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**Enhancing the clinical translation of stem cell models by focusing on standardization and international regulatory cooperation**

Wang W *et al.* Standardization and international regulatory cooperation

## **Abstract**

Granjeiro *et al*'s article provided a thorough review of the role of stem cell models in the development of advanced therapy medicinal products. It emphasizes the potential of stem cell models to refine preclinical studies and align with regulatory requirements for clinical applications. This article introduces a new perspective on enhancing the transition of stem cell research into clinical practice, focusing on the importance of international regulatory harmonization and the need for standardization in stem cell-based therapies.

**Key Words:** Stem cell models; Advanced therapy medicinal products; Tissue engineering; Preclinical studies; Clinical translation

Wang W, Song AR, Liu HW, Li YK. Enhancing the clinical translation of stem cell models by focusing on standardization and international regulatory cooperation. *World J Stem Cells* 2025; In press

**Core Tip:** Granjeiro *et al* discussed stem cells' role in advanced therapy medicinal products for tissue regeneration and drug screening. This article emphasizes the importance of international regulatory harmonization and standardized protocols to address current challenges and enhance stem cell-based therapies' global clinical translation, safety, and consistency.

## **TO THE EDITOR**

We read with great interest the article titled "Bioengineering breakthroughs: The impact of stem cell models on advanced therapy medicinal product development" by Granjeiro *et al*[1], recently published in the *World Journal of Stem Cells*. The article provides a comprehensive review of the critical role that stem cell models play in advanced therapy medicinal products (ATMPs), particularly in providing alternatives to traditional preclinical testing methods. This discussion is timely and relevant,

considering the increasing emphasis on reducing animal testing and improving the physiological relevance of preclinical models.

The freshness of this letter lies in its focus on two critical aspects that extend beyond the original review: The necessity of international regulatory harmonization and the urgent need for standardized protocols in the development of stem cell-based therapies. We believe that addressing these aspects is essential for facilitating the global clinical translation of stem cell models, which remains a significant challenge in the field[2,3]. To advance these goals, we propose the establishment of a global task force comprising regulatory agencies, research institutions, and industry stakeholders. This task force could develop unified guidelines for stem cell culture, differentiation, and quality control, leveraging existing frameworks such as the International Society for Stem Cell Research guidelines[4]. Such an initiative would harmonize regulatory approaches and foster international collaboration, ensuring that innovative therapies reach patients more efficiently and safely.

Firstly, while the original review acknowledges the role of regulatory frameworks in ensuring safety and efficacy, we propose that greater emphasis should be placed on the international harmonization of these regulations. Different regulatory approaches across regions currently create significant barriers to adopting ATMPs[5]. A more unified regulatory framework could streamline the approval process, making it easier for innovative stem cell therapies to reach patients worldwide[6]. For instance, efforts by the European Medicines Agency and the United States Food and Drug Administration to align their regulatory requirements for ATMPs have shown promising results[7]. Building on these achievements, we recommend expanding such collaborations to include emerging markets with evolving regulatory frameworks. Such alignment would ensure patient safety and foster greater collaboration among international research institutions and regulatory bodies[8].

Secondly, we underscore the need for standardization in the protocols used for stem cell cultivation and differentiation. Variability in cell characteristics and differences in isolation and culture techniques can lead to inconsistent therapeutic outcomes, posing

challenges for clinical application[9]. Recent advancements in good manufacturing practice-compliant protocols and the use of artificial intelligence for optimizing stem cell differentiation have demonstrated the feasibility of achieving high levels of standardization. For example, studies have successfully implemented artificial intelligence-driven platforms to predict and control stem cell differentiation trajectories, resulting in more reproducible outcomes[10]. Standardized protocols across laboratories could help minimize these discrepancies, ensuring that stem cell therapies are reproducible and reliable[11]. This focus on standardization is critical in clinical trials, where consistent results are crucial for gaining regulatory approval and achieving widespread clinical adoption[12].

In summary, while Granjeiro *et al*[1] have contributed significantly to understanding the role of stem cell models in ATMP development, we believe that prioritizing international regulatory harmonization and protocol standardization is crucial for realizing the full potential of these therapies. Addressing these aspects can help bridge the gap between experimental models and clinical practice, ultimately leading to more effective and accessible patient treatments. We urge the scientific community to take immediate action by forming international consortia to develop and implement standardized protocols. At the same time, regulatory bodies should prioritize harmonizing their frameworks to facilitate global access to stem cell therapies.

### ***Conclusion***

Stem cell models hold significant promise for advancing ATMPs, offering new possibilities for tissue regeneration and drug development. However, the full potential of these models can only be realized through a greater focus on international regulatory harmonization and the establishment of standardized protocols. Addressing these challenges will enhance the safety, reproducibility, and accessibility of stem cell therapies, facilitating their transition from research settings to clinical applications and ultimately benefiting patients worldwide.

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