Changes in Tumor Growth and Metastatic Capacities of J82 Human Bladder Cancer Cells Suppressed by Down-Regulation of Calreticulin Expression.

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ABSTRACT

Bladder cancer is a common urothelial cancer. Through proteomic approaches, calreticulin (CRT) was identified and proposed as a urinary marker for bladder cancer. CRT is a multifunctional molecular chaperone that regulates various cellular functions such as Ca(2+) homeostasis and cell adhesion. CRT is overexpressed in various cancers, but its mechanism of action in the development of bladder tumors remains unclear. We generated J82 bladder cancer cells lines that either stably overexpressed or knocked down CRT to investigate the physiological effects of CRT on bladder tumors. Compared with the transfected control vector cells, the knockdown of CRT suppressed cell proliferation, migration,

and attachment, whereas overexpression of CRT enhanced cell migration and attachment. We further demonstrated that the phosphorylation status of focal adhesion kinase and paxillin, important regulators of the focal adhesion complex, was also regulated in these cells. In contrast, phosphorylation of Src, a protein tyrosine kinase reported to be affected by CRT, was not significantly different between the control and CRT-RNAi groups. Most importantly, we observed that tumors derived from J82 CRT-RNAi cells were significantly smaller and had fewer metastatic sites in the lung and liver in vivo than did transfected control vector cells. In conclusion, our results suggest that alteration of CRT expression levels might affect bladder cancer progression in vitro and in vivo.

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