

# Promoting Translational Research in Academic Health Centers: Navigating the “Roadmap”

Timothy P. Cripe, MD, PhD, Blythe Thomson, MD, Thomas F. Boat, MD, and David A. Williams, MD

## Abstract

The translation of hypothesis-driven research laboratory findings about basic disease mechanisms into clinically useful tests or therapies, particularly in pediatric diseases, is time-consuming, expensive, and not well supported by traditional research grant mechanisms. Accordingly, the development of new drugs and clinical assays has typically been largely the domain of the pharmaceutical industry. Aside from partnering with for-profit companies, academic health centers are challenged to find ways to actively engage in biomedical research to bridge the gap between basic and clinical research. The Translational Research Initiative (TRI) at Cincinnati Children’s

Hospital Medical Center was launched in 2001 with the mission to build an institutional infrastructure for promoting and facilitating the clinical implementation of investigator-initiated basic research.

The TRI’s goals are to provide grant support for proposals that are translational in nature and that address serious diagnostic or therapeutic deficiencies in pediatric illnesses; to create and support specialized research cores and a specialized office that provides support for research protocol development and regulatory affairs; and to organize educational opportunities

focused on bridging communication between basic and clinical scientists and encouraging multidisciplinary interactions. The authors describe the program structure and provide an interim outcome report as measured by extramural funding obtained, Investigational New Drug applications filed, manuscripts published, clinical trials launched, and educational initiatives created. The broad success of this program suggests that it might serve as a model for other academic health centers in promoting and conducting translational research.

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**E**lucidation of basic disease mechanisms largely results from hypothesis-driven research at academic health centers, giving rise to innovative ideas for diagnosing and treating human disease. Yet translating laboratory findings into clinical practice has always been difficult. The barriers are protean,

spanning inadequate laboratory models of human disease, technical problems with large-scale production of cellular and molecular reagents with appropriate quality control, and the complexities of human research participant enrollment and outcome analysis. A recent survey of publications that included a 30-year follow-up showed that only one in five basic research articles that claimed potential human application actually led to a clinical trial, with pharmaceutical industry support being the biggest predictor of success.<sup>1</sup> Furthermore, only one in 100 clinical trials resulted in a new therapy. Due to the enormous scope of expertise and financing required for drug development and early-phase human clinical trials, much of early clinical research is conducted in the for-profit industry sector, with the goal of eventually recouping and exceeding investments through pharmaceutical sales. In addition, successful translational research has become increasingly burdened in recent years by new layers of regulatory, ethical, scientific, informatic, financial, and workforce challenges.<sup>2</sup> Phase 1 testing in humans, designed to determine safety and often to measure drug metabolism, and phase 2 testing,

designed to assess efficacy, are generally costly and labor-intensive for participants and clinicians because of the many unknowns about a new treatment. (Later stage clinical trials such as phase 3 [randomized, controlled trials] and phase 4 [postmarketing trials] are not considered by most investigators to be “translational.”) The recognition of these hurdles has led to calls at the national level for dramatic changes in the conduct of biomedical research.<sup>3</sup>

In 2003, Elias Zerhouni, director of the National Institutes of Health (NIH), announced a new “roadmap” to guide the reorganization of NIH-funded biomedical research.<sup>4</sup> An integral component of that initiative is an effort to “reengineer the clinical research enterprise,” in part by strengthening and enhancing scientist–clinician interactions and translational research. Vital to this effort is the education and training of investigators who will specialize in translational research.<sup>5</sup>

The development of translational research is particularly difficult in pediatric diseases due to the small numbers of patients in many serious

