Given the remarkable advances in bio-medicine in recent years, there has never been a better time to devote one's efforts towards bench to bedside medicine. Accordingly, well-trained physician-scientists are in high demand in the private and academic sectors, and there is increasing awareness of the need to support and nurture such individuals. Clinical fellows in hematology, oncology and hematopathology with an interest in the physician-scientist career path must be well prepared to succeed in transitioning from fellowship to their first academic position. This article will discuss some of the key elements that prospective clinical scientists need to assemble in order to survive this critical period.

Introduction

The Hematology and Oncology fields are at the forefront of translating biomedical research into clinical diagnostics and therapeutics. This elegant intertwining of molecular and clinical medicine is attractive to trainees with an interest in becoming physician scientists. Thanks to recent advances in molecular biology, genetics, nanotechnology, computational biology, and drug design, there has never been a more exciting time to devote one's career to hematology and oncology research. Bench to bedside scientific research is more feasible and impactful than ever. Physician scientists are in a unique position to perform this research and catalyze the transition to a medical era of personalized diagnosis and rationally guided therapy. Given this potential it might seem hard to understand on the surface why relatively few physicians choose to follow an academic career path and take advantage of the historic opportunity to be on the leading edge of this radical transformation. Certainly there is no lack of intelligent and creative individuals studying medicine. In fact, it is well recognized that the system is failing to provide the incentives and support necessary for more of these individuals to choose to devote their energies towards becoming physician scientists. The goal of this manuscript is to outline some of the challenges facing trainees and to provide some guidance for potential physician-scientists interested in an academic career.

Opportunities and Challenges in Medical Research

The pace of discovery in medical science continues to accelerate thanks to the progressive increase in knowledge of biological mechanisms, the development of new technologies, and the emergence or maturation of new fields or areas of research. The advent of ever more powerful and less expensive high throughput assays to capture transcriptional profiles, genetic variance, epigenomic gene regulation, proteomic profiles, etc. has the potential to accelerate the pace of discovery by allowing scientists to view cells and tissues from a systems point of view. From the oncology standpoint it is likely that these approaches will greatly improve diagnosis and selection of therapy for patients in the near future. Drug design technology is now reaching the point where investigators can generate inhibitors targeting particular disease related mechanisms of interest and potentially translate these to clinical trials. In addition the proliferation of small molecules developed by the pharmaceutical industry provides collaborative opportunities for academic investigators to study the impact of selective biological modulators on disease mechanisms of interest and develop clinical trials and marker studies. More than ever, it is possible to obtain the satisfaction that one’s research will truly have an impact on patient outcomes. From the patient’s perspective, the recruitment of more physicians into research careers could help to quickly translate basic concepts and speed the arrival of promising discoveries to the clinic. Why then are physicians not more frequently devoting their careers to research?

The Impact of the NIH Funding Crisis on MD Career Development

Certain barriers towards establishing an academic career are fairly obvious. Budgetary constraints at the National Institutes of Health have made it more difficult to obtain federal funding, a critical benchmark for the independent physician-scientist. Inspired by the increased commitment to biomedical science during the late 1990s, the number of grant applications to the NIH nearly doubled, while the purchasing power of the NIH budget has gone in the opposite direction, decreasing more than 13% since 2003. The negative impact of government policy towards the NIH over the past few years cannot be overstated. As a conse-
quence, the chance of competing successfully for a training award or first R01 is declining and the median age for a first R01 has increased to 42 years. The situation is particularly complicated for MDs, who are less likely to obtain R01 funding, less likely to attempt to renew an existing R01, and, even if they did try to renew, were less likely to be successful than PhDs (or MD-PhDs). Factors that might account for this phenomenon include lack of protected time, financial or family pressures, or lack of strong mentoring. However, funding levels alone do not account for the dearth of MDs following research careers. Although first R01s increased during the late 1990s and early 2000s, the number of MDs with such funding remained static. The increase in grant numbers was accounted for by PhDs, and, in smaller numbers, MD-PhDs. Since grants submitted by MDs are more likely to be associated with clinical or patient-based research, it seems that an opportunity was lost to foster greater growth in translational research during this period. Therefore, funding availability does not totally account for the failure to recruit more MDs into research careers, and other causes must be considered. Of particular concern for the purpose of this discussion are the failure to develop a robust career development plan and the perils surrounding the transitional period from fellowship to the next level.

