ESSAY

How to succeed in science: a concise guide for young biomedical scientists. Part I: taking the plunge

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Abstract | Biomedical research has never been more intellectually exciting or practically important to society. Ironically, pursuing a career as a biomedical scientist has never been more difficult. Here I provide unvarnished advice for young biomedical scientists on the difficulties that lie ahead and on how to find the right laboratories for training in the skills that you will need to succeed. Although my advice is geared towards succeeding in the United States, many aspects apply to other countries.

If you are contemplating pursuing a career in the life sciences, or have already embarked on one, you need to give some thought to your career prospects. So, take a study break, grab a cup of coffee and read on.

Unfortunately, I need to begin with some depressing facts. First, only a small minority of Ph.D. students will ever have opportunities to become principal investigators (PI) in academic settings and direct their own independent research programmes (FIG. 1). Second, even if you are among this elite group, the odds are that you will be well down the path towards retirement by the time you receive your first research project grant (R01) (the average age is 43) from the National Institutes of Health (NIH), the principal source of funding for biomedical research in the United States. Third, for your entire career as a PI, you will put inordinate efforts into writing grants. If you should ever lose funding, you will be at the mercy of your institution for your continued employment. Fourth, if you do achieve the 'Holy Grail' of full professorship then you will not be poor, but you will be far worse off financially than nearly all of your peers who have similar levels of talent, energy and dedication, but who chose other careers.

Your professors might tell you that this is the way it has always been, but this simply isn't true. Twenty-five years ago the situation was much rosier. Scientists gained independence a decade earlier and funding, although never easy, was more reliable and accessible. Universities were more humane institutions where accountants had less influence over institutional priorities and decisions. Our current lamentable situation is fixable, and will have to improve significantly if the United States is to maintain its position as a leader in science and technology. A positive outcome is not guaranteed, however, and fixing the current mess will require the concerted efforts of scientists, university presidents and politicians to save the biomedical goose that has laid golden eggs for US biotechnology and health care for the past 50 years.

Science rocks

But there is good news too. Society desperately needs your talents. The future health, wealth and even survival of *Homo sapiens* depend on a deeper understanding of the laws and mechanisms of nature and on using this information to develop new technologies and therapies. For rationally thinking people with an altruistic bent, life can be no more rewarding than when practising the scientific method for the benefit of all of the denizens of this fragile planet. As a budding scientist, you are trained to expertly use the scientific method. That is, you learn how to wield the body of techniques that are used to identify and investigate natural phenomena by formulating and rigorously testing hypotheses. The origins of the scientific method date back at least 1,000 years, and it is arguably the most important invention of civilized man. Armed with the scientific method, we can explore and understand nature to the limits of our intelligence. As a high priest of 'Scientific Methodism', you will be equipped for success not only in science and its allied occupations, but in virtually any career that requires rational decision making (and in some, such as politics, that ought to).

More good news: for individuals with a hunger for knowledge and an insatiable curiosity about how things work, science offers a constant challenge and, best of all, the intense thrill of discovery. What can match being the first person who has ever lived to know something new about nature? And not just the big, infrequent, paradigm-making (or breaking) discoveries, but the small, incremental discoveries that occur on a daily or weekly basis too. If this doesn't give you goosebumps and if you are not in a rush to get to the laboratory in the morning to find the results of yesterday's experiment, then you should seriously consider a non-laboratory career. Making discoveries is the core reward for the myriad of difficulties you will face in your scientific career (see Part II, in which I discuss making discoveries[1]). Although it is possible to succeed in science even if you lack this passion for discovery, you will almost certainly be miserable and make your colleagues, friends and family wretched too.

Science has other perks. Contemporary science is one of the most communal activities ever pursued by humanity, and is among the most international careers possible. You will probably be interacting on a daily basis with scientists from all over the world, both in your laboratory and over the internet. Once established in your career, you can fly to dozens of cities across the globe and be greeted by a colleague that you either know personally or through reading each other's publications. You might even train a generation of researchers in your laboratory who will disperse around the globe to pass the torch of the scientific method to the next generation of their nation.

