Reviewer’s report

Title: Circulating free plasma tumor DNA in patients with advanced gastric cancer receiving systemic chemotherapy

Version: 0 Date: 17 Oct 2018

Reviewer: Charlotte Ng

Reviewer's report:

In this study, the authors quantified cfDNA and tDNA and observed that reduced tDNA after chemotherapy was associated with longer DFS but not OS.

1. For readers and reviewers who may not be familiar with the use of ALU sequences as a surrogate for tDNA, readability of the manuscript would substantially benefit from a description of why DNA integrity would be a surrogate for tDNA and a description of how ALU sequences measure DNA integrity in the introduction.

2. The use of the phrase 'expression of ALU sequences' is potentially misleading since this does not refer to transcript expression. Suggest rephrasing.

3. The authors presumably measured the ALU sequences by qPCR, however, this was not stated in the methods. More description on how exactly the cfDNA integrity analysis was performed, the precise formula for the definition of tDNA would be crucial to interpret the results. The definition of tDNA is particularly critical since the most interesting results are directly related to tDNA.

4. A major novelty of this study is the longitudinal plasma collection, yet the authors by and large failed to capitalize on the longitudinal nature of the samples and the clinical and response data. The authors could improve the manuscript substantially by performing in-depth analysis of the evolution of tDNA per patient and to determine whether the changes are reflected clinically. Are the changes in tDNA reflected by imaging or serum markers? There was one patient with clearly elevated cfDNA levels at the 4th timepoint (Figure 1). Did this increase reflect clinical progression?

5. 20 patients had cfDNA collected at the second collection timepoint. In Figure 2, the authors compared DFS and OS of the patients below 25th percentile and above 75th percentile. This should mean that each line in the figure should be exactly 5 patients. There are clearly more than 5 patients shown in the blue line. The authors should explain this discrepancy.
Minor comment

1. Reference 16 is not correctly formatted and does not appear in the reference list.

2. Figure 2 is not of sufficient publication quality.

3. What is the unit on the y-axis of Figure 1?

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.

Yes

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

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

Needs some language corrections before being published

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?
3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal