Author's response to reviews

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

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Dear Editor,

Please find enclosed our manuscript “Amyloid-β Precursor Protein Promotes Cell Proliferation and Motility of Advanced Breast Cancer” that we submit for publication as a research article in *BMC Cancer*.

The function of amyloid-β precursor protein (APP) is extensively studied in neuronal cells and has been identified as a responsible molecule for Alzheimer disease. Recently, the potential role of APP has been proposed in several types of cancer such as pancreatic, lung, and colon cancer. In previous studies, APP expression was elevated in those types of cancer and the role of APP was defined as a growth-stimulating molecule; however, the underlying molecular mechanisms in the regulation of signaling pathways and gene regulation have not been fully understood.

In the current work, we explored the pathological significance of APP in breast cancer and its underlying molecular mechanism. We found that the expression of APP is increased in a panel of mouse and human breast cancer cell lines, especially in the cell line possessing higher metastatic potential. In addition, the analysis of human breast cancer tissues revealed a significant correlation between the level of APP and the stage of tumor development. Moreover, knock-down of APP(APP-kd) in breast cancer cells caused the retardation of cell growth *in vitro* and *in vivo*, with both the induction of p27kip1 and caspase-3-mediated apoptosis. Such anti-tumorigenic effects of APP knock-down partially came from reduced pro-survival AKT activation in response to IGF-1, leading to activation of key signaling regulators for cell growth, survival, and pro-apoptotic events such as GSK3-β and FOXO1.

These findings are the first to demonstrate the underlying molecular mechanism through which APP regulates breast cancer cell growth, migration, and invasion. We believe that these findings provide novel insights into the pathogenic role of APP and its mechanism in cancer.

We look forward to hearing from you on the disposition of this manuscript.

Sincerely,

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