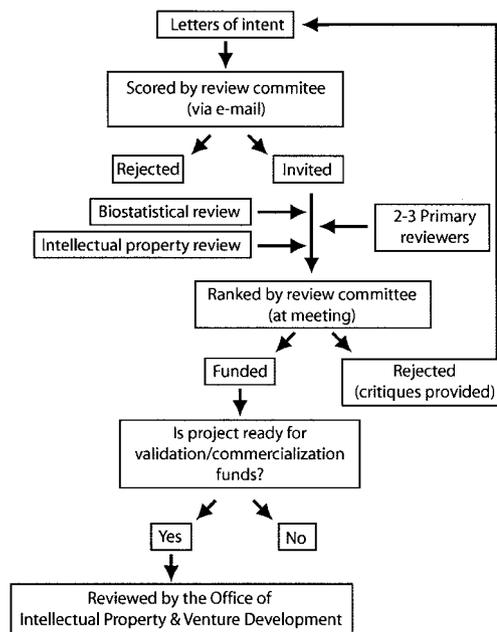
**Dr. Cripe** is associate professor of pediatrics, Division of Hematology/Oncology, Cincinnati Children’s Research Foundation, University of Cincinnati College of Medicine, Cincinnati, Ohio.

**Dr. Thomson** is clinical associate professor, Seattle Children’s Hospital and Medical Center, Seattle, Washington.

**Dr. Boat** is B. K. Rachford Professor and chair of pediatrics, Division of Pulmonary Medicine, and director, Cincinnati Children’s Research Foundation, Cincinnati Children’s Hospital Medical Center, University of Cincinnati College of Medicine, Cincinnati, Ohio.

**Dr. Williams** is Beatrice Lampkin Chair in Oncology, professor of pediatrics, associate chair of translational research, and director, Division of Experimental Hematology, Cincinnati Children’s Research Foundation, University of Cincinnati College of Medicine, Cincinnati, Ohio.

Correspondence should be addressed to Dr. Cripe, Division of Hematology/Oncology, MLC R7015, 3333 Burnet Avenue, Cincinnati, OH 45229; telephone: (513) 636-7241; fax: (513) 636-3549; e-mail: (timothy.cripe@cchmc.org).



**Figure 1** Application and review process for support for Translational Research Initiative (TRI) projects at Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio.

disease categories, the reluctance of parents to enroll children in “experimental” therapies, and the ethics of informed consent in phase 1 trials in children. Prior to the NIH's strategic proposal, in 2001 the Translational Research Initiative (TRI) was established at Cincinnati Children's Hospital Medical Center (CCHMC). Approved by the Board of Trustees and implemented by the associate chair for translational research, the TRI's mission is to stimulate translational research among local principal investigators. The strategy to fulfill this mission includes:

- providing grant support for proposals deemed translational in nature and addressing serious diagnostic or therapeutic deficiencies in pediatric illnesses;
- building an institution-wide infrastructure, including specialized research cores and a specialized office, the Translational Research Trials Office (TRTO), that provides support for research protocol development and regulatory affairs; and
- organizing educational opportunities, such as retreats, symposia, and workshops, focused on bridging communication between basic and clinical scientists and encouraging multidisciplinary interactions.

Here we describe each of these aspects of the TRI and provide a summary of its accomplishments as of 2005.

### Translational Research Initiative Financing and Business Plan

The development of the TRI was stimulated by the CCHMC Board of Trustees, which sought to increase the speed with which the investment in basic research was translated into improved patient outcomes. In an effort to stimulate this activity, the board approved using a portion of operating margins generated from the clinical activities of the hospital. This reinvestment of margins reflected the board's belief that the TRI had significant potential to advance the institutional vision and potentially expand future revenue streams. Based on a proposed business plan, this investment included \$1 million per year for a period of five years. The plan targeted \$700,000 for “stimulative funding” in the form of grant support, \$210,000 for a protocol development and regulatory affairs core (mainly personnel expenses), and \$90,000 for other expenses (such as retreats, symposia, and protocol-specific support). The CCHMC is an institution with an NIH funding base of approximately \$100 million per year. The investment in the TRI was made with the

expectation that the key missions of the institution, namely, research, education, and patient care, were optimally supported by a more proactive program that emphasized the impact on human health of the institution's research, in addition to more traditional metrics used and typically measured by medical centers, such as patient volumes and NIH grants. Additionally, long-term expectations included enhanced patient referrals on a national basis, increased intellectual property activity, and increased leverage for pharmaceutical and NIH grant opportunities. The grant support review process evolved to specifically address intellectual property issues in an effort both to assure rigorous property protection and to identify attractive opportunities for commercialization early in the development process. Royalties from any intellectual property are dispersed via institutional guidelines already in place at the CCHMC. Since there was no apparent model for this program available, the initial funding period was developed as a pilot project with external review and an opportunity for renewal of the program after the initial five years.

