Bone Microenvironment and Androgen Status Modulate Subcellular Localization of ErbB3 in Prostate Cancer Cells

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摘要

Abstract

ErbB-3, an ErbB receptor tyrosine kinase, has been implicated in the pathogenesis of several malignancies, including prostate cancer. We found that ErbB-3 expression was up-regulated in prostate cancer cells within lymph node and bone metastases. Despite being a plasma membrane protein, ErbB-3 was also detected in the nuclei of the prostate cancer cells in the metastatic specimens. Because most metastatic specimens were from men who had undergone androgen ablation, we examined the primary tumors from patients who have undergone hormone deprivation therapy and found that a significant fraction of these specimens showed nuclear localization of ErbB3. We thus assessed the effect of androgens and the bone microenvironment on the nuclear translocation of ErbB-3 by using xenograft tumor models generated from bone-derived prostate cancer cell lines, MDA PCa 2b, and PC-3. In subcutaneous tumors, ErbB-3 was predominantly in the membrane/cytoplasm; however, it was present in the nuclei of the tumor cells in the femur. Castration of mice bearing subcutaneous MDA PCa 2b tumors induced a transient nuclear translocation of ErbB-3, with relocalization to the membrane/cytoplasm upon tumor recurrence. These findings suggest that the bone microenvironment and androgen status influence the subcellular localization of ErbB-3 in prostate cancer cells. We speculate that nuclear localization of ErbB-3 may aid prostate cancer cell survival during androgen ablation and progression of prostate cancer in bone. (Mol Cancer Res 2007;5(7):675 – 84)