Reviewer’s report

Title: Metastatic susceptibility locus, an 8p hot-spot for tumour progression disrupted in colorectal liver metastases: 13 candidate genes examined at the DNA, mRNA and protein level.

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Reviewer: Yoichi Furukawa

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General comments
The authors carried out an allele-type study of metastatic colon cancer, and identified a 2Mb region of chromosome 8p with loss of heterozygosity in 73% samples. From the region, they focused on 13 candidate genes associated with progression or metastasis of cancer, and analyzed alteration in DNA, mRNA and protein. Interestingly among the 13 genes, they found a novel germ line mutation leading to protein truncation in DR5/TNFRSF10B. In addition, ADAMDEC1 showed decreased expression in mRNA and protein levels during both development and progression of colon cancer.

Major criticism
1) Although their findings are interesting and important, I think that data of polymorphisms in DR4 and PDLIM2, expression of STC1 and LOXL2, and gene relationships are less important. Therefore, I recommend that the authors may shorten or delete discussion of the data.

2) The most critical issue in this manuscript is the interpretation of genetic variant C790T in DR5. To evaluate whether DR5 is a key issue in the progression of colorectal cancer, I recommend that the authors should analyze germ-line mutation (but not somatic mutation) of DR5 in an increased number of genomic DNA from patients with metastatic colorectal cancer and that from healthy controls. Alternatively immunohistochemical staining of DR5 in a number of metastatic lesion and primary lesion of colorectal tumors is essential to study whether loss of DR5 expression is a common feature of metastasized tumors.

3) Although the authors discussed on the importance of DR5 mutation and decreased expression of ADAMDEC1, they emphasized that 8p disruption is a consequence of tumor progression. I agree that the possibility should be always taken into consideration. However description of lack of strong candidate of protein-coding gene on chromosomal band 8p gives discrepancy to their preceding discussion.
**What next?:** Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

**Level of interest:** An article of importance in its field

**Quality of written English:** Not suitable for publication unless extensively edited

**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