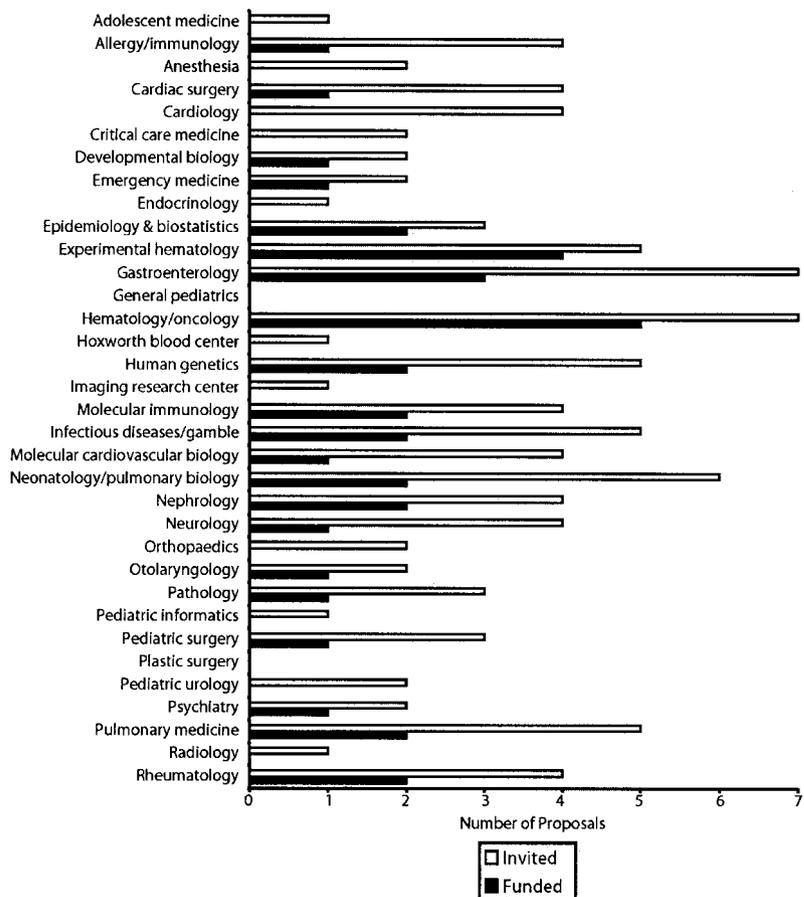
### Research project grant support

The Translational Research Initiative at Cincinnati Children's Hospital Medical Center encourages and supports researchers and clinicians undertaking translational research projects in part through a research project award mechanism. The annual budget for the awards program is approximately \$700,000. An annual competition uses peer review by a committee of 22 investigators who represent 18 divisions of the Cincinnati Children's Research Foundation (CCRF). The application and review process is outlined in Figure 1. An initial letter of intent (two-page limit) is reviewed by the full committee and scored on a 1–5 scale similar to the five-point scale the NIH uses for evaluating research proposals. Full applications are invited from 50% to 70% of investigators based on how their initial letters of intent are scored. Invited applications are assigned two to three primary reviewers, who submit written critiques. The applications are then discussed and ranked during a meeting of the review committee, and critiques are adjusted based on the discussion. Committee members involved in the project or those who have academic appointments in the

same division as an applicant or co-applicant leave the room during the discussion to avoid potential conflicts of interest. The written critiques serve as feedback for the applicants, with reviewers' names removed. Rejected applicants may resubmit during the next grant cycle. Following identification of the top-ranked applications, the review committee recommends funding priorities to the director of the CCRF. Subsequently, funded projects are re-reviewed by the separate, independent CCRF Office of Intellectual Property/Venture Development for consideration of additional commercialization or validation funds. A multidisciplinary Internal Advisory Committee, made up of CCHMC faculty leaders with appointments in ten divisions, advises the program with respect to the annual grants review process and prioritization of resources.

