

Review of: "[Research Note] Unveiling the Interplay of Klotho Protein, Chemotherapy-Induced Klotho Protein Deficiency, and the Pivotal Role of GLP-1 Agonists like Ozempic in Cancer Survivorship Patient Survival Rate after Chemotherapy Treatment"

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Potential competing interests: No potential competing interests to declare.

The topic of the Research Note is good since it focuses on the effects of chemotherapy on nephrotoxicity and the decrease in the production of the Klotho protein and its influence on the life expectancy of cancer patients, and how GLP-1 can induce its expression as a possible therapy; however, improving the writing with some suggestions is necessary.

1. On page 3/7, paragraph 2 mentions the Klotho protein and its relationship with longevity. However, the characteristics of this protein are not mentioned, such as molecular weight, if it is a protein secreted into the extracellular medium or, on the contrary, is intracellular, and in which cells it is preferentially expressed.

<u>Suggestion:</u> Extend the information on the characteristics of the Klotho protein, as it is a crucial factor in writing this paper.

2. On page 3/7, paragraph 2, the IGF-1 and mTOR signaling pathways and the inhibitory effect of the Klotho protein on them are discussed. However, the effects of the activation of the IGF-1 and mTOR pathways on cellular health and under what physiological conditions they are activated are not explained. Therefore, the true function of the Klotho protein on them and how it favors longevity is not understood.

<u>Suggestion:</u> Explain the molecular effect of activating these signaling pathways, IGF-1 and mTOR, on cellular health and under what conditions they are activated, and how the Klotho protein acts to inhibit these pathways to promote longevity.

3. On page 3/7, in the last paragraph of this page, it is mentioned that chemotherapy interferes with the expression of the Klotho protein and that this is a pivotal factor in the shortened lifespan of cancer patients. However, this idea is not supported by the bibliography.

Suggestion: Support the idea presented with a bibliography referring to what was written.

4. It is not mentioned what happens with the expression levels of GLP-1 in oncological patients and what the effects of its expression are on them.



Suggestion: Include information on GLP-1 expression in different types of cancer and its effect on pathology.