

Peer Review File

Article information: <http://dx.doi.org/10.21037/tlcr-21-3>

Reviewer A

Congratulations to the authors on this thorough review. My only suggestion would be to include one or two references to support the statement made 129-131: 'in a few patients with relatively high TMB and high PDL-1 expression, immunohistochemistry might still be false negative'.

Reply: We thank Reviewer A for reviewing our article. Thank you for pointing out, that this statement has not been correctly referenced. We have now included the citation.

Changes in text: We inserted the correct citation at the end of the respective sentence (line 132).

Reviewer B

This article presents a review of liquid biopsy in NSCLC. The paper is well-written and comprehensive. The reviewer only has a few suggestions. There are few references regarding liquid biopsies for therapeutic monitoring purposes (immune checkpoint inhibitors and other molecular targeted agents). Please add some reports about the topic. Second, there are various purposes with liquid biopsies, such as early detection of cancer and recurrences (MDR) for precancerous lesions and early-stage NSCLC and tumor aggressiveness and drug resistance for advanced NSCLC. The reviewer hopes the authors construct the paper more for classifying early-stage and advanced-stage cancers.

Reply: We are grateful to Reviewer B for the careful and critical assessment of our article. As suggested, we have now added a new paragraph where we go into detail with liquid biopsy as a tool for disease (and treatment response-) monitoring (lines 598-621).

Addressing the second statement of Reviewer B, we have added a new paragraph to the background part (lines 138-156), where we have now highlighted the role of liquid biopsy for the early detection of lung cancer. The topic of disease monitoring (i.e. detection of drug resistance) has already been addressed in the above-mentioned new paragraph (lines 598-621).

Changes in text: The newly added information on liquid biopsy and disease monitoring, including citations from the recent literature, is found in chapter 5, lines 598-621.

Moreover, we highlight the role of liquid biopsy as a tool for the early detection / screening of lung cancer in the introduction/background part, lines 138-156.

Reviewer C

Extensive review but there are many already published on the same subject.

Reply: We want to thank also Reviewer C for reading and reviewing our manuscript. We agree, that the topic of liquid biopsy has already been addressed in the existing literature. However, the pool of available data is ever-expanding, and with our article we sought to include the most recent literature about liquid biopsy, with a special focus on everyday clinical practice.

General remark: Please note, that all the changes we have made in our manuscript, as a response to the reviewers, are marked in red.