In the first three years of the program (2001–2003), letters of intent were received from 135 investigators in 34 different CCHMC divisions and programs, full applications were invited from 100 applicants in 32 divisions and programs, and funding was provided to 30 individuals for 31 separate projects in 21 divisions and programs (see Figure 2). NIH-type priority scores averaged 207 (median 194), with a range of 131–183 for funded applications and 191–366 for unfunded applications. Four of five resubmitted projects were approved and funded. The direct costs awarded through June 2004 totaled \$2.35 million.

We surveyed funded investigators in November 2004 to determine the outcome of their projects. At the time of the survey, TRI support had directly led to the publication of 26 peer-reviewed manuscripts (with three others in review). In addition, ten subsequent extramural awards (plus ten others in review), including R01, R24, P01, U01, and SBIR grants and foundation awards, were attributed to initial pilot support from the TRI. The total direct cost of these awards was approximately \$4 million, plus a single award of about \$15 million for a large multicenter clinical trial consortium (total approximately \$19 million), which suggests that investigators have been very successful in using TRI grants to secure external grant funds. Five patents have been filed that were attributed in part to TRI support.

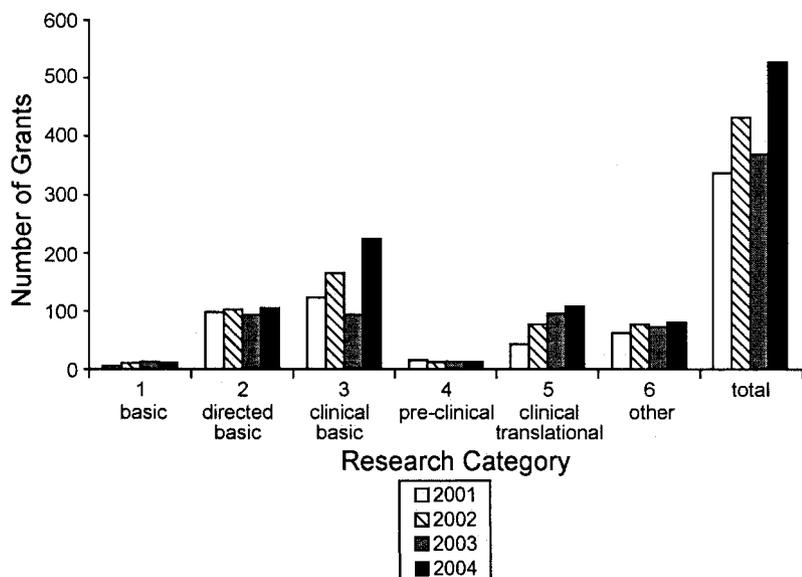


**Figure 2** Outcome of grant applications for all divisions that submitted letters of intent to the Translational Research Initiative (TRI), Cincinnati Children’s Hospital Medical Center, Cincinnati, Ohio. Those applicants invited to submit full proposals are shown as “invited,” while those who actually received funding are shown as “funded.” Divisions with no bars submitted one or more letters of intent, but none were invited to submit full proposals.

Finally, the TRI funds were instrumental in facilitating the creation and opening of five clinical trials by CCHMC investigators, with an additional trial in development.

To determine if the TRI had any overall discernable impact on the types of external grants that have been successfully awarded to investigators at the CCHMC, one author (TFB) assigned the awarded grants for the four-year period since the establishment of the TRI to one of six categories. These categories are: (1) basic research, (2) directed basic research (related to child health), (3) clinical problem-focused basic research (related to child health), (4) preclinical translational research (conceptual formulation, design, and preclinical [nonhuman] testing of a range of diagnostic and therapeutic products and procedures, as well as health services processes), (5) clinical translational research (includes phases 1 through 4

clinical trials and assessments of clinical effectiveness), and (6) other research (e.g., studies to improve or enhance teaching). As Figure 3 shows, there has been a significant increase in the total number of extramural grants received by the CCHMC since the inception of the TRI program, primarily due to an increase in problem-focused basic research related to child health and clinical translational research grants (categories 3 and 5). A relatively consistent number for grants was observed over time in the other categories. Of note, very few preclinical translational research grants (category 4) were obtained in any of the years, consistent with our supposition that these types of grants are not well supported by traditional NIH mechanisms. While these category 4 studies make up the bulk of TRI-funded proposals and are often designed to lead to category 5 studies, it is tempting to



**Figure 3** Number of grants awarded to the Cincinnati Children's Research Foundation (CCRF) by year, organized by type of grant.

speculate, but difficult to confirm, that the TRI program directly resulted in the increased category 5 studies.

### Infrastructure for Translational Research

In an effort to build an institution-wide infrastructure to support and enhance translational research, TRI organizers have focused on support for protocol development and regulatory affairs and the creation of innovative, specialized core facilities and services.

### Protocol development and regulatory support

The Translational Research Trials Office (TRTO) was established to facilitate early phase trials involving human participants. Specifically, the office targets trials requiring an Investigational

New Drug (IND) filing with the U.S. Food and Drug Administration. Members of the TRTO include a research nurse, a physician's assistant, a biostatistician (10% time), and two clinical research associates (four full-time equivalents). The CCHMC's TRTO medical director devotes 20% of his or her total time and effort to the TRTO's functions as well. The annual operating budget of the office is approximately \$200,000. While much of this financial support is derived from the originally committed \$1.1 million from clinical revenues as described in the business plan, funding for 1.1 full-time equivalents has been obtained so far via an NIH program grant. The TRTO members are well versed in regulations from both federal and local oversight bodies. These regulations are complex and change often, which highlights the

increasing need to have the individuals who are dedicated on an ongoing, daily basis to translational research remain current with these important policies. See List 1 for the services provided by the TRTO to local investigators.

The TRTO has helped manage phase 1 investigator-initiated gene transfer trials for several genetic diseases; many biological studies in hematologic, immunologic, pulmonary, and genetic research; and monoclonal antibody trials (see Table 1). The office has also provided help to over a dozen divisions in trial initiation, monitoring, and design. Additionally, the TRTO has worked with the regulatory oversight committees at the CCHMC to address patient safety in early phase human trials and to assist with an organized approach to institutional guidelines regarding data safety monitoring, data safety, and data management. The TRTO has developed a templated process for establishing Data Safety Monitoring Boards that is now widely adapted by the institution.

To ensure high quality during the execution of clinical trials supported by the TRTO, an internal oversight plan has been established. Each proposed treatment protocol undergoes scientific review by the Scientific Review Committee of the University of Cincinnati General Clinical Research Center (prior to patient recruitment) and protection of human safety review by the CCHMC Institutional Review Board. Because these committees existed at the CCHMC prior to the development of the TRI, the program added only minimally to the institutional commitment of peer review. The TRTO members meet weekly to review all active protocols. Additionally, internal quality assurance reviews and audits occur monthly on all research protocols, with quarterly and annual reports for internal quality improvement objectives.

The protocol development and regulatory affairs services of the TRTO have facilitated the successful application of one clinical trial network award, funded by the National Center for Research Resources Rare Lung Disease Consortium (U54-RR019498-01). Bruce Trapnell is the primary investigator; the award, in the amount of \$5,520,790, is for 2003–2008. Thus the TRTO receives fiscal support from the Rare Lung Disease

### List 1

#### Services Provided by the Translational Research Trials Office (TRTO), Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio

- Designing phase 1 investigator-initiated clinical studies
- Submitting protocol to local and federal regulatory bodies
- Investigational New Drug (IND) applications
- Organizing regulatory documents
- Protocol review and monitoring
- Scientific review
- Internal and external audit assistance
- Statistical support
- Data safety monitoring board management
- Data safety monitoring plan creation
- Recruiting participants
- Obtaining proper consent/assent
- Data management and analysis

Table 1

**Description of 26 Translational Research Protocols Managed by the Translational Research Trials Office (TRTO), Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio\***

Type of clinical trial protocol	No. protocols	No. patients enrolled to date
<b>Gene transfer protocols</b>		3
Active	1	
Inactive	1	
In application process	1	
In development	3	
<b>Current protocols requiring an Investigational New Drug (IND) application</b>	3	
<b>Pending protocols requiring an IND</b>	5	
<b>Active protocols requiring patient consent</b>	14	
<b>Biologic studies (nonconsenting)</b>	12	
<b>Normal donor protocols (consenting)</b>	4	
Peripheral blood stem cell		40
Bone marrow		60
Normal blood		12 <sup>†</sup>
Umbilical cord		197
<b>Studies involving clinical protocol management, excluding normal donors</b>	6	5
<b>Studies co-managed with the Division of Hematology/Oncology Clinical Research Office</b>	1	11

\* Some protocols fall into more than one category; therefore the sum of the number of protocols listed is greater than 26.

