CORRESPONDENCE

Re: Preferential Adhesion of Prostate Cancer Cells to a Human Bone Marrow Endothelial Cell Line

In their recent article, Lehr and Pienta (1) demonstrate that prostate cancer cells preferentially adhere to human bone marrow endothelial cells (HBME-1) through integrin-mediated mechanisms. They mainly base this conclusion on experiments in which the blocking effect of a panel of agents (almost exclusively antibodies) on the adhesion of the prostate cancer cell line PC-3 to HBME-1 was analyzed (1; Fig. 3). Here they show that an antibody against ‘‘pan-cadherin’’ could not interfere with endothelial adhesion of PC-3 cells.

However, this negative result for cadherins has to be reconsidered in light of the fact that PC-3 cells are known to carry a homozygous deletion of a large portion of the α-catenin gene, resulting in a complete loss of α-catenin at the RNA and protein levels (2). As α-catenin is an integral part of the cadherin/catenin complex and directly mediates the link of adherens junction proteins to the actin cytoskeleton (3), PC-3 cells have been characterized as functionally deficient in E-cadherin-dependent cell–cell adhesion (2). A loss of E-cadherin in prostate cancer has been associated with dedifferentiated tumors (4), increased lymphatic metastasis (5), and poor clinical prognosis (6).

So far, no detailed analysis has been performed on the functional importance of cadherins for the development of bone metastasis in prostate cancer. While the work of Lehr and Pienta nicely indicates some potential mechanisms involved in the preference of prostate cancer cells for the bone marrow microenvironment, the PC-3 cell model system employed makes it difficult to address the contribution of cadherins to this clinically important phenomenon. Perhaps a future modification of the authors’ successfully established in vitro system, employing cadherin-competent cell lines, might address the pathophysiological role of cadherins in bone metastasis originating from prostate cancer.

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References


Notes

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Response

We appreciate the comments of Drs. Grothey and McCrea. The authors suggest that we demonstrate that prostate cancer cells preferentially adhere to human bone marrow endothelial cells (HBME-1) ‘‘through integrin-mediated mechanisms.’’ On the contrary, we emphasize that we do not know what mediates this adhesion event. The process of prostate cancer metastasis to bone is a complex, multistep phenomenon. The adhesion of prostate cancer cells to bone marrow endothelial cells is most likely at least a two-step event involving ‘‘docking’’ and ‘‘locking’’ events. We agree that the functional significance of cadherins in the development of bone metastasis in prostate cancer is unclear. We found that the pan-cadherin antibody did not interfere with the binding of DU-145 and TSU to endothelial cells. However, we do not know the status of α-catenin or E-cadherin in these prostate cancer cell lines (unpublished data). Our system should help answer these questions.

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