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# Bridging the innovation gap and rethinking translation in biomaterials science

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https://doi.org/10.1016/j.matt.2025.102257

**Despite a surge in biomedical engineering publications, clinical translation still lags behind. To bridge this gap, we must prioritize interdisciplinary collaboration, problem-driven innovation, and an inclusive scientific culture to ensure that research has a real-world impact on global health. Moreover, translational challenges can be resolved by bridging laboratory research with industry.**

We are currently facing a scientific paradox: a few papers have been published in the field of biomedical engineering; however, these papers are not matched by a proportional increase in patents and/or commercially available products to address global health, translational hurdles, and societal challenges. For instance, the United States filed one patent in the field of nanotechnology for every three articles in 2021.[1] Approximately 20 cancer nanomedicines are approved for clinical use, and more than 100 formulations are in the (pre)clinical testing stage.[2] This striking disconnect reveals that academic productivity does not necessarily translate into practical solutions, a trend that warrants urgent investigation. This matter of opinion explores the value of key scientific aspects of biomedical engineering, supported by a discussion of various case studies that illustrate both the successes (i.e., Doxil and Abraxane) and challenges within this field, particularly in the use of nanoparticles for cancer diagnosis and treatment.

Nanomedicine therapies have revolutionized the reduction of side effects compared to free diagnostic and therapeutic molecules, ultimately improving patients' quality of life.[2] Liposomal doxurubicin (Doxil) formulation was approved by the Food Drug Administration (FDA) in 1995 for the treatment of advanced breast cancer and in 1996 by the European Medicines Agency (trademarked as Caelyx).[3] Strikingly, Doxil reduces cardiotoxicity (>3-fold reduction) and hair loss, which are significant side effects associated with free doxorubicin administration. This improvement in safety, coupled with the potential for targeted drug delivery, has significantly improved the quality of life of patients undergoing chemotherapy for various cancers. This work started with the pioneering work of Gabizon and Barenholz in collaboration with laboratories around the world, including in Jerusalem (Hebrew University-Hadassah Medical School), Canada (University of Alberta), and California (Liposome Technology, Inc.). Interestingly, several aspects of achieving therapeutically efficacious passive targeting of liposomes to cancer tissues were developed in parallel across these four locations. Throughout the Doxil development journey, there was a clear contribution from various experts, including biochemistry researchers (e.g., Barenholz), medical oncologists (e.g., Gabizon), and entrepreneurs (e.g., Papahadjopoulos). It took 16 years from the beginning of basic research on liposomal doxorubicin in 1979 to its FDA approval in 1995, highlighting the importance of long-term investment in translational science. Since 1991, when the first patient in the first clinical trial received Doxil, more than 500,000 patients have been treated with it. It should be noted that inconsistencies among regulatory agencies/bodies have been observed in defining nanomedicine because of their distinct behaviors. For example, the FDA and EMA have differently considered the approval of LipoDox, a generic version of Doxil which was approved by the FDA but rejected by the EMA due to the lack of a bioequivalence study of unencapsulated DOX drug.[4] Overall, such concerns slowdown the translational and approval progress of nanomedicines.

Another compelling example of successful nanomedicine translation is nanoparticle-albumin-bound paclitaxel, commercially known as Abraxane, nab-paclitaxel. Abraxane delivers albumin-bound hydrophobic drugs to tumors in conditions such as advanced breast cancer and metastatic adenocarcinoma of the pancreas.[5] It was the first protein nanotechnology-based chemotherapeutic, and Cremophor free, receiving FDA approval in 2005 and EMA approval in 2008.[2] Unlike traditional paclitaxel formulations, Abraxane addresses the solvent-related issues of Taxol and provides significant value for patients by simplifying administration protocols, namely enabling administration over a shorter infusion period (30 min vs. 3 to 24 h with solvent-based paclitaxel), at a higher dose (300 vs. 175 mg/m$^2$ for solvent-based paclitaxel, every 3 weeks), and without a corticosteroid and/or histamine co-mediation to prevent solvent-related hypersensitivity reactions.[5,6] Nab-paclitaxel was invented by the chemical engineer Neil Desai and a physician-entrepreneur Patrick Soon-Shiong from UCLA Medical School and Abraxis Bioscience company. Abraxane remains the leader in the paclitaxel formulation market.