The Successful Transition

Mentorship

In addition to one’s own natural interest in molecular and clinical research, mentorship is the most important factor in assuring a successful transition to a career as a physician-scientist. Selecting the right mentor is a difficult task, and the attributes of the “ideal” mentor may not be readily apparent to most trainees. Just because a senior faculty member has published 300 papers and is an internationally recognized and admired authority in the field does not necessarily translate into solid mentoring. It should be kept in mind that association with the right mentor has a lifelong impact that does not end after fellowship or after obtaining a faculty position. In addition to teaching scientific and technical principles, the mentor plays a critical role in teaching grantsmanship and scientific writing. The mentor should serve as a role model in the ethical conduct of research, the ethical review of manuscripts and grants, the ethical and open sharing of scientific information. The mentor is also the conduit for the trainee to the outside world, by providing guidance and opportunities to present at the meetings from which the trainee is most likely to benefit, by fostering the interaction of trainees with collaborating scientists, facilitating the extension of training not covered by the mentor’s expertise, and allowing the trainee to speak at high profile settings. It is crucial that mentors serve as a role model in their commitment to their trainees, their generosity in allowing them to carry their research to an independent faculty position, and continue to support their mentee’s career long after they left their laboratory. This creates a culture whereby trainees who have been through a positive experience will be inclined to repeat this pattern with their own trainees and be inspired to be excellent mentors themselves.

The qualities of the mentor should, to a certain extent, reflect the candidate’s strengths and weaknesses. It is particularly important that MDs transitioning into the laboratory enter into a strong training environment with adequate supervision from both the mentor and senior laboratory members. The laboratory should have regularly scheduled group meetings and good rapport between lab members. Prior to deciding to join a given lab, the trainee should directly talk to some of the current lab members and attend a lab meeting to get a sense for the environment and interactions between people. It is easy to get lost in a huge laboratory where post-docs and students don’t collaborate or interact in a positive manner, regardless of how many Nature papers come out of that lab each year. In contrast, a well-trained and highly experienced MD-PhD might be more suited to take advantage of the prestige and power of such a laboratory and may not need as much hands on supervision. So, how does the trainee identify the right mentor? Although there is no magic formula for choosing, some things to keep in mind include:

- MD mentors (as opposed to PhDs) are more often (but not always) attuned to issues pertaining to the career development of clinical trainees trying to develop a career in translational research.
- The trainee should inquire whether the prospective mentor has a track record of developing successful junior faculty members and supporting the submission of trainee awards, and should also find out what percentage of their trainees fail.
- When the applicant moves away, she/he will most likely continue and expand upon research performed in the mentor’s laboratory. A good mentor will have a track record of respecting the vulnerability and independence of their trainees by allowing them to take projects and to not compete with them, at least for the initial years.
- Mentors should be well-funded and have a strong record of publications in high-quality journals. Program directors and other scientists can advise the trainee of the qualifications of potential mentors.
- A very junior mentor may not be a credible sponsor for career development awards and may not be able to afford to allow trainees to take their projects with them when they leave the laboratory. That said, junior investigators may have a lot of energy and enthusiasm for supporting trainees and also may spend more time directly at the bench.
• A senior mentor may have many other obligations and academic roles that limit their access to the trainee. Moreover, mentors with established scientific and senior University positions may not be as focused on trainee career development.
• It is important to understand that one of the metrics of success for faculty members is their track record in training junior scientists. Many junior and mid-career mentors will be aware that their own career development is dependent in part on the success of their trainees.
• When choosing a laboratory, consideration should be given to whether or not the atmosphere in the lab is collaborative and interactive. Laboratories consisting of a few junior people or only technicians may not provide a robust training environment for the fellow. The trainee (especially MDs with little research experience) will need the support of experienced laboratory members and should make sure that such individuals are available.

