Reviewer’s report

Title: Molecular features of lung adenocarcinoma in young patients

Version: 1 Date: 05 Jun 2019

Reviewer: Reviewer 2

Reviewer’s report:

PEER REVIEWER ASSESSMENTS:

OBJECTIVE - Full research articles: is there a clear objective that addresses a testable research question(s) (brief or other article types: is there a clear objective)?

Yes - there is a clear objective

DESIGN - Is the current approach (including controls and analysis protocols) appropriate for the objective?

Yes - the approach is appropriate

EXECUTION - Are the experiments and analyses performed with technical rigor to allow confidence in the results?

No - there are minor issues

STATISTICS - Is the use of statistics in the manuscript appropriate?

Yes - appropriate statistical analyses have been used in the study

INTERPRETATION - Is the current interpretation/discussion of the results reasonable and not overstated?

No - there are minor issues

OVERALL MANUSCRIPT POTENTIAL - Is the current version of this work technically sound? If not, can revisions be made to make the work technically sound?

Probably - with minor revisions
GENERAL COMMENTS: The manuscript "Molecular features of young patients with lung adenocarcinoma" describes the analysis of genetic alterations in a cohort of 89 patients less than 35 years old that were diagnosed with lung adenocarcinoma. The utilized a panel of 59 cancer-associated genes and then correlated the observed mutations and fusion genes with clinical and pathologic features. The main finding were 24.7% had mutations in ERBB2, 21.3% in EGFR, 16.9% with ALK fusions, and 9.0% mutations in TP53, 3.4% in BRAF and 1.1% in PIK3CA, CTNNB1 and ROS1 fusion. EGFR, ERBB2, and TP53 mutations, gene abnormalities and ALK fusions correlated with tumor differentiation. ALK fusions and EGFR mutations correlated with a worse prognosis. The authors conclude that young patients with lung adenocarcinoma exhibit a unique molecular phenotype.

The study provides some interesting information in these patients who develop lung adenocarcinoma at an early age. The authors appear to have adequately performed these analyses and data is presented clearly. However there are several issues in the authors conclusions and other specific issues that require attention.

REQUESTED REVISIONS:

1. The title should read "Molecular features of lung adenocarcinoma in young patients" since it is the tumors and not the patients being molecularly analyzed.

2. Abstract line 2:...and have unique clinicopathological features.

3. Abstract line 12: A total of 6 mutant genes and 2 fusion genes were analyzed; ….This does not appear to be correct. The authors analyzed 59 genes and a total of 6 mutations and 2 fusion genes were detected.

4. Page 2, line 20: compared with ERBB2 mutations and no mutations or fusions (P < 0.01). This is confusing and might read compared with ERBB2 mutations and tumors that contained no mutations or fusions (P < 0.01).

5. Page 2, line 21: Conclusions: Young patients with lung adenocarcinoma exhibit a unique molecular phenotype, and the main driver genes also have unique clinicopathological features. This conclusion is not well supported and is over sold. The fact that young patients with lung adenocarcinoma demonstrate these mutations does not indicate that they are a unique molecular phenotype. They would have to show a new mutation not seen in older patients to convincingly demonstrate they are a unique molecular phenotype. Further other conclusion that the well and poor differentiated tumors distinct diseases is also not well supported and highly conjecture without defining other molecular characteristics of these tumors which the authors in this study have not done. This might include mutational burden; expression profiles, methylation status and inflammation score.
6. The authors use lung adenocarcinoma (LA) in this paper however the established nomenclature (TCGA) is LUAD.

7. Page 4, line 20: Microcut tumor tissue enrichment is not correct nomenclature. Macro-dissection of tumors to enrich for tumor cell content is what was likely being performed.

8. Page 5, line 3: according to the manufacturer's instructions.


10. Page 8, line 6: The histomorphology was mostly sieving or solid type. What is the reference for sieving? Please use IASLC-approved types.

11. Page 8, line 10: co-occurred

12. Page 8, line 21: differentiation or stage IV disease had a significantly worse prognosis (P < 0.01). Spacing is issue.

13. Page 9, line 5: remove People's.

14. Page 9, line 14: related to internal factors in the patients. This is not clear what is exactly meant here.

15. Page 10 and throughout: Ting Ye et al, do not use full names only the last name with et al.

Note: This reviewer report can be downloaded - see attached pdf file.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

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

No

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

No

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 am able to assess the statistics

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Please indicate the quality of language in the manuscript:

Acceptable

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