Training in Clinical Research in Oncology

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Objectives of the Workshop

Responding to the emerging concerns and problems relating to the training and retaining of clinical investigators in oncology described in various publications (1-5), a workshop on "Training in Clinical Research in Oncology" was conducted by the Centers, Training and Resources Program of DCBDC on September 12, 1990, in Gaithersburg, MD. The purpose of the workshop was 2-fold: (a) generally to identify the concerns and problems facing the clinical oncology research community; and (b) primarily to focus on how these problems are affecting the training of M.D.s who wish to pursue careers in clinical oncology research. The workshop agenda was designed to ensure that the participants were completely aware of the spectrum of training and research mechanisms currently available to clinical oncologists, to develop as much agreement among the participants as possible with respect to a definition for clinical oncology research, and to use this definition as the basis for further evaluation of the adequacy of the NCI training mechanisms and institutional training environments for attracting and retaining M.D.s in clinical oncology research. Pertinent issues and strategies were identified from the perspective of the extramural participants with particular attention being focused on those areas which could be pursued by the NCI within the organizational structure and authority of the NCI/NIH. Emphasis was placed on the training and retaining of M.D.s preparing for careers in innovative clinical oncology research.

All participants were informed that this workshop represented a preliminary step in a process that clearly would require further evaluations and confirmations of the problems by program staff of the DCBDC and the DCT, the advice from the DCBDC and DCT Boards of Scientific Counselors, and possibly the National Cancer Advisory Board before any definitive strategies for solving the problems could be developed.

Defining Clinical Oncology Research

The participants considered that clinical oncology research and clinical research in general are philosophically no different than laboratory research. While the same scientific principles of experimental procedure apply to both, the unique feature of clinical investigation is that it involves people and, because of individual heterogeneity, experimental results are difficult to interpret, take longer to develop, and are more difficult to reproduce. This is in contrast to laboratory research that uses in vitro and in vivo models selected for genetic homogeneity in which the experimental variables can be controlled to yield greater reproducibility and clarity in data analysis and interpretation. The challenge of scientific investigation in humans is to minimize and overcome as many variables as possible and to arrive at an experimentally valid conclusion. While there are vast inherent differences in the levels of experimental rigor and design and even purpose between laboratory research and clinical research, clinical researchers do effectively use laboratory research and preclinical research in animals as complementary and confirmatory adjuncts to their ongoing research with patients. In short, a clinical oncology investigator is a scientist developing a research program directed and applicable to his/her patients. In this respect, clinical oncology encompasses numerous medical specialties in oncology (e.g., pediatric oncology, medical oncology, surgical oncology, and radiation oncology) as well as many other related specialties that deal directly with the patient in cancer diagnosis, treatment, and reconstruction and rehabilitation.

Although there was no absolute consensus developed by the participants for the meaning of clinical oncology research, in general the following definition, which is similar to that used for clinical research in a study conducted by NIH (6), is the one that best captures the opinions and sentiments of the participants and the one that the participants mostly used in evaluating NCI training grant mechanisms and the institutional environments available for training:

Clinical oncology research is the investigative care of patients with cancer, not restricted to individual medical disciplines or practices, which is directed toward the study of biology, diagnosis, treatment, behavioral components, and/or prevention. It often involves laboratory and preclinical research with dynamic back and forth interactions between the laboratory and the clinic, but it always is motivated by observations in patients as a result of continuously ongoing activities in direct patient care.
A minority among the workshop participants considered this definition too broad and preferred a more restricted definition dealing with medical oncology (as a discipline within the group of physicians specialized in internal medicine) and patient-oriented research only. However, the majority of the workshop participants concurred with this definition as an appropriate basis for examining problems and issue related to training and training environments for clinical oncology research investigators.

Training Opportunities in Clinical Oncology Research

A decline in the number of clinical oncologists pursuing careers in innovative clinical research appears to be related to a large number of environmental factors including: heavy medical school debt; lack of exemplary role models; limited and tenuous research funding opportunities; service-oriented work pressure in order to capture reimbursements; job security pressure to obtain specialty board certifications; the rapid and demanding pace of progress in the basic sciences; and life-style attractions which are incompatible with the requirements for lengthy training periods and long-term rewards.

