How to Obtain a National Heart, Lung, and Blood Institute-Sponsored K08 and K99/R00 Grant in the Current Funding Climate

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I write this editorial in an attempt to help applicants and their mentors as they prepare their National Heart, Lung, and Blood Institute (NHLBI)-supported K08 or K99/R00 applications. In my view, these programs are critical for the future of cardiovascular research in the United States because they support talented new investigators at a particularly vulnerable period in their careers. In this issue, Circulation Research has published an article from the NHLBI that details critical aspects of these programs.1

Cardiovascular disease is still the number 1 cause of death in the United States.2 There is an obvious need to develop novel therapies to prevent or reverse the consequences of these diseases. New therapies should reduce the morbidity and mortality of cardiovascular disease, lower associated costs of health care, and improve the lives and productivity of affected patients. Basic, translational, and clinical research is the foundation on which these new therapies will be developed. High-impact discoveries that lead to medical advances are usually made by well-trained biomedical scientists, and many of these investigators have started their careers with support from NHLBI K08 (Mentored Clinical Scientist) and K99/R00 (Pathway to Independence) awards. These grants support training of young scientists in premier laboratories to prepare them for careers in what has been, in my view, the best biomedical science environment in the world, the United States. This “pipeline” of young talent is challenged by the current funding environment. In my view, the current lack of support for the biomedical research puts our leadership in a difficult position in this field at risk. I digress.

I have spent >25 years reviewing different types of grants for the NHLBI, and I have had significant experience both mentoring K08 awardees and reviewing K08 and K99/R00 applications. In this editorial, I give my personal views on who would make an ideal candidate for each of these awards. I also discuss my personal views on those aspects of K08 and K99/R00 applications that, to me, make them outstanding. I write this editorial in the hope that I can be helpful to applicants, so that their grants do not fall on the wrong side of the pay line for reasons that they can avoid. Make no mistake about where we are right now; we are in full crisis mode. The current3 NHLBI pay line of 19 (raw score, 10–90 scale with 10 being the best score) for K awards means that the application must receive some scores of 1 (the very best score, which in olden days was rarely given) by some reviewers. A score of 1 (translates to a 10) is described as “exceptionally strong, with essentially no weaknesses.”4 It is not the fault of the NHLBI that the pay line for these awards has plummeted. This pay line reflects the reduced support for the National Institutes of Health, and thereby training of the next generation of biomedical scientists. Given this highly competitive environment, every aspect of the application needs attention, because reviewers pay attention to the entire application, not just the science. What follows are my opinions of who should apply for K08 (Mentored Clinical Scientist) and K99/R00 (Pathway to Independence) awards and what makes a candidate special to me.

K08 (Mentored Clinical Scientist) Awards

K08 (Mentored Clinical Scientist) Awards are primarily for MD and MD/PhD applicants who have finished their clinical training and have or are moving into entry-level faculty positions. These individuals usually have just finished an extensive clinical training phase and are now returning to the laboratory to blaze a pathway to an independent career as a physician scientist. K08 awards are mentored awards that are designed to prepare physician/scientists for careers in academic medicine. To me, they are designed to set the stage for the applicant’s first R01 application.

When I review these applications, I am looking for a candidate with a track record that documents a sincere desire for a career in research. Past training is important and productivity, as documented by publications, is viewed as a predictor of future success by almost all reviewers. The applicant does not need to have an extensive publication record. However, if there has been a significant amount of time in the laboratory during previous training, there should be first author publications. If there are few publications or gaps in publications, then the applicant needs to state why and hope for the best.

Because K08 awards are mentored awards, the qualifications of the mentor are critical. The mentors must convince the reviewers that they will devote time and energy to the development of the K08 applicants. The current research environment is harsh and, to be successful, I think a dedicated mentor can be the factor that ultimately determines success or failure. The mentor should read the application. Many applications fail because it is clear the mentor has not reviewed the

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application. The criticism goes like this, “if the mentor has no time to read the application, then will they have time to mentor the applicant?” Sometimes a “junior” investigator is proposed as the mentor. My view is that less established investigators can provide valuable training and can be great mentors. However, junior faculty members are in the process of establishing their own career, and there can be concern that they may not be as “giving” with their ideas as established senior scientists. Therefore, if a junior faculty member is proposed as the mentor, then I think it is wise to have a senior scientist as a co-mentor. These types of mentoring teams are popular with reviewers.

The applicant must have a well-defined career development plan. The applicant needs to clearly define the goals of the training plan and tell reviewers what is going to be learned and why learning these things will enhance the scientific skill set. Applicants should tell reviewers how the science proposed will lead to the first R01. The mentors must clearly define how they will develop the young physicians/scientists and guide them to the level of an independent investigator.

The Environment and Institutional Commitment must be strong. The mentor and the sponsoring institution must provide a clear description of the resources that will be used to support the K08 candidate. Institutions that give K08 applicants entry-level faculty positions on the tenure track are viewed favorably by review committees. Protected time from clinical work, research space, and financial investments must be clearly detailed, because these are essential for success.

Of course, the research plan must be good. Good science is good training and will catapult the candidate to an independent career. It is expected that the area of study will be related to the expertise of the mentor. Although these are training awards and preliminary data are thought to be less important, reviewers still look for preliminary data to show feasibility and proof of concept for the research plan. Because the candidate is often just out of clinical training, portions of these data could be from the mentor’s laboratory. If this is the case, then it is important that the candidate and the mentor clearly detail how the applicant will eventually develop a research program that will be independent of the mentor’s research.

