Reviewer's report

Title: Amyloid-beta Precursor Protein Promotes Cell Proliferation and Motility of Advanced Breast Cancer

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Reviewer: Amit Tuli

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In this manuscript Seunghwan Lim and co-workers have presented evidence for increased expression of amyloid-precursor protein (APP) in breast cancer and highlighted the signaling pathway through which APP promotes tumor growth. In this study, APP expression level was analyzed in multiple human and mouse breast cancer cell lines and by tissue microarray array. The major findings from this study were:

• APP level was found to be elevated in breast cancer cell lines possessing higher metastatic potential;
• Silencing of APP expression was found to retarded the growth, migration and invasion potential of breast cancer cells both in vitro and in vivo;
• Knockdown of APP expression in breast cancer cells induced the expression of cell cycle inhibitor (p27kip1) and apoptosis markers; and
• APP regulate the IGF-1/AKT pro-survival pathway as silencing of APP in MDA-MB231 cells lead to decreased phosphorylation of AKT upon IGF-1 stimulation and also significantly reduced the phosphorylation of AKT substrate, FOXO.

I think these are all important findings especially in the context of APP biology and its emerging role in cancer progression. All the experiments are carefully done with appropriate controls. I have few minor comments:

1) In the materials & methods sections, the authors should provide the complete information on all the antibodies used. This will help the readers.
2) In some of the western blots (like Fig 1C, Fig 2B, Fig 3A and 3B and Fig 5), the protein size marker is missing, and that should be included.
3) In Figure 1C (top panel) blot, the author should comment why there are two bands immunoreactivity for anti-APP Ab.
4) I’m not convinced with the blot shown in Fig 5A. I’m not so sure whether EGF stimulation has worked in this case.

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:

I declare that I have no competing interests.