

Dear Na Ma,

I am grateful to You and to the Reviewers for considering my manuscript for publication and preliminary decision that it is acceptable for publication after your appropriate revision. I have been able to incorporate the requested changes within the manuscript which have been highlighted throughout. I am appreciate your willingness to revised draft of my manuscript in light of the further information now provided and to ascertain if my manuscript is suitable for publication in the *World Journal of Clinical Oncology*.

Below is a point-by-point response to the reviewer's feedback.

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade C (A great deal of language polishing)

Conclusion: Major revision

Specific Comments to Authors: thank you interesting content however it needs : English polishing and any place for the nano particles?

The manuscript has been submitted for language correction on the AJE website\*. I obtained a language certificate, which I attached as a file. I also added in Conclusion: *One of the trends in modern diagnostics and anti-leukemia therapy is the exact use of nanotechnology, which primarily offers the opportunity to improve sensitivity, selectivity and bioavailability and thus effectiveness[149]. The advantage of nanoparticles is their size, which allows them to cross biological barriers more effectively. Anticancer drug components include new classes of therapeutic agents such as siRNA, miRs and ssDNA[148]. An additional improvement is the possibility of functionalizing the surface of the nanoconstruct with specific ligands[150]. Nevertheless, nanomedicine is the domain of solid tumors[149, 151]. In the case of leukemia, however, nanoconstructions are used as noninvasive methods of diagnosis and treatment. An example would be the construction of a modern nanoparticle containing antagomiR-126 (nanoconjugate: LNP@antagomiR126@Anti-CD45.2 (lipopolyplex NPs)) for adult AML therapy[152].*

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: It is a well written review about the role of miRNAs in the development, progression and therapy monitoring of pediatric acute leukemias. No major comments. Could you please discuss further which could be the first expected added value of miRNAs in the understanding of acute leukemias development and treatment targeting. Please avoid using personal style eg : "I will focus..."

I have made corrections to my personal style:

It was :In the current review, I will focus on the role of miRNAs in the development, progression and therapy monitoring of pediatric acute leukemias.

*Now is: In the current review, the role of miRNAs in the development, progression and therapy monitoring of pediatric acute leukemias will be presented and discussed.*

*I also added a comment: MiRNAs are becoming more and more popular among scientists and oncohaematologists due to their important role in the etiology of acute leukemia. However, the prospect of their routine use in diagnostics requires further research to identify a small group of sensitive and specific biomarkers of diagnostic and prognostic significance. Undoubtedly, the results of numerous studies indicate a few promising candidates, but nevertheless there is still no one miRNA or small set selected that allows with accuracy close to 100% to diagnose acute leukemia or differentiate its subtypes, regardless of other diagnostic factors. A much more promising direction for further research on miRNAs is to utilize their potential for effective and personalized medicine. In the case of miRNA, the therapeutic challenge is also to improve targeting (one miRNA usually regulates the expression of many genes) as well as to increase the circulation time of the molecule. The therapeutic use of miRNA therefore requires a combination with a suitable nanoparticle that directs miR as well as protecting against inactivation and degradation.*

Reviewer #3:

Scientific Quality: Grade C (Good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: Although microRNAs for AL diagnostics and therapy is a challenge, especially in analysis standards. There is not so long way to understand miRNA regulatory mechanisms in childhood AL.

Thank you for this review. In my opinion, it doesn't require any comment from me.

**Below is a point-by-point response to the reviewer's and editor's feedback.**

Step 1: Please select revise this manuscript or not

Please login to the F6Publishing system at <https://www.f6publishing.com> by entering your registered E-mail and password. After clicking on the "Author Login" button, please click on the "Manuscripts Needing Revision" under the "Revisions" heading to find your manuscript that needs revision. Clicking on the "Handle" button allows you to choose to revise this manuscript or not. If you choose not to revise your manuscript, please click on the "Decline" button, and the manuscript will be WITHDRAWN.

**I decided to include comments from reviewers and submit the manuscript to the editor again.**

Step 2: Key points of revising the manuscript

(1) Scientific quality: Please resolve all issues in the manuscript based on the peer review report and make a point-to-point response to the issues raised in the peer review report.

**I tried to apply all corrections as suggested.**

(2) Language quality: Please resolve all language issues in the manuscript based on the peer review report. Please be sure to have a native-English speaker edit the manuscript for grammar, sentence structure, word usage, spelling, capitalization, punctuation, format, and general readability, so that the manuscript's language will meet our direct publishing needs.

