



## ***Science Translational Medicine Podcast***

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*Host – Kate Travis*

Welcome to the *Science Translational Medicine* Podcast for April 7, 2010. My name is Kate Travis, and I'm the editor of CTSciNet, the Clinical and Translational Science Network, an online community for scientists from *Science* Magazine's online career portal Science Careers.

This week, *Science Translational Medicine* and CTSciNet have teamed up for a discussion about a Perspective in this week's issue called, "Training Translators for Smart Drug Discovery." The article is written by Carsten Skarke and Garret FitzGerald of the University of Pennsylvania's Institute for Translational Medicine and Therapeutics in Philadelphia. In their Perspective, the authors write that translational medicine needs investigators with "a sophisticated understanding of the principles of human medicine and expertise in both basic and human pharmacology who are capable of projecting their preclinical work across the translational divide". I spoke with Garret FitzGerald last week about where he sees deficits in the translational medicine workforce and what sorts of training investigators need to truly make a difference in human therapeutics development.

*Interviewer – Kate Travis*

First off, thanks very much for speaking with me today.

Interviewee – Garret Fitzgerald

Delighted to talk to you.

*Interviewer – Kate Travis*

In your Perspective article, you used the term "translational medicine and therapeutics" as a specific subset of clinical and translational science. What are you referring to with "translational medicine and therapeutics"?

*Interviewee – Garret FitzGerald*

I use that term to try and capture the science that projects from information acquired in model systems – be they cell-based model systems, mammalian cells, yeast, or animal model systems, like fish and mice – and projects that across the translational divide to inform the design of mechanistic studies in humans to elucidate basic mechanisms of human biology but also, in this particular case, mechanisms of drug action. Clinical and translational science is a very broad tent that extends all the way from basic science through to health services research – it's the entire spectrum, if you will, of endeavor relevant to translation of the fruits of basic research through to clinical benefit. The reason I thought the term "translational medicine and therapeutics" might be one worth considering is that it captures the current interest in translation; it puts the discipline at

the heart of medicine with a small “m”, and it illustrates the ultimate focus on the delivery of novel therapeutic entities.

*Interviewer – Kate Travis*

In your article, then, you talk about deficits in the workforce in translational medicine and therapeutics.

*Interviewee – Garret FitzGerald*

Yeah.

*Interviewer – Kate Travis*

Where are those deficits?

*Interviewee – Garret FitzGerald*

Well, I think the number of people who perform mechanistic research in model systems and/or in cells and project that using contemporary quantitative sciences, as well as phenotyping, across the translational divide to similarly sophisticated mechanistic studies in humans, globally is a relatively small number of people. And the group of that number of people that have an informed and sophisticated understanding of basic and human pharmacology is an even smaller number of people still. And I think actually that human capital has dwindled to a critical restraint on the activities of academia and pharma and biotech and, indeed, the regulatory bodies, as well. And I think the consequences of that erosion of human capital really manifests themselves in the way doctors prescribe drugs, in the way drugs are regulated, and, of course, most manifestly in the unsustainable mismatch between the cost of bringing drugs to market and the actual number of new therapeutic entities that are being delivered.

*Interviewer – Kate Travis*

You mention in the paper that there’s a deficit in the number of people trained in clinical pharmacology. What’s happened with this discipline?

*Interviewee – Garret FitzGerald*

Well, I think what happened was that when in this country, and then subsequently in other developed countries, like the U.K., for example, that had a fine tradition of clinical pharmacology – when we moved to a sort of cost center model of the economics of, particularly, departments of medicine, clinical pharmacology as a discipline that was essentially an academic discipline suffered greatly from not having a procedure that could be billable. And, of course, clinical pharmacology ideally brings the clinical relevance of a department of medicine and the fundamental rigor of the basic science of pharmacology, so needs the buy in of the chairs of those two different types of departments. So, I think that change in the economics of the way medical schools went contributed in no small way to the disintegration of many of the programs in clinical pharmacology that existed in this country, and then subsequently in other countries as they adopted similar economic models.

*Interviewer – Kate Travis*

What is it about training for clinical pharmacology that makes that type of person uniquely suited to do translational medicine?

