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Implementation and Impact of a Translational Research Training Program in Pulmonary and Critical Care Medicine*

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Abstract

Background—The translation of basic research advances to the clinical arena has been slow and inefficient. With the goal of improving interactions and collaboration between basic science and clinical investigators, we instituted a Translational Research Training Program (TRTP) in acute lung injury to complement our basic science and clinical research training programs in pulmonary and critical care medicine.

Methods—We developed a TRTP in which trainees select a primary research discipline for rigorous development of skills in either basic science research or clinical research. This primary foundation is complemented by cross-training in the other discipline through a specifically designed program of study. To measure the impact of the program, we analyzed publication rates, coauthorship to reflect collaboration between research disciplines, and publication of papers with a translational focus by members of our division before and after the institution of the TRTP.

Results—We describe our new training program, including modifications to our preexisting program and development of new components. We found significant increases in multidisciplinary authorship and translational articles following institution of TRTP.

Conclusions—An explicit TRTP appears to increase collaboration between basic and clinical investigators. Our goal is to share our experiences and provide a template for other pulmonary and critical care programs interested in developing similar curricula. We speculate that this training will improve the translation of basic research findings into clinical advances, thus increasing the probability that successful treatments will be developed for patients with lung diseases.

Keywords

curriculum; education; graduate; medical; pulmonary and critical care; specialty; training

Fundamental knowledge about the biology of inflammation, injury, and repair in the lungs (and other organs) has burgeoned. However, relatively few basic science advances have been translated into clinical benefits for patients with lung diseases and critical illness. This is not limited to pulmonary and critical care medicine (PCCM); the general transfer rate of basic science findings into clinical practice is slow and inefficient.^{1,2} A previous study found that < 1 in 10 basic science studies with potential clinical applications found its way

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into clinical use within 20 years of the original publication.³ Thus, there is a clear need to build a better bridge between basic science and clinical research and practice. A new approach to meeting this challenge is the training of investigators in the field of translational research. Translational research has been defined operationally as the application of basic science discoveries to clinically relevant scenarios and concurrent generation of new basic science questions arising from clinical observations.^{4,5} We believe that dual training in basic and clinical research, although possible, is unrealistic and unnecessary, and that most translational research will be collaborations between basic and clinical investigators. We hypothesized that by expressly defining a translational research training program (TRTP), with well defined goals and an explicit curriculum, that we would increase cross-talk between clinical investigators and basic science investigators, and ultimately allow basic research advances to be more rapidly translated into clinical trials and clinical benefits, and to lead to more relevant basic science inquiries. We describe the TRTP that we developed and the impact of the program on interdisciplinary research.

Materials and Methods

TRTP Components

Our training program for translational investigators is comprised of five components: (1) primary research training in the primary research discipline of a trainee (basic science or clinical); (2) cross-training in the alternate research discipline; (3) development of a research project that includes a translational research component; (4) mentoring by a committee with membership reflecting the scope of the translational research project; and (5) enhancement of the research environment to emphasize translational research.

Primary Research Training

The program builds on the strengths of our established template for training research fellows. The fellows choose a primary research training track (clinical or basic science) and a primary mentor by the end of their first year of clinical training. For our basic science research fellows, the training program follows a traditional model in which fellows choose a mentor and work on a project related to the primary research area of the mentor. Our approach to training clinical research fellows has been described.⁶

Cross-Training in the Alternate Research Discipline

Formal Cross-Training in Basic Science Research—We designed a three-part curriculum to expose trainees whose primary expertise is in clinical research to cutting edge laboratory science and to provide the opportunity to develop meaningful partnerships with basic scientists. Course components were open to interested trainees from all divisions and departments.