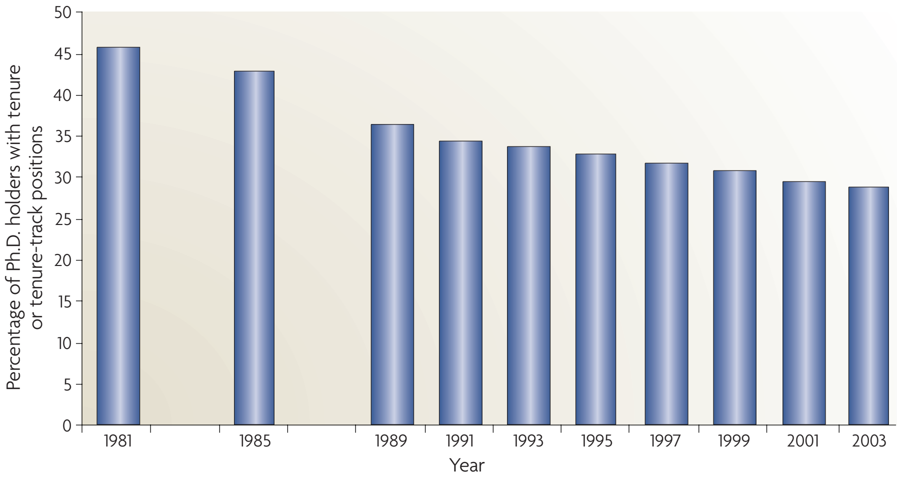

Figure 1 | **The tenure track derails.** The number of doctorate degrees awarded per year in the United States in the life sciences has increased more than threefold since 1966, whereas the number of tenured scientists has decreased slightly from a peak in 1981 (according to National Science Foundation data[3]). Consequently, in the past 25 years the fraction of Ph.D. holders with academic independent investigator positions has decreased steadily. The fraction of Ph.D. holders with tenure or tenure-track position is now ~30%. Graph reproduced from REF. 3 © (2007) FASEB.

This generational transfer of Scientific Methodism is, in fact, the most important and tangible achievement of a scientist. Discoveries are the joy and stock of our trade, but when your career is over (and probably well before this moment), few people will remember your brilliant papers. If you are successful (and lucky), you will have contributed a few lines to text books that future students will resent having to memorize. Through no fault of your own, and for reasons that you could not have anticipated, your discoveries might prove to be the artefacts that led your field in the completely wrong direction. You will be happiest in science if you are content with pursuing the truth to the best of your abilities and in passing the skills and insights you have developed to the next generation. Scientists who pursue fame are destined to be forgotten and forever dissatisfied with their achievements. In practical terms, peer recognition is needed only to maintain funding and to attract talented individuals to your laboratory who will make your daily laboratory life more productive and enjoyable. Beyond this, chasing fame is a waste of time that could be better spent on science itself, or on enjoying life outside the laboratory.

Getting started: graduate school

Choosing a graduate programme. Choosing a graduate school in which to pursue your Ph.D. should be largely based on the field that you would like to enter. Obviously, you should choose a programme that has a well-respected faculty. Size provides a large number of advantages, including a larger number of potential mentors to choose from, more students and postdoctoral fellows who can become lifelong friends and colleagues, better chances for collaboration, greater access to reagents, techniques and specialist equipment, and a more exciting intellectual environment. To minimize the insanely long 'training' period of your career, you should find a programme that takes pride in expeditiously awarding Ph.D. degrees . It should take 4 or 5 years for a decent student to finish a Ph.D., with an absolute upper limit of 6 years. Any longer than this and the student is either not suited for science or is being exploited by the mentor. Also, choose a department where the current Ph.D. students are treated as junior colleagues, with an eye towards their career development, and are not just exploited as inexpensive labour (small departments can be better in this respect).

Choosing a laboratory. Once you have chosen a school (or vice versa) to work in, your most important decision will be to choose a laboratory. The decision can be based either on the topic of research or on the mentor. I would strongly recommend the latter (BOX 1). Good scientists work on interesting and important topics, so a good mentor has this covered. Your goal as a graduate student is to become an expert in wielding the scientific method, and this can be achieved pursuing any project. The topic matters most in the types of experiments it entails. A good project will enable you to design, perform and analyse experiments on a routine basis,

Box 1 | **On the innate superiority of rabbits over wolves**

A rabbit is happily grazing one day when it is ambushed by a wolf.
"Please don't eat me Mr Wolf," pleads the rabbit, "I haven't completed my Ph.D.!"
The wolf spits out the rabbit and laughs until he almost chokes.
"Yeah right! A rabbit? Doing a Ph.D.? What about? Carrots? Duracell batteries? I just gotta hear this one!"
The rabbit clears its throat and intones: "On the innate superiority of rabbits over wolves."
"That's a crock for a start," scoffs the wolf.
"But I can prove it," says the rabbit. "Come to my hole and I'll show you my results, and if you still don't believe me, then you can eat me. Deal?"
"Sure. Can I have fries with that?" says the wolf, following the rabbit down the hole.
But only the rabbit comes out.
Months later the rabbit is grazing contentedly again when it meets another rabbit.
"How's tricks?" asks the friend.
"Wonderful," says our hero, "I've just submitted my Ph.D. dissertation."
"Congratulations! What's it called?"
"It's called 'On the innate superiority of rabbits over wolves'."
"Unbelievable — I mean, literally. Are you sure?"
"Yes, I thought it was crazy at first too. But I've tested the model rigorously and that's the result I get."
"Wow…"
"Look, if you don't believe me, why not come to my hole and I can show you the results?"
"Of course, I'd love to!"
So the two rabbits scurry down the burrow. In the first chamber is a workstation, covered with and surrounded by piles of books, papers, printouts and half-eaten carrots. In the second chamber are boxes and boxes of wolf bones, all catalogued and annotated. And in the final chamber, in a rocking chair, is a large and very satisfied looking bear.

Moral: do your Ph.D. on any subject you like, provided you have a good supervisor.
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ideally several per week, if not daily. This provides the best training and, importantly, is also the most fun. This will also develop your abilities to conceive the crucial controls that are needed to interpret the data in a meaningful way. ‘Control creativity’ is a central part of your scientific IQ; it comes only from the experience of designing and interpreting experiments. You should avoid projects that are largely based on using a single technique to develop a reagent or collect data (for example, generating a transgenic mouse).

Choosing a mentor. Although there is tremendous subjectivity in choosing a compatible mentor, there are a number of objective criteria (FIG. 2). Are the people in the laboratory happy and enthusiastic about their research? Have former students gone on to productive careers? Does the mentor treat students as junior colleagues and not as employees? Generally speaking, you should run from laboratories where a PI is referred to as Doctor X and not by his or her first name.

Frequently, you will have to choose between a small laboratory with a new investigator versus a large laboratory with a well-established scientist. Newly minted assistant professors will not have much of a track record as mentors; you might even be the first student they train. Still, you should seriously consider joining such a laboratory if the chemistry seems right. Although this has its obvious risks, you are a much more valuable commodity to a small laboratory, the survival of which could well depend on your personal success. Consequently, you will get more intense mentoring and will probably be working side-by-side with the PI. The best situation is to be the first Ph.D. student of a rising star, for you will be maximally productive, will generate well-developed ties to your field and will have an influential champion for years to come (although because academic ‘star’ formation is an inexact science, this often takes some luck).

Skills, not papers. Contrary to what you might have heard, it is not critical to have a spectacular publication record from your Ph.D. When the time comes to apply for a tenure-track job, the selection committee will focus on the productivity and promise you displayed during your postdoctoral fellowship. Furthermore, a solid Ph.D. with one good first-author paper that is based largely on your own work is all that is usually required to obtain the postdoctoral position of your dreams, particularly for citizens of the United States, who are in short supply at this level. Your focus as a graduate student should be to develop all of the skills you will need to be an independent scientist.

At some point as a graduate student you will need to take responsibility for all aspects of your career and develop the skills of an independent scientist. You need to develop confidence in your ability to make discoveries and learn new techniques, so that you will not be limited later in your career when your findings lead you to new and unexpected areas (see Part II (REF 1)). You need to do the background reading to place your results in their proper context and determine the next step in the project. You need to learn how to present a seminar in which you convey not only the data and conclusions, but also your depth of knowledge and enthusiasm for your field of research. Such public-speaking skills are critical for peer recognition of the impact of your research, for recruiting students and fellows to your laboratory, and for effective teaching. Most importantly, you need to learn how to write concisely and lucidly[2], for without this skill, you will not be able to raise grant money or place your papers in high-impact journals.

Step two: postdoctoral fellowship

In many ways the most important decision on the PI career path is where you do your postdoctoral fellowship. It should be in a field in which you envisage starting your independent career, the success of which will be almost entirely dependent on your ability to attract funding. As a newly independent scientist, study sections will be loath to fund you to embark on a project that is not a direct continuation of your postdoctoral studies. This also means that you will need access to the reagents you developed as a postdoctoral

Figure 2 | **The nine types of principal investigator.** This cartoon was kindly provided by Alexander Dent, http://dentcartoons.blogspot.com.

fellow. You will also need the blessings of your mentor and, optimally, your mentor should actively support your nascent career. So, in choosing your postdoctoral mentor, it is critical to determine whether a mentor enthusiastically supports, both materially and psychologically, the careers of their fledglings. This is easier to determine if the mentor is an established scientist with a pedigree. Established scientists will also be able to offer laboratories with a greater variety of expertise, reagents and greater financial resources, all of which will help you establish an independent line of research for you to parlay into an independent career.