Increasing evidence suggests that there is a need to train more clinical oncology researchers. Requests for trained professionals to fill such job openings are numerous and continuous. Laboratory research is progressing so rapidly that there is a shortage of properly trained research clinicians to translate salient findings to patient populations. Conversely, interesting clinical observations and problems also need to be communicated to the laboratory. A formal survey of the field of clinical oncology should be undertaken to obtain a more quantitative assessment of (a) the number of clinical oncology researchers, (b) the type of research and percentage effort, (c) the source of research support, (d) vacancies for research positions, and (e) an estimate of future needs. An assessment of research opportunities and future funding opportunities are critical in such a survey and overall report.

There was a consensus that the problems of recruiting talented medical students into clinical oncology, obtaining time and funding commitments for clinical research, writing high quality grant applications, and receiving appropriate peer review are not unique to clinical oncology compared with other clinical disciplines. However, the situation for clinical oncology may be more extreme given the importance of clinical research, the increasing number of opportunities for translating basic research findings into clinical investigations, the availability of few effective standard therapies, and the intensity of care required for cancer patients.

Furthermore, in order to entice the best young minds into clinical oncology research and retain them in research, an optimal training environment must be provided in order to maintain a high level of enthusiasm and incentive. This would require a critical mass of clinical investigators with peer-reviewed, funded research, stable funding for trainees, and proximity as well as interaction with basic research laboratories. It was estimated by the participants that only 20 to 50 institutions have all of the essential elements to develop high quality training programs in clinical oncology research. The NCI-designated comprehensive cancer centers were considered as potentially optimal training environments for clinical oncology investigators by virtue of their multiple capabilities in basic and clinical research, clinical trials, patient care, and cancer control activities.

Realistically, an optimal program for training medical oncology researchers requires prolonged, stable support and should be designed around the typical career track relative to training and research opportunities noted in Fig. 1. An unpublished NIH survey shows that it takes 4 to 5 years of "postdoctoral" training for clinicians to successfully compete with Ph.D.s for research grant support. Ideally, a training program would be individually planned since clinicians will have a variety of backgrounds, experiences, and future objectives. There must be a proper balance between the laboratory, the clinic, and didactic instruction with at least 2 to 4 years of research integrated with the American Board of Internal Medicine requirements for specialty (e.g., Medical Oncology) certifications. Finally, responsibility for the trainee's research program and progress must reside with a clearly defined mentor. There should also be a committee equivalent to the graduate student's research committee that would provide an oversight function.

More flexibility is needed in the existing NIH/NCI training grant mechanisms for the support of clinical oncology researchers. It is important for clinicians to have a protected period of research training (4 to 5 years), so that they would not have to prepare grant applications before they are sufficiently trained to be competitive. The Institutional Training Grant (T32) is a vehicle that nominally provides a maximum of 3 years of postdoctoral support. This rule could be waived to provide a fourth year for clinicians with proper justification on a case by case basis. However, the NIH/NCI should consider formalizing a prolonged T32 for a subset of promising young clinical investigators. Continuing support for trainees who have sufficiently matured to submit their own grants could be achieved.

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Fig. 1. Clinical Oncology practice and research tracks. This is a general schema which should be modified to fit the needs of individual programs. ABIM, American Board of Internal Medicine.
through greater and more flexible use of career (K08, K11) grants. However, NCI also should consider initiating “program” career grants (e.g., K12) to be awarded to excellent clinical departments and/or cancer centers; these could be utilized by trainees not yet ready to compete for their own grants. An important corollary to an array of appropriate individual and program training grant mechanisms, is a peer review system in which competent, well-qualified reviewers are used. In this regard, the review of T32 surgical oncology grants, which provides a strong component of peer clinical expertise in addition to training, educational, and administrative expertise, may serve as a model.

Since Program Project grants (PO1) currently support the majority of clinical research, NCI should consider adding training funds to this mechanism. Cooperative Group grants (U10s) should also be considered in the same context.

To encourage the best medical students to choose careers in clinical oncology research, it is essential to use early recruitment measures, expose them to successful role models, and pay particular attention to the special problems created by the high cost of medical education. Increased funding for the Cancer Education Program in the NCI, which uses the R25 grant mechanism, could provide opportunities for and more support to medical and undergraduate students to work in established clinical research laboratories during summer breaks. Also, the high costs of medical education create a heavy debt burden for many new medical graduates and this acts as an impediment to their considering long years of research training at fellowship salary levels. It was suggested that NCI/NIH should consider creative approaches to aid the trainees in paying the interest on student loans.

