Reviewer’s report

Title: Enrichment of the Embryonic Stem Cell Reprogramming Factors Oct4, Nanog, Myc, and Sox2 in benign and malignant vascular tumors.

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Reviewer: Rui Henrique

Reviewer’s report:

This manuscript from Amaya and Bryan reports on the immunohistochemical expression of embryonic stem cell reprogramming factors in benign and malignant vascular tumors. The authors claim that both benign and malignant vascular tumors are enriched in those proteins. Based on these findings, the authors suggest that the “stem cell theory of cancer” should be modified to include benign neoplasms.

Overall, the manuscript is well structured and written. Some issues, however, require clarification.

Major compulsory revisions

Materials and methods
1. Please clarify how the specificity of the antibodies was tested, although positive and negative controls were used. This is a relevant issue as the percentage of stained cells for most protein markers was high. In the case of Myc the results are quite discrepant considering the HPA reports.

2. The authors used Student’s t-test to seek for significant differences in immunostaining among tumor types. However, they actually evaluated a categorical variable, derived from the product of two other categorical variables (% of stained cells and staining intensity). Thus, this does not seem to be the more appropriate statistical analysis. Moreover, Student’s test is parametric and in the manuscript there is no mention to the assessment of the normality of the distribution(s). Please clarify these issues.

Discussion
1. Usually, cancer stem cells constitute a very small proportion of the tumor cells, usually less than 1%. Thus, how do the authors interpret the results of the immunostaining? It is not clear whether they consider that immunostaining for the target proteins is equivalent to “tumor stem cell” identification. This issue should be thoroughly discussed and clarified.

Minor essential revisions
1. Line 77: cancer = malignant tumor/neoplasm. Thus "malignant cancers" is a redundant expression. Please correct.
Level of interest: An article whose findings are important to those with closely related research interests

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