

## Peer Review File

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### Reviewer A:

**Comment:** The present review is quite helpful for the readers who are interested in the B cells in TME. It seems to be valuable to publication in TGH.

Minor issues,

1. Recently, the below paper reported about TLS in ESCC TME. If the authors are interested, it could be better to refer the below paper.

Tertiary lymphoid structures correlate with enhancement of antitumor immunity in esophageal squamous cell carcinoma.

Nakamura S, et al. Br J Cancer. 2023 Oct;129(8):1314-1326. doi: 10.1038/s41416-023-02396-7.

**Reply:** We appreciate the insightful comments made by the reviewer. The articles suggested by the reviewer is of positive significance to our manuscripts. We have added relevant content to the manuscripts and cited them.

In the revised manuscript (*4.1. Esophageal cancers, Paragraph 2*), we provide the following detailed information:

*ESCC, which constitutes approximately 90% of global esophageal cancer cases, has been studied through single-cell sequencing of tumor samples to obtain its transcription map. The tumors exhibit a presence of common immune cells, such as T cells, natural killer (NK) cells, monocytes/macrophages, dendritic cells (DC), B cells, and mast cells. **Mature TLS, which is rich in various immune cells, significantly enhances the anti-tumor immunity of ESCC.**(35) However, ESCC displays a higher infiltration of T cells and monocytes/macrophages and a lower presence of B cells compared to normal tissues and other cancers.*(36)

### Reviewer B:

**Comment:** "B Cells Present a Double-sided Effect in Digestive System Tumors: A Review for Tumor Microenvironment," offers an in-depth analysis of the dual role of B cells in the context of digestive system tumors. The authors have meticulously compiled and reviewed research studies to elucidate how B cells, a key component of the immune system, exhibit both tumor-promoting and tumor-suppressing effects within the tumor microenvironment of digestive system cancers.

We still need more research on B cells compared to T cells, and I think the key is to find out what phenomena related to B cells we observe in cancer that we can target in therapy. Thanks for a great paper.

**Reply:** Thank you very much for the reviewer' recognition of our manuscript. We will continue to pay attention to the research progress of B cells in cancer. And we are carrying out research on the immune markers of gastric cancer, hoping to help the future tumor research.