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Careers in Cardiovascular Research

Careers in Basic Cardiovascular Research

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The opportunities in basic science for graduating PhD students and for aspiring physician-scientists have never been so extraordinary. The sequencing of the human genome and the development of the human haplotype map have enabled scientists to begin to unravel the basis of complex multigenic disorders. Rapid developments in stem cell biology are affecting many areas of cardiovascular biology and may enable repair of injured myocardium. High-throughput chemical genetic screening, proteomics, and metabolomics are changing the approaches with which investigators characterize novel signal transduction pathways and develop new therapeutic paradigms. Rapidly evolving molecular imaging technologies are noninvasively illuminating the fundamental processes contributing to cardiovascular diseases. New insights into the mechanisms involved in cardiac myocyte hypertrophy and dysfunction have important therapeutic implications for an expanding population of patients with congestive heart failure.

For the young scientist looking to the future, there are major benefits in pursuing a basic science career including the excitement of discovery, the opportunity for life-long learning, and the potential to broadly affect cardiovascular science and medicine. On the other hand, the young investigator considering a basic science career is confronted by many challenges. The budget of the National Institutes of Health (NIH) has remained essentially unchanged for 5 years (when the impact of inflation is considered). The success rate of R01 grant applications has consistently declined since 2000, and the average age when an investigator receives a first R01 grant (or equivalent) increased to 42.6 in 2007 (NIH Extramural Data Book at www.report.nih.gov/index.aspx). At the same time, the increased costs of undergraduate and medical school educations have burdened potential young investigators with ever-increasing financial commitments. Many academic leaders have suggested that an entire generation of young scientists is “at risk” (www.BrokenPipeline.org). Long hours at the laboratory bench are compensated modestly compared with those of other professions. There is no doubt that embarking on a career in basic cardiovascular science has significant risks. A frequently asked question—“How do I know whether I will be successful?”—has no certain answers.

This perspective piece focuses on the young investigator or clinician (with a PhD, MD, or both) interested in pursuing postdoctoral training in basic cardiovascular science. It is based in part on the experience of the author, who has been privileged to provide advice to an extraordinary cadre of young scientists pursuing research training, often combined with clinical training, in cardiovascular medicine at the Massachusetts General Hospital. This review will focus on the steps required to secure the ideal postdoctoral fellowship and to initiate research training in a basic science laboratory. Also considered will be the optimal time commitment to research training, as well as the challenges associated with the transition to independence.

Securing a Postdoctoral Fellowship

Young scientists considering a postdoctoral fellowship in cardiovascular science have varied backgrounds. Most have PhD degrees and substantial scientific training and research experience. The PhD scientist typically undertakes postdoctoral training to gain additional expertise and experience, as well as to garner scientific productivity, before embarking on a career as an independent investigator. Other young scientists embark on postdoctoral training after completing clinical training in internal medicine and cardiology, often as part of a cardiology fellowship program. Many of these MD postdoctoral fellows have only minimal prior scientific training, whereas others received PhDs before or concurrently with MD degrees. Increasingly, cardiovascular science is attracting MD scientists from other fields such as anesthesiology and surgery. Clinically trained individuals, particularly those without substantial scientific backgrounds, must understand that postdoctoral research training in basic science is substantially different from the training they have completed thus far. Moreover, a career combining substantial clinical activities (>20% of effort) with running a basic science research laboratory is extraordinarily difficult. Clearly, postdoctoral training must be tailored to the experience, background, and aspirations of the fellow, but training clinician-investigators and PhD scientists side by side enables them to benefit from each other’s strengths.

When one chooses an optimal postdoctoral research training experience, 5 steps are recommended to successfully identify the best mentor and research program. It is critical to

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initiate the search for a postdoctoral position at least 1 year ahead—the best laboratories may have a waiting list!

**Step 1: Identify the Area of Cardiovascular Science of Greatest Interest to the Trainee**

One of the most challenging tasks for a young scientist is identifying the area of investigation to pursue. The research area should be an important question in cardiovascular biology that offers multiple possible aspects for investigation. A narrowly focused research question may be answered “prematurely” (before a young scientist has completed training). Reliance on a single assay or technique is too risky because either may be rendered obsolete by technological advances. If the area of interest is too broad, the number of opportunities may be too large to adequately investigate. If the area of interest is too narrow, it may not be possible to identify an optimal training experience. Above all, the young scientist should be passionate about the research area in which he or she is training. Scientific excitement needs to be a driving force, particularly when incubations are long, assays are repetitive, and positive results are few and far between.

