Reviewer's report

Title: Patient-derived heavy chain antibody targets cell surface HSP90 on breast tumors

Version: 2 Date: 21 April 2015

Reviewer: Smarajit Pal

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Minor essential revisions

The study by Devarakonda et al identifies a novel heavy chain antibody (HCAb2) that targets HSP90 on the more stress induced regions of breast carcinoma and shows the potential to combat dissemination of the tumor mass. The authors used a novel research strategy developed by them to identify antibodies that target tumor antigens. The manuscript is well read and has some revelatory implications in as much as the power of the strategy to screen antibodies is concerned. However, the applicability of the antibody as an anti-tumor agent is not strongly evident and stronger assays are needed to validate its relevance alongside other HSP90 inhibitory antibodies or small molecule inhibitors.

1. More powerful migration assays like transwell/boyden chamber assay alongside suitable in vivo metastasis model are needed to unhesitantly validate the potential of the antibody to inhibit migration. Moreover a positive control is missing.

2. Although the antibody seems to accumulate inside the xenograft tumor mass, it is not clear whether it has any potential to restrict tumor growth by activating immune effector mechanism like ADCC and CDC. The mere accumulation of an antibody does not suggest restriction of tumor growth.

3. Toxicity profile of the antibody is needed to determine the optimum dose. Also needed to determine is the stability of the antibody.

The study validates the potential of the technique developed by the author but since the other major objective of the study is to determine the tumor growth restriction property of the antibody, the study needs more elaboration regarding the therapeutic potential of the antibody.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

declared