Reviewer’s report

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

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Reviewer: Gabriela Dontu

Reviewer’s report:

The study has a scientifically sound experimental design and a logical, clear presentation of the data. With several exceptions, discussed below, the results are clear-cut and support the author’s conclusions. Overall the work is interesting and relevant for esophageal cancer research, although not a particularly novel contribution compared with previous publications by Okumura et al. Chemoresistance of p75NTR positive cells is probably the most significant result of this work which was not previously reported.

The authors propose that p75NTR+ cells of the normal and malignant esophageal epithelium have stem cell characteristics, such as ability to self renew and regenerate the heterogeneity of the esophageal cancer cell lines after sorting, resistance to chemotherapy, localization in the basal, proliferative layer of the epithelium, expression of markers of self-renewal (BMI1) and lack of expression of differentiation markers (involucrin).

Major criticisms:

1. The study would be considerably more convincing if in vivo functional data would be added, in addition to the in vitro results, to show difference in tumorigenicity between the p75NTR positive and negative cell populations. This would also represent an important contribution and a step forward compared to previous findings by Okumura et al.

2. Self-renewal was not demonstrated by the experiments performed. In order to demonstrate self-renewal one should separate and analyze the p75NTR positive and negative cell populations in several serial passages. The same analysis shown in Figure 2, with respect to the phenotype of the progeny population should be performed.

The same applies to sphere formation. In addition, information about the sphere formation of the p75NTR negative population should be shown.

Minor criticisms:

Figure. 1 B, C, D pictures should be replaced with better quality versions of same sections, larger details should be shown

Figure 4. It would be useful to label flow charts with marker name (instead of FL1-height)
There are numerous language, grammar, spelling errors. Manuscript should be checked and some sections re-written.

**Level of interest:** An article of limited interest

**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