It is essential to visit the laboratories that interest you to gauge the productivity, independence and happiness of the students and postdoctoral fellows. It is a good idea to contact scientists who have left the laboratory to obtain their honest opinion of their experience (in laboratories headed by evil mentors, this might be the only way to ascertain their pathology, as the current laboratory members may be too intimidated to express negative opinions). If the laboratory won't pay your travel expenses, then this does not augur well, as it indicates either limited financial resources or stinginess. All things being equal, it is advantageous to work at larger, wealthier institutions where there will be better access to expensive, state-of-the-art instruments and core facilities, greater overall intellectual ferment, more laboratories for collaboration and a better chance to impress other established scientists, who can write the crucial recommendation letters for getting your tenure-track application into the interview round. Sometimes, however, all things are not equal, and if the best mentor is at a smaller institution, this will do just fine.

What is it going to take?

Perspiration. Success in science will require a major commitment of your body and soul. As a graduate student, you should be spending a minimum of 40 hours per week actually designing, performing or interpreting experiments. As there are many other necessary things to do during the day (for example, reading the literature, attending seminars and journal club, talking to colleagues both formally and informally, and common laboratory jobs), this means you will be spending 60 or more hours per week in science-associated activities. The key to success and happiness is that most of this should not seem like work. If the laboratory is not the place you'd most like to be, then a career as a PI is probably not for you. At the postdoctoral level you will have to work at least as hard, but your most intense effort will actually begin as a tenure-track faculty member, when you are expected to fund your research (and at least some of your salary too), teach undergraduates as well as graduate and professional students, serve on committees and run your laboratory, which itself entails learning an entirely new set of skills (such as accounting, diplomacy and psychology). Ironically, you will have more to learn as a fledgling professor than as a postdoctoral fellow. Until you are well into your career, there will be time in your life for just one additional significant activity (family, active social life with friends, a sport or a hobby), but probably not for much more than that.

Talent. Enthusiasm and effort are necessary but not sufficient for a successful scientific career. Talent is a key part of the equation, and at some point in your career (not necessarily as a graduate student), you will need to objectively assess your skills and potential relative to your peers. The inexorable weight of the scientific career pyramid squeezes out all but the most talented from getting the tenure-track job that will offer you the chance of establishing your own laboratory. Furthermore, the insanely competitive funding situation is making the previously safe transition between tenure-track and tenured professor a far dicier proposition. Scientific talent is not a single parameter, but a complex mix of innate and learned skills and abilities. Deficiencies in one area can be offset by strengths in another. Some scientists achieve success by their experimental skills or insights, others by their management or political skills. There is no one path to success and each successful scientist has unique combinations of strengths (and weaknesses).

If, for whatever reason, you decide that you are better suited for life outside the laboratory, there are numerous career alternatives. Neither you nor your mentor should consider this outcome a failure. It is unfair, and even irresponsible for mentors to expect trainees to emulate their own career paths. Each mentor has only to train a single replacement to maintain the PI population at equilibrium. Even with robust growth in NIH-funded biomedical research (which is unlikely in the foreseeable future), the current investigator-to-trainee ratio dictates that most trainees will pursue careers that differ fundamentally from those of their mentors.

Networking plays a key part in providing information about potential alternative careers and in landing such jobs. Alumni of the laboratories and departments you have worked in are the most proximal source of networking partners. E-mail has opened a great portal into the academic community for initiating contacts that can be deepened by follow-up telephone conversations. It can be difficult to penetrate the corporate world by this path, but conferences provide ideal circumstances for meeting scientists out of the academic mainstream who can provide insight, advice and even job opportunities. It might be possible during your postdoctoral fellowship to develop your skills and attractiveness to potential employers by moonlighting or volunteering in the career path you are contemplating.

Final thoughts

So, your cup of coffee should be finished by now. Please don't be discouraged, but give some thought to your career path. If you are talented and passionate, you will have a good chance of becoming a PI; particularly in the United States, which still provides great opportunities for truly independent entry-level positions. If the trials and tribulations of being a PI aren't for you, there are many other ways to use your scientific training to make a decent living and a valuable contribution to society. Now get back to work.

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doi:10.1038/nrm2389
published online 10 April 2008

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Acknowledgements
The author is grateful to the many junior and senior scientists who shared their insights into scientific success. B. Dolan, K. Grebe, S. Hensley and J. Ishizuka made valuable suggestions for improvements to the manuscript.

FURTHER INFORMATION

Jonathan W. Yewdell's homepage:
http://www3.niaid.nih.gov/labs/aboutlabs/lvd/cellBiologyAndViralImmunologySection/BenninkYewdell.htm
Graduate student resources on the web:
http://www-personal.umich.edu/~danhorn/graduate.html
Making the right moves: a practical guide to scientific management for postdocs and new faculty, second edition:
http://www.hhmi.org/catalog/main?action=product&itemId=313
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