K08 and K99 Cardiovascular Training
Comparisons and Trends Among Current Awardees

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Training the next generation of independent cardiovascular investigators has been a longstanding interest to the Circulation Research community, as evidenced by an editorial in the first volume of this journal. Since then, National Institutes of Health (NIH) training mechanisms have expanded from a single offering of postdoctoral fellowships to the current offerings composed of institutional predoctoral and postdoctoral traineeships, individual predoctoral and postdoctoral fellowships, and individual early career development awards.

The transition from postdoctoral trainee to independent status has always challenged aspiring young investigators and is especially difficult during fiscally constrained times. As resources dwindle, we wanted to compare the 2 training programs (K99/R00, K08) that most often launch cardiovascular bench science careers and describe the characteristics of individuals trained under each program.

The NIH initiated the K99/R00 Pathway to Independence award to support this transition to independence for promising candidates. Participation by the National Heart, Lung, and Blood Institute (NHLBI) in the K99/R00 funding opportunity complements its long-standing participation in the K08 Mentored Clinical Scientist Award program. We compare the first 4 years of trainees in the cardiovascular K99/R00 portfolio with the concurrent experience with the K08 cardiovascular portfolio. The results highlight differences and similarities in the populations and institutions served and the training structures and skills developed. Continued analysis of this comparison will inform future approaches to maintain a vibrant, innovative, productive, and engaged biomedical research community.

The K08 and K99/R00 programs have fundamental differences. The K08 provides up to 5 years of mentored research during the assistant professor years, whereas the last 3 years of the K99/R00 (the R00) is an independent award and starts with the first faculty appointment. We analyzed 4 years of data to compare and contrast the K08 with K99/R00 programs to determine the attributes of trainees and comment on the program strengths (Table). We reviewed only grants assigned to the NHLBI Division of Cardiovascular Sciences (DCVS). We looked at records of all new K08 and K99 applications funded between 2007–2010. Grantee information was abstracted from the Principal Investigator’s (PI) biosketch associated with the initial application. A total of 150 biosketches were abstracted.

K08 Grantees
From 2007–2010, 77 new K08 awards were funded. K08 awardees are highly trained and represent a variety of clinical disciplines. More than half of the K08 recipients hold an advanced academic degree in addition to the MD, with the MD/PhD being the most common combination (Figure 1). Adult cardiologists constitute nearly half the grantees, and many hold designated subspecialties including cardiac imaging, vascular medicine, interventional cardiology, and cardiac electrophysiology. Pediatric awardees included pediatric cardiologists, critical care pediatricians, neonatologists, and pediatric cardiothoracic surgeons (Figure 2). The remaining awardees were trained in internal medicine, emergency medicine, pulmonology, veterinary medicine, pharmacy, nephrology, endocrinology, and pathology.

PhD degrees held by K08 awardees included biochemistry, immunology, pharmacology, molecular pharmacology, pathology, cell biology, neuroscience, molecular genetics, developmental biology, biophysics, and clinical virology. Master’s degrees held by K08 awardees included epidemiology, public health, and public policy.

The hallmark of the K08 award is the extended period of research mentoring, and there are several ways of tracking awardee accomplishments during the award. For example, the K08 applications require that mentoring teams and mentoring plans are carefully delineated. Mentoring roles are explained and meeting frequency defined. Multiple mentors are currently the norm, with 1 designated as the principal mentor. K08 recipients may also enlist advisors to independently assess their progress and serve as a resource to overcome unanticipated problems. Strong research mentors are critical for the awardees to achieve independence.

The K08 annual progress report, submitted by the awardee to the NHLBI, is a valuable monitoring tool for awardee, mentor, and NHLBI program staff. Progress reports summarize the year’s work including scientific progress, peer-reviewed papers, presentations, and other academic successes. The “mentor’s statement” is also a part of the annual report and attests to the awardee’s progress as well as obstacles in achieving the year’s goals.
The NHLBI program staff can also provide guidance to K awardees. Advice is sought after the award when the awardee considers changing institutions, when mentors leave or die, or when new institutional demands threaten to interfere with their 75% protected research time. We work with the K08 awardee and their institution to facilitate resolution of local questions and problems, on behalf of the awardee.

K99/R00 Grantees

The K99/R00 award was designed to “facilitate a timely transition from a mentored postdoctoral research position to a stable independent research position with independent NIH or other independent research support at an earlier stage than is currently the norm.” Between 2007–2010, the NHLBI issued a total of 73 CVD K99 awards. Awardees are predominately basic scientists (Figure 3) trained in disciplines that include biomedical sciences (biochemistry, cell biology, and pharmacology), biophysics or physiology, biomedical engineering, genetics, and epidemiology (Figure 4). The remaining K99/R00 PIs were trained in clinical specialties or in other basic fields (cardiology, clinical psychology, immunology, pathology, or neuroscience).

