATS or elsewhere, rather than trying to provide a general overview of each stage. The workshop organizer can provide any relevant background information about the basic biology of the disease in question and the pathway that was targeted for therapeutic development. Experts can then be brought in to present a summary of the assays and tools used for each stage (target ID and validation, assay design and development, hit-to-lead optimization, and IND-enabling studies) to advance the compound in the case study through the development process. Ideally, the case study will illustrate applications of different experimental approaches available to translational researchers in each stage of pre-clinical development. The workshop organizers hope to develop and implement this case study-based module in the next iteration of the TSTP.

The next section of the pre-clinical development workshop involves a guided tour of the NCATS DPI facilities for assay development, medicinal chemistry, and high-throughput screening (HTS). Participants see the advanced equipment used by NCATS researchers to

discover and develop new therapies and innovative biomedical technologies. Participants have an opportunity to ask detailed questions about how assays are automated, what types of reagents and detectors are needed for various automated assays, and how a very large compound library is maintained and organized, among others. One of the most common questions the participants ask is how to scale up an assay from a 96-well plate to a 1,536-well plate format, and to scale down assay volumes from the hundreds of microliters to the tens of nanoliters. The tour also impresses upon them the rigorous controls necessary in drug discovery.

Following the tour, the 20 participants are divided into five groups and partnered with 3–4 experienced translational scientists from NCATS DPI. As much as possible, the scientists assigned to each group have different areas of expertise that complement one another (e.g. assay development, medicinal chemistry, target validation, and PK/ADME/Tox). The focus of the small group discussions are the translational science exercises from each participant, which had previously been shared with the expert scientists. During the two hours dedicated to this session, each participant presents a brief overview of their exercise, after which the group discusses the scientific and technical aspects of the proposal. The purpose of this exercise is to facilitate dialogue between the participants and the translational scientists so that the participants could gain deeper insight into the technical aspects and challenges of pre-clinical development as they directly relate to their research area or interests. This also provides a forum wherein expert scientists can discuss ideas and seek feedback from their peers as to how the participants could translate their basic research, and whether certain approaches would be more feasible than others. One of the takeaways from these discussions is that the participants learn what additional experiments are needed to validate their targets and therapeutic concepts.

The workshop closes with an informal networking session to which all of the presenters, lab tour leaders, and small group discussion volunteers are invited. This provides the participants with time to further discuss their research and career interests and gain valuable feedback about professional and scientific development opportunities. Many of the research staff within NCATS DPI have prior industry experience and are able to provide a sense of what it is like to work in either a large or small biotechnology or pharmaceutical company. Some of the participants also seek to establish research collaborations with NCATS DPI scientists in order to implement the research plans outlined in their exercises.

Results

To assess the effectiveness of the TSTP, we utilized two different metrics. The first is a self-reporting evaluation from the participants following the bootcamp. Participants were asked to answer three critical questions on a scale from 1 to 5, with 1 indicating the participant strongly disagrees with the statement and 5 indicating the participant strongly agrees with the statement. The three questions and the cumulative score for the past five iterations of the bootcamp from 2011–2015 are described in Table VI. Participants strongly agreed (4.62 average score) that the bootcamp increased their knowledge and understanding of what translational science is and how it is conducted. We feel this is an excellent indicator of success for the first objective listed for the program. For the second objective of introducing

participants to the broad career options within the public and private sectors, participants agreed (4.12 average score) that the bootcamp met those expectations. Importantly for building a lasting program, participants strongly agreed (4.51 average score) that they would recommend the TSTP to colleagues interested in translational science.

To assess the effectiveness of building professional networks for the participants we asked a simple “Yes” or “No” question about their intentions to contact any of the speakers about their research or career. Nearly 90% of respondents indicated they would be following up with a presenter in some capacity.

In the 2014 and 2015 iterations of the two-day bootcamp we also instituted a pre- and post-bootcamp test to gauge the effectiveness of our instructors in conveying the key points of their sessions. This pre- and post-test was administered using an interactive surveying technology to poll the audience at the beginning of day one and the end of day two. At the beginning of the bootcamp a majority of the participants were unable to answer more than half of the questions correctly, demonstrating the lack of previous knowledge of translational science and the importance of having such a program focused on this field. At the conclusion of the TSTP bootcamp, a majority of participants doubled their correct response rate suggesting that they understood the material presented.

