For research article

Response to Reviewer 3 Comments

1. Summary

Thank you very much for taking your valuable time to review this manuscript. Please find the detailed responses below and the corresponding revisions/corrections highlighted/in track changes in the re-submitted files.

2. Questions for General Evaluation	**Reviewer's Evaluation**	**Response and Revisions**
Does the introduction provide sufficient background and include all relevant references?	Yes	
Are all the cited references relevant to the research?	Can be improved	I have revised the paragraph 4. Discussion based on the references you provided.
Is the research design appropriate?	Can be improved	
Are the methods adequately described?	Yes	
Are the results clearly presented?	Can be improved	
Are the conclusions supported by the results?	Can be improved	

3. Point-by-point response to Comments and Suggestions for Authors

Comments 1:

Dear Authors,

It was my pleasure to review the article titled Prediction of Mismatch Repair Status in Endometrial Cancer

from Histological Slide Images Using Various Deep Learning-Based Algorithms, a rather meaningful and well-crafted analysis centered around 127 cases of the primary lesion of endometrial cancer and aimed at investigating the potential use of H&E-stained endometrial cancer slide images to predict the associated mismatch repair (MMR) status.

The article is noteworthy and impressive, a well structured and competently assembled piece of research with strengths which cannot be overlooked: novelty, relevance in a highly sensitivr area of cancer research, and a potentially broad appeal to a relatively large

scholarly readership; also worth mentioning is the fact that in terms of pursuing its stated objective, the article comes across as thorough and well-grounded in sound and clearly explicated methodology, as far as I was able to determine; the table and figures are well framed as well, and ultimately effective in outlining key data and findings.

Some shortcomings which need to be dealt with:

The article's objective should be enunciated more throroughly in terms of what the contributions of the study's findings would be within the broader picture of cancer care, prognostics and therapeutics. I therefore advice the authors to strive for more thorough contextualization and elaboration, especially as it pertains to crafting new innovative prognostic/therapeutic avenues stemming from personalized/precision medicine, ncRnas, molecular classifications. "Biomarkers", which is one of the keywords, are not discussed exhaustively, yet such highly innovative and still evolving avenues for diagnostics and prognostics have already been harnessed in diseases such as gynecological cancers, including EC, affecting fertility prospects, with remarkably successful outcomes and considerable prospects for further development. It is therefore worth weighing said innovations within the realm of major innovations based on as AI, machine-learning and data processing.

The Discussion is in fact the section which falls relatively short compared to the high degree of insightfulness reached with respect to the article's main objective.

Even though the article is obviously not a review, greater elaboration is also advisable with regards to the personalized/precision medicine applications of AI, data analysis, clinical machine-learning from the standpoint of policy-making and evidence-based guidelines (which are incredibly relevant as the rate of innovation risks outpacing the standards we rely on when providing care in an equitable and fair fashion). When fleshing out such dynamics, broader contextualization is necessary, given the complexities at play. This would emphasize the value of this writing and make it more comprehensive.

The following sources should be drawn upon and cited:

Zhang R, Wesevich V, Chen Z, Zhang D, Kallen AN. Emerging roles for noncoding RNAs in female sex steroids and reproductive disease. Mol Cell Endocrinol. 2020 Dec 1;518:110875.

Cavaliere AF, Perelli F, Zaami S, Piergentili R, Mattei A, Vizzielli G, Scambia G, Straface G, Restaino S, Signore F. Towards Personalized Medicine: Non-Coding RNAs and Endometrial Cancer. Healthcare (Basel). 2021 Jul 30;9(8):965. doi: 10.3390/healthcare9080965.

Swanson K, Wu E, Zhang A, Alizadeh AA, Zou J. From patterns to patients: Advances in clinical machine learning for cancer diagnosis, prognosis, and treatment. Cell. 2023 Apr 13;186(8):1772-1791. doi: 10.1016/j.cell.2023.01.035.

Medenica S, Zivanovic D, Batkoska L, Marinelli S, Basile G, Perino A, Cucinella G, Gullo G, Zaami S. The Future Is Coming: Artificial Intelligence in the Treatment of Infertility Could Improve Assisted Reproduction Outcomes-The Value of Regulatory Frameworks. Diagnostics (Basel). 2022 Nov 28;12(12):2979. doi: 10.3390/diagnostics12122979.

All in all, the manuscript is well-conceived, well-written and with some adjustments and a higher degree of contextualization, can provide a considerable contribution to a highly meaningful and compelling area of cancer research vis-a-vis innovations which will broaden our horizons dramatically.

Best regards.

Response 1:

Thank you very much for your important suggestion. We acknowledge that our paper lacked discussion on both biomarkers for endometrial cancer in general and considerations related to medical AI. With reference to the papers you provided, we have supplemented our discussion primarily on the utility of ncRNA as biomarkers for endometrial cancer (Page11, Line 410-421) and addressed the issues surrounding the clinical use of medical AI (Page12, Line 450-460). We believe that the value of our paper has been enhanced thanks to your feedback.

4. Response to Comments on the Quality of English Language

Point 1:

Response 1:

Thank you for your important suggestion. The manuscript has already undergone English editing by MDPI English editing service at the "Academic" quality level. For the additional content in this revision, I also utilized the MDPI service. Please find attached pdf files of the certificate of English editing.

5. Additional clarifications