Basic Science for the Clinical Investigator: Acute Lung Injury—The first part of the Basic Science for the Clinical Investigator curriculum is a lecture series that provides a comprehensive introduction to basic science concepts, using lung injury and repair to illustrate a variety of specific topics in basic science. The topics include inflammation, cytokines, and chemokines in the lung; immunology and host defense; cell signaling; and transgenic animal models (Table 1). Each session consists of 45 min of didactic lecture, followed by a discussion of journal articles. The discussion is designed to illustrate translational aspects of the topic. The course is held three mornings per week, for 4 weeks.

“Omics for Everyone”—The second part of the Basic Science for the Clinical Investigator curriculum serves as an introduction to genomics, proteomics, and population genetics in lung biology. The course meets three afternoons per week for 3 weeks. Week 1

focuses on DNA arrays and gene expression analysis, week 2 focuses on genomics and gene variations, and week 3 focuses on proteomics.

Laboratory Workshop—The third part of the Basic Science for the Clinical Investigator curriculum is a 1-week-long “Introduction to Laboratory Techniques” workshop. The goal of the workshop is to provide hands-on laboratory-based experience that introduces the clinical research trainee to commonly used cellular and molecular biology techniques (Table 2). Each morning consists of a 1-h didactic session, describing the rationale behind the procedures to be learned and addressing the clinical applications of the techniques. The rest of the day is spent in the laboratory. We take a “Julia Childs” approach to the lab in order to ensure that the experiments are successful. All reagents and materials are prepared in advance so that if one step should fail, the necessary templates are available to continue with the next steps. The syllabus contains an overview of techniques with specific laboratory protocols. Participants are divided into small groups of 3 to 4 students, each led by an experienced research scientist.

Formal Cross-Training in Clinical Research—For trainees whose primary expertise is in basic science research, we designed a workshop that provides a focused introduction to statistical methods. The workshop addresses statistical issues relevant to basic scientists, including power, sample size, parametric and nonparametric sample comparisons, repeated measurements, and statistical instability. The last portion of the workshop is a roundtable discussion entitled “Ask the Statistician,” in which the participants bring their current work and statistical questions for discussion.

Research Project To Include a Translational Research Component

All of our fellows are required to complete a research project under the direction of a faculty mentor. Examples of ongoing fellow projects with a translational research component include: the design and implementation of a phase II randomized, controlled trial of enteral fatty acids vs placebo in patients with acute lung injury that investigates whether fatty acids cause a reduction of markers of inflammation and injury in the lungs and serum of patients with acute lung injury; and the study of the epidemiology, mechanism and outcomes of critical illness polyneuropathy/myopathy in patients with acute lung injury. These projects require input from both clinical investigator and basic science investigator mentors.

Mentoring

A formal mentoring committee reviews the training experience and career development of each of our fellows. Each trainee in the TRTP has a secondary translational research training mentor, in addition to the primary research mentor. This mentor is a faculty member in the alternate research discipline who prepares an addendum to the report of the committee. This report specifically focuses on the progress made by the trainee toward translational research training goals. The secondary mentor is a member of the formal mentoring committee for each trainee and provides overall career guidance and recommendations about all aspects of training. The secondary mentor meets with the trainee at least once per year.

Research Environment Enhancement To Emphasize Translational Research

Translational Journal Club—As part of our TRTP, we modified our journal club to incorporate a broader range of studies and to stimulate interaction between clinical and basic science disciplines. Paired articles explore the same disease from complementary scientific perspectives, usually one that focuses on basic mechanisms and another that demonstrates how those mechanisms are related to disease in patients (Table 3). Designated faculty moderate the discussion to illustrate the bridges between the basic and clinical ideas in the

two articles. The discussion of a basic science article might include comments about the additional steps that would be necessary before the concept would be ready for testing in the clinical setting or what type of other studies might result in the development of an intervention. The discussion of a clinical study might include discussion about the basic mechanisms involved in the clinical disease and potential basic science studies that could be used to elucidate them.

