

FGF-8 is involved in bone metastasis of prostate cancer

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Prostate cancer is the most common malignancy in males in Western countries. Patients with advanced prostate cancer invariably suffer from bone metastases. These incurable metastases are nearly always osteoblastic (bone-forming). It is not known why prostate cancer cells have a predilection to bone. Recent data indicates that interactions between prostate cancer cells and osteoblasts or their precursors are essential for formation of bone metastases. FGF-8 is widely overexpressed in prostate cancer. We have previously shown that FGF-8 produced by cancer is a novel regulator of osteoblast differentiation. The aim of this study was to examine the role of FGF-8 in bone metastasis of prostate cancer by an in vivo mouse model of bone metastasis and by immunohistochemical staining of samples of metastatic tumor tissue of prostate cancer patients.

We used immunohistochemistry to study FGF-8b, the most transforming isoform of FGF-8, in tissue array samples of prostate cancer bone metastases. We next injected PC-3 prostate cancer cells transfected with FGF-8b (PC-3/FGF-8b) or a control vector (PC-3/Mock) intratibially into nude mice. The occurrence of bone lesions was monitored weekly with small animal X-ray (Faxitron). 4 weeks after the cancer cell injection tibiae and tissue samples were collected for histological analysis. 3D structure of the intratibial tumors is currently being analyzed with micro-CT.

Immunohistochemical analysis of tissue array samples showed that 78 % of bone metastasis samples (n=27) were positive for FGF-8b. PC-3/FGF-8b intratibial tumors were radiographically visible earlier compared to PC-3/mock intratibial tumors and larger than PC-3/Mock tumors at the end of the experiment. Histological analysis showed that both osteoblastic and osteolytic activity was present around the intratibial tumors. The results demonstrate that there is expression of FGF-8 in bone metastases of human prostate cancer and that expression of FGF-8 in PC-3 prostate cancer cells increases their growth as intratibial tumors in an in vivo model of prostate cancer metastasis.