

## **ANSWERING REVIEWERS**

### **REVIEWER 1**

However, I would insert a small introductory paragraph to all the descriptions of specific organ pathologies on the sources of inflammation that may lead to cancers (bacterial and viral infections, autoimmune conditions, others) and the pathways mainly involved. Thus, this streamlines the individual paragraphs on the description of WNT or TGF- $\beta$  and the authors defer to the reference only, as the general pathways have been described previously.

**Paragraph has been added**

Maybe adding an explanatory figure

**Explanatory figure has already been added.**

### **REVIEWER 2**

There are some typos in the manuscript.

**Typos have been corrected.**

Whit respect to the following phrase: "Of note, some authors do not include immune cells as a component of stroma, however, as immune cells are integral to the function of parenchymal cells and can have far-reaching effects on tumour biology and consequent behaviour, they will be classified as a stromal component in this review." Please give some names of immune cells that are considered as a component of stroma.

**Examples of immune cells considered as stroma have been added.**

In the introduction section, the authors should include the most common signaling mechanisms caused by the inflammation and fibrosis for cancer development.

**Description has been included.**

In my opinion, column 3 (Mechanism) should also contain references.

**References have been added.**

Some acronyms were written in different ways, such as TNF-a.

**Appropriate changes have been made.**

I recommend the next good reference for the table 1, which are related to this interesting manuscript (PMID: 36612019).

**Reference has been added to the table.**

I suggest an additional figure or table that globally indicates the cytokines or specific markers of inflammation and fibrosis with each cancer, respectively.

**As each cancer mostly have similar cytokines and markers of inflammation with minimal differences, we have included the information in the mechanism section of Table 1 to avoid repetition.**

Please check the next phrase and confirm if the acronym is NASH or NAFLD according to reference 80: "NASH-related cirrhosis is also associated with the development of HCC, with multicentred cohort studies showing 1.6 to 23.7 times increased risk 80."

**Appropriate changes have been made.**

There some mistakes in the following: "adipocytes are involved in HSC activation.87-89prob split refs Fibrosis impairs the hepatic"

**Mistakes have been corrected.**

Please check if is correct the following: "IF-alpha".

**Mistake has been corrected.**

According to the abstract section: "Strategies including the application of various therapeutic agents with stromal manipulation potential and targeted cancer screening for certain inflammatory diseases which can reduce the risk of cancer will also be discussed." However, this is little addressed.

**Various therapeutic agents that target inflammation and fibrosis to help reduce the risk of cancer have been discussed for specific cancers in the manuscript from pages 14-18.**

In addition, the authors should add a table that indicates the main anti-inflammatory and anti-fibrotic agents for the different cancers considered in this manuscript.

**Table 1 has included a section with the main anti-inflammatory and anti-fibrotic agents specific to each cancer discussed in the manuscript.**