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PROSTATE CANCER

ROLE FOR EGFR & HER2 IN BONE METASTASIS

ErbB family members ErbB1 (EGFR) and ErbB2 (HER2) are involved in prostate cancer metastasis to the bone, according to new data published in *Cancer Research*.

ErbB receptor tyrosine kinases are implicated in prostate cancer development, progression to castration resistance and metastasis, but the mechanisms underlying their function in these processes have not been fully clarified. Mark Day from the University of Michigan and colleagues evaluated how HER2 and EGFR might contribute to prostate cancer metastasis.

Immunohistochemical analysis of tissue microarrays showed that HER2 and EGFR were overexpressed in prostate cancers compared with normal prostate tissue. The increased HER2 protein levels were not caused by an increase in *ERBB2* gene copy number, but correlated with expression of receptor activator of NF-κB (RANK), which is thought to have a role in cancer progression and HER2 regulation.

Using two C4-2B cell populations that either expressed high or low HER2 and EGFR levels, the researchers showed that sphere formation was dependent on high EGFR expression levels but was independent of HER2 levels, suggesting that cells with high EGFR levels might be involved in metastasis. The team then tested EGFR expression on circulating tumour cells (CTCs) from 10 men with metastatic prostate cancer and bone involvement and found $EGFR^+$ CTCs in 9 of these men.

In intratibial C4-2B tumour xenografts, pharmacological inhibition of HER2 and EGFR resulted in smaller tumours and staining for cytokeratin 8, RANK and Ki-67 indicated loss of C4-2B cells and proliferation.

Clemens Thoma

ORIGINAL ARTICLE Day, K. C. *et al.* HER2 and EGFR overexpression support metastatic progression of prostate cancer to bone. *Cancer Res.* http://dx.doi.org/10.1158/0008-5472.CAN-16-1656 (2016)