Research Work-in-Progress Sessions—An essential ingredient of translational research training is to create a forum in which clinical and basic investigators can meet to discuss research in progress. We currently hold two separate research work-in-progress sessions: one dedicated to clinical researchers and the other dedicated to basic science researchers. The goals of the work-in-progress sessions are to provide fellows and faculty with a supportive environment in which to present ongoing research projects for critical evaluation and discussion, to provide a forum to present research proposals and preliminary results, and to provide fellows with experience critiquing the work of their colleagues. Fellows interested in translational research now attend and participate in both sessions to gain facility in the vocabulary and methods of the research area that is the alternate to their primary research track, to obtain additional experience evaluating both forms of research, and to facilitate the creation and refinement of translational research projects.

Survey Instruments

We designed survey instruments to evaluate the individual components of the program. Participants were asked to evaluate course content, topics, speakers, organization, course materials, audiovisuals, administrative support, and environment/facilities on a qualitative scale from 1 (poor) to 5 (excellent). In addition to numerical grading of components, free text responses provided qualitative assessment of the different courses. Focus groups with PCCM fellows and junior faculty were conducted using scripted topics and an agenda to assess barriers to translational research. Responses were recorded, transcribed, and used to inform the design of TRTP components.

Analysis of Publication Record

We analyzed all peer-reviewed publications for which a member of the PCCM Division at the University of Washington (UW) was a coauthor in 1995 and 2000 (prior to initiation of the TRTP) and in 2006 (after two cycles of courses). UW PCCM Division members include faculty based at the UW Medical Center, Harborview Medical Center, the Veterans Administration Puget Sound Health Care System, and the Fred Hutchinson Cancer Research Center. We excluded book chapters, letters to the editor, and responses to letters. For each publication, we counted total number of authors, number of authors from UW PCCM, and number of other divisions and departments. Only primary appointments were used. For large multicenter trials, only writing committee members were counted. To determine the number of authors from UW PCCM Division, we compared author list to the faculty and staff list of the Division at the time of publication. For additional authors, we used the primary affiliation as listed in a manuscript, supplemented by review of institutional departmental listings as needed. For example, if an author affiliation was listed as being in the “Department of Medicine,” we queried institutional directories to determine divisional affiliation.

For each publication, we calculated the percent of authors from outside the UW PCCM Division and the number of different medicine divisions and departments represented among the authors. In addition, our pulmonary faculty and fellows have primary affiliation with one of the following three tracks: Clinical Research, Integrative Physiology, and Respiratory Cell and Molecular Biology Research. To determine whether there was increased cross-talk

between researchers within these tracks, we scored each manuscript with more than one UW PCCM Division author as either 0 (only one pulmonary track represented) or 1 (more than one track represented). Our training tracks were not formerly defined in 1995; therefore, this parameter was only analyzed in 2000 and 2006. We analyzed the data for all publications and analyzed the subset of publications with more than one author. In addition, four independent readers rated each publication as translational or not translational. A publication was counted as translational if it was rated as such by three or more of the readers. For each publication in 2006, we also determined whether any of the authors had participated in any of the formal TRTP course components.

To determine potential impact of TRTP on fellow productivity, we analyzed the number of publications per fellow during > 5 years from two cohorts of fellows: fellows beginning in 1995 (n = 6), prior to TRTP, and fellows beginning in 2000 (n = 7), following institution of TRTP.

Statistical Analysis

Comparison of three or more groups of normally distributed data were performed using one-way analysis of variance (ANOVA) followed by a Tukey *post hoc* honestly significant different test. Statistical significance was set at $p < 0.05$. For comparison of two groups, an unpaired Student *t* test was used to determine statistical significance. The data are presented as the average $\pm$ SD. Assessment of agreement between scorers of translational articles was determined by κ coefficient.⁷

Results

Course Components

Over the course of the program, 57 individuals participated in one or more of the TRTP courses. Of the 57 participants, 35 were members of the PCCM Division, of which 20 were members of the Basic Science Track and 15 were members of the Clinical Research Track. The additional participants represented nine different divisions and departments from the UW. Of the PCCM participants, 25 (71%) currently hold faculty positions at 10 different institutions, 8 (23%) are still in training, and 2 (6%) are in private practice. This is similar to the follow-up of PCCM graduates from the past 10 years, in which approximately 62% have faculty appointments.

Participants filled out evaluations at the end of each course (Table 4). Survey response rate was 55%. Survey responses from the course evaluations indicated that the time frame and format for the courses worked well. Participants indicated that the courses met the stated objectives and their personal objectives in all cases. Evaluations of topics and lectures were all in the very good-to-excellent range. Evaluations from the basic lecture series confirmed that they provided a great bridge between basic research and clinical significance and applications. Additional benefits included increased exposure to leading experts in various fields as potential resources. One survey participant wrote, "Now I know who to go to for questions or advice." Attendees at the basic science lectures included not only clinical researchers, but also basic science researchers, including PhDs who sought clinical context for their projects. Similarly, attendance at the statistics workshops included clinical researchers. At times, this led to discussions that became too complicated. Thus, it is important for lecturers to maintain focus on the target audience. For the laboratory workshop, small groups with supervision by a senior technician were indicated to be critical for the success of the workshops. Successful journal clubs tended to have significant faculty involvement and commitment to facilitate the translational aspect of the session. These

discussions have helped to make active consideration and promotion of translational research part of the culture of the UW PCCM Division.

Publications

To obtain objective measurements of interactions between clinical researchers and basic science researchers within our division and interdivisional and interdepartmental interactions, we used coauthorship as a surrogate marker of interdisciplinary work. The total number of publications from UW PCCM Division members increased from 1995 ($n = 43$) to 2000 ($n = 52$) and 2006 ($n = 83$). Part of this increase could be attributed to an increase in the size of the faculty from 28 to 48 members. The number of articles published per fellow in the 5-year period prior to institution of TRTP was 2.5 (range, 0 to 5). In the 5-year period that coincided with the institution of TRTP, the number of articles published per fellow increased to 4.7 (range, 0 to 10), although this did not reach statistical significance. Between 1995 and 2000, there was not a significant change in any of the authorship parameters analyzed. However, between 2006 and either 1995 or 2000, every measured criterion of interdisciplinary work increased (Fig 1, 2). The average number of authors per manuscript increased from 3.79 in 1995 to 5.54 in 2006 ($p < 0.05$). The percent of non-PCCM coauthors per publication increased significantly in 2006 to 48% from 31% in 2000 or 31% in 1995 (Fig 1). Similarly, significant results were found when singleauthor articles were excluded (57% in 2006 vs 37% in 2000% and 39% in 1995). The average number of different departments represented in authorship per publication increased significantly to 3.4 in 2006 from 1.8 in 2000 and 2 in 1995 (Fig 2). Finally, the number of publications that included PCCM Division members from more than one training track increased from 8% in 2000 to 32% in 2006 ($p < 0.005$).

We also analyzed the percentage of articles determined to be translational in the three time points studied. The percent of translational articles was similar in 1995 and 2000 (9% and 11%, respectively) but increased to 22% in 2006 ($p < 0.05$) [Fig 2]. In addition, the translational articles were enriched in authorship by TRTP participants. Articles designated as translational were more likely to have a TRTP participant as a coauthor than nontranslational articles (60% vs 30%, respectively; $p = 0.013$).

Discussion

Our TRTP is based on the concept that translational investigators can be trained by providing targeted complementary cross-training in the alternate research discipline to the primary research discipline of the trainee. Therefore, we modified our existing fellowship training curriculum and added novel components. Importantly, we decided that it was critical that the TRTP not extend the overall time period required for research training.⁸ Thus, the cross-disciplinary components are designed to be concise, introductory, and representative rather than comprehensive. While the program has focused on fellow training, the long-term objective of the program is to change in the overall culture of our division and of the PCCM research community in order to facilitate bench-to-bedside translational research. Therefore, attendance at the courses and components was open to all members of the PCCM Division, as well as other interested trainees and faculty. Furthermore, assignment to the TRTP training track was informal and not prespecified.

