Elias Zerhouni

The former National Institutes of Health (NIH) director lays out the numerous challenges facing the translation of academic discoveries.

As an inventor of groundbreaking technology, a founder of several startups, a leader of major public research institutions and now head of research at Sanofi-aventis, Elias Zerhouni has a unique perspective on the complex process of bringing drugs and technologies to market. Here the former NIH director spells out some of the major problems facing translation.

Is the current model for translation misaligned with the healthcare challenges facing society?

Elias Zerhouni: First and foremost, there's a fundamental gap of knowledge. Despite much progress in the biological sciences, we do not yet know how to interpret complex human biology to the point where we can reliably identify safe and effective therapies. This is leading to a misalignment between growing research spending and decreasing translational productivity. This has multiple downstream consequences. First, venture capital funding for academic startups and early-stage biotech companies is drying out due to the long development times and high failure rates. The second misalignment is that government policy is swinging to rationing reimbursement to control healthcare costs. Many payers see innovation as a main culprit of rising costs; it's almost like an anti-innovation spirit in the policy makers. In addition, an increasingly stringent regulatory system is making it more difficult to develop new therapies, especially primary-care drugs for large populations. This means that industry is being pushed into what I call specialty-care products that can [be] more easily developed rather than the primary-care products aligned with the current and future public health needs, such as chronic diseases. Then the last misalignment is allocation of human resources. In other words, there are too few MD-PhD scientists able to bridge the gap between understanding basic science and human disease. When you look at academia, it has moved away from translational research by necessity. Those who could do this type of work are either consumed by what clinical service demands or would rather go into the basic, rather than translational, side of things because you can get grants, publish papers and get promoted more easily. Eighty-five percent of US MD-PhDs are at the bench, not at the bedside.

What can be done to correct the human resource problem?

EZ: When I was at the NIH, I pushed very hard to establish the concept of translational medicine. And when I first started talking about the need to rebuild translational research as a new discipline so that it would have its mechanisms of promotion, recognition and funding—some people were outraged. They felt that this was not the role of NIH. Well, I think otherwise; it *is* the role of major government agencies to find solutions to the translation problem. That's why I created the CTSA [Clinical and Translational Science Awards] program to provide a kernel of support that will be independent of clinical services, which eat up an enormous amount of our scientists' creative time. The point is to fundamentally challenge academic institutions to come up with their own ecosystem that will encourage translational research and bridge the widening gap between basic research and clinical impact. In many top-line medical schools today there's no such thing as a pharmacology department, let alone research in chemistry or toxicology. So we've tried to incentivize such activities. Another important facet of course is to provide a high-tier journal to acknowledge excellence in translation research, which is why I supported the creation of *Science Translational Medicine*.

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How can one encourage fruitful industry-academia collaborations and avoid duplication of R&D?

EZ: It's really important to stress that translational work should never be done at the expense of continuing fundamental research. That would be a huge mistake. We cannot slow down our efforts in understanding the behavior of complex biological systems—what I've called the fundamental gap of knowledge. My philosophy at NIH was 60% of the budget went to fundamental research, and then 25% to what I would call translational research and 15% to public health. Having said that, one area where academic centers can help is understanding the biology of disease in human populations as early as possible using whatever method—biomarkers, adaptive clinical trials, exploratory INDs [investigational new drugs] or phase-zero trials. If you look at the behavior of the industry, it used to be closed-in R&D shops that worked within themselves and really didn't have access to external innovation or external centers of innovation. That is changing for the better. Every company you hear now is saying, "I want to be connected. I want to work with academia. I want to have problems posed to folks who have direct interactions with the diseases themselves in human populations." The NIH will also have a role to play in helping in the biological validation of core therapeutic hypotheses. I also see a major need for us to align research with patient organizations. If you're going to solve the Alzheimer's problem, you won't be able to do it with no participation in research by patients.

What do you see as the way forward?

EZ: It is imperative that we narrow the gap between regulatory science, the gap between financing and the gap between academic organizations, industry strategies and patient groups around one central concept, and that is that we cannot ignore the public health requirements. Basically, we have to realize that without innovation in our innovation ecosystem, we won't achieve the innovation that will serve the public and that needs the leadership of government agencies for it to happen. So it's a time of change. It's a time of reform. It's a time of not being timid about identifying the problem and allowing people to try different ways of changing the innovation system itself.