Choosing projects
Choosing the right project is critical. For trainees who do not have an extensive research background, it is best to avoid starting a project that is outside the usual scope of the mentor’s laboratory or that involves an area with which the mentor and her/his lab are not familiar. A project that builds on the strengths of the laboratory in terms of methodologies and availability of the proper resources is most likely to get off the ground quickly. The project should be relevant from the scientific and bio-medical point of view, for example, not limited to an epiphenomenon observed in a single cell line, and, if possible, should be disease oriented. Projects should involve the opportunity for the trainee to learn a range of methodologies to gain broad experience, a point that will become crucial when the trainee needs to start their own research group. A trainee who has spent their entire time performing one or two assays is unlikely to be prepared to supervise more complex projects.

The trainee should be aware of the rhythms of scientific research. A project may steam along and then suddenly stall for many months due to a technical glitch or experimental difficulties. One of the strengths that MDs can bring to the lab is the ability to multitask. Having the experience of caring for dozens of sick patients at the same time engenders the ability to keep calm while handling multiple different situations accurately, each with its own complexities and nuances. The trainee can capitalize on this ability in his/her laboratory work. Specifically, it is a good idea for the trainee to have more than one project. Then, when one project stalls, the other can proceed and vice versa. It is OK to take on a more risky mechanistic study or a “fishing expedition” if these can be complemented by other more straightforward projects.

Finally, the trainee needs to be aware that her/his research project will become the basis for his/her future career. The project should have the potential for long-term development; i.e., it should lead to additional important questions and possible translation into clinical practice. It is not feasible for the trainee to start an entirely new project in a different field upon becoming independent. It should be understood that the mentor will allow the trainee to take their project with them and continue to expand and develop the ideas initiated during the training years. Ideally, the mentor will continue to advise the newly independent former trainee during this time and will refrain from directly competing on the same project.

The career development plan
The hematology/oncology trainee needs to prepare a career development strategy as early as possible. This strategy must take into account educational requirements, the need for co-mentors to provide guidance and feedback in complementary areas, the timing and type of grant funding the trainee should seek, a plan for manuscripts, and a plan for sufficient penetrance into field so that the trainee’s work is recognized by scientific peers.

Educational requirements
Clinically trained MDs can greatly benefit from exposure to graduate-level classes in areas related to the biomedical science and Public Health programs, along with courses in statistics and the design and conduct of clinical research. Trainees should budget abundant time to enroll or audit relevant courses during their research training. The trainee should take advantage of a number of other important training resources. ASH has created the Clinical Research Training Institute (http://www.hematology.org/education/training/crti.cfm), which is an outstanding yearlong mentoring program to develop skills in clinical research. AACR (http://www.aacr.org/home/scientists/meetings—workshops/educational—workshops—special-courses.aspx) and ASCO (http://www.asco.org/ASCO/Education+%26+Training/Training/Resources+for+Fellows) provide intensive training courses devoted to translational and clinical research as well as useful guides and resources. Other institutions offer high-quality training courses in areas of scientific research. One example is Cold Spring Harbor Laboratories (http://meetings.cshl.edu/courses.html). These courses are intensive and can have a major impact in providing the trainee with the necessary tools to become an independent investigator. The education plan should begin as early as possible and be planned over the course of several years (usually 3 to 5 years). It should include components of these and other resources the trainee is able to identify with the mentor and program director. The trainee will be expected to be describe their educational plan and timeline in great and convincing detail when they apply for NIH “K” or other similar career development grants.
Co-mentoring
More than ever, biomedical research is a multidisciplinary endeavor. It is unlikely that a single mentor can provide the necessary breadth and depth of teaching required for the trainee to become an independent expert. For example, the increasing importance of statistical modeling, computational biology, and bioinformatics in the Systems Biology era requires that individuals with these backgrounds work together with a team. The scientific background that allowed the mentor to become independent several years ago may not be sufficient for trainees planning a career today. The trainee should therefore choose several additional co-mentors who can provide complementary expertise and guidance in areas crucial to the conduct of the research plan. It is critical for the trainee to receive feedback from the mentor and co-mentors. MD trainees should be advised to have the co-mentors meet once every 6 to 12 months to review progress in a “thesis advisory committee” type meeting, which would include direct feedback to the trainee. In addition the trainee should have regularly scheduled meetings with the mentor and co-mentors. These should be included in any grant application as part of the educational plan.