**Step 2: Get Sage Advice From More Than 1 Person**

Choosing a research program/laboratory in which to pursue postdoctoral training represents a “career-determining” decision. Senior faculty in the graduate or medical school in which the young scientist has trained often can provide an overview of available opportunities. Thesis advisors and committee members, as well as Residency Program Directors and Division and Department Chairs, are sources of valuable advice. Often these advisors can provide introductions to potential mentors and/or other advisors. The young scientist should seek advice from experts in his or her chosen field of interest. Not infrequently, it is necessary to gently remind an advisor, who is trying to “sell” his or her own research program, to provide a broad perspective. On the other hand, the best advisors, who provide unbiased and unselfish advice, may also be outstanding mentors.

**Step 3: Interview as Many Potential Mentors as Possible**

Much has been written about mentorship and the qualities of an outstanding mentor.1-3 The Mentoring Handbook published by the American Heart Association and American Stroke Association (www.americanheart.org/downloadable/heart/1233694796037MentorHbook2e.PDF) is an outstanding resource for trainees and mentors. Lee and colleagues4 have summarized the key features of an outstanding mentor, which include availability, inspiration/optimism, and the ability to provide direction while encouraging creativity. Please also see “Choosing a Research Project and Research Mentor,” published previously in this series.

Several additional considerations in choosing a mentor deserve mention. First, the optimal mentor for one postdoctoral fellow may not be optimal for another. For example, a fellow without extensive research experience might benefit from working with a less senior, more available mentor. In contrast, a fellow with a PhD or prior postdoctoral experience may choose to be mentored by a more senior, established scientist and may not require as frequent interactions with the mentor as would a less experienced trainee.

Second, although many postdoctoral fellows choose mentors with backgrounds similar to their own, training with a mentor who has a scientific background different from the trainee may result in a spectacular postdoctoral fellowship. For example, a young scientist who obtained PhD training in a laboratory focused on fundamental aspects of cardiovascular development in Drosophila may benefit from a postdoctoral fellowship with a mentor who has an MD or MD/PhD and who is focused on translational medicine or cardiovascular physiology. Similarly, a clinically trained scientist may benefit from a postdoctoral fellowship with a PhD scientist in a basic science department. Often, it is optimal for a trainee to have 2 or more mentors with complementary mentoring expertise or experience, but it is critical that 1 mentor be ultimately responsible for the trainee’s career development.

A third important consideration is the mentor’s track record in the research field of interest to the trainee. Has the mentor been successful in terms of publications and grant support? Information on the grants funded by NIH (including a brief description) is publicly available from the Computer Retrieval of Information on Scientific Projects (CRISP) database (www.crisp.cit.nih.gov). Information on grants currently funded by the American Heart Association (grant application title only) is available on the American Heart Association Web site (www.americanheart.org). A final consideration about choosing a research mentor/research program is that the best basic science training opportunity is frequently located at an institution different from that where the trainee attended graduate school or pursued clinical training.

**Step 4: “Interview the Laboratory”**

A critical determinant of success in a postdoctoral training experience is the laboratory environment. The laboratory environment is an important reflection of the mentor, as are the scientists and students recruited to participate in the mentor’s research program. It is strongly recommended that a potential postdoctoral fellow meet with several of the current postdoctoral fellows and graduate students. Ideally, the candidate should sit in on a laboratory meeting. Key questions include the following:

1. Where are past trainees, and what are they doing? Did they continue along research directions begun in the mentor’s laboratory? If possible, the candidate should e-mail/call former trainees for additional insights. Successful mentors have successful trainees.
2. How available is the mentor for scheduled and unscheduled consultation? Are there routinely scheduled laboratory meetings? Is the mentor’s door always open to postdoctoral fellows, or are appointments necessary? There are merits to both approaches.
3. Who is responsible for teaching new postdoctoral fellows the techniques they need for their research program? The mentor? Senior fellows in the mentor’s laboratory?
4. Do the scientists in the mentor’s laboratory collaborate?
Are more senior fellows willing to teach more junior trainees? Do the scientists in the mentor’s laboratory know about each other’s research projects? Do members of the laboratory meet as a group to solve problems together?

