Translational Insights
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Editorial

Translational Insights: A Paradigm Reversal in Translational Research

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Received: 9 March 2026; Accepted: 9 March 2026; Published: 16 March 2026

How To Cite: Liang, Y.; Marincola, F.M. *Translational Insights*: A Paradigm Reversal in Translational Research. *Translational Insights* **2026**, *1*(1), 1.

Translational Insights is intended to support and foster the bidirectional learning for early development, proof-of-concept studies in humans. We aim to publish early-phase translational studies that meaningfully connect breakthrough biological discovery with first-in-human or early human testing, and that clarify the mechanistic and clinical potential of new therapeutic concepts through realistic and efficient development pathways. We particularly welcome submissions that provide high-value human ex vivo evidence, mechanistically anchored correlative analyses, and early clinical datasets that improve prioritization decisions. In doing so, we hope to help accelerate rigorous bidirectional translation while maintaining the scientific, ethical, and clinical standards that patients deserve.

In the opening editorial for the ***Journal of Translational Medicine*** in 2023 [1], I argued that translational research should be cultivated not only in the traditional bench-to-bedside direction, but also from bedside to bench. At the time, translational efforts were still largely framed by preclinical experimentation, with therapeutic development relying predominantly on in vitro systems and in vivo animal models before any meaningful learning could occur in humans.

Quoting the editorial [1]:

> "*Translational research should be regarded as a two-way road: Bench to Bedside and Bedside to Bench. However, Bedside to Bench efforts have regrettably been limited because the scientific aspects are poorly understood by full time clinicians and the difficulty of dealing with humans poorly appreciated by basic scientists. Translational research would be most useful to the scientific community at large if journals would foster specific interest for the publication of* ex vivo *human observation. The review process for such work should be assigned to clinical scientists competent not only in the intricacies of molecular or cell biology but also intimate with the reality of Internal Review Boards, ethics committees, Governmental Regulatory Agencies and most importantly the humane aspects of dealing with sick individuals and their families. This approach may focus both basic and clinical scientists and those struggling to fill the gap between them on the effective treatment of diseases affecting women, men and children making translational research more than an interesting concept.*"

Since then, the technological landscape has advanced rapidly. Tools for comprehensive patient monitoring and biological discovery—including high-throughput genomics and proteomics, spatial transcriptomics, single-cell sequencing, and multi-omics integration—have become increasingly powerful. These developments, together with improvements in computational modeling, artificial intelligence, and machine learning, have greatly expanded our ability to learn from both success and failure in early-phase clinical studies.

Thus, the paradigm has changed since then and, while bed-side-to-bench efforts have transformed the way we understand the genetic, somatic and environmental determinants of diseases and their response to therapy [2], the bench-to-bedside is languishing due to excessive proof-of-concept and safety studies required before allowing early phase evaluation of treatment efficacy. Thus, the majority of potentially ground-breaking approaches miss the mark of reaching clinical stage not because of the quality of the science upon which they stand, but failure to obtain sufficient support to endure an extremely long and costly path [3]. Indeed, The bench-to-bedside time course is a lengthy, multi-stage journey from lab discovery to patient testing, typically taking 10–15 years or more, involving basic research, pre-clinical testing (mostly expensive animal models), multi-phase clinical trials (Phase I–III for safety/efficacy), regulatory approval, strict manufacturing requirements, and post-market surveillance, with most discoveries failing along the way due to dwindling financial support.

Outside a limited number of self-contained academic programs, bidirectional translation is therefore costly, complex, and difficult to support through government or academic funding alone. Industry and venture capital can provide the necessary resources [3] but their appetite is dampened by the discouraging amount of time required to test biomedical concepts from conception to clinical evaluation due to the red tape that slows translational processes overburdened by (a) disproportionate requirements for proof-of-concept studies in questionably relevant pre-clinical animal models; (b) ever more burdensome regulatory requirements that limit access to new therapeutic concept for terminal patients, whose demise often occurs without the opportunity to test promising, scientifically legitimate though yet unproven therapies [4].

Thus, fresh approaches are vital. One priority is to accelerate early proof-of-concept testing in humans through biologically relevant ex vivo human models that complement, and in selected contexts help de-risk reliance on, contrived animal systems. Another is to identify early signals of target engagement and clinical activity in carefully designed early-phase studies, so that the most promising agents can be prioritized for further development and commercialization [5]. For instance, phase 0 clinical trials are early-stage explorations designed to quickly and inexpensively determine if a new drug behaves in humans as expected from laboratory and animal studies, before committing to more extensive and costly traditional clinical trials [3].

At the same time, the power of AI and machine learning should not be overstated in the absence of high-quality human data. These technologies are only as informative as the datasets on which they are trained. For translational medicine, such data must increasingly come from longitudinal study of human tissue and biofluids collected before, during, and after treatment in early-phase clinical investigations. Generating these data responsibly requires not bypassing ethics or safety standards, but designing more efficient, risk-proportionate, and scientifically informative pathways into the clinic.

Translational Insights is intended to support this mission. We aim to publish early-phase translational studies that meaningfully connect breakthrough biological discovery with first-in-human or early human testing, and that clarify the mechanistic and clinical potential of new therapeutic concepts through realistic and efficient development pathways. We particularly welcome submissions that provide high-value human ex vivo evidence, mechanistically anchored correlative analyses, and early clinical datasets that improve prioritization decisions. In doing so, we hope to help accelerate rigorous bidirectional translation while maintaining the scientific, ethical, and clinical standards that patients deserve.

Conflicts of Interest

The authors declare no conflict of interest.

Use of AI and AI-Assisted Technologies

No AI tools were utilized for this paper.

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