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Translational Biomedicine: a clinician's view

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Introduction

If I have to name the most momentous concept for biomedicine in the last decade, I would certainly go for the term "translational" without any hesitation. Not only it describes the vast array of biomedical research activities that relate to the study of human disease, their treatment and prevention; it also directs the processes of novel drug discovery and medical devices invention that directly or indirectly affects our economy as a whole.

Definition of "translational" in research and biomedicine

We all know what translation is all about in language when you need to express ideas and concepts from one common set of symbols and semantics to another set. How about in science and medicine? Merriam-Webster Dictionary defines "translational research" as "medical research that is concerned with facilitating the practical application of scientific discoveries to the development and implementation of new ways to prevent, diagnose, and treat disease." Professor Lee Nadler, senior vice president for Experimental Medicine at the Dana Farber Cancer Institute also epitomises a translational researcher as "someone who takes something from basic research to a patient and measures an endpoint in a patient"(1). That undoubtedly has been the a leading definition and scope for translational research in the last decade, a bench-to-bedside (N2B) mode as I would call it. But is that the whole picture for translational research? Or, should this be only direction that we use?

Bench-to-bedside (N2B) translational research

Biomedicine is based on science which equates human life and health to a conglomeration of molecules and chemicals interacting with each other intricately in a dynamic equilibria. Most often than not, diseases in human can be reduced to disturbances of these equilibria and can be rectified with chemical intervention in the form of drugs. A drug is designed to interact with target receptors on the cells which in turn modify the internal milieus of the cell via subsequent signalling mechanisms. Given this logic, novel drug discovery in Big Pharma can start with wet-bench biochemistry to produce compounds that interact with the target receptors with higher affinity, better specificity, longer duration or action or less side-effects. These compounds are known as new chemical entities (NCEs) in the drug industry. Having said, from sketch board to the actual NCEs, it may have already taken 3-5 years of research and development (R&D) and thousands of babies will have been thrown out of the bath tub, burning millions of dollars in such process. These NCEs will then be subjected to a long and cost-intensive process of drug trialling from Phase I/II toxicity trials in cells lines, perfused organs (2-3) and animals to Phase III/IV clinical trials in humans. This drug trialling period may take another 5-10 years and hopefully, these NCEs will successfully evolve as block-buster drugs that will both recoup the costs of R&D and bring in additional profits. Such business model is now under severe crisis compounded by the increasing stringent standards of drug approval by regulatory bodies in developed countries. In 2006, it has been estimated that 43% fewer NCEs have become drugs in the 21st century than did so in the past years of the 20th(4).

Bedside-to-bench (B2N) translational research

Clinicians always want to know what causes diseases and how they can be treated to enhance the health and life-span of patients. In other words, clinicians will poise their set questions and research targets from the bedside and addressing them with bench research will then become bench-to-bedside (B2N) translational research. From the standpoint of cost-effectiveness, B2N translational research commences with a clinical perspective and seeks a patho-physiological or pharmoco-therapeutic answer. It gives clearer directives of research and can embrace multiple basic scientific disciplines in its construct. If N2B translational research is like making an array of keys and trying out each of them for an unknown padlock, B2N translational research will be having a known padlock as a reference keyhole to make a best fitting key. A practical scenario for B2N will be to focus on various folklore or traditional medicines that have known therapeutic values for particular diseases, hence narrowing down the scope of wild-hunting for NCEs and drastically reduce the cost and wastage in R&D. One must not forget

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the natural herbs and traditional medicines have always been goldmines for novel drugs. Oseltamivir, better known as Tamiflu© which is the indicated drug for our global swine flu epidemics, is in fact isolated from a common Oriental spice called Illicium anisatum, or star anise(5).

Known hurdles to B2N translational research

It makes perfect sense for B2N translational research to complement the prevailing N2B approach but unfortunately it has never been given due respect from the academia, appropriate support from the grant funding bodies or proper attention in the Big Pharmas. Other known hurdles confronting B2N translational research include lack of mutual communications between bench scientists and clinicians(6), and insufficient clinician-scientists with solid training and expertise in basic sciences to facilitate B2N translational research. Moreover, the present legal pathway for any novel drug/device development is invariably a N2B direction from Phase I to Phase IV as described. It is almost unheard of for any treatment even with renowned clinical efficacy to proceed to Phase III/IV trial directly without going back to the wet-bench sciences first. That is a major hurdle for translational research in alternative and complementary medicine it is often not possible to identify the NCEs for drug trialling as there would be more than one interacting with each other in a synergistic way for the normal clinical efficacy.

Suggested solutions

For a start, N2B translational scientists have to think in reverse gear from the desired end-products to the building blocks. They also need to maintain constant clinical input from bedside physicians as they develop the blueprints for their NCEs or prototypic devices. At the other end, clinicians with basic sciences training are desperately needed as B2N translational researchers to maintain a constructive dialogue with N2B scientists. At present, B2N translational clinician-researchers are still a minority group and our federal government should inject more funding and incentive to aspire clinicians to take up a career in this rapidly developing field. A solid B2N translational input will no doubt be able to streamline development of new treatments and enhance the efficacy of medical care, which will then equate to billions of savings for both the Big Pharma and our Government in the long run. President Obama's 2011 budget has enunciated US$32 billions for National Institute of Health's investment in biomedical research, in particular "to focus on priority areas including genomics, translational research, science to support health-care reform, global health, and reinvigorating the biomedical research community." It is high time that B2N translational research should be highlighted in the agneda to ensure that President Obama's budget is well spent.

Conclusions

Translational research has always been a N2B-B2N two way traffic(7) and the author believes that it should also be an incessant N2B-B2N loop to sustain the best and most fruitful biomedical research activities. Using the author's "padlock and key" simile, there is no faster and cost-efficient way to unlock future biomedical secrets than maintaining a continuous N2B-B2N looping.

Bibilography

1. Birmingham K. What is translational research? Nat Med. 2002 Jul;8(7):647.
2. Curtis CG, Bilyard K, Stephenson H. Ex Vivo Metrics, a preclinical tool in new drug development. J Transl Med. 2008;6:5.
3. Leung L. Perfused human organs versus Mary Shelley's Frankenstein. J Transl Med. 2009;7:9.
4. Barden CJ, Weaver DF. The rise of micropharma. Drug Discov Today. 2010 Feb;15(3-4):84-7.
5. Bradley D. Star role for bacteria in controlling flu pandemic? Nat Rev Drug Discov. 2005 Dec;4(12):945-6.
6. Marincola FM. Translational Medicine: A two-way road. J Transl Med. 2003 Jul 24;1(1):1.
7. Marincola F. Translational Medicine: A two-way road. J Transl Med. 2003 Jul;1(1):1.