Author's response to reviews

Title: Neural protein gamma-synuclein interacting with androgen receptor promotes human prostate cancer progression

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Dear Editor:

We would like to submit the manuscript entitled “Neural protein gamma-synuclein (SNCG) interacting with androgen receptor promotes human prostate cancer progression”, which we wish to be considered for publication in Molecular Cancer.

The incidences of prostate cancer are increasing rapidly worldwide, while mortality rates resulting from prostate cancer are stable. Metastasis is one of the hallmarks of advanced prostate cancer and contributes to high rates of morbidity and mortality in patients with this disease. Neural protein gamma-synuclein (SNCG) protein has been demonstrated to have a significant correlation with metastatic malignancies such as breast cancer. However, the in-depth investigation of SNCG in prostate cancer is lacking. In the present study, we first investigated the biological roles of SNCG in LNCaP cells in vitro and in vivo. Silencing SNCG by siRNA in LNCaP cells contributed to the inhibition of cellular proliferation, the mediation of cell-cycle arrest at G1 phase, the suppression of cellular migration and invasion in vitro as well as the decrease of tumor growth in vivo with the exception of castration mice. We found castration in the host mouse reduced SNCG protein expression in engrafted prostate cancer cells. Next, our mechanistic studies indicated that SNCG is a new androgen receptor (AR) coactivator. It interacts with AR and promotes cellular growth and proliferation of prostate cancer by activating AR transcription in an androgen-dependent manner. Interestingly, we demonstrate SNCG may be a hormone-related protein. Our results support the application of androgen-deprivation therapy (ADT) regimen in clinical for the treatment of advanced prostate cancer patients because ADT could reduce some androgen-induced risk factors, such as SNCG. Finally, immunohistochemical analysis in a tissue array revealed that SNCG protein was almost undetectable in normal or
benign human prostate tissues. However, it elevated in metastatic PCa tissues. Overexpression of
SNCG was significantly correlated with peripheral and lymph node metastases. We suggest
SNCG may serve as an early diagnosis biomarker for predicting human prostate cancer
progression and metastasis. It also would become as a novel target for anticancer therapy in
advanced prostate cancer. For these reasons, we hope this work is suitable for your journal.

We confirm that this manuscript has been prepared in accordance with Molecular Cancer for
authors, and that the manuscript meets the requirements as outlined in the submission checklist.
All authors have participated in the preparation of the original article. The manuscript has not
been published previously, and has not been considered for publication elsewhere, either in
whole or in part or in any other language. None of the authors has any conflict of interest with
any organization or company to disclose.

We deeply appreciate your consideration of our manuscript, and we look forward to receiving
comments from the reviewers. If you have any queries, please don’t hesitate to contact me at the
address below.

Thank you and best regards.

Yours sincerely,

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