

A 45-kDa ErbB3 secreted by prostate cancer cells promotes bone formation

鄭建睿

Lin SH;Cheng CJ;Lee YC;Ye X;Tsai WW;Kim

J;Pasqualini R;Arap W;Navone NM;Tu SM;Hu

摘要

Abstract

ErbB3 is a transmembrane growth factor receptor that has been implicated in the pathogenesis of human cancer. After finding that a truncated form of ErbB3 was present and upregulated in metastatic prostate cancer cells in lymph nodes and bone, we explored the pathophysiological functions of this unusual form of ErbB3 in the context of mouse calvaria as well as osteoblasts in vitro and the femur microenvironment in vivo. Here we demonstrate that prostate cancer cells expressed an alternatively spliced transcript that encodes a 45-kDa glycosylated protein (p45-sErbB3). The recombinant p45-sErbB3 purified from conditioned medium stimulated calvarial bone formation and induced osteoblast differentiation. Overexpression of p45-sErbB3 in the osteolytic prostate cancer cell line PC-3 converted its phenotype from bone-lysing to bone-forming upon injection into the femurs of immunodeficient mice. Further, we detected sErbB3 in plasma samples from patients with castration-resistant prostate cancer with bone metastasis. These observations establish that p45-sErbB3 is a structurally and functionally unique gene product of ErbB3 and suggest that p45-sErbB3 is likely one of the factors involved in the osteoblastic bone metastases of prostate cancer.