

Peer Review File

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Reviewer A: Minor Revisions

Comments:

Authors reported the impact of neutrophils in the development of Lung cancer.
This is a very complete and good written review.
Just few things in the introduction.

Comment 1: Please be focused directed on the topic. I would suggest to remove the first sentences about lung cancer incidence.

Reply 1: As suggested, the introduction “Lung Cancer” has been amended to give greater focus on the topic.

Comment 2: Please add some references about the sentences written between line 62 and 68

Reply 2: As suggested, appropriate references have been added between lines 62 and 68 – currently lines 65-67.

Reviewer B: Minor Revisions

Comments:

This review by Christian Aloe et al is well written and provides an interesting summary of research into the role of neutrophils in NSCLC. My only issue is that I think the structure could be improved to help the reader follow the major points described. Some suggestions for improvements in this area are provided below.

Comment 1: Given the focus on neutrophils these cells are not properly introduced until quite a long way into the review. It would be nice to have a section introducing neutrophils at the beginning or following the first section on lung cancer to set the scene for the rest of the review. This information is mostly covered in the two paragraphs starting at line 176 and 192, but could be improved by also covering the mechanisms of neutrophil recruitment and activation in non-cancerous lung tissues to allow for comparison between these processes and the mechanisms activated in lung cancer.

Reply 1: We agree and have included a section introducing neutrophils following the section “Lung Cancer” to better tie-in the subject matter that follows. Additionally, the mechanisms of neutrophil recruitment have been expanded upon and the introduction under subheading “Lung Cancer” has been amended to better lead into the sections on neutrophil recruitment/activation and COPD.

Comment 2: I would also suggest that the section on “chronic inflammation may be pathogenic in lung cancer” could be reversed. Starting with the section on cancer and the TME (paragraph starting line 125) and then following this up with the link to COPD.

Reply 2: As suggested, the section starting on line 125 - “The connection between inflammation and cancer development.....” - was brought up – currently commences on line 142.

Comment 3: Finally, it would also be helpful for the authors to describe whether the N1 and N2 phenotypes are specific to tumour associated neutrophils or if these phenotypes are also found in other diseases/tissues.

Reply 3: To better highlight the plasticity of neutrophils a section describing some of their observed phenotypes in healthy tissue has been included. The N1 and N2 neutrophils typically refers to the TAN populations, however we have identified that this naming convention has been utilised to describe pro- and anti-inflammatory neutrophils isolated from infarcted left ventricles in mice, and has been included in the review.