Reviewer's report

Title: Tissue-Infiltrating Lymphocytes Signature Predicts Survival in Patients with Early/Intermediate Stage Hepatocellular Carcinoma

Version: 0 Date: 20 Jan 2019

Reviewer: Xianbo Wang

Reviewer's report:

The authors in their manuscript address the interesting issue to construct a novel predictive index with tissue-related immune signature (TRIS) for patients with early/intermediate HCC: to this purpose they studied 14 immune markers of intra- and peri-tumoral immune cells in 745 HCC patients. The further analysis showed, γ-glutamyl transferase (GGT), tumor diameter, tumor differentiation, and TRIS (CD3T, CD27T, CD68P, CD103T and PD1T) were independent prognostic factors of OS in HCC patients. In general, it is an impressive study with merits in clinic.

1. One major issue I have with this is that the C-index values of the ICPI were 0.691 and 0.686 in the training and validation cohorts, which were lower than 0.7, suggesting that the discrimination ability of the new model is not very well. We know that the nomogram could offer a more precise and individualized prediction compared with the traditional models (such as the Logistic regression model, Cox regression model). So, is it better when analyzed the C-index values of the nomogram and compared with other 7 traditional staging systems?

2. The study firstly carried out Correlation analysis in the TCGA dataset and immune features were examined by IHC analysis, I wonder if is it better to provide the QPCR results of tissue expression to support this?

3. It is necessary to predict the prognosis of patients by using the expression of immune markers in tumor tissues. But in the future, for patients without hepatectomy or liver puncture, it will be more meaningful to detect the expression of relevant immune markers in serum and draw similar conclusions.
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.

Yes

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?  
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I am able to assess the statistics

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