Translational Cancer Research: Challenges and Opportunities

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Pesquisa Translacional em Câncer: Desafios e Oportunidades

Investigación Traslacional del Cáncer: Desafíos y Oportunidades

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In the last two decades, it has been seen unprecedented advances in understanding the subjacent biological mechanisms to the development and progression of cancer. Efforts of the scientific community targeted to mapping cancer genome produced an extraordinary vision of genetic and epigenetic alterations occurring during carcinogenesis. The translation of this wisdom into clinical practice has granted specific innovative treatments for molecular targets in certain tumors. However, the progress in more effective treatments has been slower than expected. Our ability to translate this knowledge in approved therapies is still challenging[1,2].

The traditional frontiers between basic and clinical research generated the concept of translational research (or translational medicine, translational science etc.) whose goal is to facilitate the application of ideas, insights, and discoveries within the scope of basic investigation in clinical and communitarian environments for the treatment or prevention of human diseases; a concept many times shortened as from "bench to bedside"[3]. Although the term "translational research" has been used for the first time in the decade of 1990[4], the concept had been discussed by Stewart Wolf in a pioneer editorial of the New England Journal of Medicine (NEJM) in 1974[5].

In a more comprehensive vision, the main objective of translational biomedical research in biomedicals is to ensure that new products found have more odds of success in terms of safety and efficacy in studies with humans. In other words, reject new products with probability of failure in the process start-up can reduce the overall cost of the development significantly. Therefore, the ultimate end of the translational research is to lead the first pre-clinical discoveries to the point of investment, mainly those conducted in the academia or industry[6].

According to this simplified vision, translational research is part of a unidirectional *continuum* in which the first stage of research transfers knowledge from basic research (T0) to clinical research (T1) and the second stage (T2) transfers findings from clinical studies to practice settings. In stage T0, basic investigation defines the cellular mechanisms, its relation with the disease, the identification of therapeutic targets, development of treatment methods among other. In stage T1, the research is conducted with volunteers who establish the safety of a product (phase I clinical trials). Phase 2 and phase 3 clinical trials are part of stage T2, necessary to test the efficacy of the therapeutic agents in cohort of patients with the disease. Stages T1 and T2 translational research bring off-lab and clinical practice scientific discoveries but that do not fully apply to the real world[7].

Some authors suggest additional stages (T3 and T4). In stage T3, research reaches the communities to test whether new treatments and interventions which succeeded in minor scale within controlled setting, will work in less controlled settings (the real word, ambulatorial or medical practice, for instance). Examples of T3 translational research include community-based participatory research – CBPR and Phase IV clinical trials[8-10]. The next stage (T4) comprehends the translation of researches from clinical practice to population health impact, including the development of public health policies and programs. T4 translational research can include cost-benefit analysis, policy analysis, surveillance studies, evaluation of the program and so forth[1,11].

Although the illustration of translational research indicates a linear model (with beginning, middle and end), actually, it must be considered as a continuous and bidirectional process with interdependent operational phases and subject to continuous complex feedback cycle[12,13]. Translational research moves bidirectionally from a type of research to another (from basic research to patient-oriented research to populational-based research and vice-versa) involving the collaboration among scientists of various disciplines.

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By definition, translational research in cancer concentrates in the necessities of individuals affected and prevention of individuals in risk. Even with the implementation of future "discoveries" we may be unable to prolong the life of a considerable subset of patients with cancer significantly. This means the necessity of weighing researches in prevention too. As in the case of translational research for therapeutic ends, the different components of the *continuum* of researches in cancer prevention will not be sufficiently connected and have important gaps between basic research and results of primary, secondary, and tertiary prevention strategies[13].

As widely discussed in the literature, the increasing problem of cancer can only be modified significantly through concurring actions involving prevention, early detection and treatment and promotion of personalized medicine (of accuracy) that allows to associate early detection and treatment to tumor biology, increasing survival and improving the quality of life of patients with cancer.

In the last years, translational research became object of great discussions in biomedicals and policy, generating expectations, promises and concerns and is a constant reference in research programs, academic articles, policies reports and education programs worldwide[3,6]. However, various barriers delaying this process need to be overcome to make translational cancer research more than an interesting concept. Functional interactions among academia, government, community, incentive agencies, industries (pharmaceutical, biotechnology) among others[14] should be in place for translational research to work more effectively.

REFERENCES

1. Khoury MJ, Gwinn M, Yoon PW, et al. The continuum of translation research in genomic medicine: how can we accelerate the appropriate integration of human genome discoveries into health care and disease prevention? Genet Med. 2007;9(10):665-74. doi: https://doi.org/10.1097/GIM.0b013e31815699d0
2. Zhang H, Klareskog L, Matussek A, et al. Translating genomic medicine to the clinic: challenges and opportunities. Genome Med. 2019;11(1):9. doi: https://doi.org/10.1186/s13073-019-0622-1
3. Rubio DM, Schoenbaum EE, Lee LS, et al. Defining translational research: implications for training. Acad Med. 2010;85(3):470-5. doi: https://doi.org/10.1097/ACM.0b013e3181ccd618
4. Mulshine JL, Jett M, Cuttitta F, et al. Scientific basis for cancer prevention. Intermediate cancer markers. Cancer. 1993;72(3 Suppl):978-83. doi: https://doi.org/10.1002/1097-0142(19930801)72:3+<978::aid-cncr2820721305>3.0.co;2-t
5. Wolf S. The real gap between bench and bedside. N Engl J Med. 1974;290(14):802-3. doi: https://doi.org/10.1056/NEJM197404042901411
6. Seyhan AA. Lost in translation: the valley of death across preclinical and clinical divide - identification of problems and overcoming obstacles. Transl Med Commun. 2019;4:18. doi: https://doi.org/10.1186/s41231-019-0050-7
7. Woolf SH. The meaning of translational research and why it matters. JAMA. 2008;299(2):211-3. doi: https://doi.org/10.1001/jama.2007.26
8. Vukotich CJ Jr. Challenges of T3 and T4 translational research. J Res Pract. 2016;12(2):P2.
9. Zarbin M. What constitutes translational research? Implications for the scope of translational vision science and technology. Transl Vis Sci Technol. 2020;9(8):22. doi: https://doi.org/10.1167/tvst.9.8.22
10. Westfall JM, Mold J, Fagnan L. Practice-based research- "Blue Highways" on the NIH roadmap. JAMA. 2007;297(4):403-6. doi: https://doi.org/10.1001/jama.297.4.403
11. Khoury MJ, Gwinn M, Ioannidis JPA. The emergence of translational epidemiology: from scientific discovery to population health impact. Am J Epidemiol. 2010;172(5):517-24. doi: https://doi.org/10.1093/aje/kwq211
12. Mata HJ, Davis S. Translational health research: perspectives from health education specialists. Clin Transl Med. 2012;1(1):e27. doi: https://doi.org/10.1186/2001-1326-1-27
13. Ringborg U. Translational cancer research – a coherent cancer research continuum. Mol Oncol. 2019;13(3):517-20. doi: https://doi.org/10.1002/1878-0261.12450
14. Berns A. Quality-assured research environments for translational cancer research. Mol Oncol. 2019;13(3):543-48. doi: https://doi.org/10.1002/1878-0261.12441

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