Reviewer's report

Title: The mitochondrial transporter SLC25A43 is frequently deleted and influences cell proliferation in HER2-positive tumours

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Reviewer: Liza Makowski

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The mitochondrial transporter SLC25A43 is frequently deleted and influences cell proliferation in HER2-positive tumours.

The purpose of this study was to screen tumors to establish novel targets. Found 40 loci with CNV: 16 amplifications and 24 deletions. First time identifying SLC25A43 in relation to cancer. Authors found that SLC25A43 is deleted in HER2 positive breast cancer and state that it causes an increase in proliferation through influencing the S phase of cell cycle ultimately increasing proliferation. Sample size is adequate (85 HER2+).

The authors show that deletion was present in about 50% of HER2+ and 10% of HER2-.

Major Compulsory Revisions
1) Can the authors discuss how this LOH in SLC25A43 affects the S phase in these HER2 negative tumors?
2) How does SLC25A43 IHC (protein levels) correlate in HER2 negative?
3) Low/negative SLC25A43 staining in HER2+ correlated with lower S phase fraction. There is no description of how S phase is measured.
4) The authors state that differences in SLC25A43 influence S phase fraction—but really this is just a correlation. The abstract and manuscript need to be edited to reflect this correlation, not causation.
5) Variability at the SLC25A43 protein level did not correlate with ER status or age of diagnosis, but what about metastasis, responsiveness to chemo, recurrence?
6) The authors state similar deletions in lung cancer—there are several types of lung cancer, please describe.

Minor Essential Revisions
7) Unclear sentence “the prognostic value of S-phase fraction in BC has been discussed due to inconclusive data.” What does this mean? In the abstract you suggest a difference due to SLC25A43 and now say it is inconclusive? Please clarify.

In sum the manuscript is interesting and spans sequencing and protein expression. The authors identify a novel LOH of SLC25A43 at Xq24 in breast cancer (and other cancers, although poorly described), suggesting it is a TSG.
Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
'I declare that I have no competing interests'