<sup>†</sup> Opened in the spring of 2005.

Consortium to assist in development and monitoring of clinical trials related to rare lung diseases.

### Specialized cores

Specialized core research facilities and services are designed to centralize services in order to improve quality control, provide shared services that are difficult to establish by individual investigators, produce an economy of effort, and/or save overall costs for investigators. Cores supported by the TRI may include laboratory and clinical facilities, equipment, and services that are shared by multiple investigators. The TRI has been primarily interested in supporting new, innovative cores that promote the mission of building a local or networked infrastructure for conducting preclinical or translational research. Established cores seeking bridge or supplemental funding, or cores that primarily support basic (discovery) research, have not been a targeted priority for TRI funding.

Applicants hoping to implement a new core are asked to provide a description of the services to be provided and the

background and significance for the core, as well as a clear description of methods and services to be provided and, where appropriate, discussion of human participants protection and inclusion and a data safety monitoring plan. Cores may contain a non-hypothesis-driven research activity, provided that the research is designed to improve core services. Proposals for new cores also need to include a discussion of the decision making processes for core activities such as prioritization of services and allocation of resources, the establishment of any necessary oversight committees, and the planned mechanisms for promoting communication and collaboration among users of the core. The TRI supports an initial two years of funding for each core; a plan for funding beyond this period is an essential part of a new core proposal.

To date, two innovative cores have been created by the TRI through the award mechanism: the Fanconi Anemia Cell Repository and the Human Milk Bank. A third core, the Normal Human Hematopoietic Stem Cell Core, is

managed by the TRTO. In this program, there are four different normal donor protocols directed to the collection of umbilical cord blood, peripheral blood, G-CSF mobilized peripheral blood stem cells, and bone marrow. All three of these cores include de-identified collection of human biological samples and clinical data accessible to any investigator for use in an IRB-approved research study.

Each of the cores is being actively used by multiple investigators. The Children's Hospital Fanconi Anemia Comprehensive Care Center has opened eight phase 1 trials that use the Fanconi Anemia Cell Repository. After two years of research, 86 samples have been collected and tracked in the repository from 17 different subjects with this rare disease. Eight active projects involve the Human Milk Bank. These eight projects involve multidisciplinary teams from nine internal CCHMC divisions (Center for Epidemiology and Biostatistics, Infectious Diseases, General and Community Pediatrics, Neonatology, Immunobiology, Allergy and Immunology, Human Genetics, Endocrinology, and Neurology) as well as external collaborators. The projects span a variety of topics, including the presence and roles in milk of adiponectin, CMV, vitamins E and Q10, contaminants, interleukin-11, beta-defensins, and oligosaccharides. A description of this core has been published.<sup>6</sup> Finally, 11 projects being conducted by 11 different investigators in three CCHMC divisions have been supported by specimens procured through the Normal Human Hematopoietic Stem Cell Core.

To help manage collection, storage, and distribution of biological samples through the cores, the TRTO has worked with the CCRF Division of Biomedical Informatics to create a Health Insurance Portability and Accountability Act (HIPAA)-compliant specimen repository database linked to a protocol management system, the Biological Specimen Tracking System (BSTS) and Protocol Manager. Researchers use Protocol Manager to track the protocol from the concept stage, through regulatory oversight, to informed participant consent, data acquisition, and management. The system sends reports to both internal and external regulatory agencies with electronic reminders to the principal investigator. It is important to

note that Protocol Manager is linked to the companion system, the BSTS, allowing samples to be collected, de-identified with a bar coded system, and tracked throughout processing and storage using handheld technology. Protocol Manager enables researchers to control the scope and accuracy of data collection for multiple research studies at different sites. From participants' enrollment and physical examinations to specimen collection and lab reports, use of the Protocol Manager system helps investigators cover many aspects of data collection while ensuring complete security and ongoing compliance with regulatory guidelines. Investigators can request new services from laboratories and track the status of their requests. Using handheld technology, lab managers can scan samples with barcodes, annotate any activities they perform, and synchronize with a centralized Web-based database. Lab personnel can also run customized reports, including inventory and dispense summaries. This template can be used for all divisions of the CCHMC that need to create a complete biological database. Protocol Manager is distributed by ItCube, Inc.<sup>7</sup>