An alternative model would be to increase the overall duration of training and provide in-depth training in both basic science and clinical disciplines. While this may be appropriate for select individuals, we feel it is unlikely to produce a significant number of translational researchers, particularly in PCCM where the clinical training requirement is already extensive. Feedback from moderated, small-group focus groups that included increased time commitment was perceived as a major barrier for translational research training. While there

are no studies directly comparing different methods of translational or interdisciplinary training, there is evidence supporting our model. The National Cancer Institute instituted a similar program for fellowship training in Cancer Prevention, featuring interdisciplinary work-in-progress sessions and short, defined courses to introduce fellows to related disciplines.⁹ The adoption of the curriculum increased the publication rate of fellows over that in previous years.¹⁰

Our original plan for training basic science investigators in clinical research methods was to take advantage of relevant sections of preexisting programs in clinical research available at the UW, such as the National Institutes of Health-funded K30 lecture series and programs offered by the General Clinical Research Center. However, we found that there was general reluctance on the part of the basic science research fellows to participate in these series because of time constraints and the perception that the material was not tailored to the needs of the pulmonary research fellows. We held discussions with mentors and trainees, and determined that the greatest perceived need was for a short, focused introduction to statistical methods. Therefore, the statistics workshop was designed based on this feedback.

Previously, we held a monthly journal club in which fellows selected articles, often prominent clinical trials, to present to faculty and fellows. The principal goals of the traditional journal club were to teach skills in critical evaluation of the medical literature and to discuss issues related to the clinical management of patients. Our current format features discussion of both basic and clinical aspects of pulmonary issues.

The percentages of translational peer-reviewed publications and interdisciplinary authorship increased after the institution of the TRTP. In addition, translational articles authorship was enriched with TRTP participants. However, this must be interpreted with caution, as researchers already participating in translational research may be more likely to participate in the TRTP program. The majority of TRTP participants remained in academic settings. However, the follow-up is too short to determine whether they will ultimately increase the amount of translational research performed. Long-term success will be measured ultimately by a more rapid and efficient translation of basic research advances to clinical practice. There are also limitations in using historical controls, including the impact of factors other than the development of the PCCM TRTP, such as the National Institutes of Health Initiative in Clinical and Translational Science Awards¹¹ and our establishment of a formal clinical research training program.⁶ However, all of the measured indicators of translational research increased after initiation of the TRTP, while there were no changes in the time periods preceding development of the program.

In summary, we describe the components of the newly implemented TRTP and demonstrate a statistically significant increase in interdisciplinary authorship that coincides with the development of the TRTP. The results are consistent with a benefit of the program and explicit efforts to alter the division-wide culture to enhance translational research. Thus, it is our contention that a program of limited, focused training in the alternate discipline is suitable to increase the pool of translational researchers in PCCM.

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Abbreviations

ANOVA analysis of variance

PCCM	pulmonary and critical care medicine
TRTP	translational research training program
UW	University of Washington

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Figure 1.

Fraction of nonpulmonary authors in 1995, 2000 (before TRTP), and 2006 (after TRTP). For each peer-reviewed publication, the fraction of nonpulmonary authors was calculated. The mean fraction $\pm$ SD is shown. Comparison of three time periods was performed using one-way ANOVA followed by Tukey HSD *post hoc* test. * = $p < 0.05$. Line graph represents total number of publications for each time period.

Figure 2.

Number of departments represented per publication. For each peer-reviewed publication, the number of different primary affiliations was determined. Mean $\pm$ SD is shown. Comparison of three time periods was performed using one-way ANOVA followed by a Tukey *post hoc* honestly significant difference test. * = $p < 0.05$. Line graph represents percentage of publications designated as translational for each time period.

