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Loss of P53 facilitates invasion and metastasis of prostate cancer cells

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Abstract Prostate cancer is a lethal cancer for the invasion and metastasis in its earlier period. P53 is a tumor suppressor gene which plays a critical role on safeguarding the integrity of genome. However, loss of P53 facilitates or inhibits the invasion and metastasis of tumor is still suspended. In this study, we are going to explain whether loss of P53 affect the invasion and metastasis of prostate cancer cells. To explore whether loss of P53 influences the invasion and metastasis ability of prostate cancer cells, we first compared the invasion ability of si-P53 treated cells and control cells by wound healing, transwell assay, and adhesion assay. We next tested the activity of MMP-2, MMP-9, and MMP-14 by western blot and gelatin zymography. Moreover, we employed WB and IF to identify the EMT containing E-cad, N-cad, vimentin, etc. We also examined the expression of cortactin, cytoskeleton, and paxillin by immunofluorescence, and tested the expression of ERK and JNK by WB. Finally, we applied WB to detect the expression of FAK, Src, and the phosphorylation of them to elucidate the mechanism of si-P53 influencing invasion and metastasis. According to the inhibition rate of si-P53, we choose the optimized volume of si-P53. With the volume, we compare the invasion and metastasis ability of Du145 and si-P53 treated cells. We find si-P53 promotes the invasion and metastasis in prostate cancer cells, increases the expression and activity of MMP-2/9 and MMP-14. Also, si-P53 promotes EMT and cytoskeleton rearrangement. Further analyses explain that this effect is associated with FAK-Src signaling pathway. Loss of P53 promotes the invasion and metastasis ability of prostate cancer cells and the mechanism is correlated with FAK-Src signaling pathway. P53 is involved in the context of invasion and metastasis.

Keywords P53 · Invasion · Metastasis · EMT · Prostate cancer cells

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Introduction

The public health burden of prostate cancer is substantial. A total of 241,740 new cases of prostate cancer and 28,170 deaths from the disease are anticipated in the United States in 2012, making it the most frequent non-dermatologic cancer among U.S. males [1]. Invasion and metastasis of primary cancer are the major cause of death, and over 70 % of men have lymph node metastases at the time of diagnosis [2–5]. It accounts for 29 % of all male cancers and 9 % of male cancer-related deaths [1]. Therefore, there is an urgent need to explore novel targets for prostate cancer.

The tumor suppressor p53 is a well-known transcription factor controlling the expression of its target genes involved in cell cycle, apoptosis, and DNA damage [6, 7]. In about half of all human cancers, p53 is either lost or mutated in a way that compromises its function [8]. Two