Reviewer's report

Title: Tumor hypoxia, in association with inflammation, angiogenesis and MYC, is a critical prognostic factor in patients with hepatocellular carcinoma after surgery

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Reviewer: YUTAKA YAMAMOTO

Reviewer's report:

This is an interesting paper reporting clinical significance of the expression of hypoxia-inducible factor 1alpha (HIF-1alpha) in hepatocellular carcinoma (HCC). HIF-1alpha is an independent prognostic factor and associated with several factors showing aggressive phenotype including COX-2, PDGFRA, MMP7, MMP9 and MYC in HCC. This paper is generally well written and of scientific value.

However, this paper has a critical issue. Hypoxic condition in tumor is not identical the expression levels of HIF-1alpha although HIF-1alpha is a master regulator of essential adaptive responses to hypoxia. In tumor cells in addition to the oxygen-dependent regulation of HIF-1alpha, multiple other oxygen-independent oncogenic pathways serve to regulate HIF-1alpha, including growth factor signaling such as phosphatidyl inositol3-kinase and loss of function of tumor suppressor genes such as pVHL. The authors did not demonstrate that the expression levels of HIF-1alpha were equal to the status of hypoxic condition in HCC in this paper. The authors cannot use “hypoxia” instead of HIF-1alpha expression.

Major Compulsory Revisions
#1. The authors should change from tumor hypoxia to HIF-1 alpha in Title.
#2. The authors should change or delete the word “hypoxia” in line 3, 16 and 18 in Abstract, last line in Background session, line 7, 22, 59, 60 and 61 in Discussion session and line 3 and 4 in Conclusions session.

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: Yes, and I have assessed the statistics in my report.