So, who moves to the top of my list when I review these applications? My “walk on water” K08 candidate has been productive in previous research training and has a number of first author publications in solid journals. My top candidate would already have an entry-level tenure track faculty position, with documented protected time and an institutional commitment that includes space (in or next to the mentor’s laboratory) and a financial investment specifically for the work proposed (a start-up package). The mentor would be an established investigator with a track record for training independent scientists. The mentor would have the intellectual and financial resources to support the applicant through this K08 training period. There is not sufficient funding in the K08 award to support the proposed science. Therefore, the applicant, mentor, and institution must provide the reviewer with evidence that there will be financial support for the science. The career development plans should clearly define what will be accomplished to help ensure that the candidate is ready for an independent scientific career within a few years. The applicant and the mentors should be saying the same thing about the training plan, performance expectations, and the road to independence. The science should be innovative and independent from the central theme of the mentor’s laboratory. The project should have the capacity to develop into an independent R01-supported area of research for the applicant.

**K99/R00 (Pathway to Independence) Awards**

K99/R00 (Pathway to Independence) awards are for young investigators who are currently working as postdoctoral fellows in their mentor’s laboratory. They should be finishing their postdoctoral research and approaching the time when they will transition to an independent faculty position. The K99/R00 award has partially mentored (K99 phase) and partially independent (R00 phase) components. Those with MD, MD/PhD, and PhD degrees who are working as postdoctoral fellows and approaching the time when they will transition to an entry-level faculty position would be appropriate candidates for this award.

When I review these grants, I am looking for candidates with a strong publication record in their graduate and postdoctoral training phases. There is no substitute for publications. Reviewers might not understand your science but they all can count, and they will count the number of first author publications you have. I find that reviewers expect to see that the applicants have first author publications from both their graduate and postdoctoral research training experiences. If there is a reason why this is not the case, then it needs to be explained. I also look to see if the applicant has been involved in collaborative research with laboratories outside of the mentor’s laboratory. To me, the richness of the research experience is a useful predictor of an applicant’s ability to thrive in the current collaborative research environment.

The career development plans presented by both the applicant and the mentor are important. The applicants need to clearly describe what they will do in the remainder of their mentored training (K99 phase) and then state the work they will perform during the R00 phase. The mentors need to discuss how they will guide the applicants to the independent (R00) phase and clearly state how the science in the independent phase will be distinct from things being accomplished or planned in their laboratories. It is fine if the plan is to transition to a faculty position in the institution where the postdoctoral work is being performed. However, I have found that most reviewers do not like candidates to stay where they are, and they reward the applicants who seek a new position where they can be independent of previous mentors. Again, given the current environment in which every little factor can push the applicant to the wrong (and much larger) side of the pay line, every factor must be considered. Therefore, having a plan to look broadly for the best possible opportunity, even if you end up staying where you are, will be better-received by the most reviewers.

The research plan for the R00 phase must be independent of the mentor’s research and be viewed as an area that the candidate could explore in depth for a significant period of time. My view is that the science proposed in R00 applica-
tions must be something that reviewers feel will be a fruitful area of study for many years and will launch the candidate’s independent career.

My “walk on water” K99/R00 candidate has been productive in previous research training and has first author publications as a graduate student and as a postdoctoral fellow. The career development plan must have details of the work that will be performed to finish the postdoctoral experience as well as the science that will be performed during the R00 (independent) phase. The research in the R00 phase must be viewed as independent of the central theme of the postdoctoral mentor’s laboratory. I look for research in the R00 phase that is innovative and career-building. I need to see something that can build to an R01 within a few years.

My favorite applicants discuss how they will search for an independent faculty position and the type of environment they are looking for. The applicants should be looking for an entry-level tenure track faculty position in an institution with strength in their research areas. Obtaining a tenure track position in an institution where there are no collaborators is a formula for failure. Tell reviewers what type of environment you are looking for. Stating what institutional resources are essential for you shows clarity of thought and is good planning. The ideal institution would be able to provide independent research space, start-up funds, collaborators, and senior leaders with a history of developing junior faculty. The current mentors need to discuss how they will help the successful candidate make the transition to the R00 phase. The mentor needs to state that the science described in the R00 phase will be the applicant’s independent work.

Attention must be given to every aspect of the application because different reviewers focus on different things. I cannot overemphasize the suggestion that attention to every detail is essential. If either you or your mentor fails to address everything requested, then you can lose points, and you cannot afford to lose any points with the current pay line. These awards are extremely competitive, and we will clearly eliminate great people from careers in biomedical research because of the current funding climate. The NHLBI pay line for K awards has gone from 30 (in 2011) to 19 (in 2012), so there is no debating the fact that we are excluding qualified young scientists from careers in academic medicine and the private sector (where many people eventually would find themselves).

In summary, the K08 and K99/R00 awards are, in my view, essential for the future of cardiovascular science in the United States. They have always been significant awards, but given the trying funding climate they are, in my view, essential. This is the most challenging funding climate in my >30 years in biomedical science. It is sad because we have so many wonderful tools to use today and there are great opportunities to develop new therapies that would benefit patients in need. I have always been a glass half-full person, and I still am. However, I have purchased a smaller glass. My hope is that sometime soon our political leaders will recognize the merits of the National Institutes of Health and the contributions it makes to the private sector and to patient care. In the interim, K08 and K99/R00 awards can help our best young people weather this storm, and hopefully things will be better before their awards are completed. To me, K08 and K99/R00 awards are career-launching grants. They often determine if someone gets an opportunity to pursue biomedical science as a career. My advice to K08 and K99/R00 applicants is to be productive (publish papers) during your training phases. You cannot publish too much or too soon. As applicants prepare an application, they should work with their mentoring team to develop a thoughtful proposal that allows reviewers to know who they are, what they have done, what they plan to do in the future, and how their mentoring team will guide them to a faculty position as an independent investigator. Good luck!

Disclosures

None.

References


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