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BPI Review Form 070520

Book Name:	Innovations in Biological Science
Manuscript Number:	**Ms_BPR_1437**
Title of the Manuscript:	**Cell Reprogramming and Differentiation Utilizing Messenger RNA for Regenerative Medicine**
Type of the Article	**Book chapter**

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PART 1: **Review Comments**

	Reviewer's comment	**Author's comment***(If agreed with the reviewer, correct the manuscript and highlight that part in the manuscript. Authors must write his/her feedback here)*
Is the manuscript important for the scientific community? Please write a few sentences explaining your answer	Yes, this manuscript is likely important to the scientific community. It discusses the use of mRNA in regenerative medicine, a rapidly developing field with the potential to revolutionize the treatment of various diseases and injuries. The manuscript also highlights the work of Karikó and Weissman, who won the Nobel Prize for their discoveries on mRNA, further emphasizing the significance of this research area.	
Is the title of the article suitable? Do you have any alternative Title in your mind?	The title, "Cell Reprogramming and Differentiation Utilizing Messenger RNA for Regenerative Medicine," is suitable as it accurately reflects the content of the article, which discusses using mRNA for cell reprogramming and differentiation in regenerative medicine. An alternative title could be: "mRNA: A Novel Tool for Cell Reprogramming and Differentiation in Regenerative Medicine." This title is more concise and emphasizes the novelty of using mRNA in this field.	
Is the abstract of the article comprehensive? If your answer is No, please provide suggestions	1. The abstract mentions mRNA's potential use in vaccines and regenerative medicine but could briefly elaborate on the specific applications within regenerative medicine (e.g., direct reprogramming, protein supplementation). 2. Briefly touch upon the challenges associated with mRNA therapeutics, such as delivery methods and immunogenicity. This would provide a more balanced overview. 3. The abstract could end with a sentence hinting at the future directions or potential impact of mRNA research in regenerative medicine.	
Do you think the English quality of the article is suitable for scholarly communications? If your answer is No, please provide suggestions	No, the English quality of the article could be improved for scholarly communication. There are several grammatical errors and instances bad phrasing. For example: • In the first sentence of the introduction, "With the recent spread of coronavirus disease 2019 (COVID-19), attempts to apply mRNA as a medicine have attracted attention (1)," the phrase "attempts to apply mRNA as a medicine" could be rephrased to "the potential applications of mRNA as a medicine." • In the second sentence of the introduction, "In addition to being used as a vaccine against cancer and viral and bacterial infections (2), it is also expected that mRNA will be used as a drug for protein supplementation therapy and tissue regeneration to restore function, enabling the generation of missing proteins in genetic diseases (3)," the phrase "enabling the generation of missing proteins in genetic diseases" could be rephrased to "thereby addressing protein deficiencies in genetic diseases."	
Please provide your comments regarding the appropriateness of different sections of the manuscript.	**Introduction** The introduction provides a good overview of mRNA and its potential applications in medicine, particularly regenerative medicine. It effectively highlights the significance of mRNA research, especially in light of the COVID-19 pandemic, and sets the stage for the rest of the chapter.	

	Synthesis of mRNA This section is well-structured and informative. It covers the two main methods of mRNA synthesis (post-capping and in vitro transcription) in sufficient detail, making it easy for readers to understand the process. The inclusion of recent advancements, such as the PureCap method, adds to the relevance of this section. **Key Technologies for mRNA Therapeutics** This section is crucial as it discusses the key technologies that have enabled the development of mRNA therapeutics. The explanation of lipid nanoparticles (LNPs) and their role in mRNA delivery is clear and concise. The discussion of modified nucleobases and their impact on immunogenicity is also well-presented. **mRNA-Based Protein Supplementation for Regenerative Medicine** This section effectively introduces the concept of regenerative medicine and the potential of mRNA in this field. The examples of mRNA-based treatments for heart failure and fractures are relevant and illustrate the practical applications of this technology. However, the section could benefit from a more in-depth discussion of the challenges and limitations of mRNA-based protein supplementation. **mRNA for Cell Reprogramming** This section provides a comprehensive overview of cell reprogramming and the various techniques used to achieve it. The discussion of Yamanaka factors and the risks associated with viral vectors is informative. The comparison of different reprogramming methods, including mRNA-based methods, is well-structured and easy to follow. **mRNA-Induced Cell Differentiation from iPSCs** This section delves into the application of mRNA for inducing cell differentiation from induced pluripotent stem cells (iPSCs). The example of generating neurons from iPSCs derived from Gaucher's disease patients is a compelling illustration of the potential of this technique. However, like the previous section, this section could also benefit from a more thorough discussion of the challenges and limitations of mRNA-induced differentiation. **mRNA for Cell Reprogramming and Differentiation Induction and Direct Reprogramming without Passage through Pluripotent Stem Cells** This section explores the combined use of mRNA for cell reprogramming and differentiation, as well as direct reprogramming. The examples provided, such as the transformation of fibroblasts into muscle tissue and the generation of hepatocyte-like cells, are interesting and demonstrate the versatility of mRNA. However, the section could be improved by providing more context and explaining the significance of these findings in the broader field of regenerative medicine. **Conclusions** The conclusion effectively summarizes the key points of the chapter and reiterates the potential of mRNA therapeutics in regenerative medicine. It also acknowledges the	

	challenges that need to be addressed for the successful translation of this technology into clinical practice. The emphasis on the need for further research is appropriate and encourages continued exploration in this field.	
Do you think that the references in the manuscript are proper, recent and sufficient? If you have any suggestions, please write here.	The reference list in this manuscript is extensive, with 147 references cited. The references are mostly recent, with a majority published within the last decade (2010-2023). This demonstrates the authors' efforts to incorporate the latest research in the field. However, there are a few areas where the references could be improved: • **Older References:** While most references are recent, some are older (e.g., 1984, 1987, 1989). While these may be seminal papers in the field, it might be beneficial to include more recent citations that build upon or update these foundational works. • **Lack of Review Articles:** The reference list primarily consists of primary research articles. Including a few relevant review articles could provide readers with a broader overview of the field and a deeper understanding of the context of the research presented in the chapter. • **Self-Citation:** The author has included several self-citations. While it's acceptable to cite one's own work when relevant, excessive self-citation can be perceived as self-promotion. The author could consider replacing some of these with citations of other researchers' work in the same area.	

PART 2:

	Reviewer's comment	**Author's comment***(if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)*
Are there ethical issues in this manuscript?	*(If yes, Kindly please write down the ethical issues here in details)*	

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