Reviewer's report

Title: Pluripotency-associated genes in human nasopharyngeal carcinoma CNE-2 cells are reactivated by a unique epigenetic sub-microenvironment

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Reviewer: Lifu Hu

Reviewer's report:

The authors have identified non-SP single clone cells can generate SP phenotype when they are co-cultured with macrophages, which had an effect on cell-cycle specific changes and enhanced migration.

Comments:

1. There are several NPC cell lines, CNE-1, CNE-2, CNE-3,... Why authors select CNE-2 for this study? The authors have cited the previous work by Wang et al.( 2007), but there is no reference.

2. It is good that authors used neuroblastoma for validation of lab system and showed the effect from macrophage interaction, although is an indirect evidence to CNE-2.

3. What is the reason to have such big range of SP cells from 0.1% to 73.7%? How to exclude the introduced errors due to changes of cell culture condition or manipulation?

4. The present result is from a single NPC cell line, CNE-2 and it would be interest to know if the results are producible and represent a common character of NPC from several NPC cell lines, whereas if these involved genes were found in other NPC cell lines as well.

5. From SSH, there are so many genes involved, why those gene are selected from up-regulation and what is the evidence of these gene linked to cell growth and metastasis of NPC?

6. NPC is 100% association with EBV virus. It is more interesting to see if CNE-2 cell (EBV negative) was infected with EBV.

Minor comment:

1. What is the difference of human nasopharyngeal cancer cell line THP-1 from original CNE-2?

2. CNE-2-2 cell line should be described in Materials and Methods.

3. Clone ID 2 in text was not showed in Fig. 1C.

4. There are no (D) in Fig. 4 legend

5. There are several misspellings (from to form, page 7, line 3), and un-properly term (lysed cells in Trizol, not homogenized cells, page 8, line 4 from bottom).....
Conclusion: This manuscript can be accepted for publication after revised

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

**Quality of written English:** Acceptable

**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