PROSTATE CANCER

Under pressure—physical force promotes tumour growth

New data, published in *Cancer Research*, have shown that tumour-generated pressure in the bone microenvironment can promote the growth of prostate cancer bone metastases.

Sottnik and colleagues report the first evidence that tumour modulation of their microenvironment can enhance cancer progression in bone through physical force. *In vivo* mice studies revealed that prostate cancer tumours growing in bone significantly increased intramedullary pressure, raising it to approximately 40 mmHg from a baseline of about 20 mmHg. These *in vivo* measurements were then used to investigate the effects of increased pressure on prostate cancer cells and osteocytes (which co-ordinate bone remodelling by releasing biochemical mediators) *in vitro*.

Pressure increased the viability of osteocytes but not prostate cancer cells; however, the viability of cancer cells increased when they were grown in conditioned media from pressurized osteocytes. Analysis of the cytokine

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profile of preconditioned media from osteocytes grown at 0 mmHg, 20 mmHg and 40 mmHg revealed several factors with altered expression. Neutralization experiments showed that CCL5 was important for cancer cell migration and invasion. Application of pressure to

osteocytes induced a dose-dependent increase in CCL5 RNA and protein expression. Pressurization also increased osteocyte secretion and activation of MMP2 and addition of CCL5 to osteocyte media also increased MMP expression. Inhibition of MMPs present in osteocyte-conditioned media reduced the invasive ability of prostate cancer cells.

These results suggest that physical force could induce MMP expression, partly through increased CCL5 expression in osteocytes, and these factors can then promote prostate tumour growth in bone. Further research could help to identify protumorigenic pressure-induced pathways and lead to therapies targeted at manipulating these pathways or modulating the pressure in the tumour microenvironment.

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Original article Sottnik, J. L. *et al.* Tumor-induced pressure in the bone microenvironment causes osteocytes to promote the growth of prostate cancer metastases. *Cancer Res.* doi:10.1158/0008-5472.CAN-14-2493