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Carboxyl terminus of Hsp70-interacting protein(CHIP) functions as a tumor suppressor and enhance the radiosensitivity in cervical cancer

Hui Yang, Qiaoli Wang, Shaobo Ke, Lei Yang, Yunman Luo, Lin Wu, Xiaojia Gao, Fuxiang Zhou, Yunfeng Zhou
Wuhan university, China

Cervical cancer recurrence and metastasis after radiotherapy is one of the main reasons lead to cervical cancer treatment failure. CHIP serves as a chaperone-associated Ubox-containing E3 ligase that can modulate a lot of tumor-related proteins and has been reported to act as an tumor suppressor in pancreative cancer, breast cancer, colorectal cancer and so on. But we know little about its roles in cervical cancer. In this study, we show a significant difference in the expression of CHIP between the normal squamous cervical epitheilia, high grade squamous intraepithelial lesions and invasive squamous cell carcinoma of the cervix tissues. Gene set enrichment analysis(GSEA) shows that the CHIP is related to cell cycle progression, cell apoptosis and DNA damage pathways. So we hypothesis that CHIP can modulate the radiosensitivity in cervical cancer. Here, we established two radioresisitant cervical cancer cell lines C33AR and HelaR by exposing their parental C33A and Hela cells to repeated X-ray irradiation with a total dose of 60Gy and 72Gy respectively. The radiosensitivity of these two pairs of radiosensitive and radioresistant cell lines were confirmed by clonogenic assays. We then examine the cell cycle distribution and cell apoptosis by flow cytometry and found that the radioresisitant cell lines prolonged G2 arrest and lesser apoptosis which compared to their parent cell lines after 6Gy X-ray irradiation. Furthermore, transwell, real-time PCR and TeloTAGGG telomerase PCR ELISA Kit were performed to examine cell invasion, telomere length and telomerase activity in these two pairs of cell lines separately and the C33AR and HelaR cell lines show a significant difference in cell invasion, telomere length and telomerase activity. In addition to this, real-time PCR and western blot were used to examine the expression of CHIP and hTERT respectively and show that the CHIP is low expressed in radioresistant cell lines, whearas the hTERT is high expression in radioresisitant cell lines. In order to further explore the relationship between CHIP, hTERT and radiosensitive, we use real-time PCR to detect the expression of CHIP and hTERT at different time points after 2Gy, 5Gy and 10Gy irradiations, the results show that the CHIP expression is accompany with the changing of hTERT, a few minutes after the high expression of hTERT, the CHIP is high expression and then the expression of hTERT is declined. Overexpression of CHIP in C33AR and HelaR cell lines show an enhancement of radiosensitivity and down regulate telomerase activity. These results showed that CHIP can be seen as a tumor suppressor and high expression of CHIP can enhance the radiosensitivity by negatively regulates telomerase activity. Hence, CHIP may served as a novel target radiosensitizer.

Biography

Hui Yang is a PhD candidate of Wuhan University, China. She took part in the group of Prof. Yunfeng Zhou who has been the head of Zhongnan Hospital of Wuhan University and research on the telomere/telomerase in anti-cancer therapy and radiation-guided gene therapy of cancer.

yanghui.whu@qq.com

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