

Peer Review

Review of: "Cancer: Being or Becoming? A Whiteheadian Process Ontology Perspective"

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Dear Authors,

I read with great interest the hypothesis/perspective paper entitled: Cancer: Being or Becoming? A Whiteheadian process of ontology perspective. It is very well-written, clear, and well-justified. I think it is the right time to propose something else after the clear failure of the current understanding and view of cancer, which has led to almost no change in cancer survival for many cancer types, let alone the suffering of the patients. When I first read it, it seemed like a paper on ontology or epistemology that is somewhat difficult to be understood by mainstream scientists in the field, especially when it comes to comparing Whitehead vs. Dupré and Nicholson: A Comparative Analysis. However, after careful reading, I enjoyed much of what has been written, feeling that it will help us change our view of cancer and hence research directions and, above all, treatment, which will impact patients' quality of life.

Minor revisions:

1- **Page 1; line 1:** Not only Cancer Research but also, above all, cancer treatment, and I would ask you to add this.

2- **Page 1; line 3.** I am not sure if you can call what you propose a paradigm shift; it is one step towards it.

Many authors advocated the use of multiple therapies, and therefore, your approach is not very novel, but the advantage is that you gave it a theoretical framework that is really a strong one.

Please see:

Liao, C., Xiao, Y. and Liu, L., 2020. The dynamic process and its dual effects on tumors of therapy-induced senescence. *Cancer Management and Research*, pp.13553-13566.

Strobl, M.A.R., Gallaher, J., Robertson-Tessi, M., West, J. and Anderson, A.R.A., 2023. Treatment of evolving cancers will require dynamic decision support. *Annals of Oncology*, 34(10), pp.867-884.

3- **Page 4; Line 12:** I am not sure if the journal would allow putting page numbers in the text citations.

4- I think there are trials now going on to shift viewing cancer from a genetic disease to a metabolic disease.

Please see: Seyfried, T., 2012. *Cancer as a metabolic disease: on the origin, management, and prevention of cancer*. John Wiley & Sons. From electrons to cancer (Romain Attal et al., 2023)

Attal, R., Bakkar, A., Bouillaud, F., Devin, A., Henry, M., Pontie, M., Radman, M. and Schwartz, L., 2024. From electrons to cancer: Redox shift as a driving force of tumorigenesis. *Advances in Redox Research*, 10, p.100087.

In addition, the same authors tried to link the Warburg effect to the microenvironment, and they did find a reasonable therapeutic target, i.e., Glutamine.

Please see:

Mahout, M., Schwartz, L., Attal, R., Bakkar, A. and Peres, S., 2024. Metabolic modeling links Warburg effect to collagen formation, angiogenesis, and inflammation in the tumoral stroma. *PloS one*, 19(12), p.e0313962.

I think the authors should refer to these trials, put them in perspective, and recognize their role in changing the attitudes of cancer research and treatment. Therefore, the authors should put all this into the context of Whitehead's process.

5- Viewing cancer as a genetic or a metabolic disease does not all the time mean a static view. The alterations of major tumor suppressor genes accelerate the rate at which cells acquire other alterations and hence accelerate their progression and aggressiveness. Therefore, targeting these alterations at an early stage would interfere with the dynamic nature of the disease. Please refer to this in your article with the relevant references.

6- **Page 4; line 21:** Can you provide an example where cancer progresses systematically rather than chaotically and apply it to a treatment plan that takes into consideration cancer as a becoming rather than a being? This would be more convincing to the readers rather than a detailed philosophical explanation of Whitehead's process

In conclusion, this hypothesis/perspective paper is accepted for publication provided that the authors take into consideration the minor revisions that I suggested.

Thank you.

Declarations

Potential competing interests: No potential competing interests to declare.