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Picking a Research Problem -- The Critical Decision

There is probably no question that plagues investigators, especially young investigators, more than how to pick a research project. This decision is not one that must be faced only once in a lifetime; rather, it must be continually revisited. Although it is easy to assume that success in research is just the difference between good and bad luck (and indeed there is a certain amount of luck in research), most highly regarded investigators will have many successful research experiences during their careers.

For the new investigator and junior faculty member just starting his or her career, the decision about a research project is further complicated by many other questions. How should one weigh high-risk, high-interest projects against lower-risk projects of lower interest? How similar or different should the project be from work done during one‘s postdoctoral fellowship? Can one remain in the same institution as one‘s postdoctoral mentor and still make an impact, and if so, how is this best achieved? How many different projects should an investigator attempt to be involved in or undertake? How important is complete independence? When is collaboration good, and with whom? Should the M.D. investigator do anything differently from the Ph.D. investigator in picking a research project? What do you do when you are faced with some aspect of a project for which you are not technically prepared? How should one balance projects funded by the National Institutes of Health (NIH) against projects without such funding? In contrast to the rich scientific base that underlies the research itself, little has been written to help the investigator facing these challenges[1,2,3,4,5,6]. Clearly the answers to these questions depend on the exact circumstances, background, expertise, and desires of the individual investigator, but every investigator should have a strategy for picking a research problem that optimizes the chances of success.

The first step in picking a research project is to understand what makes research “good.“ Indeed, considering the extremely competitive nature of research funding and the rigorous review process used by top academic institutions for promotion, this question should be more accurately phrased, “What makes a research project outstanding?“ Certainly, there are fundamental characteristics that everyone would agree are important. The study should be well performed and use appropriate and up-to-date forms of technology. The data should be carefully analyzed and accurately reported. For studies involving animals and humans, ethical considerations must be dealt with appropriately. But is this enough? Are these the variables that make us feel that the work of one investigator is superior to the work of another? Usually not.

In my opinion, there are several features that make a research project “outstanding.“ First, it must ask important questions. If the question is not important, then it is likely that no matter how carefully the study is performed, how accurately the results are tabulated, or how well the work is reported, this will not be viewed as an outstanding piece of work. Second, if possible, the project should have the potential to yield a “seminal“ observation -- one that creates truly new knowledge, leads to new ways of thinking, and lays the foundation for further research in the field. We often recognize a seminal observation as the first major publication in an area, which sets the stage for subsequent work and will be followed by many reports from the same and other laboratories extending and developing the point and expanding it to related areas. If these first two criteria are met, the remaining criteria for good research are usually easily fulfilled. Thus, the resuits of the project will be publishable in respected journals, recognized and cited by peers, presentable at high-quality meetings in the field, and of course, fundable on competitive grant review.

It is important to recognize, however, that frequently, at the earliest stages, work leading to a seminal observation goes counter to existing dogma. Thus, peers may be skeptical, making it difficult to publish the work in the "best" journals and difficult to obtain competitive grants. Over the past several years, very tight NIH funding has made this problem much worse and no doubt has led to a loss of creativity in science, as more and more investigators attempt to ride the trends in science rather than seek new avenues for investigation[1,2,3]. In such cases, the wise investigator must determine, by discussion with trusted colleagues, whether the work has the potential for real importance, find the capacity to stick with the project, and fight to obtain financial support until the rest of the scientific community recognizes its value.

With these points in mind, picking a research project can be viewed as a series of discrete steps or thought processes that might be termed the "Ten Commandments for Picking a Research Project."

I. Anticipate the Results before Doing the First Study

First and foremost, before beginning a project, anticipate the results you might obtain. If the most interesting outcome is not very interesting, then certainly this is not an area worthy of much effort (although often it may be necessary to perform uninteresting experiments as part of the complete characterization of a process). On the other hand, if you can imagine some interesting outcome of the experiments, then anticipate what the next step or next series of experiments might be. If you are not prepared to follow up the most interesting result, then perhaps it is not worth beginning at all.

II. Pick an Area on the Basis of the Interest of the Outcome

As you look through various possible research projects, try to pick areas that are not only of interest to you, but also of interest to a large fraction of the scientific community. Studying a minor aspect of a rare phenomenon may be a reasonable project if the outcome can affect some broader aspect of science. If the most interesting result is of interest only to two other people in the field, however, the research is never likely to be viewed as truly important or seminal. Although studying some aspect of a large biologic or clinical question does not necessarily ensure that the findings of the study will be of major importance, broad interest in the field will certainly help with both publication and funding.

III. Look for an Underoccupied Niche That Has Potential

This is an especially good strategy for someone completing a postdoctoral fellowship who would like to continue his or her basic line of investigation but avoid competing head-on with a mentor or with other recognized figures in the field. Even in the best studied areas, there are often very important aspects that are not being studied by the major investigators, either because they have not yet thought of these particular aspects or because they lack the specialized expertise necessary to move in a specific direction. Finding an underoccupied niche with potential may be difficult, but it can be made easier by following Commandment IV.

IV. Go to Talks and Read Papers outside Your Area of Interest

In my opinion, some of the best ideas come from listening to talks and from reading papers outside your area of interest. Indeed, it is wise not to read too many papers or to listen to too many talks in your own area of interest before picking a project, since they may strongly bias your choice and stifle your creativity. By contrast, papers and presentations outside your area may point you in truly new directions and allow you to anticipate the evolution of the field. Once you are involved in a particular area, of course, it is absolutely essential to be conversant with the literature and to attend important conferences. However, you should be careful not to put excessive weight on this information when considering your own direction, since this may lead you to move in the same direction as other investigators rather than in a novel direction.

V. Build on a Theme

Although it is important to avoid fragmenting research reports, publishing incomplete or redundant papers, or dividing work into “least publishable units,“ it is also true that the effect of two papers on a single topic is greater than that of a single paper. By their very nature, seminal or important discoveries create a need for further exploration. In a new and highly competitive area, preliminary studies should be followed quickly by additional studies that provide a more complete characterization of the findings, including many of the aspects that take time to work through.

VI. Find a Balance between Low-Risk and High-Risk Projects, but Always lnclude a High-Risk, High-lnterest Project in Your Portfolio

Whether one has a small research program or a large one, it is important to find a balance between low-risk and high-risk projects. Nonetheless, you should always include a high-risk, high-interest project in your research activities. Such projects may or may not prove successful, but a higher-risk, higher-interest project is truly your opportunity to move out in front of the field and make a seminal observation. They often turn into the most interesting and most productive projects in the laboratory.

VII. Be Prepared to Pursue a Project to Any Depth Necessary

Several years ago, the Nobel laureate Dr. Joseph Goldstein described a problem in his presidential address to the American Society for Clinical Investigation that he termed PAIDS, an acronym for paralyzed academic investigator‘s disease syndrome[4]. Goldstein pointed out that an investigator studying an interesting physiologic observation may eventually come to a point when it is necessary to purify some new factor or clone some new gene that underlies the basic mechanisms being studied. If the investigator is not adequately trained in biochemistry or molecular biology, he or she may become paralyzed and not pursue the work to the next important level, but rather move laterally in a safe and less challenging direction. To be recognized for important research accomplishments often requires a willingness to pursue a project to any depth necessary. If part of the project requires specialized expertise that you do not have and you may not need in future investigation, this is the proper time to involve collaborators. If, on the other hand, it seems likely that you will need the new techniques tor many aspects of your current or future studies, then it is important to learn these skills and bring them into your own laboratory.

VIII. Differentiate Yourself from Your Mentor

Although having a strong mentor during the early phase of a research career is one of the most important determinants of long-term success[1], it is crucial to differentiate yourself from your mentor. This is especially necessary when you remain at the same institution, since the mentor by virtue of his or her seniority will already have more recognition than you do as a young faculty member or trainee. For peer review of grant proposals, faculty promotions committees, and election to selective societies, the issue of independence is often used as a criterion. On the other hand, this does not mean that it is absolutely necessary to move or change institutions, or even to change general project areas. In many cases, the greatest scientific progress is made through the efforts of two or more investigators, acting as a team, who have complementary interests in a common problem. It is often relatively easy to define a project in a large and complex biologic area that will distinguish you effectively from your mentor. However this is achieved, you must be recognized as more expert than your mentor at least in some area.