**The manuscript has been submitted for language correction on the AJE website. I obtained a language certificate, which I attached as a file.**

(3) Special requirements for figures: Figures must be presented in the order that they appear in the main text of the manuscript (numbered as 1, 2, 3, etc.). The requirements for the figures and figure legends include: (A) All submitted figures, including the text contained within the figures, must be editable. Please provide the text in your figure(s) in text boxes; (B) For line drawings that were automatically generated with software, please provide the labels/values of the ordinate and abscissa in text boxes; (C) Please prepare and arrange the figures using PowerPoint to ensure that all graphs or text portions can be reprocessed by the editor; and (D) In consideration of color-blind readers, please avoid using red and green for contrast in vector graphics or images.

**I am attaching a PowerPoint file containing editable figures.**

(4) Special requirements for tables: Tables must be presented in the order that they appear in the main text of the manuscript (numbered as 1, 2, 3, etc.). Please verify that the tables are referred to in the text by their respective Roman numerals and that the numbering order is correct, and format the tables. Please verify that there are no missing or multiple spaces in the text and tables, e.g. before or after parentheses, between words, or before or after symbols like +, ×, ±, <, >, ≥, and ≤. Please verify that the special words or letters in the text and tables are correct, e.g. P (uppercase), n (lowercase), via, vs (lowercase, no punctuation), in vivo, in vitro, and et al (no punctuation) are italicized.

**I checked and corrected the mistakes that I noticed.**

(5) Special requirements for references: Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout. The author should provide the first page of the paper without PMID and DOI numbers. NOTE: The

PMID is required, and NOT the PMCID; the PMID number can be found at <https://pubmed.ncbi.nlm.nih.gov>. (Please begin with PMID:) The DOI number can be found at <http://www.crossref.org/SimpleTextQuery/>. (Please begin with DOI: 10.\*\*).

Please verify that the references are cited by Arabic numerals in square brackets and superscripted in the text, and that the numbering order is correct. There should be no space between the bracket and the preceding word or the following punctuation. When references in the text and tables are cited with author name(s), it is necessary to manually verify that the name(s) is consistent with the first author's surname in the corresponding reference list.

I prepared the list of publications in EndNote. DOI and PMID are correctly entered to my knowledge. I have bolded the volume number and the name of the first author. I removed unnecessary spaces between the bracket and the preceding word or the following punctuation.

(6) Special requirements for article highlights: If your manuscript is an original study (basic study or clinical study), meta-analysis, systemic review, the “article highlights” section should be provided. Detailed writing requirements for “article highlights” can be found in the Guidelines and Requirements for Manuscript Revision.

(7) Ethical documents: Please double check the accuracy of all ethical documents and verify the completeness of the documents according to the type of manuscript.

I checked the attachments.

(8) Approved grant application form(s) or funding agency copy of any approval document(s): If your manuscript has supportive foundations, the approved grant application form(s) or funding agency copy of any approval document(s) must be provided.

The manuscript was not financed from any sources.

Step 3: Manuscript revision deadline

We request that you submit your revision in no more than 14 days.

Step 4: Verify the accuracy of general information for your manuscript

Name of journal: World Journal of Clinical Oncology

Manuscript NO.: 54438

Column: Review

Title: Role of miRNA dysregulation in childhood acute leukemias: diagnostics, monitoring and therapeutics. A comprehensive review

Authors: Joanna Szczepanek

Corresponding author: Joanna Szczepanek, PhD, Associate Research Scientist, Centre for Modern Interdisciplinary Technologies, Nicolaus Copernicus University, Wileńska 4, Toruń 87-1001, Poland. [szczepanekj@umk.pl](mailto:szczepanekj@umk.pl)

Received Date: 2020-01-31

First decision: 2020-04-18

The data is correct. The manuscript was prepared on the invitation received on 2019-10-10 from Lian-Sheng Ma, Founder and CEO

Step 5: Peer-review report(s)

The authors must resolve all issues in the manuscript based on peer-review report(s) and make a point-to point response to the issues raised in the peer-review report(s) which listed below:

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Thank you for this review. In my opinion, it doesn't require any comment from me.

Step 6: Editorial Office's comments

The author must revise the manuscript according to the Editorial Office's comments and suggestions, which listed below:

(1) Science Editor: Recommend for potential acceptance. 1 Scientific quality: The manuscript is a review on the role of miRNA dysregulation in childhood acute leukemias: diagnostics, monitoring and therapeutics. The topic is within the scope of the WJCO. (1) Classification: 2C and B. (2) Summary of the peer-review report: The reviewer#00506472 thinks it is a well written review and the author should discuss further which could be the first expected added value of miRNAs in the understanding of acute leukemias development and treatment targeting. The reviewer#03026651 suggests the author could discuss more about the nano particles in leukemia in children. (3) Format: 5 figures and 2 tables. 164 references were cited, including 26 references published in the last three years. No self-citation. 2 Language evaluation: A, B and C. The language editing certificate was not provided. 3 Academic norms and rules: The authors signed the conflict-of-interest disclosure form and the copyright license agreement. No academic misconduct was found in the CrossCheck investigation and the Bing search. 4 Supplementary comments: (1) Invited Manuscript (2) Without financial support. (3) The topic has not been published in the WJCO. (Han Zhang)

