Author's response to reviews

Title: PKC alpha regulates netrin-1/UNC5B-mediated survival pathway in bladder cancer.

Authors:

Jiao Liu (546439049@qq.com)
Chui ze Kong (syliujiao@sohu.com)
Da xin Gong (2046401688@qq.com)
Zhe zhang (494222088@qq.com)
Yu yan Zhu (15840259855@163.com)

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Authors’ contributions

The study was conceived by JL, DG, YZ and CK. Experiments were carried out by JL, ZZ and CK. Statistical analysis was carried out by JL. Manuscript was written by JL. All authors read and approved the final manuscript.

Jiao LIU (546439049@qq.com)
Chui-ze KONG (syluijiao@sohu.com)
Da-xin GONG (2046401688@qq.com)
Zhe ZHANG (494222088@qq.com)
Yu-yan ZHU (15840259855@163.com)

Abstract

Background

Netrin-1 and its receptor UNC5B play important roles in angiogenesis, embryonic development, cancer and inflammation. However, their expression pattern and biological roles in bladder cancer have not been well characterized. The present study aims to investigating the clinical significance of PKC α, netrin-1 and UNC5B in bladder cancer as well as their association with malignant biological behavior of cancer cells.

Methods

Netrin-1 and UNC5B expression was examined in 120 bladder cancer specimens using immunohistochemistry and in 40 fresh cancer tissues by western blot. Immunofluorescence was performed in cancer cell lines. PKC α agonist PMA and PKC siRNA was employed in bladder cancer cells. CCK-8, wound healing assays and flow cytometry analysis were used to examine cell proliferation, migration and cell cycle, respectively.
Results

Netrin-1 expression was positively correlated with histological grade, T stage, metastasis and poor prognosis in bladder cancer tissues. Immunofluorescence showed elevated netrin-1 and decreased UNC5B expression in bladder cancer cells compared with normal bladder cell line. Furthermore, cell proliferation, migration and cell cycle progression were promoted with PMA treatment while inhibited by calphostin C. In addition, PMA treatment could induce while calphostin C reduce netrin-1 expression in bladder cancer cells.

Conclusions

The present study identified netrin-1/UNC5B, which could be regulated by PKC signaling, was important mediators of bladder cancer progression.