Recently, additional nanomedicine platforms, such as Lipoplatin and mRNA-4157/V940, have emerged, offering new

**Table 1. Translational landscape of nanomedicine: Successes, challenges, and enablers**

| Aspect | Doxil | Abraxane | Lipoplatin | mRNA-4157/V940 | Common challenges in translation | Key enablers of translation |
|---|---|---|---|---|---|---|
| Type of nanomedicine | liposomal doxorubicin | albumin-bound paclitaxel | liposomal cisplatin | lipid nanoparticle-encapsulated mRNA | complex, multi-layered nanoparticles with limited clinical relevance | simple, biocompatible, and scalable designs |
| Approval timeline | FDA (1995); EMA (1996 as Caelyx) | FDA (2005); EMA (2008) | phase III trials completed; EMA orphan drug status granted | phase IIb trial positive; FDA Breakthrough Therapy and EMA PRIME designations granted | many nanomedicines remain in early clinical stages for extended periods | early regulatory engagement and translational planning |
| Time from basic research | ~16 years (1979–1995) | ~10 years | ~10–15 years | ~6 years (2017–2023) | extended development timelines without clear commercial pathways | long-term funding and institutional support |
| Inventors/leaders | Gabizon, Barenholz, Papahadjopoulos | Desai, Soon-Shiong | Boulikas, Stathopoulos | Moderna and Merck collaboration | academic-led projects often lack entrepreneurial infrastructure | entrepreneurial leadership and industry collaboration |
| Clinical advantages | reduced cardiotoxicity, improved tolerability | Cremophor-free; higher dosing, shorter infusion | reduced nephrotoxicity; improved tumor targeting | personalized vaccine; significant reduction in recurrence risk | insufficient tumor accumulation; toxicity; delivery barriers in tumor microenvironment | targeting tumor biology and simplifying administration |
| Multi-disciplinary input | clinicians, biochemists, entrepreneurs | engineer, physician-entrepreneur | oncologists, pharmacologists, nanotechnologists | bioinformaticians, immunologists, clinicians | siloed academic research with limited real-world input | cross-disciplinary teams (clinicians, engineers, regulatory experts, etc.) |
| Market/clinical impact | 500,000 patients treated | leader in paclitaxel market | demonstrated efficacy in NSCLC; reduced toxicity compared to cisplatin | 49% reduction in recurrence risk in high-risk melanoma patients | low success rates in phase II/III trials despite high phase I success | clinical relevance, market need, and patient-centric design |
| Translation barriers | N/A | N/A | N/A | N/A | overengineered particles, lack of tumor penetration, weak translational strategy | problem-driven innovation with focus on patient needs |
| Cultural/systemic issues | N/A | N/A | N/A | N/A | hierarchical lab cultures, exclusionary practices, lack of diversity | inclusive and collaborative research environments |
| Innovation ecosystem | supported by Liposome Technology Inc. | backed by Abraxis Bioscience | developed by Regulon Inc.; EMA orphan designation | developed by Moderna and Merck; leveraging mRNA technology | limited commercialization training and support in academia | participation in translational/ entrepreneurial programs (e.g., NSF I-Corps, IMFAHE) |

