Reviewer’s report

Title: Analysis of the EGFR, HER2, and TOP2A gene status and chromosomal aneusomy in gastric adenocarcinoma from Chinese patients

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Reviewer: Akishi Ooi

Reviewer’s report:

The authors reported the numerical changes of EGFR, HER2 and TOP2A genes in gastric cancers using FISH. In addition, they also correlated the FISH data with the respective gene expressions detected by IHC. Although there have already been a few preceding reports, this paper handles the theme in an up-to-date manner and these findings seem to represent the first such report about Chinese. To the reviewer this paper seems to have several major flaws in the processing data and its presentation would thus have to be revised before the paper could be considered for publication.

Major Compulsory revisions

1. The word "polysomy" is defined as an excess of a particular chromosome. Therefore, the terms "EGFR polysomy" and "EGFR aneusomy (non-disomy)" make no sense to me. Please carefully define and explain the meaning of these terms

2. p8: The EGFR gene status was classified into six categories: disomy, low trisomy, high trisomy, low polysomy, high polysomy and gene amplification. In this categorization, two standards are used. Polysomy 7 and the EGFR gene amplification are not mutually exclusive phenomena. For example, cases with either "gene amplification and disomy" or "gene amplification and polysomy could also exist. Of course, this confusion could be avoided by changing the present categorization. In general sense trisomy is a low polysomy. The reason why trisomy was isolated from low polysomy is unclear and difficult to understand. Furthermore, it is extremely unclear regarding the reason for dividing trisomy into two categories, namely "low" and "high". Tables 1 and 2 have no column of "high trisomy", in these tables only 5 categories are observed. Furthermore the discussion does not mention anything about high and low trisomies.

3. The authors also used an additional categorization#EGFR-positive and -negative. The authors stated in the abstract (p2, line 17) "Chromosome 7 polysomy correlated significantly with EGFR FISH-positivity." This line of reasoning is very difficult to understand because EGFR FISH-positive includes high polysomy by definition. These complicated and duplicated categorizations thus lead to a great deal of confusion.

4. One of the major findings of this paper is that not the EGFR FISH-positive status but EGFR aneusomy showed a significant association with EGFR overexpression (p10 & p13). Does this means that trisomy 7 and low-polysomy 7
have a major impact on the aEGFR overexpression? Authors should clearly state
which of the 6 categories for the EGFR gene status is supposed to be closely
associated with EGFR overexpression.

Minor Essential Revisions
1. Reference 2: second author "Kuntomo K" --> "Kunitomo K"

Discretionary Revision
1. On page 14, line 16: " a small number of cases showed .co-expression of
EGFR and HER2. "

In this section, the precise number of cases should be written. Thereafter, an
expanded discussion of the dual inhibition therapy against EGFR and HER2
would be possible.

**Level of interest:** An article whose findings are important to those with closely
related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the
statistics.

**Declaration of competing interests:**

I declare that I have no competing interests.