Reviewer's report:

In this manuscript the authors reported that LAT1/4F2hc was overexpressed in gliomas, localized both in tumor cells and vascular endothelial cells; in addition, the expression levels significantly correlated with the pathological grade and Ki-67 LI of gliomas, as well as microvascular density. As the author mentioned previous studies had already shown that that LAT1/4F2hc is highly expressed in a variety of human tumors including gliomas, and LAT1 over-expression is associated with glioma progression and poor prognosis of glioma patients, but the exact tissue location of LAT1/4F2hc in gliomas and its precise role is unclear. From their findings the authors concluded that LAT1/4F2hc over-expression was correlated with the malignant phenotype and proliferation of gliomas, and LAT1 was associated with glioma angiogenesis.

Major Compulsory Revisions

1. Abstract (background): Lines 1-2: The sentence… is a large neutral amino acid transport agency and… should be deleted.
2. Abstract (background): line 7: “glioma progression” should be replaced with “glioma grade”. In the same line it is not clear to me what you mean with the words “the exact tissue location”
3. Abstract (Results): The same question what you mean with the words “in all the glioma tissues examined”. Do you mean “all cells”?
4. Abstract (Conclusions): Re – write the conclusions as follows: LAT1/4F2hc over-expression was closely correlated with the malignant phenotype and proliferation of gliomas, and LAT1 was associated with glioma angiogenesis. LAT1/4F2hc, especially LAT1, may become a novel potential molecular target for glioma biological therapy.
5. Background: Replace the phrase “(LAT1) is a Na+-independent neutral amino acid transport agency” with “(LAT1) is a membrane glycoprotein”. In addition, in this section it needs to be mentioned that LAT is highly expressed in brain capillaries that form the blood brain barrier relative to other tissues, with the appropriate references.
6. Methods: The median age of patients rather than mean needs to be reported (or both).
7. Methods (Evaluation of staining results): “The cases that contained equal to or
less than 50% positive cells were considered patchy staining, and those that contained more than 50% positive cells were considered diffuse staining”. I don’t think this is a correct statement. The authors should delete the terms “patchy” and “diffuse” and only mention staining less/equal and over 50% respectively.

8. Results (under Correlation of LAT1 and 4F2hc staining..): The authors state that the immunoreactivity of both LAT1 and 4F2hc enhanced significantly with the glioma pathological grade ascending (r=0.526, P=0.000; r=0.413, P=0.001). However, in table 1, apart from the grade IV gliomas it appears that in grades I-III there is overall equal distribution of LAT1 and 4F2hc immunoreactivity. The statistics need to be rechecked concerning this issue.

9. Discussion (2nd paragraph). Similar to the above point (#8) the authors state that both LAT1 and 4F2hc expression levels significantly correlated with the glioma pathological grade, which was obviously higher in high grade gliomas than in low grade gliomas. Although it seems that this is true for glioblastoma (grade IV) it does not appear that the LAT1 and 4F2hc expression is correlated with any other grade.

10. Discussion (2nd paragraph). The authors state that both LAT1 and 4F2hc expression levels were markedly associated with Ki-67 LI of glioma tissues. These results indicate that LAT1/4F2hc may play a crucial role in the malignant proliferation and progression of gliomas. Again I think this statement is true for glioblastomas but not for any other glioma grade. Thus I don’t think that the statement LAT1/4F2hc may play a crucial role in the malignant proliferation and progression of gliomas is true, according to these findings.

11. Conclusion. The statement that LAT1/4F2hc over-expression is closely correlated with the malignant progression and proliferation of gliomas, has not been proven in this manuscript.

Discretionary Revisions
None

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**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 interest