



## JOURNAL EDITORIAL BOARD'S REVIEW REPORT

**Name of journal:** World Journal of Stem Cells

**Manuscript NO:** 89034

**Title:** Effects of different concentrations of nicotinamide on hematopoietic stem cells cultured in vitro

**Journal Editor-in-Chief/Associate Editor/Editorial Board Member:** Shengwen Calvin Li

**Country/Territory:** United States

**Editorial Director:** Jia-Ping Yan

**Date accepted review:** 2023-12-27 02:42

**Date reviewed:** 2023-12-27 05:54

**Review time:** 3 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair		<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Major revision

### JOURNAL EDITORIAL BOARD COMMENTS TO AUTHORS

Comment: The present manuscript lacks coherence in connecting its research questions to the corresponding data sets, which is evident in inconsistencies in logical terminology definitions and methodological justifications. Numerous loopholes persist in the narrative, as highlighted in specific comments below. The authors have not adhered to the standard revision practices for scientific manuscripts, failing to furnish - point-by-point - meticulous rebuttals in response to the reviewer's comments (Refer to all three reviewers' reports below after EIC comments) and neglecting to include tracked changes in their revisions. Specific comments: 1) Page 4: "RESULTS Compared with the control group, the proportion and expansion folds of hematopoietic stem and progenitor cells (CD34+CD38-) incubated with 5 mmol/L or 10 mmol/L of NAM were significantly increased (all  $P < 0.05$ )." Neither logic nor meticulousness were manifested in the context: concrete statements have been used. How did they differentiate "hematopoietic stem and progenitor cells?" What was the



**Baishideng  
Publishing  
Group**

7041 Koll Center Parkway, Suite  
160, Pleasanton, CA 94566, USA  
**Telephone:** +1-925-399-1568  
**E-mail:** office@baishideng.com  
**https://www.wjgnet.com**

proportion? 2) Pages 5-6: "NAM may mediate the metabolic transition of aging stem cells by upregulating the expression of young genes such as sirtuin 1 (SIRT1), thereby maintaining stemness." Definition of young? Timelines? Influential factors of aging? Citations? 3) Page 7: "Based on the different concentrations of NAM, the cells were divided into control group (0 mmol/L), low concentration group (5 mmol/L), and high concentration group (10 mmol/L)." How did these relate to physiological conditions in vivo? Citations? 4) Fig 1 D Cell size for each group of cells. How did NAM affect the cell sizes? 5) Fig 1 E: Viability of each group of cells. There were no effects of 10 mmol/L on viability, which contradicted the apoptosis data. Why? 6) Fig 2B: Fold expansion of total nucleated cells. How did they determine the data - Excel spreadsheets of duplications? Why did they not do proliferation assays? 7) Fig 2A: Scale bars should be embedded in Figures. 8) Fig 2A: All four panels of cell images looked like HSCs in suspension culture: Neither the morphological nor the adherent justified like 40X magnification of any microscope - rechecking these images should be a must if not suspension culture (Refer to "Establishment of an adherent cell layer from human umbilical cord blood" DOI:10.1590/S1415-4757200000300002Corpus ID: 1999346). If yes, they should mark in the method! Utilizing the colony-forming unit (CFU) cell assay, also known as the CFC assay, is mandatory when investigating the proliferation and differentiation of HSCs. Have they examined CFU assays? 9) How did they define ST- and LT-HSCs with biomarkers in a continuous in vitro culture relevant to in vivo microenvironment? Citations? 10) Fig 3B, C: Why did they not plot the data of 15 mmol/L NAM? 11) Figure 4 Effect of different concentrations of nicotinamide on reactive oxygen species content, cytokine levels, and gene expression in cultured hematopoietic stem cells. How did NAM affect these molecules? Why did CXCR4 not change? How did they define functional HSCs without CXCR4 [PubMed PMID: 21466480] and engraftment? 12) Fig 4A: the tickmarks are missing in the Y-axis. 13) Page 14: "CONCLUSION In conclusion, different concentrations of NAM have distinct effects on proliferation and differentiation of HSCs." Where were their data sets for either one - how did they do differentiation of HSCs? Cell cycle analysis is not sufficient to claim that. 14) Page 15: "Research motivation The effects of different concentrations of NAM on the proliferation and differentiation of HSCs, as well as whether it affects sirtuin 1 (SIRT1) transcription levels, have not been reported yet. This is crucial for selecting the working concentration of NAM and predicting small molecules that have a synergistic effect with NAM." Where is their data for SIRT1 synergistic effects? How did they define SIRT1 synergistic effects? Synergic with what? 15) Page 16: "Research conclusions Low concentration NAM did not inhibit but upregulated the transcription of SIRT1, promoting cell proliferation by activating the SIRT1-HIF1A pathway." Where is the data of the hypoxia SIRT1-HIF1A pathway (page 12) (did they use The hypoxia condition)? A schematic diagram should be provided to illustrate that pathway coupled with the data. Not sufficient alternatives related to stem cell reports were discussed, such as NAM-regulated ROCK and casein kinase 1[ doi: 10.1016/j.stemcr.2018.10.023]. 16) Grammar errors crawl around pages (A corrected form is within square brackets [...]): e.g., i. Page 3: "cultured for 10-12 d in [a] serum-free medium." ii. Page 5: "Hematopoietic stem cells (HSCs) are cells that can self-renew and give rise to mature cells of all