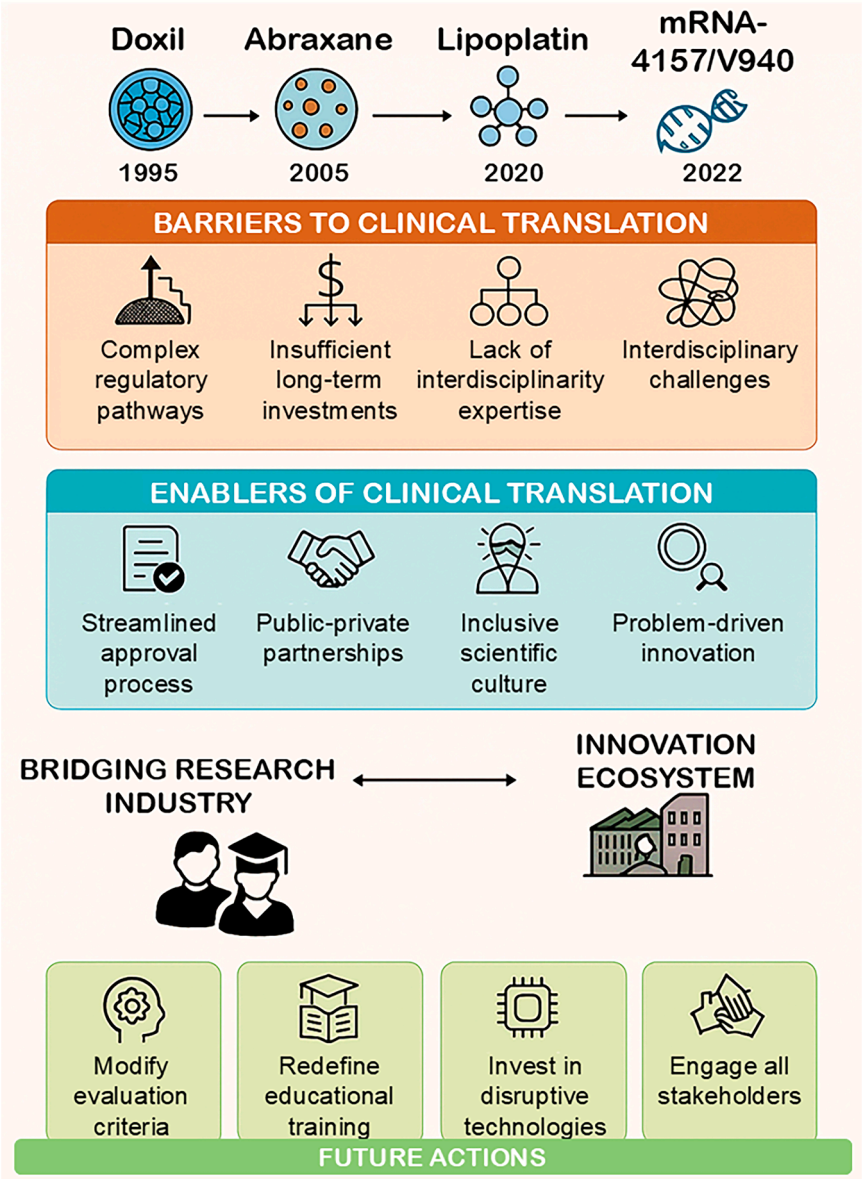


**Figure 1. Translational pathways and innovation ecosystem in biomaterials science**

A roadmap highlighting key milestones in nanomedicine development (Doxil, Abraxane, Lipoplatin, mRNA-4157), major barriers to clinical translation (e.g., complex regulations, insufficient investment, lack of interdisciplinary expertise), and enablers of success (e.g., inclusive culture, public-private partnerships). The bottom section emphasizes the importance of bridging research with industry and outlines future actions needed to close the innovation gap, including modifying evaluation criteria, redefining educational training, investing in disruptive technologies, and engaging all stakeholders.

perspectives on successful translation. Lipoplatin, a liposomal formulation of cisplatin, has demonstrated reduced nephrotoxicity and improved tumor targeting in patients with non-small cell lung cancer, with promising outcomes in phase III trials. Meanwhile, the personalized cancer vaccine mRNA-4157/V940, developed by Moderna and Merck, leverages lipid nanoparticles to deliver tumor-specific mRNA and has shown a 49% reduction in recurrence risk when combined with checkpoint inhibitors in high-risk melanoma patients, leading to an FDA breakthrough therapy designation. These cases reflect a shift toward patient-specific, immune-responsive, and biocompatible platforms that address safety and efficacy. Notably, while the success of mRNA-4157/V940 underscores the value of integrating immunotherapy and nanotechnology, it also illustrates the importance of early alignment with regulatory bodies and strategic partnerships in the industry.

