

VIEWPOINT

Under-Investigated Area in Prostate Cancer: Cross Talk Between the Bone Microenvironment and Prostate Cancer Bone Metastasis[†]

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It is estimated that in 2003, there will be 220,900 new cases of prostate cancer and 28,900 estimated deaths [American Cancer Society, 2004]. In patients with advanced prostate cancer, the incidence of bone metastasis is extremely high, which contributes heavily towards morbidity and mortality. The debilitating symptoms of bone metastasis include bone pain, spinal cord compression, pathological fractures, partial paralysis, hypercalcemia, and eventual death. Recognizing this, the United States Congress in the FY2001 National Cancer Institute's Budget, encouraged the NCI "to conduct research to develop a better understanding of the unique role the bone microenvironment plays in metastasis of cancer to bone, in particular breast cancer, prostate cancer, and myeloma, including the development of animal models of bone metastasis and identification of novel therapeutic targets and modalities to prevent and treat bone metastasis." Subsequent NCI budgets, in FY 2002 and FY 2003 convey a similar emphasis to encourage research in this area.

The NCI organized several "think tank" style workshops focused on tumor–host interactions and the role of proteases in cancer with special sessions devoted to bone metastasis [Matrisian et al., 2001, 2003]. In addition, a special multidisciplinary workshop on understanding the molecular mechanisms of bone metastasis was

organized to assess: (a) the current state-of-the-science on the available experimental models to study bone metastasis, (b) the current knowledge about the molecular mechanisms of tumor–bone stroma interaction, and (c) critical unresolved issues in tumor metastasis to the bone. Speakers and participants agreed that areas of high priority included identifying unique features of bone that encourage homing of tumor cells, delineating the role played by growth factors and cytokines in this process, elucidating the bidirectional interactions between tumor and bone stroma and exploiting the resulting information for diagnostics or therapeutics [Reddi et al., 2003].

The study of tumor–host interactions continues to be an area of high priority for the NCI [The Nation's Investment in Cancer Research, 2004, 2005]. Several initiatives to provide funds for NCI-funded grantees to pursue this area of science have been awarded, and a recent initiative, "Molecular Interactions between Tumor Cells and Bone" supported by three NIH institutes has also been funded to promote research in this under-funded area.

The following three "Prospect" articles focus on providing comprehensive reviews written by experts. The articles examine prostate cancer metastasis to the bone, covering the basic biology, clinical aspects, and animal models; the role of extracellular matrix, cell adhesion molecules, proteases, growth factors and cytokine signaling, steroid hormones and immune aspects, and the bidirectional interactions between tumor–bone stroma in bone metastasis.

Overall, these timely papers will provide a comprehensive overview of the current understanding and management of prostate cancer skeletal metastases.

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