Reviewer’s report

Title: Heterogeneous components of lung adenocarcinomas confer distinct EGFR mutation and PD-L1 expression

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Reviewer: Lucia Anna Muscarella

Reviewer's report:

Cai and co-Authors reported in their manuscript a molecular and IHC dissection of EGFR and PD-L1 in adenocarcinoma tumors by microdissecting and analyzing tumors with different histological components. The paper is interesting and well written and provides additional informations in the field of immunotherapy and targeted therapy interference.

Here are my comments:

Major comments:

Abstract. The last sentence was not really supported by the results of the manuscript.
M&M section. Page 8 lines 17-23. The Authors described the ALK analysis, but no mention was made about this in the abstract and in the title of the paragraph. Please, clarify this point and add this informations.

Results. Through the manuscript (i.e. Title, Abstract and Results) the Authors generally reported an "EGFR mutation screening". However in the M&M ("Digital PCR detection of EGFR mutations on LMD tissues" paragraph) they declared that only Ex19del, L858R and T790M mutations were investigated by ddPCR. Moreover, they not indicated the cut-off for positivity used to discriminate between positive and negative samples. Since we are talking about the tumor heterogeneity, please, reconsider any sections in light of these restricted molecular analysis and report positivity cut-off especially for naive T790M.

Results. "Patient Characteristics and Histopathological feature" section. Results about possible correlation of PD-L1 expression with ALK fusion were missed. Please, provide evidences about any results obtained about this.

Minor Comments:

Genes name must be written in Italic.
Some grammatical errors should be corrected
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Unable to assess

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

Quality of written English
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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