Reviewer's report

Title: The gene-reduction effect of chromosomal losses detected in gastric cancers

Version: 1 Date: 3 August 2010

Reviewer: Yong Sung Kim

Reviewer's report:

The gene-reduction effect of chromosomal losses detected in gastric cancers

The manuscript by Hong et al. examined LOH events in gastric cancers to investigate if the cell-adverse effect by the gene reduction was a rate-limiting factor for the LOH events in two different histologic types of gastric cancers. They concluded that the cell-adverse effect by the gene reduction is more tolerated in intestinal-type gastric cancers than in diffuse-type cancers and that the loss of high-dose genes is associated with hematogenous metastasis.

Overall this paper is an impressive body of work on clinicopathologic significance of LOH events in gastric cancers, showing a distinct difference between intestinal types and diffuse types of gastric cancers.

Major Comments:

Q1: This study initially started based on that the eight chromosomes as those having a low density of genes or the gene-poor chromosomes and having no stomach-specific genes in line 20 of P6 and line 5 of P18. Then authors should explain the definition about the gene-poor chromosome. If the parameter is due to the difference of mean value compared to other chromosomes in Table 2, is it significant? Can authors present some evidence for the eight chromosomes having no stomach-specific genes?

In this study, LOH events were examined by five microsatellite marker sets for each chromosome. Is it possible to estimate overall LOH events on each chromosome with the small number of MS marker set? So can you say “This indicates that the LOH events tend to target the chromosomes with a low dose of genes and transcription”? Is there any other data supporting it?

Q2: It is not clear how LOH-H and LOH-B gastric cancers can be grouped into the high-risk genotypes against the low-risk genotypes of LOH-L and MSI in bottom line of P14 or in middle line of P16. What is a factor to divide gastric tumors into two groups, high-risk or low-risk genotypes? The rational argument should be answered.

Q3: In conclusion section, authors insisted that the cell-adverse effect by the gene reduction is more tolerated in intestinal-type gastric cancers than in diffuse-type cancers. In other word, it means that the cell-adverse effect by the gene reduction is less tolerated in LOH-B tumors of diffuse type, although only
zero and one chromosomes was lost in diffuse type of gastric cancers. Can you find a diffuse type-specific LOH event? Or could you consider other genetic factor during carcinogenesis of diffuse type of gastric cancer?

Minor Comments:

P10: Authors performed the autoradiograph of PCR product to determine the amount of DNA of the tissue lysates or to detect LOH or MSI in tumor DNAs. Then the procedure for radioisotope labeling during the PCR should be described in Materials and Methods section of text in detail.

P29: in legend of Figure 1, authors defined the extent of chromosomal losses as follows: “Zero and one chromosomal loss was dually classified into low-level (LOH-L) for the intestinal-type and into the baseline-level (LOH-B) for the diffuse-type.” But in Figure 1B, LOH-L in intestinal type was figured as 0-3 chromosomal losses. It should be defined accurately.

P13: in line 3 from bottom, “because most - - - - - - - had two or more chromosomes,” chromosomes have to be corrected to “chromosomal losses”

P18: In line 12, Table 3 is replaced to Table 2.

In figure 2: Title on Y axis may be simplified.

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

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.