Participant evaluation of the pre-clinical development workshop also indicated a strong level of effectiveness and support. Of the 20 participants in the 2015 workshop, nearly all strongly agreed that it increased their knowledge and understanding of how the pre-clinical phase of translational science is conducted (4.85 average score) and would recommend the workshop to colleagues interested in learning more about translational science (4.95 average score) (Table VII). A vast majority also reported favorably on their experiences in the small group discussions and indicated they walked away with a better understanding of how to translate their own particular research project (4.7 average score). Additional comments from participants emphasized that more time should be allocated to the tour of the research facilities, and that the small group discussions should have a more defined and uniform structure.

Conclusions

The Translational Science Training Program exposes graduate level scientists to a budding scientific field with great potential. Through the program, graduate students and postdoctoral trainees at the NIH learn about the field of translational science and the process by which a basic science discovery leads to a tangible benefit to patient and public health. They are also introduced to a variety of career options within the translational field both at and away from the bench. Overall, we have found the program to be very successful. The data from the surveys strongly indicates that the program is expanding the participants’ understanding of translation and careers within the field. *Also, we have been able to identify the career status of 119 past participants of the program. 45 (37.8%) of those fellows are still in the same training positions as when they participated in the course. Of the remaining 74 fellows, 56 (75.7%) currently hold a position within the translational science field while the remaining 18 (24.3%) have scientific career positions outside the field. Anecdotally, many of those 53*

fellows currently work in translational science have told us that that the program was a strong factor in either their decision to pursue their current line of work, or in providing them with the knowledge and confidence to obtain their current positions. We have utilized the alumni/ae from the TSTP to both contribute to the course as panelists, to participate in the program as project scientists for the pre-clinical development workshop and as networking contacts for other TSTP fellows. In the future, we hope to more formally engage alumni/ae from this program to further strengthen the professional networking opportunities. We hope that the TSTP structure described here can be a model used by academic institutions and other translational research organizations to continue to educate and train tomorrow's translational scientists.

Acknowledgments

The authors would like to acknowledge the leadership, guidance and support of Dr. Sharon Milgram, OITE, and Dr. Dorit Zuk, NCATS. Special thanks is owed to previous co-organizers of the TSTP, including Dr. Rajesh Ranganathan and Ms. Neely Gal-Edd, who were instrumental in launching the program. We would also like to thank the multiple scientific and administrative staff at NCATS who volunteered their time to help implement the workshop component, in particular Dr. Nathan Coussens and Dr. Stephen Kales. Financial support for the TSTP was provided by the NIH Office of Intramural Training and Education.

Figure 1.
Flowchart of the Translational Science Training Program.

Table I

Agenda of the TSTP Bootcamp.

Day 1	Duration	Day 2	Duration
Welcome & Introduction	0.5 h	Clinical Trial & Drug Development Planning	2 h
Bench-to-Bedside Overview	1.25 h	FDA – New Drug Evaluation & Review	1 h
Target Validation	2 h	Marketing and Product Launch	2 h
Intellectual Property & Patenting	1 h	Panel Discussion on the Realities of the Biopharmaceutical Industry	2 h
Pre-clinical Development & IND-Enabling Studies	2 h		
NCATS Clinical and Translational Science Award (CTSA) Program	1 h		

Table II

TSTP Bootcamp modules, key terms and key concepts.

Module	Key Terms	Key Concepts
Bench-to-Bedside Overview	<ul style="list-style-type: none"> - Drug - Drug Discovery - Drug Design - Pharmacodynamics - Pharmacokinetics - Toxicity - Therapeutic window 	<ul style="list-style-type: none"> - Different factors involved in disease causation - How pharmaceuticals work - Perceptions versus realities of pharmaceutical companies' profits and motives - Drug development pipeline, timeline and costs - "Eroom's law" - <i>In vitro</i> Diagnostics' (IVD) role in the patient treatment scheme - Challenges facing the IVD market
Target Validation	<ul style="list-style-type: none"> - Target - Node - Serendipity and folk medicine - Human genetics - Fast followers - Pathway genetics 	<ul style="list-style-type: none"> - Different ways to choose a target - Contrast the organization of basic research (disease specific) versus industry research (common targets for multiple indications) - How common target approach can help eliminate lost revenue in clinical trials development
Intellectual Property and Patenting	<ul style="list-style-type: none"> - Non-Disclosure Agreement - Material Transfer Agreements - Cooperative Research and 	<ul style="list-style-type: none"> - Purpose of the patent is to encourage the sharing of ideas - Rights a patent grants

Module	Key Terms	Key Concepts
	<ul style="list-style-type: none"> - Development Agreements - Patents 	<ul style="list-style-type: none"> - Different types of patents - The requirements, cost and timeline for filing a patent - Sections of a patent and key points to each, especially the "Claims" section
Pre-clinical Development and IND-Enabling Studies	<ul style="list-style-type: none"> - Efficacy - Safety - ADME - Bioavailability - Toxicity - Animal Modeling - New Molecular Entity (NME) - NME properties - cLogP - Solubility - Permeability - <i>In vivo</i> clearance - Investigative New Drug (IND) 	<ul style="list-style-type: none"> - The cost of development increases exponentially as it moves through the development process - Pre-clinical development that is predictive of failure or success in clinical trials can lower the overall cost of drug development - Efficacy and safety responsible for 80% of failures for drug candidates in clinical trials - Where in the drug development pipeline diagram ADME, PK, bioavailability, toxicity and animal modeling determined - Highlight the team science dynamic of drug development - The PD properties of the drug, formulation and dosing - The IND filing process: timing and cost of moving through the submission process

Module	Key Terms	Key Concepts
		<ul style="list-style-type: none"> - Good Laboratory Practices: why there were started and the purpose they serve
NCATS Clinical and Translational Science Award (CTSA) Program	<ul style="list-style-type: none"> - CTSA - Translational science workforce - TL1 research training grant - KL2 mentored career development grant 	<ul style="list-style-type: none"> - CTSA program is an innovative national network of medical research institutions working together to improve the translational process - CTSA hubs train and cultivate the translational science workforce and provide opportunities for pre- and post-doctoral training in clinical translational science - The CTSA program offers grant support for research training, mentored career development, and workforce development - Training is provided in non-traditional skills such as regulatory science, entrepreneurship and team science - Degrees (MS and PhD) are offered in clinical and translational science
Clinical Trial and Drug Development Planning	<ul style="list-style-type: none"> - Drug Development Plan - Phase I, II, III and IV - Dose Tolerance - Dose Escalation - Dose range 	<ul style="list-style-type: none"> - Successfully taking a product through clinical trials requires preparation - Requirements and determinations for each Phase (I–IV)

Module	Key Terms	Key Concepts
	<ul style="list-style-type: none"> - Dose limiting Toxicity - Placebo - Efficacy - Standard of Care - Surrogate endpoint - Draft package insert - cGMP 	<ul style="list-style-type: none"> - Reasons to stop a trial in each phase and ramifications of such decisions - Review the actual data from the clinical trial of Imatinib, emphasizing how unusual it is - Consider how a drug development plan differs for a large pharmaceutical compared to a small company - Emphasize the overall goal of the drug development plan is to submit a New Drug Approval to the FDA and receive approval
FDA – New Drug Evaluation and Review	<ul style="list-style-type: none"> - NDA - Fast Track - Breakthrough Therapy - Priority Review - Accelerated approval 	<ul style="list-style-type: none"> - Introduce the seven person review team assigned to each application - Place the timing of submitting an NDA in the context of the entire drug development pipeline - Lay out six step process of review: Pre-submission activities, Process the submission, Create a review plan, conduct the review, take official action and handle post action feedback - Walk through a case study submission that raised concerns and how the concerns were addressed - Different expedited programs and the

Module	Key Terms	Key Concepts
		consideration for each
Marketing and Product Launch	- Marketing	- The critical elements of marketing
	- Sales	-
	- Features	- Why marketing is important
	- Advantages	- Differentiate between marketing and sales
	- Benefits	-
	- Market Dynamics	- How market dynamics affect the product development
	- Product levers	- How marketing levers drive a product's market value
	- SWOT	- Introduce marketing messages and the SWOT analysis.

Table III

Agenda of the TSTP Pre-clinical Development Workshop.

Module	Duration
Welcome & Introduction to Pre-clinical Development	0.75 h
Target Identification & Validation	0.5 h
Assay Development & Design	0.5 h
Therapeutic Development and De-risking	0.5 h
Pre-clinical Development for IND Submission	0.5 h
Tour of Pre-clinical Innovation Research Facilities	0.5 h
Small Group Discussions	2 h
Networking with Translational Scientists	0.75 h

Table IV

Outline and evaluation questions for the translational science exercise.

