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| Journal Name: | [**Asian Journal of Pediatric Research**](https://journalajpr.com/index.php/AJPR) |
| Manuscript Number: | **Ms\_AJPR\_140218** |
| Title of the Manuscript: | **Circular RNA (circRNA) and the Role in Pediatric Disease Pathogenesis** |
| Type of the Article |  |

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| PART 1: Comments | | |
|  | Reviewer’s comment **Artificial Intelligence (AI) generated or assisted review comments are strictly prohibited during peer review.** | **Author’s Feedback** (It is mandatory that authors should write his/her feedback here) |
| **Please write a few sentences regarding the importance of this manuscript for the scientific community. A minimum of 3-4 sentences may be required for this part.** | The current manuscript involves a very topical and new field of research in pediatric oncology. Circular RNAs are more recent types of non-coding RNAs and have become interesting studies by virtue of their functions in regulating genes and disease pathogenesis. Such emphasis on pediatric diseases is additionally very relevant since circRNAs can potentially provide new relevant diagnostic biomarkers and therapeutic targets in childhood malignancies, with these known to have different molecular signatures than their adult counterparts. That is why the full-scale analysis of circRNA participation in several pediatric solid tumors (medulloblastoma, neuroblastoma, rhabdomyosarcoma, osteosarcoma, Wilms tumor, hepatoblastoma, and retinoblastoma) is a useful contribution to scientists and clinicians dealing with pediatric oncology. This work might help set the way of future studies and influence the implementation of precision medicine strategies in children with cancer. | Thank you for the comprehensive feedback. |
| **Is the title of the article suitable?**  **(If not please suggest an alternative title)** | The title is suitable and reveals the content of the manuscript. It shows the emphasis on circular RNAs and their importance in the pathogenesis of child illnesses. The title is descriptive, and it would be easily recognized by a researcher studying this topic. | Okay, thank you for the assurance. |
| Is the abstract of the article comprehensive? Do you suggest the addition (or deletion) of some points in this section? Please write your suggestions here. | The abstract gives a fair preview of what this manuscript is about discussing the major concepts of circRNAs biology, the regulation of miRNA in them, and their connection with pediatric cancer. It can be improved, however, by:   * Incorporation of further information as to the specific examples of circRNAs discussed in the review. * The inclusion of a short declaration of the clinical implications and future directions. * Giving more definite data concerning the size of the review (i.e., how many studies were reviewed, what types of pediatric cancers were included). | Noted and modifications were made to the abstract. |
| Is the manuscript scientifically, correct? Please write here. | Overall, the manuscript does not seem to have any scientific issues. The authors are also well aware of the biology of circRNA and the mechanisms of action. The data introduced regarding the existence of certain circRNAs in various pediatric malignancies are in accordance with the existing body of knowledge. Nevertheless, there are some aspects, into which it is possible to enhance:   * Certain parts are not detailed enough in mechanistic explanations. * The relationship between circRNA dysregulation and clinical outcomes bear explanation. * The manuscript would be improved with more comments about the difficulties and constraints of circRNA research. * Enlighten the source of data (original vs literature source). | Okay, thank you for pointing out the areas of improvement. |
| **Are the references sufficient and recent? If you have suggestions of additional references, please mention them in the review form.** | The sources are mainly up-to-date with the majority of the references dated 2020-2025, which is suitable due to the fast-changing nature of this industry. There is a good selection of primary research articles by the authors. Nevertheless, here are a few improvement tips:   * Add more instructional articles on circRNA biology and discovery. * Insert citations of recent circRNA in cancer reviews. * It can be discussed to mention circRNAs in clinical trials or translating studies. * There are a few landmark articles in pediatric cancer genomics that one can include. | Okay, noted and relevant references have been added. |
| Is the language/English quality of the article suitable for scholarly communications? | The quality of English is good in general, and it is good enough to be published. The writing of the manuscript is appropriate and concrete. There are commonplace grammar mistakes and awkward wordings, though they do not have a strong effect on the readability. An extensive language editing would enhance the general quality. | Noted and grammatical issues corrected. |
| Optional/General comments | Format: It would be good to have a more organized format including specific headings and an adequate organization across general biology of circRNA to its specific applications in pediatrics.  Figures/Tables: There are no visuals used in the manuscript. To make it less dense, it would be optimal to include figures illustrating the processes of circRNA biogenesis, mechanisms of action, tables reflecting the main findings.  Clinical Relevance: The manuscript can be strengthened further with more information on clinical implications of the studies like what are the existing challenges to convert circRNA research in clinical practice.  Future Directions: A summary of future directions and their clinical application of studies would be beneficial.  The issue touched upon in this manuscript is an essential and topical one in the field of pediatrics in oncology. The information is scientific and exhaustive and relates to various forms of pediatric cancer. Nevertheless, structural rears and integration of visuals, further mechanistic deliberations, and improvement of clinical significance chapters in the manuscript are also in prospect. This would be of significant contribution to the body of literature with such revisions.  **Concrete Suggestion of Improvement:**  Include figures or tables to design a better view  Enlarge the introduction to clarify more about circRNA biology  Make available a special area with clinical implications and challenges  Include comments about directions of future research  Become more organized by defining subheadings more clearly  Expand the abstract by giving further specific details  Small editing of language to provide clarity | Thank you for pointing out the areas of improvement. |

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| **PART 2:** | | |
|  | Reviewer’s comment | **Author’s Feedback** (It is mandatory that authors should write his/her feedback here) |
| **Are there ethical issues in this manuscript?** | There are no grave ethical concerns found in this manuscript. The relevant consent forms and ethical approval disclaimers have been mentioned by the authors, which is the standard practice in the review articles since it might cite some clinical studies. |  |