

Are we really translating pain knowledge to clinical practice?

Estamos mesmo translacionando o conhecimento da dor para a prática clínica?

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Scientific research in health care takes many different forms, from preclinical laboratory research (basic research), observational studies and clinical trials (clinical research) to the direct application in the population (patients). It is not safe to make the direct transition from studying individual cells or organ systems and begin tests in patients, and this is where translational research comes in. Translational research is designed to link basic research and innovation in health in order to generate products such as vaccines, drugs, non-pharmacological therapies, equipments, or services and policies that can benefit the population. In this context, the objective is to apply laboratory research findings and preclinical studies to the design and development of clinical trials, as well as the adoption of the best clinical practices^{1,2}.

Although the terminology is recent, this discussion about the link between basic scientific knowledge and the development of innovative products and processes has its origin in ancient research practices and was established after the Human Genome Project in 1990. The discussion strengthened after the publication of an editorial in the Journal of the American Medical Association (JAMA) in 2002, where it discussed the need to apply advancements acquired through basic research to improve patient health through new knowledge in the fields of disease prevention, diagnosis, prognosis, and treatment. In 2003, the National Institute of Health (NIH) in the United States began to prioritize translational research³ and, in 2022, the International Association for the Study of Pain (IASP) launched the worldwide campaign entitled Global Year for Translating Pain Knowledge to Practice, whose objective is to raise awareness about pain knowledge and how it can benefit individuals living with pain.

In addition to the new terminology, a systematization for its practice has also been developed through improved methodologies and more effective information systems, such as network systems. But how can we ensure that the discoveries generated through basic research promotes gains for the health of the human population?

In more clear terms, a basic pain researcher can identify, for example, an important receptor for a particular analgesic therapy. Based on this information, translational science researchers can evaluate a range of therapeutic combinations to develop a drug or a nonpharmacological intervention that achieves the expected effect by performing evaluations in laboratory animal models and determining a protocol with suggested dose, therapeutic effect, and adverse effects or toxicity. Next, after testing the effect and safety of the therapy, applied science researchers can initiate clinical trials in humans with specific pain conditions to test the efficacy, responsiveness, and clinical safety. Although translational research is considered to be this link between basic and applied science, in most cases, there is no articulation between the two.

The knowledge produced via basic science is often not well utilized, or at best, its use occurs in a very slow and not promising manner. With the advent of translational research, there is a tendency for the researcher's work to continue with the articulation between the laboratory and the clinic.

However, in the current global scenario of translational research, there is a real gap between basic research, the ready access of patients to new products and the provision of care, which results in a great challenge to be overcome. In recent years, investment in this type of research has greatly grown and several discoveries about the neuroscience of pain have occurred, but the impact on the application of new pain diagnostics and treatments has not achieved corresponding progress regarding the development of new diagnostics and long-term interventions for the treatment of chronic pain, and therapeutic milestones have not been produced in the same proportion. This is a quintessential problem, since the prevalence of people affected by chronic pain has increased greatly in all age groups, increasing the global economic impact of pain, and, at the same time, no major advances in pain management interventions have occurred in the last 20 years. On the other hand, there has not been as much progress in methodological strategies of translational research from the development and evaluation of preclinical models to the design and execution of clinical trials.

In what proportion does pain in laboratory animals resembles the human condition? Do preclinical pain models mimic the chronic pain condition to the same magnitude as acute pain? Are we becoming accommodated to existing models? Is it not now the time to reflect and seek new methodological options for a better comprehension of new concepts in pain in order to promote effective translational optimization? Are the questions being asked and answered in preclinical studies relevant for diagnostic or clinical treatment studies? Have the most appropriate and relevant questions been asked by the scientists? Has the solution of real health problems been considered in contemporary basic science? Who is asking and testing the questions? What is the level of articulation between scientists and clinicians? These questions are important, and while there are no ready-made or unique answers in the different settings, they trigger important reflections.

Despite its importance, the knowledge acquired through basic science should not be assumed *ipsis litteris* to promote better patient care, that is, it is not possible to ensure that the phenomena that happen in laboratory animals replicate and reproduce exactly in the same way and to the same extent in human beings with clinical pain. It is not that simple! This shallow understanding perhaps contributes to the failure of the translational potential of science.

All in all, caution is needed when criticizing translational science or scientists, as different factors affecting progress need to be considered, such as the lack of relevant pain models; limited strategies of evaluation; species differences between laboratory animals and humans; flaws in reporting, execution, analysis, and/or interpretation of clinical trials; regulatory constraints; and differences between countries.

There is no doubt that the understanding of pathophysiological mechanisms of diseases, as well as the mechanisms of action of pharmacological and non-pharmacological interventions for pain, especially chronic pain, are important and add value and safety to the clinical reasoning of professionals, as well as induce the reasoning of scientists to create new hypotheses and investigations in order to generate advances in the clinical area that reflect the investment of time and financial resources.

However, in the current context, probably the most adequate and viable strategy is to perform the reverse translational reasoning, from the verification of occurrences with the patients and, then, the proposition of pain models and assessment methods consistent with the problem-situation. This feedback thinking (from clinic to science) favors the improvement of basic science, promoting progress and effective contribution to the health of the human population.


Knowledge about pain cannot die on the bench of basic science. It needs continuity to be promising and actually influence, at some point, the assistance of patients with pain. On the other

hand, although clinical decision making is based on therapeutic efficacy derived from randomized clinical trials and, to a greater extent, systematic reviews with meta-analysis, the knowledge produced by basic and translational sciences are essential to provide pain specialists with accurate and reliable information about not only what works and how it works, but why it works.

In this sense, clinical relevance must be the priority of decision making for translational pain science researchers. Simultaneously, comprehending the complexity of the phenomena and the magnitude of health problems is necessary, assuming that future advances in clinical performance in the setting of chronic pain will have to be solved by teams that involve interdisciplinarity, in a collaborative way, by means of multiple knowledge and complementation of skills, as well as scientists engaged together to seek the solution to a single problem. Furthermore, organizations, societies, institutions, and funding agencies must encourage and induce leadership so that scientists realize and focus on the need for innovative techniques and strategies with emphasis on real clinical goals for pain management. All these factors together tend to favor the future success of translational pain research.

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