Section	Instructions	Evaluation Questions
Research Project Title	Provide a brief title describing your hypothetical translational science project mentioning your target and the disease you are intending to develop a treatment for.	
Target Biology and Disease Relevance	Provide a brief overview of the role of your target in normal human physiology and its disease relevance as a potential target for therapeutic development. If you are studying a particular disease without a known molecular basis, describe what targets could potentially play a role in disease etiology. If you are having difficulty establishing a link between your particular area of research and therapy development, you are welcome to discuss an alternative therapeutic target you are interested in. <i>(250 word limit)</i>	<p>Did the applicant:</p> <ul style="list-style-type: none"> - Identify a specific biological target? - Clearly explain the known or hypothetical relationship between the function of the target and its role in normal human physiology? - Clearly explain the known or hypothetical relevance of the target to a human disease?
Specific Aim 1 – Target Identification/Validation	Describe how you would identify and validate a molecular target that plays a role in disease development or progression. If your target is already known and validated, provide a brief summary of the available information to demonstrate this. <i>(250 word limit)</i>	<p>Did the applicant:</p> <ul style="list-style-type: none"> - Describe a methodology that either was used or could be used to identify the target? - Describe a methodology that either was used or could be used to validate the target? - Demonstrate a general understanding of the types of methods used at this stage of pre-clinical development?
Specific Aim 2 – Assay Development	Describe at least one type of assay you could use to screen compounds against your target. Include the appropriate cellular environment, assay technology needed, and what the assay readout would be. <i>(250 word limit)</i>	<p>Did the applicant:</p> <ul style="list-style-type: none"> - Describe at least one screening assay that is scientifically plausible? - Include sufficient detail to provide the reviewer with a general understanding of the parameters of the assay?

Table V

TSTP Pre-clinical development workshop presentations and associated key concepts.

Presentation	Key Concepts
Introduction to Pre-clinical Development	<ul style="list-style-type: none"> - The need for translational science to be conducted as a team sport engaging experts from diverse backgrounds - Examples of deliverables from each stage of the pre-clinical development pipeline - Description of exemplary cases of drug development at the institution
Target Identification & Validation	<ul style="list-style-type: none"> - Methods for detecting and visualizing RNAi off-target effects - Bench-level controls for small interfering RNA experiments
Assay Development & Design	<ul style="list-style-type: none"> - Types of high throughput screening (HTS) assays and current examples of HTS assay design - Equipment and materials needed to conduct HTS assays, such as low volume liquid dispensers, compound transfer devices, fluorescence and luminescence detectors, and the robotic systems enabling HTS automation - Impact of assay artifacts on data quality, demonstrated through an example of compound fluorescence overlapping with the assay readout - Importance of investing the time to differentiate a true hit from a false positive during the design phase
Therapeutic Development and De-Risking	<ul style="list-style-type: none"> - Overview of the experimental steps needed to optimize compounds once they have been identified, and subsequently verified, as hits in HTS assays - Evaluation of compound efficacy in pharmacologically-relevant assays - Measurement of pharmacokinetic and pharmacodynamic properties/parameters in model organisms - Continual medicinal chemistry optimization - Strategies for selecting a suitable method of drug formulation and delivery
Pre-clinical Development for IND Submission	<ul style="list-style-type: none"> - Experimental data required to submit an investigational new drug (IND) application to the FDA in order to receive approval for a Phase I first-in-human clinical trial - PK/ADME/Tox studies and correlative histopathology in vertebrates - <i>In vitro</i> genetic toxicity studies - Good manufacturing practices (GMP) to ensure compound quality - Assessment of compound stability - Initial planning of clinical trials

Table VI

TSTP Bootcamp Satisfaction Survey Results; responses based on a Likert scale, 5=strongly agree.

Evaluation Statement	Response Average
The TSTP increased my knowledge and understanding of what translational science is about. (n=95)	4.62
Participation in the TSTP provided me essential career exploration and development opportunities. (n=94)	4.12
I would recommend the TSTP to colleagues interested in learning more about translational science. (n=96)	4.51

Table VII

Pre-clinical development workshop participant survey results; responses based on a Likert scale, 5=strongly agree.

Evaluation Statement	Response Average
The NCATS Workshop increased my knowledge and understanding of how the pre-clinical phase of translational science is conducted. (n=20)	4.85
I would recommend the NCATS Workshop to colleagues interested in learning more about translational science. (n=20)	4.95
The small group discussions with NCATS scientists helped me better understand how to translate my research. (n=20)	4.7