Reviewer's report

Title: Genetic and epigenetic characteristics of human multiple hepatocellular carcinoma

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Reviewer: Yutaka Midorikawa

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Comment on the manuscript by Taniguchi, et al.

One of the clinical distinction of hepatocellular carcinoma (HCC) is multiple carcinogenesis, and discrimination of intrahepatic metastasis (IM) and multicentric carcinogenesis (MC) is critical for decision making of therapy. The authors investigated genetic aberrations of 15 pairs of multiple HCCs consisting of 11 MCs and 4 IMs using mutation analysis, array CGH, and methylation analysis. However, they could not demonstrate dominant conclusion, for example, difference of genetic alteration between MC and IM. And that, several conclusions the authors came to would not have the readers acceptable.

First, the authors' assertion in 'Somatic mutation analysis' in Results is not clear. It seems just a negative data.

Second, the authors concluded the multiple tumors were derived from common precancerous or cancerous ancestors due to common chromosomal aberrations. However, the number of common chromosomal aberrations in pair samples is quite few (Table 2), and I don't think they could form such a conclusion. ('Chromosomal aberration' in Results).

Third, as with ‘Somatic mutation analysis’, the aim of ‘Methylation analysis’ is quite obscure. Why did the authors perform methylation analysis for multiple HCC?

Through genome research using IM and MC samples, the readers would like to know what is the difference of genetic change between two groups, I guess. That is, is it possible to make a molecular diagnosis about multiple HCC as IM or MC?

Level of interest: An article of limited interest

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.

Declaration of competing interests:
I declare that I have no competing interests.