A comprehensive approach to structuring programs for training clinical oncology researchers should set both short-term and long-term goals that will train young physicians in research and prepare them to compete successfully for individual investigator-initiated research project grants (e.g., RO1s) so that they can foresee a reasonable opportunity to pursue long-term careers in clinical research. Finally, the means and mechanisms for evaluating training programs should be an integral part of the overall plan.

Environmental Resources for Training in Clinical Oncology Research

The environmental resources available for training in clinical oncology research depend largely on the extent and type of funding available to clinical researchers, as well as on the various support mechanisms available for training young M.D.s wishing to pursue careers in research. The availability of peer-reviewed research funds from the NIH, in particular the training grants (e.g., T32s), the investigator-initiated research grants (e.g., RO1s) and project grants (e.g., PO1s), is what provides academic recognition and success for clinical researchers, maintains high morale and purpose within the clinical research community, and sustains a culture that promotes high standards of experimental vigor within the field. It was the general feeling of the extramural clinical researchers who participated in this workshop that opportunities for peer-reviewed support in clinical oncology were severely limited. Instead of spending a significant portion of their time and effort on peer-reviewed research, senior clinical investigators are forced to do research which depends on funds from various tenuous sources (e.g., industry) in a piecemeal fashion and to spend the majority of their time in service activities. Thus, senior clinical investigators are placed at a considerable disadvantage compared to senior basic investigators in their ability to provide adequate environments for attracting, training, and retaining young M.D.s in clinical research.

A number of unique problems intrinsic to the clinical oncology research community were identified by the participants in this workshop. They concluded that these problems, if addressed, would enhance the environmental resources for training and would also increase the number of young M.D.s pursuing research careers in clinical investigations. The following areas were considered of importance:

1. A lack of access to the RO1 grant mechanism is the main problem faced by a researcher wishing to pursue innovative clinical oncology research. Most clinical investigators simply do not submit research proposals to the NIH because they perceive that this type of research will always fare poorly in NIH study sections and, as a result, will not be funded by the NCI. Yet there is no doubt that innovative clinical research could be accomplished using the RO1 grant support mechanism, and, if RO1s were used for this purpose, they would serve as direct resources for training individuals at the graduate and postdoctoral levels in the same way that basic cancer research RO1s are used. The surfeit of clinically oriented RO1s submitted to NIH does not mean that there is a lack of interest in doing research by the clinical research community. Clearly, the recent response of the research community to the DCT RO3 initiative (160 submissions with only 12 weeks notice) demonstrates the widespread interest of clinical researchers in obtaining investigator-initiated, peer-reviewed support.

Currently, there are no NIH Study Sections predominantly oriented toward the review of clinical oncology research as defined in the workshop. Although the Experimental Therapeutics 2 Study Section in the NIH DRG consists of highly qualified scientists and physicians in their respective areas of expertise and is one example of an initial review group charged with reviewing clinical oncology research, it has a fairly broad review responsibility and as a whole would not serve as the most suitable peer review group for evaluating more focused, patient-oriented clinical oncology research. The workshop participants noted that an ad hoc initial review group in DRG was created nearly 10 years ago that was designed to review clinical oncology research. After a short time this peer review group was discontinued at the very time it appeared to some of the participants that it was beginning to have a positive effect. The factors that led to the establishment and termination of this initial review group should be determined.

The workshop participants recommended either a study section in DRG be realigned to consist primarily of peers who are actually doing innovative clinical oncology research directly with patients or create a new study section with this kind of charge and expertise even if it has to be done as an “experiment.” The group also was very supportive of continuing the RO3 grant support mechanism but believed the NCI had unintentionally sent the research community the wrong message when funds available to pay the awarded RO3 grants were so restricted.

2. While the PO1 grant mechanism has proved to be a good way to obtain peer-reviewed funding for clinical studies, the funding of clinical studies is limited relative to laboratory research. It was pointed out that the successful clinical research grants are those linked to good basic laboratory research. In the opinion of the workshop participants, good clinical oncol-
ogy research is seldom allowed to stand on its own by the currently structured peer review groups. The peer review of these types of applications should be reassessed by the NCI to ensure that clinical studies are being treated fairly relative to laboratory studies.

