Answering Reviewers – Point-by-point answers

Specific Comments To Authors

05224959   Conclusion: Accept (High priority)
Scientific Quality: Grade A (Excellent)
Language Quality: Grade A (Priority publishing)

The author is dealing with the Artificial Intelligence in Cancer. In this paper, Coulouarn proposes a tour of Artificial Intelligence in cancer from different points of view and shows the importance of the area. I think it would be interesting to include some small reference to Soft Computing, as an emerging field of IA in the treatment of uncertainty. I include some references on soft computing techniques, which have provided solutions for cancer, regarding diagnosis, prediction, inference, classification, and so on: - Mitra, S., Das, R., & Hayashi, Y. (2009). Genetic networks and soft computing. IEEE/ACM Transactions on Computational Biology and Bioinformatics, 8(1), 94-107. - Bandyopadhyay, S. (2007). Analysis of biological data: A soft computing approach (Vol. 3). World Scientific. - Purohit, H. J., Kalia, V. C., & More, R. P. (Eds.). (2018). Soft Computing for Biological Systems. Springer. - Malone, J. (2008). Soft computing in Bioinformatics: Genomic and proteomic applications. In Soft Computing Applications in Industry (pp. 135-150). Springer. - Yardimci, A. (2007, September). A survey on use of soft computing methods in medicine. In International Conference on Artificial Neural Networks (pp. 69-79). Springer. - Bhatia, A., Mago, V., & Singh, R. (2014, September). Use of soft computing techniques in medical decision making: A survey. In 2014 IEEE International Conference on Advances in Computing, Communications and Informatics (ICACCI) (pp. 1131-1137).

The manuscript is very interesting. The motivation and justification are appropriate. The paper is well written in correct English. Now I include some typographical errors in References: For: a model was build for predicting read: a model was built for predicting; In references 3, 5, 6, 8, 11, 12, 15, 25, 29, For: Cancer Genome Atlas Research N read: Cancer Genome Atlas Research Network; In ref. 2, For: The L. GLOBOCAN 2018: counting the toll of cancer read: The Lancet. GLOBOCAN 2018: Counting the toll of cancer; In ref. 7: Remove "Electronic address aadhe, Cancer Genome Atlas Research N."; In ref. 8: Remove "Electronic address wbe, Cancer Genome Atlas Research N."; In ref. 19: Remove "manuscript does not cover any product under development. RG, YK, BL, PA and EC's employment by Medial does not alter the authors' adherence to PLOS ONE policies on sharing data and materials."; In ref. 23: Add title of the paper: "Pathway-based biomarker identification with crosstalk analysis for robust prognosis prediction in hepatocellular carcinoma"

I thank the reviewer for her/his evaluation of my manuscript. The manuscript has been revised to correct the typographical errors, notably in the references (due to automatic software). Some references on soft computing techniques applied to cancer have been included following the reviewer recommendations.

03093768   Conclusion: Accept (High priority)
Scientific Quality: Grade A (Excellent)
Language Quality: Grade A (Priority publishing)

The author briefly reviewed some examples of supervised and unsupervised big data derived from TCGA programs, especially AI models fueled by multi omics data (e.g. genetic, epigenetic, transcriptomic, proteomic, metabolomics profiles, radiomics). It was also commented on how AI algorithms have been applied to improve the management of patients with cancer. This is a high-level editor's note, introducing the current research results of artificial intelligence in the field of cancer, and pointing out the future research direction. Although refined, it is still worth reading for those concerned.

I thank the reviewer for her/his evaluation of my manuscript. The manuscript has been revised to take into account all the comments raised by the reviewers.

03892684   Conclusion: Minor revision
Scientific Quality: Grade C (Good)
Language Quality: Grade A (Priority publishing)

The paper presents an review of the recent use of AI methods in oncology. The manuscript is interesting and well-written, but there are a number of issues that need to be dealt with in order to achieve the required quality level for the journal: - some illustrations would help explaining the topic - the issue of translation between research and clinical practice should have been discussed deeper - same for the hurdles affecting the use of AI in oncology - probably it would be worthwhile mentioning the issue of clinically approved algorithms, such as SAMD (Software as Medical Devices) by US-FDA - a number of quite relevant studies appeared in the literature have not been listed or discussed - there is no mention of the issue of reproducibility - there is no mention of the issue of interpretability.

I thank the reviewer for her/his evaluation of my manuscript. The manuscript has been revised to take into account all the comments raised by the reviewers. A figure has been included to explain the topic and introduce future directions.

I mentioned the issues raised by the reviewer in the revised version, taking into consideration the word limit of this editorial. The objective is not to provide to the readers an exhaustive review of the literature that is expanding over the last few years, but rather an overview of AI & omics in cancer.

02856239   Conclusion: Minor revision / re-review
Scientific Quality: Grade A (Excellent)
Language Quality: Grade A (Priority publishing)

This is a generally well-written editorial on the role of AI in cancer omics research. The topic is of very high interest. This paper can be improved in following points. Many discussion points are binary and dichotomous (eg, signal upregulation vs. downregulation). It is a bit misleading because many biological characteristics form or represent continuum. There are many environmental, dietary, and lifestyle

factors that influence the microbiome, immune system, pathogenic mechanisms, and response to drugs. The authors should discuss these points; influence of those factors, eg, smoking, diet, obesity, etc. AI can model effects of those factors. Actually those factors are called "exposome", which should be examined in omics research. In these contexts, as a future direction, research on dietary / lifestyle / genetic factors, microbiome, immunity, and molecular tissue biomarkers is needed in omics research using AI. The author should discuss molecular pathological epidemiology (MPE), which can investigate those factors in relation to molecular pathologies, immunity, and clinical outcomes by means of computational analyses. MPE, its strengths and challenges have been discussed in Gut 2011, Annu Rev Pathol 2019, etc. MPE research is a promising direction.

I thank the reviewer for her/his evaluation of my manuscript. The manuscript has been revised to take into account all the comments raised by the reviewers.

I fully agree with the reviewer as regard to the influence of exposome and the role of AI in modeling these effects. Molecular pathological epidemiology has been mentioned in the revised version, taking into consideration the word limit of this editorial. A figure has been added for this purpose.

03251421   Conclusion: Accept (High priority)
Scientific Quality: Grade B (Very good)
Language Quality: Grade A (Priority publishing)

This article introduces the application of big data and AI algorithms in cancer. The title reflects the main subject of this manuscript. The abstract summarizes and reflects the work described in the manuscript. The key words reflect the focus of the manuscript. And the manuscript describes the background, present status and significance of the study adequately. References are cited properly. The manuscript is well organized and presented.

I thank the reviewer for her/his evaluation of my manuscript. The manuscript has been revised to take into account all the comments raised by the reviewers.