Science Translational Medicine – improving human health care worldwide by providing an interdisciplinary forum for idea exchange between basic scientists and clinical research practitioners

Science Translational Medicine – ein Forum für den interdisziplinären Wissensaustausch zwischen Grundlagenforschern und klinischen Forschungsärzten mit dem Ziel, die Patientenversorgung weltweit zu verbessern

Abstract

Science Translational Medicine's mission is to improve human health care worldwide by providing a forum for communication and interdisciplinary idea exchange between basic scientists and clinical research practitioners from all relevant established and emerging disciplines. The weekly journal debuted in October 2009 and is published by the American Association for the Advancement of Science (AAAS), the publisher of Science and Science Signaling.

The journal features peer-reviewed research articles, perspectives and commentary, and is guided by an international Advisory Board, led by Chief Scientific Adviser, Elias A. Zerhouni, M.D., former Director of the National Institutes of Health, and Senior Scientific Adviser, Elazer R. Edelman, M.D., Ph.D., Thomas D. and Virginia W. Cabot Professor of Health Sciences and Technology, Massachusetts Institute of Technology. The Science Translational Medicine editorial team is led by Katrina L. Kelner, Ph.D., AAAS.

A profound transition is required for the science of translational medicine. Despite 50 years of advances in our fundamental understanding of human biology and the emergence of powerful new technologies, the rapid transformation of this knowledge into effective health measures is not keeping pace with the challenges of global health care. Creative experimental approaches, novel technologies, and new ways of conducting scientific explorations at the interface of established and emerging disciplines are now required to an unprecedented degree if real progress is to be made. To aid in this reinvention, Science and AAAS have created a new interdisciplinary journal, Science Translational Medicine.

The following interview exemplifies the pioneering content found in Science Translational Medicine. It is an excerpt from a Podcast interview with Dr. Samuel Broder, former director of the National Cancer Institute and current Chief Medical Officer at Celera. The Podcast was produced in tangent with Dr. Broder’s Research Perspective “Twenty-Five Years of Translational Medicine in Antiretroviral Therapy: Promises to Keep”, published in Science Translational Medicine, 7 July 2010; Volume 2, Issue 39 [3].

Dr. Broder’s perspective marks the 25th anniversary of modern antiretroviral drug discovery and development. In the early 1980s, Dr. Broder’s research team adapted the nucleotide analog AZT for treating HIV infection, thus ushering in the era of antiretroviral therapies that have enabled HIV-positive individuals to live longer. The Podcast interview was conducted by Annalisa VanHook, Associate Online Editor, AAAS.

Katherine Forsythe

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Zusammenfassung


Dr. Broders Perspektive markiert das fünfundzwanzigjährige Jubiläum der Entdeckung und Entwicklung moderner antiretroviraler Medikamententherapien. Zu Beginn der achtziger Jahre stimmte Dr. Broders Forschungsteam das Nukleosidanalogon AZT auf die Behandlung von HIV-Infektionen ab, wodurch die Ära der antiretroviralen Therapien eingeleitet wurde, die HIV-positiven Patienten ein längeres Überleben ermöglichte. Das Podcast-Gespräch wurde von Annalisa VanHook durchgeführt, Online-Mitherausgeberin, AAAS.
The time in between when HIV was identified as the causative agent of AIDS, and before HTLV-1 was identified as the causative agent of a subset of T cell lymphomas, researchers didn’t seem to think it was likely that retroviruses would cause disease in humans. And even once HIV and HTLV were identified as causing disease, then people seemed to think that it might be futile to try and treat these retroviruses. Why was that idea prevalent in the scientific community?

Interviewee – Dr. Samuel Broder: The existence of animal retroviruses – that is, RNA viruses that replicate by reverse transcriptase – was already well known and widely accepted. But, there was a widespread belief that activating – that means replicating retroviruses – did not exist in human beings, partially because there had been an extensive search for them that was entirely negative. Then there was a secondary belief that even if human retroviruses did exist, they were not really involved in the pathogenesis of major human diseases. While there were some exceptions – you mentioned HTLV-1 as a cause of certain subacute T cell leukemias or, in some cases, tropical spastic paraparesis – many people felt that they, at most, played a minor role in the general public health. And then, when it was discovered and formally proven, by Gallo and Montagnier, that retroviruses really were the principle causative agent for AIDS, there was a sense of futility because it was felt that retroviruses, by their very nature, were inherently untreatable (Figure 1). This is for two reasons: They had a capacity to integrate into DNA of the host, and they could rapidly mutate due to the error-prone reverse transcriptase that they possessed, and both of those factors were felt to be essentially impossible barriers to the development of effective antiretroviral therapy. So, I think that was the feeling, that was the prevailing mood that we faced in 1984 when we began thinking very seriously about trying to develop antiretroviral agents, of which the first that went through our pipeline into human beings was AZT. That was done in a collaboration of what was then called the Burroughs-Wellcome Company and also academic investigators at Duke University.

Interviewer – Annalisa VanHook: Before HIV was identified as the causative agent of AIDS, and before HTLV-1 was identified as the causative agent of a subset of T cell lymphomas, researchers didn’t seem to think it was likely that retroviruses would cause disease in humans. And even once HIV and HTLV were identified as causing disease, then people seemed to think that it might be futile to try and treat these retroviruses. Why was that idea prevalent in the scientific community?

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constantly shift, in any case. But, if you’re totally afraid of crossing into the line of what might be impossible, if you’re very fearful that that will make you somehow look bad or that you’ll look foolish or something, you can’t really make major advances, in my opinion. And the NCI really strongly supported translational medicine, although that term was not in use at the time.

A: In your Perspective, you mention the need to adopt new paradigms for funding and for expediting the process of developing treatments and getting them into patients. And specifically, you mentioned the need for collaboration between the public and the private sectors. Why is neither sector ideally suited to successfully manage these large studies on their own, and how would the collaboration of the two be able to improve translational efforts?

SB: It isn’t merely the large studies that we’re talking about – that’s part of the equation – but actually there’s a larger issue. I think that certain types of drug discovery and certain types of drug development can be done in the private sector extremely well, but the private sector cannot undertake certain types of basic research or translational research when there is a significant chance of failure and when many of the assumptions are not proven. And so, it becomes very difficult to take on certain types of very far-reaching, paradigm-shifting experiments and to move them into the clinic and to move them to registration. That requires collaboration with the academic community and with the Intramural Program of the National Institutes of Health. So, a translational medicine approach, in which the probability of success or time to completion can’t be precisely quantified, would be beyond the reach of many drug development programs – quite frankly, either private or publicly funded. The other thing that I want to stress is that we need to have a wholeness of motion between the lab and the clinic. I think a compartmentalization – in which people do discovery in the lab and then almost like a relay race, turn it over to people in the clinic who are possibly in a different administrative structure or geographic location – can work, but it does not really take the best advantage of what translational medicine means, in my opinion. So, we need to restore and replenish the notion of the wholeness of motion where clinical investigators can actually do basic research and vice versa. And I think that that is becoming more and more difficult. Think there is a specialization – it’s an understandable specialization – but I think it would be important to have as many opportunities to fund, support, and train individuals who can do this wholeness of motion – that is, moving from the lab to the clinic and vice versa, from the clinic back to the lab.

References

Erratum
The authorship was originally attributed to Samuel Broder (Celera, Alameda, CA, USA) and Annalisa VanHook (American Association for the Advancement of Science, Washington D.C., USA).

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