5. Is the mentor’s laboratory a fun place to work? Do colleagues treat each other professionally and with cultural sensitivity? Or, is there an atmosphere of competitiveness? Do the scientists in the mentor’s laboratory get along? Do they spend time together outside the laboratory? Do they have lunch together?

6. What do the postdoctoral fellows and graduate students think about their mentor? If they had it to do all over again, would they choose to pursue research training in the mentor’s laboratory?

7. Are resources sufficient to accomplish the trainee’s research program? Does each fellow have adequate desk space and laboratory space? Are equipment and supplies available? Is there ample opportunity to establish collaborations with other research groups?

8. Does the department or institution have programs that support postdoctoral fellows? Is there a Postdoctoral Fellow Association? Are there institution- or department-sponsored lectures on how to write a grant and on the responsible conduct of research? Does the institution have ample research core facilities that enable the young investigator to utilize cutting-edge technologies?

Step 5: Seek Additional Advice
Having investigated opportunities in a variety of laboratories with a spectrum of mentors, it is highly worthwhile for the young scientist to report back to his or her advisors. The advantages and disadvantages of each opportunity should be reviewed. Experienced advisors can add perspective to a young scientist’s observations.

Beginning in the Laboratory
Many resources are available that offer advice for the young scientist beginning a postdoctoral fellowship, including the American Heart Association Mentoring Handbook (cited above), the ScienceCareers Web site (www.sciencecareers.sciencecareers.org), and a recent perspective piece written by J.W. Yewdell.

Having chosen a mentor and research laboratory (and having been accepted), it is optimal for the mentor and trainee to establish a list of shared expectations. This list should include a description of the nature and frequency of the fellow’s interactions with the mentor(s) and the laboratory meetings and journal clubs in which the trainee will participate. Course work should be included in the training plan to complement the fellow’s experience and prior training. The list should also include the methods by which the mentor will help the trainee to develop independence (encouraging the fellow to give presentations locally and nationally, teaching the “art” of grant preparation, and teaching methods to review a manuscript). The mentor and trainee should agree on a series of anticipated benchmarks by which the mentor and trainee can judge the latter’s progress. It is critical that the mentor and trainee meet on a regular basis to review progress toward achieving these benchmarks and make appropriate course corrections as necessary.

The methods by which a mentor and trainee select a research project vary depending on the mentor and the trainee. For example, a trainee with little prior basic science training (eg, an MD completing clinical training) will need significant direction from the mentor. In contrast, a more experienced scientist (eg, a fellow with a PhD degree) may have a specific line of inquiry in mind and/or may have joined the mentor’s laboratory to learn a specific technology or expertise.

In general, it is desirable to choose a project focused on an important biological question. Often such a project requires collaborations with members of other laboratories. Collaborations enhance scientific programs by bringing together groups of scientists with complementary expertise and resources. Increasingly, multiple research groups are working together to undertake research projects that cannot be accomplished by 1 group or even a few groups. For example, genome-wide association studies often require international collaborations to identify and confirm the association of genomic variants with phenotypes. Ideally, responsibilities for the research work (designing and performing experiments) and the credit (authorships) should be agreed on in advance, but, in reality, such agreements are not always feasible, in part because the research work may change as the project progresses.

Although collaborations are a means to enhance productivity during a postdoctoral fellowship, the fellow should also undertake a project in which he or she may take the lead. Ideally, the research project should have achievable short- and long-term goals. There are a number of advantages to completion early in a postdoctoral fellowship of a body of work worthy of presentation at a scientific meeting and publication in a scientific journal. Participation in scientific meetings, both large and small, permits the fellow to learn how to effectively communicate research findings and to network with scientists with shared interests. Publishing an article early in a postdoctoral fellowship affords the fellow the opportunity to learn or refine scientific writing skills with the guidance of the mentor. An early publication makes it easier to secure extramural funding (see below) and, perhaps most importantly, convinces the trainee that the basic science career choice is indeed feasible.

