



PEER-REVIEW REPORT

Name of journal: *World Journal of Medical Genetics*

Manuscript NO: 76177

Title: EPIGENETICS IN THE ETIOLOGY AND MANAGEMENT OF INFERTILITY: A REVIEW

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03814201

Position: Editorial Board

Academic degree: PhD

Professional title: Associate Professor, Senior Researcher

Reviewer's Country/Territory: China

Author's Country/Territory: Nigeria

Manuscript submission date: 2022-03-05

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-04-08 07:53

Reviewer performed review: 2022-04-16 15:01

Review time: 8 Days and 7 Hours

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|---------------------------|---|
| Scientific quality | <input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish |
| Language quality | <input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection |
| Conclusion | <input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection |
| Re-review | <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No |



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Publishing
Group**

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

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|-------------------------------------|---|
| Peer-reviewer statements | Peer-Review: [<input checked="" type="checkbox"/>] Anonymous [<input type="checkbox"/>] Onymous Conflicts-of-Interest: [<input type="checkbox"/>] Yes [<input checked="" type="checkbox"/>] No |
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SPECIFIC COMMENTS TO AUTHORS

The authors introduced the basic concepts and epigenetic mechanisms of DNA methylation, histone modification and microRNA. They also addressed the importance of epigenetic modification on gametogenesis and embryogenesis through literature collection and collation. Additionally, the authors summarized the common molecular mechanisms of infertility due to DNA methylation, histone modification and microRNA abnormalities, involving ovaries, oocytes, testes, sperm and embryos. Finally, this review has described an epigenetic detection method that can recognize the DNA state of spermatozoa and some epigenetic drugs that may be used to treat infertility. Generally speaking, this article has some reference value for the research in the field of reproductive biology. However, to further improve the quality of the manuscript, I have some suggestions as follows: 1. In page5, "These mechanisms may alter gene expressions individually or interact to control gene expressions" should be added with references. 2. It is suggested that Figure 2, Figure 3 and Figure 4 should be merged into one figure. Also, the figure legends should be more detailed. 3. Carefully check all references in the article citation position are accurate, such as the Ref. 76 matches the content described in the article or not.



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Reviewer's code: 03259512

Position: Peer Reviewer

Academic degree: MSc, PhD

Professional title: Assistant Professor, Lecturer

Reviewer's Country/Territory: Australia

Author's Country/Territory: Nigeria

Manuscript submission date: 2022-03-05

Reviewer chosen by: Dong-Mei Wang

Reviewer accepted review: 2022-04-27 07:15

Reviewer performed review: 2022-04-29 01:46

Review time: 1 Day and 18 Hours

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|---------------------------|---|
| Scientific quality | <input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish |
| Language quality | <input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection |
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| Re-review | <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No |



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|-------------------------------------|---|

SPECIFIC COMMENTS TO AUTHORS

The review discussed the epigenetic basis of infertility. The topic is interesting and important. Available information shows that epigenetic mechanisms (DNA methylation, histone modification, and microRNA interference) are necessary for normal gametogenesis and embryogenesis. However, the study requires a lot of improvement. 1. The manuscript requires serious English editing. Grammar and style are below average. The very 1st sentence in the Abstract requires editing ("Epigenetic disruptions have been implicated in some cases of infertility, which can be targeted to help individuals expressing such an etiology conceive"). Wrong English grammar makes this sentence unclear for understanding (meaningless). 2. Abstract/Introduction are very vacuous and does not point to the main epigenetic targets associated with infertility. For instance, author could mention that epimutations (often hypermethylation) in several genes, namely MTHFR, PAX8, NTF3, SFN, HRAS, JHM2DA, IGF2, H19, RASGRF1, GTL2, PLAG1, D1RAS3, MEST, KCNQ1, LIT1, and SNRPN, have been reported in association with poor semen parameters or male infertility. See this publication <https://pubmed.ncbi.nlm.nih.gov/21540125/> 3. Figure 3 and 4 should be combined. 4. Figure 7 is very poorly designed. Authors should improve or remove this figure. 5. miRNA up- and down-regulation should be illustrated. A figure (or table) should be designed. 6. Successful epigenetic-targeting drugs as infertility treatment should be also organized in a table. 7. Conclusions should be improved. Authors should provide solid data-supported insights (not vacuous generalizations). The 1st sentence is very vacuous ("The review established that normal epigenetic modifications are necessary for proper gametogenesis and embryogenesis"). What is "normal"? The phrase is poorly constructed.



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Your review did not "establish" anything. You just reviewed/discussed published data.



RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Medical Genetics*

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Title: EPIGENETICS IN THE ETIOLOGY AND MANAGEMENT OF INFERTILITY: A
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Professional title: Associate Professor, Senior Researcher

Reviewer's Country/Territory: China

Author's Country/Territory: Nigeria

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Reviewer chosen by: Ji-Hong Liu

Reviewer accepted review: 2022-07-07 01:55

Reviewer performed review: 2022-07-07 02:05

Review time: 1 Hour

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| Scientific quality | <input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish |
| Language quality | <input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection |
| Conclusion | <input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection |
| Peer-reviewer | Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous |



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statements

Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The authors have made some changes to the manuscript and answered some of my questions. The manuscript can be considered for publication.



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Author's Country/Territory: Nigeria

Manuscript submission date: 2022-03-05

Reviewer chosen by: Ji-Hong Liu

Reviewer accepted review: 2022-07-08 01:24

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Review time: 1 Hour

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Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

my comments were addressed. The revised version of this manuscript is improved.