### Translational Research Training

To encourage translational research, the TRI has developed both formal and informal educational programs for the academic community at the CCHMC. The TRTO organizes an annual symposium attended by members of the CCHMC and University of Cincinnati communities. The focus of each symposium is to address current issues facing investigators involved with translational research (see Table 2). Keynote speakers for each symposium have been national experts in translational research, and attendance has ranged from 60 to 140 participants. Additionally, the TRTO has provided matching funds for 11 retreats organized by investigators in different divisions.

The TRI has also been instrumental in developing a postgraduate translational research training track primarily for persons currently undergoing subspecialty training. Highlights of the program include basic courses in epidemiology and biostatistics, components of an IND application, design of early phase clinical trials, and

Table 2

**Symposia, Workshops, and Retreats Sponsored by the Translational Research Trials Office (TRTO), Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio**

Educational session type	Program title
TRTO-initiated education	Phase 1 Research in Children: Legal, Ethical, and Regulatory Issues
	Developing Phase 1 Trials
	Negotiating Clinical Research at the CCHMC
	Good Clinical Practices
Division-initiated program development	Translational Research in Allergy and Immunology
	Research and Education in Intestinal Disorders*
	Strategic Planning in Bone Marrow Transplantation Research
	Local FOCIS (Federation of Clinical Immunology Societies) Chapter*
Research presentations that facilitated collaborations	Gene Therapy
	Cystic Fibrosis
International workshops	Stem Cell Clonality and Genotoxicity (San Diego, CA)
	Second Stem Cell Clonality and Genotoxicity (St. Louis, MO) <sup>†</sup>
	Rare Lung Diseases (Cincinnati, OH)

\* These workshops proved useful in developing subsequent grant applications.

<sup>†</sup>Frederickson RM. Report from the 2nd stem cell clonality and genotoxicity retreat. *Mol Ther.* 2005;12:379–383.

courses reviewing disease-specific translational research. This program is now supported by a National Center for Research Resources K30 grant, the University of Cincinnati Clinical Research Curriculum Award (K30-RR022273). Joel Tsevat is the principal investigator; the \$1,500,000 award is for 2005–2010. The program is in the final stages of development, with the expectation that it will be open for enrollment beginning in 2006.

### Conclusions

The successful conduct of translational research poses a unique set of challenges, which have only recently begun to be addressed at the national level. Fostering preclinical and early phase human research is essential to advance the practice of medicine. The difficulties inherent in performing such work have been imposing for academic physicians and scientists, especially in the area of pediatric diseases. An organized approach to conducting translational research is therefore essential for academic health centers to succeed at the frontier of clinical research.

To encourage translational research by local investigators, we have developed the

Translational Research Initiative at Cincinnati Children's Hospital Medical Center. In its first three years, the TRI has facilitated a grants program that has led to extramural funding and numerous publications, developed several central repositories of normal and diseased tissues that are widely available to basic researchers, assisted multiple investigators in filing IND applications, and helped establish and/or manage over 25 clinical trials. As an example, the largest users of the TRI are the CCHMC's Divisions of Hematology/Oncology and Experimental Hematology. In the four years prior to the implementation of the TRI, the only IND applications filed by these divisions were for compassionate-use, single-patient INDs. Since the initiation of the TRI, these divisions have successfully filed four IND applications for new therapies. Several of these are highly complicated gene therapy trials. One IND application has been filed for compassionate use. To foster physician–scientist interactions and education, the TRI has organized an annual educational symposium and provided support for many interdisciplinary retreats and workshops. Registration for the 2005 symposium on good clinical practices reached the room capacity of 220 within

three weeks of the announcement, and more than 50% of the registrants were physicians. The TRI has also developed a new postgraduate training track in translational research. As a result of this initial effort, the CCRF has also developed a standing Working Group on Interdisciplinary Collaboration and Coordination to further enhance cross-disciplinary interactions.