A closer look at the comparative analysis of clinically approved and emerging nanomedicine platforms (Table 1) reveals that successful translation hinges not only on innovative design but also on multidisciplinary collaboration, patient-centric development, and early alignment with regulatory and commercial pathways. Moreover, it reveals three key insights: (1) successful nanomedicine translation consistently involves early and sustained multidisciplinary collaboration across academia, industry, and clinical practice; (2) designs that are clinically practical and scalable and address a clear unmet medical need, rather than merely novel, are more likely to succeed; and (3) regulatory foresight and entrepreneurial leadership are crucial in navigating the long, uncertain path from bench to bedside (Figure 1). The disconnection between the original goals of nanomedicine research and the outcomes produced is evident. There is excessive emphasis on creating new (and complex) nanoparticle designs, while insufficient effort is focused on understanding how these nanoparticles accumulate in tumors. For instance, studies on inorganic nanoparticles used at least one coating layer (89.6%) and a medium NP coating complexity (that is, 3 or 4 functionalization steps, 35.2%).[7] The scientific path often lacks sufficient focus on identifying and addressing the reasons why nanomedicine therapies are frequently unsuccessful in clinical trials. A key barrier is the tumor microenvironment, which presents formidable physiological and biological challenges to drug delivery.[8] An extensive analysis of the efficacy of inorganic nanoparticles on tumor reduction concluded that arming nanoparticles with multiple therapeutic modalities (i.e., photodynamic, ultrasound, hyperthermia) is associated with greater efficacy, addressing both intra- and intertumoral heterogeneity more efficiently.[7] The key advantages of using combinatorial therapies are yet to be clinically proven as a more customizable mode of administration and a more effective treatment. Moreover, these therapies are facing

challenges in standardization, clinical trial design, and regulatory alignment.

By analyzing the success of nanoparticle-based drugs such as Doxil and Abraxane, scientific breakthroughs require time and multidisciplinary team efforts. It is crucial for governments to maintain funding and support to provide scientists with stable careers in which they can seed and nurture their novel ideas. The global community plays a vital role in recognizing the importance of science. To achieve this, scientists must continue their outreach efforts from a young age (e.g., European Research Night and SoapboxScience initiatives). Moreover, both founders of commercially available nanoparticles emphasized the significant challenges they faced in securing funding and regulatory approval. Therefore, it is of great importance not to dissociate innovation from an early stage, particularly in terms of assembling multidisciplinary teams (e.g., clinicians, computer scientists, bioengineers) and conducting customer discovery. For instance, one of the goals of the conference workshop in Colorado was to consistently promote fundamental research in nanomedicine, despite the lack of immediate benefits for patients and to acknowledge that translational research is built on a long and gradual process.[9]

Participation in entrepreneurship programs (i.e., NSF i-corp) can also enhance participants' vision, help them identify the "sweet spot" for their technologies, and help researchers understand product-market fitness and accelerate translational pathways. It is obvious that there is no room in science for closed mindsets, racism, outdated hierarchical structures, or misogynistic environments. Such conditions hinder the open and healthy atmosphere crucial for questioning and improving initial concepts. Promoting an inclusive culture is not just a moral imperative, it is a strategic necessity for innovation. To overcome these limitations, female leadership serves as a powerful example that can empower and inspire the next generation of women and girls in science (e.g., IMFAHE Foundation and Non-Conformist Scientist program), encouraging them to lead with a confident voice and entrepreneurial mindset and ultimately pursue translation research into real-world applications. Finally, the importance of maintaining high standards and quality in the peer-review process must be emphasized. A robust peer-review system not only ensures the credibility and reproducibility of research but also helps uphold the integrity of scientific debate, which is the cornerstone of translational success.

