Reviewer 1 Comments

Comments and Suggestions for Authors

The review article is well written and on an important and relevant topic.

Specific points.

1. The main focus is on breast cancer. Should it be reflected in the title and abstract, following the structure of the manuscript: breast cancer-circadian clock-breast cancer plus circadian clock? Otherwise, the title and abstract are read as too general, while the manuscript focuses on a specific group of cancers, and some information is not universal.

We agree that the primary focus of the manuscript is breast cancer and that this should be reflected in both the title and the abstract. Accordingly, we have revised the title to "The Interplay Between Circadian Clocks and the Tumour Microenvironment in Breast Cancer" to explicitly specify the disease context. In addition, we have revised the abstract to more clearly position the review within the context of breast cancer biology.

2. Figures are of good quality. Figure legends are detailed enough for accessibility.

Thank you very much for the positive feedback.

3. Figure 2. Font sizes are inconsistent for the text. Sometimes the text starts with a capital letter, sometimes not. Kindly consider making it more consistent. Applies to all the Figures when relevant.

We thank the reviewer for pointing out this inconsistency. We have revised Figure 2 and the remaining figures to standardize font sizes and capitalization throughout. We also used this opportunity to harmonize the colour scheme for circadian clock genes across all three figures.

4. Lines 455-487. This paragraph is too long. Consider changing for more comfortable reading (shorten, split up). It is beneficial for the presentation of the manuscript to avoid long paragraphs.

Thank you very much for pointing this out. We have revised sentences throughout this entire section to improve reading flow (now lines 463 – 494). Likewise, we have adapted the respective paragraphs from the following three comments 5–7 and note the updated line numbers behind each comment.

5. Lines 517-543. Long paragraph. Consider restructuring it.

We have updated sentences throughout this section accordingly (now lines 523 – 555).

6. Lines 544-570. Long paragraph.

We have updated sentences throughout this section accordingly (now lines 555 – 586).

7. Lines 590-619. Long paragraph.

We have updated and removed sentences throughout this section accordingly (now lines 603 – 631).

8. Conclusions are too long, more like a concluding section than a sharp bullet point conclusion. Optionally, this section can be renamed or significantly shortened.

We thank the reviewer for this constructive comment. In response, we revised and streamlined the Conclusions section to improve coherence, focus and readability. In the revised version, we reduced repetition of mechanistic details already discussed in the main text and shifted from an extended summary toward a more focused conclusion. We now emphasize three key aspects more clearly: (i) the conceptual framing of circadian clocks and the TME as a bidirectional and clinically relevant interface in breast cancer, (ii) the translational implications for chronotherapy and rhythm-based interventions, and (iii) the most pressing methodological and conceptual gaps in the field.