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TMPRSS2:ERG gene fusion expression regulates bone markers and enhances the osteoblastic phenotype of prostate cancer bone metastases

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Abstract

Prostate cancers have a strong propensity to metastasize to bone and promote osteoblastic lesions. *TMPRSS2:ERG* is the most frequent gene rearrangement identified in prostate cancer, but whether it is involved in prostate cancer bone metastases is largely unknown. We exploited an intratibial metastasis model to address this issue and we found that ectopic expression of the *TMPRSS2:ERG* fusion enhances the ability of prostate cancer cell lines to induce osteoblastic lesions by stimulating bone formation and inhibiting the osteolytic response. In line with these *in vivo* results, we demonstrate that the TMPRSS2:ERG fusion protein increases the expression of osteoblastic markers, including Collagen Type I Alpha 1 Chain and Alkaline Phosphatase, as well as Endothelin-1, a protein with a documented role in osteoblastic bone lesion formation. Moreover, we determined that the TMPRSS2:ERG fusion protein is bound to the regulatory regions of these genes in prostate cancer cell lines, and we report that the expression levels of these osteoblastic markers are correlated with the expression of the TMPRSS2:ERG fusion in patient metastasis samples. Taken together, our results reveal that the *TMPRSS2:ERG* gene fusion is involved in osteoblastic lesion formation induced by prostate cancer cells.