Funding strategy
It is critical that trainees obtain their own fellowship funding at the earliest possible time during their training. Although being funded by a training grant might be easier, it is more prestigious and also more useful for trainees to obtain their own grant funding. A list of awards and strategies for writing grants has been described elsewhere. In general the most desirable awards are the mentored career development grants (including the “K” awards) given by the National Institutes of Health. K awards are very competitive and applicants with stronger MD-PhD backgrounds, or in more powerful institutions are naturally well positioned to be competitive for these awards. However, the spirit of these awards is to foster the career of any meritorious candidate, and study sections are very supportive of quality applications from MDs who do not have an extensive previous track record of research. Applicants will be seriously considered if they propose solid, rational and realistic research projects, and thoughtful, well-organized and comprehensive educational plans. The program director/department chair and mentor must document in writing that they are committed to the trainee, will protect their time, and have a well-developed plan to facilitate transition to an independent career.

It is possible and even likely that applications to the NIH will not be funded after the first attempt and will need to go through additional submission cycles. The study section will make recommendations to the trainee to strengthen the application for the next round. The critiques written by the grant reviewers are generally very helpful and well intentioned, in the spirit of intending to be constructive to the trainee. These should be taken into account and carefully considered when re-submitting. Naturally it is critical that the mentor and co-mentors participate in helping the trainee to draft the initial application as well as any eventual resubmissions. It is also useful to ask other senior faculty/program directors to read and make constructive comments. While it is always frustrating to have a grant rejected, it is important for the trainees to realize that this is part of the scientific funding process and that they should not give up. With strong mentoring and good science it is very likely that the applicant will be funded even if it takes time and several attempts.

A number of Foundations (e.g., Leukemia and Lymphoma Society, Lymphoma Research Foundation, Kimmel Foundation) as well as ASH, AACR and ASCO offer 1- to 3-year grants to support fellows during this transitional period. These awards also tend to be extremely competitive and are very prestigious. All undergo rigorous scientific review. Of particular interest to hematology and oncology fellows, both ASH and ASCO offer transitional fellowships that are meant to provide a year of additional protected time after fellowship for trainees while they attempt to obtain more long-term career development funding. Trainees should consider applying for some of these awards in addition to NIH funding requests. If the applicant is funded by more than one source, they can decline one of the awards. Trainees might not feel pressured to scramble for funding if there are alternative sources that will cover their salaries. While this might be comforting in the short term, it is a serious tactical error. A solid track record of competing successful for competitive funding is one of the most important attributes for candidates who are hoping to be hired for a tenure-track faculty appointment. Moreover, the experience of writing a scientific grant allows for thoughtful analysis and planning of the project and an opportunity to carefully review the published literature and is thus a very useful exercise.

Publications
A strong publication record is critical for academic achievement and for consideration as a potential faculty candidate. Learning how to write a scientific manuscript is a core competency for the academic physician; thus, trainees should write their own manuscripts with editing help from the mentor. In addition to publishing their results, it is a good idea for the trainee to publish a scholarly review. Not just a rehashing of reported results, but a thoughtful interpretation of the literature with useful tables and figures. A solid review will serve the purpose of really learning the field, gaining recognition in the field, and helping to provide a background for the applicant in their presentations and grant applications. There is no formula for the number of papers one needs in order to be offered a faculty posi-
tion. It is the combination of funding, publication, commitment to scholarship, leadership skills and academic commitment that create the overall package.

