Reviewer's report

Title: Comparative analysis of histologically classified oligodendrogliomas reveals characteristic molecular differences between subgroups

Version: 2 Date: 25 Jan 2018

Reviewer: Aaron Diaz

Reviewer's report:

The authors have revised their manuscript, acknowledging what both reviewers pointed out, their comparison of "molecular subtypes" of "histologically classified oligodendrogliomas" amounts to a comparison between oligos and astros, that were all originally classified as oligos based on histology. My concerns, raised in my original review, are however still unaddressed. I detect a resistance to fundamentally re-write the manuscript. major:1. The authors have compared oligos to astros, but have described those classes as molecular subtypes of "histologically classified" oligodendrogliomas. There is only one classification of oligos, it is the WHO 2016 classification. The discussion of "histologically classified" vs. WHO 2016 in the current manuscript would only add confusion to the literature, in my opinion. Moreover, if the authors want to compare astros to oligos, which is what they are currently doing by their own admission and regardless of how it is described then they need to include all available data from astrocytomas and not just the astros that were previously classified as oligos. Otherwise, it is unclear if astros are adequately sampled. The authors state "...a reclassification of the analyzed tumors is not straightforward and would require expert knowledge of neuropathologists that have to consider histological and molecular data." This statement is false, a comparison between 1p/19q co-del and ATRX/p53 in a IDH mutant background could be easily done from public data (much of which the authors have already analyzed). In fact Ventiecher 2017 does exactly that and the authors have not even compared the data or conclusions of Ventiecher 2017 as I asked in my last review.2. The authors have still not stated what conclusions can be drawn from their work. In their re-written conclusions section they state that they have identified "...novel putative major regulators and characteristic stemness signatures...". But, this is not a conclusion, this is a result. Putting aside that this result is not novel, e.g. the role of SOX genes in astrocytic lineage regulation is well known and extensively studied, it is also entirely expected given that the authors obtained the signature by comparing oligodendrogliomas to astrocytomas. minor: the figures still contain numerous illegible components and all the references are all still replaced for some reason by ?? marks.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

No
Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

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I am able to assess the statistics

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