Reviewer's report

Title: Quantitative proteomic analysis shows differentially expressed HSPB1 in glioblastoma as a discriminating short from long survival factor and NOVA1 as a differentiation factor between low-grade astrocytoma and oligodendroglioma.

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Reviewer: Donat Kögel

Reviewer's report:

In this study the authors used an iTRAQ-based quantitative proteomic approach to compare global proteomic differences between astrocytoma grade II, glioblastoma (short and long survival) and oligodendroglioma. They found that expression of nucleophosmin, GRP78, nucleolin and HSP90B1 were increased, while expression of the Raf kinase inhibitor protein (RKIP) was decreased in glioblastoma. They also report that expression level of heat shock protein 27 (HSPB1/HSP27) allowed to discriminate glioblastoma presenting short (<12 months) and long survival (>16 months). In addition, expression level of RNA binding protein nova 1 (NOVA1) differentiated low-grade oligodendroglioma and astrocytoma grade II. The authors propose that nucleophosmin, GRP78 and RKIP together with NCL and HSP27/HSPB1 are acting in a signaling network related to tumor progression.

This is a potentially interesting study and well-written manuscript, but a number of concerns need to be addressed.

Major Compulsory Revisions

1. To this reviewer, it is unclear how/why the proteins shown in Table 1/Fig.1 were selected for further analysis. Were these really the only found proteins "known to participate in the process of tumor progression" or did the authors narrow their selection based on their previous research on these candidates? Please explain. Along the same line, how does this selection relate to the model shown in Fig.5?

2. Although there is a difference between the groups (Fig. 3 A and B), the considerable overlap makes it somewhat questionable whether HSP27 really would be truly useful in discriminating between good and bad prognosis.

3. The discrimination between diffuse astrocytomas and oligodendrogliomas remains a diagnostic challenge and the new findings on NOVA1 expression are interesting. How do the authors reconcile their findings with the data of Zhi et al. (PLoS One. 2014 Oct;9(10):e109124.) who have shown that NOVA1 is expressed in astrocytoma of all grades with an increase in expression in relation to tumor grade?
Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests