Title: Expression of Hiwi in human esophageal squamous cell carcinoma is significantly associated with poorer prognosis

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Author's response to reviews: see over
Dear Editor,

We have been working on tumor stem cells, especially on the expression of stem cell factors in tumors since 2006. To characterize the expression status of Hiwi in esophageal squamous cell carcinomas, we firstly investigated Hiwi expression in a series of 153 esophageal squamous cell carcinomas materials from a high risk population area in China using immunohistochemistry and explored its associations with clinicopathological features. The follow-up data for these patients were obtained through an international collaboration project sponsored by the Norwegian and Chinese governments. In our study, the expression of Hiwi was observed in tumour cell nuclei or/and cytoplasm in 137 cases. 86 (56%) were strongly positive in cytoplasm, while 49 (32%) were strongly positive in nuclei. The expression level of Hiwi in cytoplasm was significantly associated with higher histological grade ($P=0.011$), higher T stage ($P=0.035$), and poor clinic outcome ($P<0.001$), while there was no correlation between the nuclear Hiwi expression and clinicopathological features. Given the function of proliferation and self-renewal of Hiwi, our data may indicate that the expression of Hiwi in cytoplasm enables the tumours to have higher degree tumour cell stemness, which in turn results in poorer clinical outcome for the patients with esophageal squamous cell carcinomas. Therefore, cytoplasmic Hiwi expression may be used as an independent prognosis factor for the clinical outcome of esophageal squamous cell carcinomas patients. We all believe that the findings should be of interest for the readers of BMC Cancer and the tumor stem cell research community. We have followed all the guidelines of your journal for manuscript submission, and hope that our manuscript could be considered for publication.

Sincerely yours,

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