*Interviewee – Garret FitzGerald*

Well, although many years ago I trained in clinical pharmacology, I'm not really advocating a sort of Lazarus-style resurrection of clinical pharmacology because I just don't think, on the one hand, it would work, and, on the other hand, I think time has moved on. And what we really want to do is embed the skill sets of people who have an understanding of drug action in humans with other skill sets that reflect the opportunities of contemporary science and an understanding of basic pharmacology that was a variable, in terms of many clinical pharmacologists in the past, but also an understanding of how the omic sciences, sophisticated model systems, etc., and the power of scale can be applied to therapeutic development. So, I think clinical pharmacology is one—and a core, but one—of the disciplines that we need to integrate in essentially a new interdisciplinary science that requires a new brand to attract people. And that's why I threw out the name "translational medicine in therapeutics."

*Interviewer – Kate Travis*

What are some of the other sciences that should be a part of that?

*Interviewee – Garret FitzGerald*

Well, I think clearly where there's a great opportunity is genomics as we move to a more cost effective way of getting highly detailed and particulate information there. But, the integration of genomics with metabolomics I think will be very important, as well the integration of those sets of informations with measures of drug exposure in the construction of systems biological networks that can predict how drug action may play out, both in terms of the recognized targets, which may have prompted the development of a particular drug, but also off-target effects. So, I think you're talking about the integration of what we might call systems biology, the omics sciences, pharmacology, and pharmacokinetics modeling together with basic and human pharmacology.

*Interviewer – Kate Travis*

So, what should any one researcher do to get all of that training?

*Interviewee – Garret FitzGerald*

Right. Well, I think first of all the primary responsibility is on those of us in the business, together with the funding agencies, to decide that this is an important thing to do. And then we have the complex task of establishing training programs to actually facilitate the integration of these presently segregated disciplines that are yet so relevant to drug development. And a first step in that regard has been made by the Wellcome Trust, which has funded four centers, in the U.K., in translational medicine and therapeutics. And there they've prompted precisely this type of integrative science in collaboration with industry, and the appropriate site for training will always be, I think, academia as the hub. But obviously, for this type of science, you want trainees to be exposed to the for-profit environment, where this is pursued, and also the regulatory body. So, I would see rotations out to industry to the regulatory body to, in this country, places like the NIH

Clinical Center, as being very attractive modules within training in translational medicine and therapeutics.

*Interviewer – Kate Travis*

So, what should people who are doing their training now, how should they steer their training to really make an impact in the future on translational medicine?

*Interviewee – Garret FitzGerald*

Well, I think, you know, the nice thing is that if you're attempting to do that there are many different ways to do something, and what I'm not trying to suggest is a sort of Marxist one-size-fits-all central planning–approach to this. Clearly, the likelihood is that most people, who who pursue this endeavor, will be expert in one part of it and then pursue the endeavor in teams of researchers who bring other types of expertise to the table that is then integrated. And, for that reason, I think an ideal way to begin is with an introductory degree, like a Masters, which sort of says, "Here's the challenge, here's the reason these types of different endeavors are relevant to meeting the challenge, and here's an introduction to what they are." So, many of the Masters programs that are being initiated by institutions that have clinical and translational science awards in the U.S. and similar awards elsewhere, have elements that are pitched either entirely or partly towards providing that type of expertise. And then having chosen the area within translational medicine and therapeutics where you want to develop your particular expertise, you would follow these Masters programs with postdoctoral training before applying for a faculty position.

*Interviewer – Kate Travis*

Thank you very much.

*Interviewee – Garret FitzGerald*

Okay. Thanks, Kate.

*Host – Kate Travis*

FitzGerald is the director of the Institute for Translational Medicine and Therapeutics, and Chair of the Department of Pharmacology at the University of Pennsylvania School of Medicine. You can read FitzGerald's Perspective article in the April 7 edition of *Science Translational Medicine* at <http://stm.sciencemag.org/>. And to discuss issues such as training and funding in translational medicine, visit CTSciNet at <http://community.sciencecareers.org/ctscinet/>.

*Music*

For *Science Translational Medicine* and CTSciNet, this is Kate Travis. Thanks for listening.