

# Interested in a career as a clinician-scientist?

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**The clinician-scientist is uniquely well positioned to determine when an animal disease model is a true representative of a human disease**

I wave to the graduate student at the door to come in, and continue discussing a patient problem over the phone with my nurse. I need to meet with the student today about upcoming experiments because tomorrow I will be in the clinic all day. I was hoping to finish a grant that is due later this week, but my day is rapidly slipping away. As I hang up the phone, my e-mail chirps that an editor from *Disease Models & Mechanisms* would like to know if I would be interesting in writing an article about being both a clinician and a scientist. On a day like today, my first thought is 'Why would anyone want to try to do both?' There are obvious disadvantages, with the constant demand on your time from multiple directions being one of the primary challenges. Fortunately, not all of my days are quite as hectic as today. I appreciate the distinct advantages to being both a clinician and a scientist, so I quickly respond that I will write the article, after sending out my grant!

## The advantages of being a clinician-scientist

The potential for translational medicine

The obvious advantage for clinician-scientists is their involvement in all aspects of translational medicine. Many times this is termed 'bench-to-bedside' medicine, which aims to test new therapeutic concepts in the lab and bring new treatments into the clinic. Although this is the desire of most, if not all, clinical-scientists, I now realize that ideas and experience move in both directions and more frequently flow from 'bedside to bench'. Clinician-scientists interact with patients, see the clinical features of their diseases, and then develop basic science experiments to test new ideas that stem from this experience.

As a fellow, I became interested in a rare neurodevelopmental disorder, called Rett syndrome, and the role of biogenic amines (the neurotransmitters: dopamine, norepinephrine and serotonin) in this disease. Many of the clinical features found in Rett syndrome suggest alterations in these neurotransmitters. Therefore, I designed a human study to collect spinal fluid from affected individuals and analyze the metabolite concentration of these neurotransmitters. In this study, we found that the concentrations of these metabolites were decreased in affected individuals. This initial discovery led to experiments in an animal model of Rett syndrome, where we explored the molecular consequences associated with decreased neurotransmitters and how they contributed to the disease phenotype. We hope that this knowledge will ultimately lead back to the clinic and generate novel therapies, however this story demonstrates how information can flow from the clinic into the laboratory. In this way, a clinician who also carries out basic science has an advantage in that they can push ideas between the laboratory and the clinic. In addition to moving ideas, clinician-scientists have direct access to patient samples that can be utilized experimentally in the lab.

Bringing information, ideas, and materials from the clinical world into the lab serves an important role in translational medicine. 'We function as bridges between the clinical and the scientific worlds, and currently most of the information flows from the clinic to the lab,' commented Stephen Maricich, MD, PhD, Case Western Reserve University. Clinician-scientists see a 'big picture' extending from patient symptoms and needs to

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the underlying mechanisms. They recognize the relevance and utility of scientific discovery and how it changes patients' lives. The converse is also true: clinician-scientists bring a sense of curiosity and scientific rigor into the clinic. Medical schools sometimes discourage curiosity through their teaching of 'the right way to do things', whereas basic science training encourages skepticism and an attempt to understand problems at a deep level. The two views together provide an interesting balance.

Sitting at this intersection between the clinic and the lab provides great opportunities to interact with a wide variety of people with unique experience, training and expertise. In the clinic, I gain knowledge and inspiration from my clinical colleagues and patients, where I also have the chance to teach, and learn, from the clinical residents. In the basic science lab setting, I learn new ideas and techniques from other scientists and seminars, and instruct students and postdoctoral fellows. Bridging both worlds not only lets me shuttle information and ideas back and forth, it keeps me 'on my toes' such that I am forced to keep abreast of aspects of both worlds. For someone who loves learning new things, this is a great position.

A clinician-scientist is at the intersection of diverse information, combining ideas and knowledge from a diverse spectrum of sources and people. Many of my clinical colleagues do not routinely read basic science journals and may not be up to date on the newest technologies or concepts. I can help inform them about this information when it relates to areas of interest for them. Likewise, I have had a number of opportunities to help my basic science colleagues recognize the clinical significance of their scientific findings or to direct their research in clinically meaningful ways.

#### Evaluation of the validity of animal models

The clinician-scientist is uniquely well positioned to determine when an animal disease model is a true representative of a human disease. 'It is important to realize that what we find in models is merely what might be, and what needs to be, confirmed and validated in humans,' quips Brendan Lee, MD, PhD, Baylor College of Medicine, 'working both as a clinician and a scientist provides the opportunity to do this.' The validation of animal models of human disease benefits from the human experience that clinician-scientists bring with them into the laboratory.

#### Funding opportunities for clinician-scientists

A clinician-scientist is optimally positioned to recognize important, clinically relevant questions and to design experiments to test these questions. This ultimately helps to identify and acquire sources of research funding from a variety of sources. For people who are early in their career, there are a number of funding opportunities in the USA that are restricted to people with clinical training, such as the K08 or K23 career development awards. These training awards are a great way to learn about securing National Institutes of Health (NIH) funding, to gain resources that protect your time, and to allow the development of an independent research project. In some NIH institutes the K02 award is also restricted to people who have a clinical degree and functions as an extension to the K08/23 pathway.

Another source of funding that is not exclusively restricted to clinician-scientists, but in which clinician-scientists have advantages, comes from disease-related foundations. Because most disease-related foundations have an explicit mission to target research to understand or treat specific diseases, successful funding often depends on recognizing the most important disease-related questions.

Finally, clinician-scientists are well positioned to obtain the holy grail – an NIH R01 grant. Obviously, the work of clinician-scientists is often consistent with the mission

of the NIH to apply scientific knowledge ‘to extend healthy life and reduce the burdens of illness and disability’ (<http://www.nih.gov/about/>). Furthermore, clinician-scientists often approach questions with health significance in mind, which is a major component of the new, enhanced review criteria (<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-09-025.html>). Clinician-scientists can also be more able to target specific disease-oriented requests for applications (RFA).

#### Fun and job satisfaction

A significant advantage to being a clinician-scientist is that this path gives people who enjoy both clinical medicine and basic science the opportunity to do both. Not everyone fits into this category, but for people that do, it really is fun and the experience provides a great deal of job satisfaction. I think back to times when an experiment did not go well and I went to the clinic and felt a sense of realignment after seeing patients and reconnecting with my desire to help them with their problems. There are also times when I am at a loss to suggest any clinical solutions to a patient’s problem, and then I realize that there are experiments that I can design in my lab to try to get at the fundamental problem.

#### **The downside to being a clinician-scientist**

##### Length of training

Many clinician-scientists have both an MD and a PhD, which in the USA typically involves 7-10 years of training after college. After these degrees, residency training lasts between 3 and 7 years depending on the specialty. Many people who are interested in academic medicine also require additional sub-specialized fellowship training, which typically lasts for 2-5 years after residency. Establishing a research project in the laboratory is also necessary. Often, laboratory work can be started during a clinical fellowship, but frequently, additional ‘postdoctoral fellowship’ time in the lab is required to develop a project that could become independently funded. Adding up all this training leads to nearly 15-20 years of post-baccalaureate training before a person is in a position to be an independent clinician-scientist.

##### Publication gaps

A consequence of this long training is that it leads to significant publication gaps because research is disrupted by long periods of clinical training in which no manuscripts are published. A number of my colleagues heard this criticism when they were applying for their first grants after finishing clinical training. Part of the problem is that reviewers may not be accustomed to the training program for clinician-scientists and expect all applicants to have the same continuity of publications. Perhaps funding agencies that value the contribution of clinician-scientists will implement procedures that do not penalize people who take the time to train in both fields. The K-award series are good examples of funding mechanisms that are geared toward clinician-scientists and that are reviewed with the training schedule in mind (see above).

##### Your place in the community

People who attempt to work in both the basic science and clinical arenas may be viewed with suspicion on both sides of the fence. Some clinicians feel that only a full-time clinician has the acumen to be a really good physician and some basic scientists view clinician-scientists as just MD lab dilatants. ‘I have to keep reminding people that I have a PhD,’ said James Dowling, MD, PhD, Assistant Professor of Pediatrics, University of Michigan. There are a few ways to address this problem. ‘It’s important to make

yourself visible in both worlds,' advises Stephen Maricich, 'make sure you attend the clinical case conferences, go to the departmental seminars, serve on student theses committees. That way people know who you are and hopefully can recognize your abilities in the lab and in the clinic.'

It is important to have realistic expectations and priorities. 'I consider myself a scientist-clinician,' explains Brendan Lee, 'because I am a scientist first. I think when you are starting out, it is critical to establish yourself scientifically. At that time, my advice is to recognize that you are not going to be the greatest generalist clinician in the world, but rather you should pick a clinical area and develop an expertise in that niche.' I personally have followed this advice by focusing the bulk of my clinical work on Rett syndrome. This provides a great opportunity to intersect my clinical work with my basic science endeavors. Although this is not always easy to do when starting out, I think that it is an important idea to being a successful clinician-scientist and should be considered by both the individual, as well as institutions seeking to foster clinician-scientists.

### **Finding solutions**

#### **Alternative training paths**

Although a PhD is extremely useful in learning how to approach problems in a scientific manner, it is not absolutely necessary to become a successful clinician-scientist. Eric Kandel, Stanley Prusiner and Huda Zoghbi are just a few of the many clinician-scientists who have made major discoveries with solely an MD behind their name. For the type of person who can acquire the scientific training 'on the job' during a postdoctoral fellowship, this could be a method to streamline the overall training time slightly. Unfortunately, I suspect that many people, when faced with the prospect of additional low-paying training at a point when they have the expertise to utilize their clinical skills as a physician, will not resist the urge to leave training and start practicing medicine.