Time Commitment
If the goal is to become a leader of a productive and self-renewing research program, a young scientist should plan on at least 3 years of postdoctoral training, and most will require longer. Research training is incredibly demanding. Many scientific disciplines do not lend themselves to a 40-hour, 5-day work week. On the other hand, many postdoctoral fellows are successful without working 80 hours per week. There is no doubt that productivity and success are correlated with the amount of time invested, but the correlation is not perfect.
It is critical to maintain scientific focus, but opportunities to work with colleagues and collaborate generously may enhance scientific productivity (as discussed above). On the other hand, it is important to avoid distractions during postdoctoral training such as writing reviews unrelated to the fellow’s research program. Some “distractions” cannot be avoided such as clinical responsibilities mandated by the Accreditation Council for Graduate Medical Education (eg, continuity clinic) or teaching responsibilities required by university departments.

Clinically trained scientists frequently “moonlight” during postdoctoral research training to supplement their income. Some moonlighting may be unavoidable because of financial constraints associated with medical school loans. It is critical, however, that moonlighting not interfere with research training. Mentors need to monitor trainees for signs of fatigue that can impair learning and productivity, as well as health and safety.

Some clinically trained fellows attempt to pursue postdoctoral research training concurrently with advanced subspecialty training. With rare exceptions, fellows who undertake simultaneous clinical training and basic science research training do not become successful independent investigators. Clinical leaders (Department and Division Chairs and Clinical Laboratory Directors) need to understand that a sustained, uninterrupted, and protected period of research training time is required to enable a clinically trained scientist to become an independent investigator in basic cardiovascular science.

**Funding Opportunities at Different Stages of Postdoctoral Training**

Multiple mechanisms are available to support the training of postdoctoral fellows. Sometimes support is available from the mentor’s laboratory/research grants. Often international fellows will come with partial funding from their home institutions. Despite constraints on the overall NIH budget, support for postdoctoral fellows remains a priority. One mechanism by which NIH supports training of postdoctoral fellows is by providing funding for institutional training programs (T32 grants). A list of active National Heart, Lung, and Blood Institute (NHLBI)–supported T32 training programs is provided at www.app.nhlbi.nih.gov/trainingt32. In parallel, the NIH also awards individual postdoctoral fellowships (F32 grants). The 2 programs are similar except that the postdoctoral fellow applies to institutional training programs for T32 support and directly to the NIH for F32 support. In 2007, 30% of the F32 applications to the NHLBI were funded (www.report.nih.gov/award/success/Success_All_2007.xls).

Additional opportunities are available for postdoctoral fellows training at NIH, as well as for fellows from underrepresented racial and ethnic groups and fellows with disabilities. Details are available at www.nhlbi.nih.gov/funding/training/redbook/phdintro.htm. It is important to note that F32 and T32 awards are limited to US citizens and permanent residents.

A variety of foundations provide support for postdoctoral fellowship training. Notably, the American Heart Association Affiliates funded 252 new postdoctoral fellowships in 2007–2008 (www.americanheart.org/downloadable/heart/1202158110957Research%20Facts%202008.pdf). Additional funding sources may be found on a variety of Web sites including www.grantsnet.org and www.infoed.org/new_spin/spinmain.asp.

After a period of time in the basic science laboratory sufficient to generate adequate preliminary data and, ideally, to publish an article, a postdoctoral fellow should consider applying for a mentored career development award. These awards generally provide greater salary support than a postdoctoral fellowship award and are of longer duration. Mentored career development awards are designed to enhance the transition from postdoctoral fellow to independent investigator. At NHLBI, 2 types of mentored career development awards, K08 and K23, are targeted to individuals with clinical doctoral degrees. K23 awards are directed toward patient-oriented research. K08 awards support clinician-scientists training in biomedical and behavioral research, including translational research. In fiscal year 2007, 35% of K08 grant applications to NHLBI were funded (www.report.nih.gov/award/success/Success_ALL_2007.xls). NIH institutes other than NHLBI provide mentored career development award opportunities (K12 awards) to PhD scientists. NHLBI provides K01 awards to MD or PhD scientists from underrepresented racial and ethnic groups, as well as individuals with disabilities. A new NIH-wide funding mechanism, the K99/R00 award, is designed to provide postdoctoral scientists (either MD or PhD) with both mentored and independent research support. The American Heart Association has a similar program designed to foster the transition of clinically trained scientists from fellow to faculty: In 2007, 13 new Fellow-to-Faculty Transition Awards were funded.