Peer recognition
A good mentor will provide opportunities for the trainee to speak at national and international meetings. It is very helpful to the trainee to present their data at such venues and have a chance to network with established investigators. Most established investigators are appreciative of and interested in new talent. Gaining the notice of colleagues is very helpful at multiple levels. Some of these instances may not be visible to the candidate but yet can have a major impact. For example, investigators who have interacted with a given trainee at a national meeting may then provide positive feedback about this individual during a grant study section, or could be inclined to suggest the trainee as a potential recruit to their department chair, etc. Most importantly, the trainee should establish links with their future colleagues in the field to foster brainstorming and collaborations that could enhance their success in performing research both at the training and independent stages of their career. It is not always easy to meet prominent scientists at large meetings. It is therefore important that trainees also have the opportunity to present at smaller, more specialized meetings where it is easier to find and approach people. In addition the concentration of topical and detailed presentations in the specific area of interest is very helpful in gaining an understanding of the state of the art in a particular field. A good mentor will also introduce the trainee to colleagues and include the trainee in the process of developing and negotiating collaborative research projects.

Protected time
Establishing a body of work in research can only be accomplished if one has time to focus. Both for clinical and laboratory investigators, it is obvious that it takes a lot of time to think, write and perform research. Most physicians love clinical work and are dedicated to their patients. It is very hard to balance an equal love for biomedical discovery with clinical duties. The average physician-scientist requires 80% protected time in order to accomplish meaningful research. The mentor and training program must guarantee this time and the trainee must be disciplined in not letting other activities invade research time. There are of course many hidden time sinks associated with clinical work in addition to direct contact in the clinical, such as phone calls, following up on results of tests, and emergencies. The trainee needs to factor these issues into their time to gain a realistic appreciation for how they must organize their schedules. In addition, non-clinical duties such as teaching and committee work can also take a huge amount of time. The mentor can help the trainee learn how to balance these different aspects of the job and also help the trainee ensure that the protected time is truly protected.

Transitioning to a Faculty Position
A career in academic medicine can be incredibly rewarding. The principal motivation of the physician-scientist to embark on such a career is their natural curiosity and appreciation of the elegance and complexity of biology, the excitement of discovering how things work, and the fulfillment and satisfaction of making contributions to medical science that meaningfully improve the lives of patients. Another important motivator should be the pleasure of engendering a passion for discovery in trainees and fostering their career development.

It is important to be honest with oneself about internal motivation since the decision to “go academic” also implies many sacrifices. First of all, it implies even more time as a trainee, since it takes several years after fellowship for most physician scientists to be ready for a tenure track position. The average age for a first time assistant professor position in medical schools had climbed to 37.7 years in 2006. In addition to delaying the time to “professional adulthood,” trainees in transitional (pre-tenure track) positions will have lower salaries than colleagues who move immediately to a clinical position. It is frustrating to bear the pain of having grants and manuscripts rejected. It is stressful to balance grant writing, manuscript writing, traveling to meetings, supervising the lab, managing the financial and personnel needs of the laboratory, academic duties such as committees and teaching, and clinical care. There is also the stress of academic timelines and promotion and the fact that tenure track physician scientists receive less compensation than their clinical counterparts. The trainee will be prepared for these challenges if they have followed a well-designed career development plan. The key factors in maintaining confidence and perseverance are one’s motivation and the support and guidance of a strong mentor to help put things in perspective and continue to move forward.

The Dangers of Accepting a Faculty Position Prematurely
It is very tempting to try to obtain a faculty position as soon as possible after fellowship. One is tired of being a perennial student, may have financial needs, and eager for the prestige of finally getting to be an Assistant Professor. Accordingly, trainees commonly make the mistake of rushing into their first faculty position prematurely, which can seriously derail a physician-scientist career. Timing is key, and knowing when the right time has come requires insight, patience, and mentoring. The perils in moving too quickly are that:

• Once a tenure track position is obtained the academic clock starts ticking. If the trainee is not sufficiently prepared she/he will not reach the bench-
marks for promotion, which include items such as sustained R01 or equivalent grant funding, quality publications, and national recognition. The applicant who has invested the extra time to acquire in-depth training with a team of mentors, has a strong publication and funding track record, and is already known in the scientific field will begin their first faculty appointment in a stronger position.