3. Although the clinical cooperative groups of the NCI are aggressively and extensively evaluated, their focus is primarily on large scale confirmatory phase III clinical trial studies. Many of the participants believed that cooperative group studies could contribute to the encouragement of innovative studies. Although the issues in Paragraphs 1 and 2 are the primary objectives for creating environments for innovative clinical research, greater flexibility in the use of cooperative group funds could serve to promote innovative clinical research as well as maintain a higher interest level among investigators at institutions within the cooperative groups. An example of this would be to recognize and support institutional protocols that might be the basis of future group-wide studies.

4. In examining the career track of a clinical researcher, a critical 2-year gap was noted during which the clinical research trainee must face the termination of his/her trainee fellowship support while struggling to obtain NIH grant support. The training mechanisms used by the NCI should take into consideration the special time constraints that M.D.s must deal with. Awardee institutions should be given greater flexibility in their use of the T32 grants. The NCI should consider the advantages of using the K12 grant and the individual training grant mechanisms such as the K08, K11, and K07. These should be examined carefully to ensure that the best young M.D.s are encouraged to pursue careers in clinical research and that the financial stress during the critical 2-year gap is alleviated. Specifically, longer training periods (from 3 to 5 years) or several consecutive mechanisms may be considered to allow young physicians, many of whom have not had previous research experience, to learn to do clinical research to the point where they can write a competitive RO1 application. (Some of the workshop participants have used special institutional awards in the past very successfully, but these were discontinued by the NIH.)

To summarize, the training grant mechanisms such as T32, K07/K08, K11, and K12 should mediate a tightly linked transition to the research grant support mechanisms like R29s and RO1s. These must be made more available to young M.D.s to effectively promote the transition and continuum of traineeship to independent investigation. Otherwise, the problems in training, retaining, and sustaining M.D.s in clinical oncology research will become increasingly severe. It is possible that within a very short period of time, the downward trend in the number of clinical oncology researchers will become the rate-limiting issue for translating laboratory findings into medical practice.

5. Academic institutions should find more ways of independently promoting the research careers of clinical investigators. The method currently adopted by Johns Hopkins University may serve as a useful model for others. In this model, the dean of the medical school controls a fund established by private donations that is dedicated to the support of research by young basic and clinical investigators. Such support enables the young clinical investigators to concentrate on the acquisition of an NIH grant within the critical 2-year period. Participants from the Cancer Centers suggested that the developmental funds within the center support grants (P30) may be considered as one possible source for financial support of this nature at the discretion of the Cancer Center Director.

General Conclusions

The National Cancer Institute (NCI) should reassess its current training programs in both programmatic adequacy and flexibility to meet the needs of M.D.s wishing to pursue careers in clinical oncology research. In particular, the institutional T32 training grants should be examined for possible modification to serve the special career needs of young physicians. The use of institutional awards (e.g., K12, K16) which have not been used by the NCI in the past would serve to complement the individual K08 and K11 awards and, more importantly, provide institutions with the best training environments greater flexibility in selecting and sustaining young physicians during the critical period when they are beginning to prepare their own research grant applications. The NCI should also review the current spectrum of research support mechanisms available to M.D.s wishing to do innovative clinical oncology research and to implement whatever ways and means to promote more investigator-initiated research. Access to the investigator-initiated RO1 grants through an appropriate peer review system was considered to be of critical importance. It was concluded that DCBDC and DCT would be the primary organizational components that would follow up on these issues and that training and access to research support is a continuum requiring a coordinated approach if the training, retaining, and sustaining of M.D.s in clinical oncology research is to meet the needs of the future.

A Note in Added Support for the Conclusions of This Workshop

After this workshop was completed the Institute of Medicine released a report entitled Funding Health Sciences Research: A Strategy to Restore Balance (5). This report supports nearly all of the conclusions of this workshop from the more general perspective of resources available for supporting clinical research and for the training of clinical researchers. Furthermore, the Division of Cancer Treatment in the National Cancer Institute has compiled considerable data on the success of grant applications submitted in RO1s and PO1s in clinical oncology which also supports the views of the participants in this workshop.

References

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