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hematopoietic lineages following extensive proliferation and differentiation[1,2].” iii. Page 7: “Based on the different concentrations of NAM, the cells were divided into [the] control group (0 mmol/L),” iv. Page 12: “The basic HSCs in vitro culture system consists of [a] serum-free medium supplemented with cytokines.” v. Editorial Certificate manifested in a typo: “Paper Title: The effect of different concentrations of niacinamide [nicotinamide] on hematopoietic stem cells cultured in vitro Author: 燕妮 崔 Reviewer 1 Critiques: \*\* Specific Comments to Authors: Thank you for asking my opinion about the manuscript entitled "Nicotinamide Concentration Determines the Fate of Hematopoietic Stem Cells". I believe that this manuscript should be major revision: Q1. It is very important to change and modify the title. the title is not appropriate. Q2. Are the objectives and the rationale of the study clearly stated? Q3. In the abstract, the research gap was not clearly stated. In addition, the authors need to rewrite the study objectives to be more academic writing Q4. In the introduction, include the study's significance and novelty. What makes the study different from the rest and what does it add to the current knowledge?. Q5. In the introduction, the authors should have explained the purpose of this study and the existing gaps in this field and explained why this study was conducted. Q6. Are the methods clear and replicable? Do all the results presented to match the methods described? Q7. If relevant are the results novel? Does the study provide an advance in the field? Is the data plausible? Q8. References are relevant, correct, and not recent. The number of references should be increased. please add some references. since this is a scientific review, all the sentences need to be supported with references. This study is very beautiful. I liked the sequence and enjoyed reading. Please add more references on similar studies. Q9. There are a lot of grammatical errors. This must be taken care of and addressed. Q10. What are the limitations of the study? A description of limitations is missing at the end of the discussion section. • If your manuscript is related to mine, you can cite it (ORCID: <https://orcid.org/0000-0002-5107-5550>). Reviewer 2 Critiques: Specific Comments to Authors: The article presents the possible role of nicotinamide on hematopoietic stem cells. The study needs improvement and requires grammar revision. I also recommend taking into consideration the following: - Abstract: „RT-PCR detection of gene expression levels, and Reactive Oxygen Detection assessment of intracellular ROS levels. ” rephrase - Abstract: „Low concentration of NAM is beneficial to the expansion of short-term repopulating HSCs (ST-HSCs,CD34+CD38-CD45RA-CD49f+), which can inhibit the differentiation of HSCs by reducing the production of ROS, increase the proportion of cells in S and G2 phase to significantly promote the proliferation of HSCs, and SIRT1 may be one of the related factors” rephrase - Rephrase: „Many studies by Horwitz have shown that nicotinamide-based methods are beneficial for rapid recovery of neutrophils in patients after transplantation” - use the same verbal tense throughout the hole material and methods chapter - I recommend using a short acronym for the sequences of cells “CD34+CD38-CD45RA-CD49f+” and “CD34+CD38-CD45RA-CD49f+CD90+” to make the text easier to read - Rephrase “In addition, the proportion of CD34+CD38-CD45RA-CD49f+cells in the 5mM NAM group was significantly higher than that in the control group and the 10mM NAM group (both P