Reviewer's report

**Title:** Self-renewal and chemotherapy resistance of p75NTR positive cells in esophageal squamous cell carcinomas

**Version:** 4  **Date:** 20 May 2008

**Reviewer:** Gabriela Dontu

**Reviewer's report:**

The authors addressed the reviewers' criticism by performing additional histopathological examination of the tumors and investigating correlations between p75NTR positivity and histoclinical characteristics. Moreover, the in vitro self renewal ability of p75NTR negative cells was tested as well as the tumorigenicity of the sorted populations in NOD/scid mice. The results of these last experiments, however, are in contradiction with the authors' conclusion that esophageal tumors are driven by a cancer stem cell component and the discussion included in the revised version of the manuscript is in disagreement with the rest of the paper.

The tumors generated by the sorted populations should be a) analyzed for expression of p75NTR and b) passaged several times in order to assess if the proliferation potential of the tumor is unlimited for both populations. Alternatively, lower number of cells should be injected. If all cell fractions generate tumors that recapitulate the cell heterogeneity of the parental tumor and have similar tumorigenic and proliferation potential in vivo (latency and size of the tumors), one can only conclude that these tumors are not hierarchically organized, but rather homogeneous, with a large cancer stem cell component that cannot be identified by expression of P75NTR (heterogeneous with respect to this marker).

**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.

**Declaration of competing interests:**

'I declare that I have no competing interests'