## ACKNOWLEDGMENTS

J.C. acknowledges the European Research Council (ERC) under the European Union's Horizon 2020 Research and Innovation Programme (ERC-StG-2019-848325). B.B.M. acknowledges Liga Portuguesa Contra o Cancro. This study was funded by the Fundação Ciência e Tecnologia, IP national support, through the Comprehensive Health Research Centre (UID/04923). R.P. acknowledges the Anusandhan National Research Foundation (ANRF) ANRF/IRG/2024/000620/LS for funding support.

## DECLARATION OF INTERESTS

J.C. is a co-founder and shareholder of TargTex S.A. – Targeted therapeutics for Glioblastoma Multiforme. J.C. is also a member of the Global Burden Disease (GBD) consortium of the Institute for Health Metrics and Evaluation (IHME), University of Washington (USA).

## REFERENCES

1. Zhu, H., Jiang, S., Chen, H., and Roco, M.C. (2017). International perspective on nanotechnology papers, patents, and NSF awards (2000–2016). J. Nanopart. Res. *19*, 370.

2. Lammers, T. (2024). Nanomedicine Tumor Targeting. Adv. Mater. *36*, 2312169.

3. Barenholz, Y. (2016). (Chezy). Doxil® – the First FDA-approved Nano-drug: from Basics via CMC, Cell Culture and Animal Studies to Clinical Use. In Nanomedicines: Design, Delivery and Detection, M. Braddock, ed. (The Royal Society of Chemistry). https://doi.org/10.1039/9781782622536-00315.

4. Youden, B., Jiang, R., Carrier, A.J., Servos, M. R., and Zhang, X. (2022). A Nanomedicine Structure-Activity Framework for Research, Development, and Regulation of Future Cancer Therapies. ACS Nano *16*, 17497–17551.

5. Hawkins, M.J., Soon-Shiong, P., and Desai, N. (2008). Protein nanoparticles as drug carriers in clinical medicine. Adv. Drug Deliv. Rev. *60*, 876–885.

6. Gradishar, W.J., Tjulandin, S., Davidson, N., Shaw, H., Desai, N., Bhar, P., Hawkins, M., and O'Shaughnessy, J. (2005). Phase III Trial of Nanoparticle Albumin-Bound Paclitaxel Compared With Polyethylated Castor Oil–Based Paclitaxel in Women With Breast Cancer. J. Clin. Oncol. *23*, 7794–7803.

7. Mendes, B.B., Zhang, Z., Conniot, J., Sousa, D. P., Ravasco, J.M.J.M., Onweller, L.A., Lorenc, A., Rodrigues, T., Reker, D., and Conde, J. (2024). A large-scale machine learning analysis of inorganic nanoparticles in preclinical cancer research. Nat. Nanotechnol. *19*, 867–878. https://doi.org/10.1038/s41565-024-01673-7.

8. Mendes, B.B., Conniot, J., Avital, A., Yao, D., Jiang, X., Zhou, X., Sharf-Pauker, N., Xiao, Y., Adir, O., Liang, H., et al. (2022). Nanodelivery of nucleic acids. Nat. Rev. Methods Primers *2*, 24.

9. Anchordoquy, T., Artzi, N., Balyasnikova, I.V., Barenholz, Y., La-Beck, N.M., Brenner, J.S., Chan, W.C.W., Decuzzi, P., Exner, A.A., Gabizon, A., et al. (2024). Mechanisms and Barriers in Nanomedicine: Progress in the Field and Future Directions. ACS Nano *18*, 13983–13999.