The manuscript has been submitted for language correction on the AJE website\*. I obtained a language certificate, which I attached as a file. I tried to include all comments received and supplemented the text as suggested. I also added citations of my own publications:

1. Szczepanek J, Jarzab M, Oczko-Wojciechowska M, Kowalska M, Tretyn A, Haus O, Pogorzala M, Wysocki M, Jarzab B, Styczynski J. Gene expression signatures and ex vivo drug sensitivity profiles in children with acute lymphoblastic leukemia. *J Appl Genet* 2012; 53: 83-91 [PMID: 22038456 DOI: 10.1007/s13353-011-0073-x]

2. Szczepanek J, Styczynski J, Haus O, Tretyn A, Wysocki M. Relapse of acute lymphoblastic leukemia in children in the context of microarray analyses. *Arch Immunol Ther Exp (Warsz)* 2011; 59: 61-68 [PMID: 21246408 DOI: 10.1007/s00005-010-0110-1]

(2) Editorial Office Director: 1 Scientific quality: I have checked the comments made by the science editor, and I basically agree with the science editor. The topic of the paper is the MicroRNA as a diagnostic and prognostic biomarker in pediatric acute leukemia, and is within the scope of the WJCO. (1) Classification: Grade B, Grade C, and Grade C; (2) Summary of the Peer-Review Report: Reviewer#03026651 thinks this is an interesting paper. However, it needs major language polishing. Reviewer# 00506472 pointed out it is a well written review on the role of miRNAs in the development, progression and therapy monitoring of pediatric acute leukemias. The reviewer suggested the authors to discuss further which could be the first expected added value of miRNAs in the understanding of acute leukemias development and treatment targeting. Reviewer# 03656580 thinks introduction of microRNA assays to diagnostics and therapy is a challenge, especially in analysis standards. There is not so long way to understand miRNA regulatory mechanisms in childhood AL; and (3) Format: There are 5 figures and 2 tables. A total of 164 references are cited, including 26 references published in the last 3 years. The authors need to update the references. There are no self-citations. Regarding the review paper, we suggest the authors to cite some their own research works. 2 Language evaluation: The authors need to provide the language certificate of professional language company. 3 Academic norms and rules: I have checked the documents, including the Conflict-of-Interest Disclosure Form, and Copyright License Agreement, all of which are qualified. No academic misconduct was found in the CrossCheck detection and Bing search. 4 Supplementary comments: This is an invited manuscript. This study is without financial support. 5 Issues raised: The authors need to provide the editable figures. 6 Recommendation: Conditionally accepted.

Thank you for your comment. I made comments to the best of my knowledge - as I commented above. I added several items in the list of references.

(3) Company Editor-in-Chief: I have reviewed the Peer-Review Report, the full text of the manuscript and the relevant ethics documents, all of which have met the basic publishing requirements, and the manuscript is conditionally accepted with major revisions. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report and the Criteria for Manuscript Revision by Authors.

Thank you for your comment.

Step 7: Revise the manuscript

Please update your manuscript according to the Guidelines and Requirements for Manuscript Revision and the Format for Manuscript Revision for your specific manuscript type: 'Review'. Please visit <https://www.wjgnet.com/bpg/GerInfo/291> for the article type-specific guidelines

and formatting examples. We only accept the manuscript in MS Word format, and the manuscript in other formats will be rejected.

#### Step 8: Submit the revised manuscript and all related documents

When you are ready to resubmit your revised paper and all required accompanying documents (listed below), you can begin the uploading process via the F6Publishing system.

- (1) 54438-Manuscript File
- (2) 54438-Answering Reviewers
- (3) 54438-Audio Core Tip
- (4) 54438-Conflict-of-Interest Disclosure Form
- (5) 54438-Copyright License Agreement
- (6) 54438-Approved Grant Application Form(s) or Funding Agency Copy of any Approval Document(s)
- (7) 54438-Non-Native Speakers of English Editing Certificate
- (8) 54438-Video
- (9) 54438-Image File
- (10) 54438-Supplementary Material

If your manuscript has no “Video” or “Supplementary Material”, you don’t need to submit those two types of documents.

Corrections after the revision send back (my suggestions, have been added using the Track Changes function):

- language edition
- formatting changes (font and space correction)
- editing the text indicated after CrossCheck
- obtaining permission to use figures from their authors
- removal from the list of references without DOI (except for 2 items)
- title page correction in accordance with the guidelines
- Audio core tip re-recording