Author's response to reviews

Title: Latexin is downregulated in human carcinomas of gastric body and cardia and exhibits tumor suppressor potential

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Dear Sir or Madam:

Enclosed please find the manuscript titled “Latexin is downregulated in human carcinomas of gastric body and cardia and exhibits tumor suppressor potential” for *BMC Cancer*. The latexin gene encodes the only known inhibitor of carboxypeptidase A in mammals and its physiological activities have been studied relatively little. As a result its effects on cell growth are only now being discovered. The fact that the latexin gene acts as a negative regulator of mouse stem cells and mouse lymphoma cell proliferation raise the possibility that this gene functions as a tumor suppressor. Our previous study also suggested there is a correlation between the latexin gene expression and malignant transformation of immortalized human gastric epithelial cells. In this work, we prepared monoclonal antibody against human latexin protein and examined latexin expression in human gastric body and cardia carcinomas, and further investigated whether ectopic latexin expression was sufficient to affect the proliferation of gastric cancer cells in vitro and in vivo. Our results showed reduced expression level of latexin protein in human gastric body and cardia carcinomas as compared with normal control tissues. Stable transfection of the latexin gene in human gastric cancer cells attenuated cell growth in vitro and in vivo. Conversely, gastric cancer cells transfected with antisense latexin gene exhibited enhanced capacity for colony formation and tumorigenicity in nude mice. Consistent with its tumor suppressor potential, ectopic expression of latexin gene induced differential expression of several tumor-related genes, including Maspin, WFDC1, SLPI, S100P, and PDGFRB, in gastric cancer cells. In addition, latexin gene expression in human cells was indicated to be deeply correlated with CpG methylation status of promoter region. Taken together, our results strongly suggest that the latexin gene is a potential tumor suppressor. These findings may open a door for understanding the physiological activity of the latexin gene and related molecular mechanisms in regulation of cell growth.

This whole work or substantial part of it has not been published in any scientific journals and is not submitted to others. This study was performed with the approval of the Ethics and the Academic committees of Peking University School of Oncology, and informed consent was obtained from all participants. All authors have read and agreed to its contents. No potential conflicts of interest were disclosed.

Thank you very much for your nice help.

With best wishes,

Sincerely yours,

Yang Ke, Professor

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