Applying for research grants is a fundamental part of a career in basic science. Writing a postdoctoral fellowship grant application before joining a research laboratory is an ideal method to become immersed in the scientific topic and to learn where the scientific cutting edge lies. Importantly, establishing research training goals and career development milestones is typically a required component of a postdoctoral fellowship grant application. Writing an application for a career development award or a first independent grant during postdoctoral training enables the fellow to benefit from the grant writing experience of the mentor. Examples of first independent grants include the American Heart Association Scientist Development Grant and Grant-in-Aid. Moreover, the NIH has enacted several new programs to help new investigators to obtain and renew their first R01 grant (www.grants.nih.gov/grants/new_investigators/resources.htm).

**Transition to Independence/ Career Opportunities**

The transition to independence is perhaps the greatest challenge for the postdoctoral fellow and mentor. In some cases, mentors are reluctant to see successful postdoctoral fellows leave the laboratory. In other cases, fellows are reluctant to leave the security of the mentor’s laboratory and confront the risks associated with establishing an independent research program. Difficult questions that must be addressed openly and candidly include the following: Can the fellow take his or her research project from the mentor’s laboratory? Which
career opportunity offers the best chance of long-term success? Again, there are multiple resources with advice for the postdoctoral scientist transitioning to an independent position including the ScienceCareers Web site (cited above) and the Howard Hughes Medical Institute Web site (Resources for the Development of Early-Career Scientists; www.hhmi.org/resources/labmanagement/).

In considering whether it is the right time to initiate an independent research program, the postdoctoral fellow should consider several additional questions:

1. Have I trained long enough?
   Most postdoctoral fellows with a PhD degree train for ≥6 years (including graduate school) before establishing an independent research program. MD postdoctoral fellows without prior research experience should expect to train for a similar period of time. Leaving the mentor’s laboratory too early may leave the young scientist with insufficient experience to establish a self-renewing laboratory.

2. Have I contributed to the scientific literature?
   Productivity, in terms of publications, increases with duration of training (often exponentially). Too few publications can impair the ability of the young scientist to obtain grant funding. On the other hand, promotions committees are often reluctant to promote investigators who do not publish independently of their mentors.

3. Have I written a research grant?
   As noted above, it is optimal to write grant applications with input from the mentor, who best knows the young investigator’s research program and scientific interests.

4. Have I found the right position?
   Will there be sufficient protected research time (generally ≥80%)? For physician-scientists, it is critical to avoid situations that have excessive or incompletely defined clinical commitments. For PhD scientists, it is important to limit teaching commitments until the laboratory becomes established. Is the environment conducive for the success of newly independent investigators? Are there sufficient resources (salary, supplies, space, and personnel) to enable the young scientist to establish an independent research program (including successful application for grant support)? Is there a “critical mass” of faculty with common research interests? If the soon-to-be-independent investigator is changing institutions, are there interested and willing mentors available to foster the new investigator’s research program and help him or her “learn the ropes” at the new institution?

For scientists initiating an independent research program, a variety of types of opportunities exists. Some investigators pursue careers in medical centers wherein the faculty appointment and laboratory are based in a clinical division. The emphasis is on teaching medical students, residents, and fellows. For clinically trained scientists, a clinical commitment is often required, generally 1 to 2 months per year. Other investigators pursue careers in university settings. The investigator’s faculty appointment and laboratory are in a basic science department. Basic science faculty members typically are responsible for teaching undergraduate and graduate students and often medical students. There are many variations in these career settings, with scientists based in medical centers playing an active role in teaching undergraduates and graduate students at universities, and investigators based in university settings contributing to the education of medical students, residents, and fellows.

Many young scientists pursue careers in the pharmaceutical or biotechnology industry after completing postdoctoral training. Although careers in industry typically do not bring academic acclaim, they often offer the rewarding opportunity to focus efforts on the development of new therapeutics. Generally, careers in industry do not require a substantial clinical or teaching commitment.

In summary, a career in basic cardiovascular science offers many benefits and poses an equal number of challenges. To maximize the probability of a successful career in cardiovascular science, it is critical to take the time to identify the right science, the right mentor, and the right laboratory. Having identified the best postdoctoral training experience, the probability of success is correlated with the time and effort put in at the bench. Clearly defined expectations and milestones can facilitate the mentor-trainee relationship and enhance the postdoctoral training experience. The successful transition to independent investigator in basic cardiovascular science offers the promise of life-long learning and discovery, advances in scientific knowledge, and contributions to therapeutic advances.

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