Reviewer’s report

Title: Activation of SNAT1/SLC38A1 in human breast cancer: correlation with p-Akt overexpression

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Reviewer: Aihua Gong

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Major Compulsory Revisions
In this manuscript, Wang and colleague investigated detected SNAT1 expression profiles in breast cancer tissues and cell lines, and explored its underlying mechanism in promoting breast carcinogenesis. The authors showed that SNAT1 were significantly up-regulated in breast cancer tissue chips associated with tumor size, nodal metastasis and advanced disease stage, and knocking down SNAT1 inhibited the growth of breast cancer cell lines and the efficiency of colony formation. This study at the first time established correlation between glutamine transporter SNAT1 and the pathological significance of breast cancer and potentially provides important insight about SNAT1 expression associated with p-AKT. However, the authors did not provide the functional evidence of SNAT1 knockdown (sh-SNAT1) and correlation with p-AKT, and there are several important issues that need to be addressed to strengthen the conclusions.

Major criticisms:
1. In Figure 3A, it is too preliminary to draw the conclusion that the conclusion that SNAT1 functions via Akt signaling pathway. The evidence that SNAT1 resulted in decreased p-Akt level couldn’t support directly the above conclusion. Therefore, the author must address this issue and provide direct evidence, such as Akt agonist rescue assay.
2. Although the author used CCK8 assay and Colony formation assay to assess the tumor growth, it is necessary to further analyze the reason of inhibition of SNAT1 down-regulation-induced cell growth, such as cell cycle or apoptosis analysis.

Minor criticisms:
1. In introduction and discussion, the roles of other amino acid transporters in cancer should be mentioned and discussed.
2. In results, the title ‘Knockdown of SNAT1 by shRNA inhibits proliferation and colony formation of breast cancer cells by blocking Akt phosphorylation’ should be revised.
3. In the final paragraph of results, Fig. 4 should be Fig.5.
4. It would be nice if the whole manuscript can be polished by native English spoken professional.
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 interests'