The 2-phased K99/R00 program is unique. The “K99 phase” includes research as well as a job search, and K99 recipients are encouraged to explore employment opportunities at multiple institutions. This approach reinforces important “survival skills” that include oral presentation, negotiation, and the planning needed for successfully assuming a faculty-level position. The initiation of R00 funding requires the K99 investigator to accept a tenure-track assistant professorship or an equivalent appointment as an independent researcher and an internal review by NHLBI staff of the awardee’s progress during the K99 phase, of plans to complete the remaining aims of the original K99/R00 proposal, and a time table to seek new independent funding. The provisions for protected time, research support, and laboratory space of the new position are also reviewed. When concerns arise, the NHLBI staff work with the hiring university and the PI to resolve them.

The K99 awardees have been largely successful in making the transition to R00. Of the 73 researchers funded from 2007–2010, 54 have fully transitioned to R00 through fiscal year 2011. Two-thirds of K99 researchers transitioned to new institutions as R00 independent investigators. This transfer rate contrasts dramatically with the 4% rate of the K08 awardees for the same time period where, in most cases, transfers to a new institution only occur in response to events that were unforeseen at the time of initial application.

K99/R00 applicants may request 1 or 2 years of K99 support, and the NHLBI asks that transitions occur no sooner than 1 year after the initial K99 award date. Eleven awardees or 15% of our cohort requested a single year of support. Although 8 of these PIs fulfilled their plan to attain an independent position at the end of year 1, 2 awardees required supplementary funding to extend their K Phase and 1 was lost to follow-up. Thus, unforeseen delays may adversely affect applicants who propose a single year of mentored training, and we now strongly encourage K99 applicants to request 2 years of K99 support, noting that they may transition to independent status any time during year 2 of K99 funding.

Among all K99/R00 recipients, most transition between 19–24 months after their K99 start date (Figure 5). Most of the others transition early, either at the end of year 1 of the K99 or in the first 6 months of year 2. Only 3 awardees (4%) have left the program, with 1 taking a research position in the pharmaceutical industry and the others being lost to follow-up. These findings reflect the exceptional talent and ambition
of these investigators who are highly sought by universities across the country.

R00 awardees are viewed as “independent,” starting with their appointment to a tenured track assistant professor position. With most transitioning to new institutions for the R00, they separate from their K99 mentors, which may create a period of vulnerability, particularly at institutions that lack robust programs to support newly hired faculty. The impact of transfer on academic independence must be tracked. We also must seek feedback from R00 recipients to fully evaluate the merits of this program.

Awardees by Institution
We ranked K08 and K99 awardee institutions by “Total NIH Funding” as a marker for institutional research intensity. We categorized all awardee institutions into groups by NIH Funding: Top 1–20, 21–50, 51–100, and >100, and found no difference in the distributions of K08 and K99 awardees among these categories (Figure 6, P>0.8, Mann-Whitney test). Roughly 47% of awardees trained at a top-20 school, and 27% trained at institutions ranked 21–50.

In a similar manner, we compared “institutional research intensity” for K99 awardees who transitioned to new institutions for their R00 grant and found that the R00 awardees who changed institutions dispersed to less research-intensive institutions (Figure 7, P<0.02, Wilcoxon signed-ranks test for matched pairs). This result is consistent with the view that top funded universities generally draw large numbers of trainees but do not hire all they train. We also know anecdotally that the K99 faculty applicant is attractive to most universities because they bring substantial funding to support their first 3 years. The result also suggests that the K99/R00 program serves as a valuable resource to expand the research expertise at a wide variety of institutions throughout the nation.

The Common Goal
The K08 and K99/R00 programs share a common goal to develop new investigators to maintain a highly skilled cadre of innovative and productive biomedical researchers. To this end, an important outcome is the success of each awardee in attaining independent grant support. We encourage each investigator to apply for an R01 grant in the latter years of K08 or R00 support. DCVS staff has sponsored K awardee meetings by scientific focus. Last year, we sponsored a vascular biology meeting, a part of which focused on “K to R” transition for K08, K23, and K99/R00 recipients as well as K12 scholars supported by an institutional career development program in vascular medicine. A total of 40 K awardees attended. A highlight was a panel of current K08 grantees who had received their first R01 awards. Their discussions emphasized planning and shared their R01 application experience. In addition, NIH staff provided sessions on grant review, grant referral, linking to Clinical and Translational Scientific Award (CTSA) research centers, and on how to identify additional funding opportunities through NHLBI ongoing clinical networks or through the NHLBI Ancillary Studies programs. The meeting was enthusiastically received. We hope to expand DCVS K outreach activities to the full range of subject areas and highlight the K to R transition.

Looking Forward
Determining Which Award to Pursue
The decision of which career development award to pursue is largely determined by award requirements. The NHLBI K08 award requires that applicants hold a professional degree (MD, DO, DMV) and US citizenship or permanent resident status. K08 applicants may be either postdoctoral trainees or
hold junior faculty positions. The K99/R00 award is a hybrid program, and US citizenship is not an award requirement. The K99/R00 mechanism requires applicants to be postdoctoral trainees with less than 5 years of experience and is not available to those holding an assistant professor or higher faculty appointment.

In deciding what award to pursue, it is critically important to determine which Institute or Center (IC) of the NIH will support the science, and whether the IC supports the mechanisms being sought. Consulting program officers is strongly encouraged. Program officers can advise whether a research falls within the IC’s mission. Talking with program staff at multiple NIH ICs should help determine the best IC and funding mechanism. Program officers can also keep applicants posted on important program or review changes, such as the policy change regarding number of grant revisions permitted.

**Characteristics of Successful Applications**

Preparing successful applications takes considerable time and effort. There are 5 key review criteria for K applications: Candidate; Career Development Plan/Goals and Objectives; Research Plan; Mentor(s); Co-Mentor(s); Consultant(s); Collaborator(s); and Environment and Institutional Commitment to the Candidate. Reviewers want to know the applicant’s prior research experiences as well as their passion and enthusiasm for research. Evidence of prior scientific productivity such as peer-reviewed papers and abstracts are important to include. A key question that the reviewers must determine is whether the candidate has the skills and capabilities to become an independent investigator. The mentoring team is of paramount importance and must be thoughtfully assembled. The research mentoring team must generally include at least 1 currently funded NIH investigator, and each mentor should have a strong record of mentoring K awardees who have entered successful academic careers. The role of each mentor must be clarified. Career Development plans must be clear and explicit, including the frequency of mentor meetings as well as “mentoring team” meetings. Institutional support refers to evidence that the candidate will have protected time and that the institute has made a firm commitment to the candidate to support their pursuit of research. This generally translates into letters from Deans of Research, Department Chairs, and Division Heads about protected time but also laboratory and office space/resources and access to administrative personnel. The research plan must be written in clear, concise, and measurable terms. The K awards are reviewed by IC-based special emphasis panels rather than subspecialty study sections. K applications must be written for a scientific audience. Terms and abbreviations must be defined, and specialty jargon must be avoided. The final element is the career development plan. Whether the K applicant has a single degree or multiple degrees, the career development plan must be clearly spelled out for the duration of the award.

Applications must to arrive at NIH in pristine condition. Typing, spelling, and grammatical errors are not viewed kindly. The application must undergo review and revisions until every portion of the grant can be truly rated as exceptional. If an application is not pristine at the time of submission, the applicant should keep revising and wait for the next submission date.

**Framing New Research**

A question that frequently comes up is, how different should the proposed K research be from the applicant’s prior work? The PI’s potential to develop an independent line of research can be an issue, particularly when he or she is associated with a large laboratory. Yet, proposing research that is too divergent from the candidate’s past record or from the mentor’s expertise can be seen as a lack of focus or as overly ambitious. Thus, applicants must work closely with their mentors and other colleagues to assess their plans both in relation to their present state of expertise and to their long-term goals. This assessment should culminate in clear objectives that are most often a mix of present skills that will benefit from further development and new skills to be mastered. When this assessment is understood by both the mentor and the PI and is made clear in the application to the reviewers, it can form a strong rationale for the proposed experiments and other activities such a course work and instruction from committed experts to achieve the long-term goals. Overall, the research plan must be feasible, focused, and structured so that even unanticipated or negative results will yield new knowledge rather than cripple the intended time table. Preliminary findings that support these characteristics are included in virtually all successful applications. Reviewers make some allowance for the background of the candidate; those who hold PhDs or who have substantial research experience are held to a higher standard for publication history and previous work. However, all candidates are expected to have some research experience relevant to their proposals as evidence of a bona fide commitment to their long-term goals. Applications from candidates who lack a research background are often found to be scientifically naive in review.

**Conclusions**

The K08 and K99/R00 have substantial differences that arise in large part from their eligibility requirements and structures. These differences are reflected in the proportion of each population that has clinical experience and the frequency of transfer to a new institution. However, more than half of the K08 cohort holds a PhD or an academic Master’s degree, so the basic science background for this group is more comparable to the K99/R00 awardees than if the K08 recipients had only MDs.

The mentoring provisions of these awards follow 2 models that have complementary strengths and weaknesses. K08 awardees pursue a program of mentored training through the entire duration of the award, most often for a total of 5 years. Thus, those proposals that merit funding include long-term commitments from the institution and the mentors to a well-crafted plan for the career development of the candidate. This arrangement when executed as planned is the proven strength of the K08 program, as indicated by recent NIH-wide data showing that K08 recipients achieve greater success in attaining subsequent funding to sustain their research ca-
reers,\textsuperscript{2} as compared with individuals starting research careers without the benefit of K funding. However, this structure could delay the independence of the most productive PIs and leave the skills needed by PIs who seek to change institutions underdeveloped. In contrast, the requirement for K99 recipients to transition to an independent position within 2 years should avoid these pitfalls but may be premature for PIs who encounter unexpected obstacles to their development or who would benefit from additional career guidance. As these two populations progress, we will need to follow their success in gaining continued funding and research productivity to determine if the K99/R00 fosters a level of success similar to that of the K08 and to see which model best serves the needs of the varied populations to be served.

**Disclosures**

None.

**References**

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