Another way to reduce the training time is to seek out opportunities to combine aspects of training. For example, I followed an alternative Neuroscience Track for Child Neurology. In this pathway, I was able to substitute one year of clinical training in pediatrics with a year of basic science training. Fortunately, in this pathway, it is possible to leave the science portion until the end of clinical training, which easily allows the extension of an ongoing project into additional years of postdoctoral training. There are other similar 'fast-track' training options for people interested in being both a clinician and a basic scientist. These combine residency and fellowship training to shorten the overall training time by approximately a year. Bench research is carried out during fellowship.

Unfortunately, these 'fast-track' programs are often belittled by clinicians, and discouraged or actively prohibited by residency training programs. This seems short-sighted because it discourages clinicians from engaging in research. My personal feeling is that someone in training who is interested in combining these two worlds should seek out training environments that are supportive of these options (discussed further below).

Even when research time is present, it is often in one-month blocks that are too short to effectively establish a research project and often still requires clinical activities such as night or weekend calls. This is especially true in surgical specialties. Protected blocks of time with minimal clinical duties, concentrated near the end of clinical training, are the most beneficial for career development.

One of the hurdles to this training model is finding mechanisms to pay for it. In the USA, clinical residency training is typically paid for by a combination of funds from

the hospitals and Medicare. During this time, both of these payers are expecting clinicians to be actively engaged in clinical work and not to be off in the lab running experiments. Perhaps funding agencies who appreciate the importance and value of clinician-scientists, and who would like to increase their numbers, could come up with funding mechanisms to 'buy' the clinical time from the residencies to allow for research experience. Because of the overall length of training, I do not think that fellowship money should pay for additional years of basic science training on top of clinical training, but rather a program should be developed to help encourage residency programs to create 'fast-track' residency opportunities by paying for part of the training.

#### Environment

One of the most important aspects of a successful career as a clinician-scientist is a supportive environment. The environment becomes crucial during clinical training and is even more crucial for junior faculty. The institution needs to value clinician-scientists and appreciate the unique set of skills that these individuals provide. The institutional support is typically shown by providing adequate protected time that is free of clinical obligations. This protected time is usually guaranteed by the department chair. Beyond protected time, some commitments in terms of resources, both space and financial, are needed to successfully start a research career.

Another significant factor to consider when evaluating the institutional environment is the number, depth and qualities of your colleagues. Are there enough clinicians to shoulder the majority of the clinical responsibilities? If not, even an institutional commitment towards protected time may not be able to fulfill this requirement and meet their clinical demands. High-quality clinical colleagues with different expertise who you can consult with, or refer patients to, and that have clinical experience outside your specific region of expertise are an important, and yet under-recognized, aspect of the professional environment.

#### Mentoring

It is important to develop a variety of mentoring relationships to help navigate grants, as well as institutional requirements. The career development awards mentioned previously (K08, K23) are mentored grants, so someone will need to be identified as your scientific mentor. However, it is also useful to seek out additional, potentially informal, mentors for their expert guidance for specific elements or your career. For example, it is worthwhile having someone guide you in the realm of promotions. This may be your scientific mentor, but it is better to have a separate person in this role so as to avoid any possible conflict of interest.

#### Time management

Time management is one of the largest challenges that faces a clinician-scientist, especially when trying to balance clinical tasks with science. Clinical work has a way of spilling over beyond the well-defined period of time spent in the clinic. Probably the most common way that this happens is with patient phone calls. Of course, as a clinician, we are obligated to care for our patients when problems arise. One solution is to have someone who can address these issues immediately and who is able to discern the urgency of the problem. I am fortunate to work with an excellent nurse who calls families and gets the information from them. If it is a non-urgent issue, she enters the information into a phone note within the electronic record that I can then address later. For urgent issues, she gets in contact with me and we discuss a solution on the phone. Hiring a qualified person, such as a nurse or a clinic coordinator, really facilitates effective

time management. The source of such funding might come from institutional funds (a great sign of institutional support), philanthropic sources, or from start-up funds.

On the personal side, compartmentalizing your time is crucial. By compartmentalizing time, I mean trying to define specific times during the day to devote to particular tasks. For example, I find it helpful to try to have a set period of time during the day that I use to address clinical issues, such as at the very end of the day. The staff who I work with are also crucial because they try to respect my basic science work by only contacting me during the day about important, emergent clinical issues, thereby leaving the routine issues for me to address during the defined period of the day that I have planned to consider clinical problems.

### Conclusion

Although the career of a clinician-scientist has some distinct disadvantages, it was the best career choice for me. I cannot think of another career that truly provides such great opportunities to impact patient health, both immediately in the clinic and over time through basic science. The ideas that I have listed here as possible solutions to the challenges relate to issues that I have considered, and I probably missed some alternative strategies. Even in the best situation, this is a challenging career path, but for me it is a lot of fun.

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