The TRI appears to have succeeded in its short-term goals of assisting in the development of clinical trials and beginning to build an institutional infrastructure of projects and cores in translational research. There has been a concurrent increase in funded awards in clinical translational research since the inception of the program, though due to the many variables that determine funding trends, it is not possible to definitively ascribe this increase to the TRI program. A long-term goal of actually changing health outcomes for patients, while likely to result in part from these efforts, has yet to be realized.

To date, the TRI has continued to be largely supported by hospital clinical revenues, with only a minor portion of its operating budget derived from extramural grant support. When the original five-year funding expires, as proposed in the renewal of the program, NIH funding opportunities will be aggressively pursued, and a "charge-back system" based on an extensive menu of available services offered by the TRTO to principal investigators will be used to offset in part the institutional commitment. Charge-backs will be focused on use of the TRTO, the protocol development and regulatory affairs office. In addition, translational cores will be expected to become largely independent of CCHMC funding, relying instead on external funding and charge-back

mechanisms. We believe the development and funding of the NIH roadmap<sup>4</sup> will allow new opportunities for funding these activities, even in the face of the ongoing constraints on overall NIH funding. The TRTO portion of the TRI has already been included for funding in several NIH program project grant submissions and NIH center grant applications. The structure and success of the TRI grant process has also been used in multiple NIH grant applications as an example of both institutional commitment and successful experience in "Pilot and Feasibility" grants.

One of the unresolved issues that has arisen with the increased emphasis at our institution on translational research is the criteria used for faculty evaluations, reappointment, and tenure. As pointed out in a report by the Clinical Research Roundtable of the Institute of Medicine, there are career disincentives to conduct translational research.<sup>2,3</sup> For example, preclinical translational research is not as readily fundable by traditional funding mechanisms as is hypothesis-driven research. In addition, the effort and time required to complete IND applications, early phase protocol development, and all of the required regulatory steps are extensive. Moreover, the results of these efforts in and of themselves are not publishable, so investigators' accomplishments per unit time are fewer. Thus, the traditional metrics of grants and publications may not be valid indicators of faculty performance. Changes may be necessary at academic health centers in the realm of faculty evaluation and promotion.

As we have described, the TRI has led to extramural grant support, help with protocol development and management of regulatory affairs, an increase in IND application filing, and substantial

attendance at symposia. By these measures, the TRI has been a success. But have we changed health care for any one patient in a meaningful way? This lofty, long-term goal may take years to accomplish, but is likely to be reached earlier as a result of programs such as the TRI. We have presented our experience as a possible model for other centers that wish to engage in translational research. We suggest that through an organized, focused approach dedicated to enhancing translational research, academic health centers can leverage outstanding discovery research in an efficient manner and gain a more prominent role in the integration of basic science research findings with clinical practice.

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## References

- 1 Contopoulos-Ioannidis D, Ntzani E, Ioannidis J. Translation of highly promising basic science research into clinical applications. *Am J Med.* 2003;114: 477–84.
- 2 Sung N, Crowley WJ, Genel M, et al. Central challenges facing the national clinical research enterprise. *JAMA.* 2003;289:1278–87.
- 3 Rosenberg R. Translating biomedical research to the bedside: a national crisis and call to action. *JAMA.* 2003;289:1305–6.
- 4 National Institutes of Health. NIH Roadmap: Accelerating Medical Discovery to Improve Health (<http://nihroadmap.nih.gov/>). Accessed 25 July 2005.
- 5 Crowley WJ. Translational of basic research into useful treatments: how often does it occur? *Am J Med.* 2003;114:503–5.
- 6 Geraghty S, Davidson B, Warner B, et al. The development of a research human milk bank. *J Hum Lact.* 2005; 21: 59–66.
- 7 ItCube, Inc. Cincinnati, OH. ([www.itcube.net](http://www.itcube.net)) Accessed 28 July 2005.