

Up-regulation of MDA-BF-1, a secreted isoform of ErbB3, in metastatic prostate cancer cells and activated osteoblasts in bone marrow

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摘要

Abstract

Prostate cancer (PCa) has a propensity to metastasize to bone. The identification of molecules that mediate the biological interactions between PCa cells and the bone environment is crucial to the understanding of PCa bone metastasis. The present study has used protein purification to identify bone metastasis-related factors present in bone marrow aspirates from PCa patients with bone metastasis. MDA-BF-1 was the first bone metastasis factor to be identified and is a secreted isoform of the ErbB3 growth factor receptor. To determine which cell types in PCa bone metastases express MDA-BF-1, MDA-BF-1 expression was studied in both primary and metastatic PCa cells, using an antibody to the extracellular domain (Ab10) and another to the cytoplasmic domain (RTJ.2) of ErbB3 to distinguish MDA-BF-1 from p180-ErbB3. It was found that epithelial cells in primary PCa did not express MDA-BF-1. In contrast, epithelial cells in 41 of 45 PCa metastases (18 of 19 lymph node metastases and 23 of 26 bone metastases), and activated osteoblasts in bone metastases, expressed MDA-BF-1. In addition, newly formed bone matrices adjacent to activated osteoblasts were also immunopositive for MDA-BF-1, suggesting that activated osteoblasts secrete MDA-BF-1. These observations indicate that MDA-BF-1 is up-regulated in metastatic PCa and raise the interesting possibility that MDA-BF-1 may play a role in the metastasis and progression of PCa, particularly in bone. Copyright 2004 Pathological Society of Great Britain and Ireland. Published by John Wiley & Sons, Ltd.