IX. Do not Assume That Outstanding, or Even Good, Clinical Research Is Easier Than Outstanding Basic Research

The young M.D. investigator who has limited basic-research experience often finds his or her initial experiences in basic research frustrating. In many cases, this is because he or she has primarily a clinical background and feels inadequate in the techniques required. The M.D. investigator is then tempted to switch to clinical research. Outstanding clinical research is by no means easy, however. First, it is more difficult to design well-controlled and informative studies, since often one cannot perform all the procedures needed for an optimal study in a given population. Second, the studies usually take longer and are more complicated. Finally, the questions that can be asked may be more limited. Thus, although outstanding clinical research is an important element in biomedical progress, it is not necessarily the fastest or easiest way to academic success, even for the M.D. investigator.

X. Focus, Focus, Focus

Finall, as a starting investigator, and even as a more senior investigator, you should not forget the need to focus. Trying to make an impact in three or four different areas is extremely difficult and is something that can be done effectively only by a very few. The beginning investigator should focus his or her efforts on one or at most two projects and should define very limited goals. The more senior investigator with more resources may be involved in more projects, but in each he or she should maintain a focused attitude.

These Ten Commandments will heip any investigator tackle the problem of choosing a research project. However, choosing a good research question is not all that is required for success in research. Therefore, I suggest the following complementary dictums that can further increase the likelihood of academic success.

Be prepared to sell your ideas. This does not mean to sell your ideas to a pharmaceutical or biotechnology company, but to sell your ideas to your academic colleagues. If you are not enthusiastic about your work, they will not be enthusiastic about your work, no matter how important the results may be.

Become the locally recognized expert in some area -- any area. This is a good practice for both research and clinical work. If you are an M.D. investigator trying to spend a large fraction of your time doing research, your area of expertise may be rather narrow. If you are a clinical investigator or have considerable time for clinical activities, your area of expertise may be broader. In either case, it is critical that you be recognized locally as the expert in whatever field you choose. This strongly improves your local credibility, and local credibility helps build national and international credibility.

Even if you are an independent investigator and have completed your training, find a mentor or colleague with whom you can discuss ideas, plan approaches, and express frustrations. This helps tremendously with both the reinforcement of positive issues and the buffering of negative forces. The mentor does not necessarily have to be in the same discipline or have the same research interest, but he or she should have the personal characteristics that make an outstanding scientist or physician.

No matter how well trained and how creative you are, take sabbatical leaves regularly to retrain and refresh yourself. During such leaves, it is not enough simply to take time to think and to talk to other investigators; you must also take time to do hands on research. The best sabbaticals are usually spent working in areas at some distance from your own interest, but in laboratories that might use forms of technology or have problems that have some relevance to your overall goals. This allows you to learn much about the area of expertise of this new laboratory or investigator without becoming a competitor.

Do a lot of experiments: the more times the centrifuge spins, the more likely you are to find an interesting result. Novel findings are, to some extent, a matter of luck. Thus, you can increase the probability of a lucky find by having more experimental results. As the great movie producer Samuel Goldwyn once said, “The harder I work, the luckier I get.“ However, as Louis Pasteur pointed out, “luck favors only the prepared mind.‘ Hence, as experimental data are accumulated, you must not simply look for the expected results, but also focus on the unexpected results. These are often more informative and may lead the research in new and more important directions.

Finally, although it is important to work hard and do many experiments, take time to think. This is a substantial problem for almost all investigators. The M.D. investigator is especially overburdened with tasks in research, clinical work, and teaching. In addition, he or she is expected to perform each of these tasks at the highest level. Obtaining research funding, seeing patients, conducting experiments, preparing papers, and training students are all very time consuming. Frequently, once these have been done, there is no energy left for thinking. It is critical to make such time somehow.

In summary, conducting outstanding research is difficult. Nonetheless, there are rules and processes that can improve your chance of success and progress. By using these rules, as well as your own special variations of them, you will be more likely to have a career that is both successful and rewarding.

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