- A number of grants tailored specifically for individuals starting their first faculty position are available from a variety of sources. These grants provide critical bridge support until R01 or equivalent grant funding is obtained. An accomplished applicant with a strong track record will be in a better position to compete for these awards. A weaker applicant will not be competitive and by the time they have developed more of a track record may no longer be eligible for such grant support.
- An applicant searching for a faculty position who already has funding, a strong publication record and national recognition will be better positioned to obtain meaningful written guarantees of protected time and more resources when negotiating for their faculty start-up package.

One motivation to jump to a faculty position is financial. Although loan repayment programs can be extremely helpful, there is currently no solution to the fact of lower salaries for individuals on the pathway to a career in academic medicine. The amount of money awarded to trainees for salaries on career development awards has increased but still remains relatively low. It is recognized that this remains a problem that needs to be addressed by institutions and granting agencies.

The “In Between Time”
Most trainees, especially those who are MDs, require additional years of training after fellowship in order to be sufficiently well trained to become independent investigators. The time gap between finishing fellowship and starting a tenure track faculty position is somewhat nebulous and is often dependent on local policies and traditions, and thus may vary greatly between institutions. Trainees should be aware that significant salary resources are usually not available to support individuals who are in this transitional period. A trainee who stays on after completing fellowship could easily be forced into taking on a heavy clinical load that could disrupt and permanently derail their career development plan. One way to avoid this pitfall is to rapidly obtain independent career development funding. In addition, the trainee should set up discussions with the mentor and department chairs during fellowship to discuss the transitional phase and organize a plan that will facilitate accomplishment of career goals. Even if the fellow has applied and has so far failed to obtain funding, the presence of strong mentorship, with implementation of an aggressive educational and professional development plan with clear benchmarks and objectives may allow the applicant to be retained in a protected position (such as a “fourth” fellowship year).

The vagaries of the “in between” position can be discouraging and represent a critical weak spot in our medical education and career development system. The problem was recently studied by a committee from the Association of Professors of Medicine,1 which came up with a series of recommendations, the top four of which are paraphrased and summarized here:

- **Transitional period:** That institutions should focus on trainees in transition and provide resources, protected time for research, competitive salaries, and mentoring; and that the NIH strengthen the K awards and increase first time R awards.
- **Mentors:** That institutions should create formalized mentoring programs, reflective of the team approach and with generational diversity to reflect diversity of attitudes; that mentors should reflect the diversity of the population of trainees, and should be trained to mentor and be compensated for their efforts; that formalized training along the lines of the career development plan be implemented by institutions, and that NIH expand the scope of K awards to support the mentor of junior physician scientists and thus free up R grants.
- **Promote advancement and reduce attrition of female scientists:** by providing equal resources and start up packages, etc; create a more flexible promotions track for advancement, and support child care, schools, etc.
- **Identify early on and intellectually prepare trainees** so they are better able to enter the physician scientist track: by adopting pre-med undergrad and medical school curricula to reflect the importance of molecular, quantitative, computational skills, etc. that are required for today’s research; working to create an earlier track for physician-scientist career development and provide more time for research.

Hopefully these recommendations will lead towards a national solution to maintaining a healthy supply of physician-scientists.

**Conclusions**
Advancements in medical science have reached the stage whereby the advent of modern mechanism-based molecular medicine is already reaching the clinical and will soon dominate the practice of hematology and oncology. Medical schools, research institutes and the private sector need physician-scientists to drive these advances forward. At most 8% of trainees graduating from hematology oncology fellowship programs follow the physician-scientist career track.1 MDs have a relatively poor track record of obtaining and retaining NIH funding. The Clinton-era increases in the NIH budget did not impact on these figures. Nonetheless, physicians who find good mentorship and follow the guidelines

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stated herein have tremendous opportunities and are in a "sellers" market in terms of obtaining a faculty position. From the scientific standpoint there has never been a better time to be a physician-scientist. Trainees with an interest in this track should feel encouraged to take advantage of these new opportunities and become part of the effort to reform the system and create a culture that is every more conducive towards helping new generations of physicians to realize these goals.

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Correspondence
Ari M. Melnick, MD, Weill Cornell Medical College, 1300 Morris Park Ave., Chanin 517, New York, NY 10461-1926; Phone 718-430-4238; Fax 718-430-8567; e-mail: amm2014@med.cornell.edu.

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