Table 1
Mechanisms of Lung Injury and Repair Lecture Series*

Topics
Molecular pathogenesis of ARDS
Cytokines/chemokines in lung injury
Life and death decisions in the lung
Immunology/host defense in the lung
Matrix remodeling in lung repair
Genomics: SNPs and sepsis
Monoclonal antibody development, therapeutic uses and limitations
Transgenic mouse models for lung injury
Proteomics for post translational modifications in lung injury
The matrix: not just a movie
Cell signaling
Gene array for lung injury and repair

*
SNP = single-nucleotide polymorphism.

Table 2
Laboratory Workshop Overview*

Laboratory Techniques
Protein isolation
Western blot analysis
ELISA
Immunohistochemistry
Bacterial transfection
Plasmid DNA isolation
Restriction enzyme digest
PCR

* ELISA = enzyme-linked immunosorbent assay; PCR = polymerase chain reaction.

Table 3
Journal Club Article Pair Examples

Clinical Article	Basic Science Article
Golbot S, Kolopp-Sarda MN, Béné MC, et al. Plasma level of triggering receptor expressed on myeloid cells-1: its diagnostic accuracy in patients with suspected sepsis. <i>Ann Intern Med</i> 2004; 141:9-15	Bouchon A, Facchetti F, Weigand MA, et al. TREM-1 amplifies inflammation and is a crucial mediator of septic shock. <i>Nature</i> 2001; 410:1103-1107
Wilkinson TMA, Donaldson GC, Hurst JR, et al. Early therapy improves outcomes of exacerbations of chronic obstructive pulmonary disease. <i>Am J Respir Crit Care Med</i> 2004; 169:1298-1303	Hogg JC, Chu F, Utokaparch S, et al. The nature of small airway obstruction in chronic obstructive pulmonary disease. <i>N Engl J Med</i> 2004; 350:2645-2653
Morgan WJ, Crain EF, Gruchalla RS, et al. Results of a home-based environmental intervention among urban children with asthma. <i>N Engl J Med</i> 2004; 351:1068-1080	Zhu Z, Zheng T, Homer RJ, et al. Acidic mammalian chitinase in asthmatic Th2 inflammation and IL-13 pathway activation. <i>Science</i> 2004; 304:1678-1682
Raghu G, Brown KK, Bradford WZ, et al. A placebo-controlled trial of interferon γ -1b in patients with idiopathic pulmonary fibrosis. <i>N Engl J Med</i> 2004; 350:125-133	Zuo F, Kaminski N, Euqui N, et al. Gene expression analysis reveals matrilysin as a key regulator of pulmonary fibrosis in mice and humans. <i>Proc Natl Acad Sci U S A</i> 2002; 99:6292-6297
Shepherd FA, Rodrigues Pereira J, Ciuleanu T, et al. Erlotinib in previously treated non-small-cell lung cancer. <i>N Engl J Med</i> 2005; 353:123-132	Tsao MS, Sakurada A, Cutz JC, et al. Erlotinib in lung cancer: molecular and clinical predictors of outcome. <i>N Engl J Med</i> 2005; 353:133-144
Seymour JF, Presneill JJ, Schoch OD, et al. Therapeutic efficacy of granulocyte-macrophage colony-stimulating factor in patients with idiopathic acquired alveolar proteinosis. <i>Am J Respir Crit Care Med</i> 2001; 163:524-531	Huffman JA, Hull WM, Dranoff G, et al. Pulmonary epithelial cell expression of GM-CSF corrects the alveolar proteinosis in GM-CSF-deficient mice. <i>J Clin Invest</i> 1996; 97:649-655

Table 4
Summary of Course Evaluation Surveys

General Questions	Mean Score
Did the course meet its stated objectives (yes/no)?	100% Yes
Did the course meet your personal objectives (yes/no)?	100% Yes
Lecture evaluations *	
Topics	4.8
Speakers	4.6
Organization and support *	
Audiovisuals	4.6
Course materials (syllabus)	4.6
Speaker handouts (eg, articles and slides)	4.4
Environment	4.3
Administrative support	4.4

* Scale, 1 (poor) to 5 (excellent).