

VIEWPOINT

## Advances in Prostate Cancer Research

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These state-of-the-art Prospect articles on Prostate Cancer offer a series of novel perspectives on the current status of prostate cancer research, and provide a framework for study to tutored as well as untutored scientists. Research on prostate cancer has made significant progress in the last few years, although this disease continues to be a leading cause of death among men in the United States and Western Europe. In 2002, an estimated 189,000 men were diagnosed with prostate cancer and there were an estimated 30,200 deaths due to this disease [Nelson et al., 2003].

The series of Prospect articles which follows is divided into three Parts to be published in three separate issues: Part I emphasizes new discoveries in the area of the basic mechanisms of Prostate Cancer; Part II elucidates translational and clinical studies that concern this disease. Finally, Part III highlights our current knowledge in an underinvestigated area of study: the cross-talk between bone microenvironment and prostate cancer bone metastases. An overview of Parts II and III will accompany the two groups of articles (Clinical and Translational Prospects and Prostate Cancer Bone Metastases Prospects, respectively) and will be presented in subsequent issues. Additional Prospects will be published separately in subsequent issues of the *J. of Cellular Biochemistry* in 2004. Page constraints prevent a comprehensive coverage of the progress made in this area of research.

Part I covers a broad range of topics and describes the progress recently made in the

study of the molecular mechanisms that contribute to prostate cancer progression. Classic topics in prostate cancer research such as alterations of the androgen receptor signaling pathways (see Prospects by Miyamoto et al., and by Weber and Gioeli) or dysregulation of expression of extracellular matrix proteins, their “integrin” receptors and their downstream pathways (see Prospects by Demetriou and Cress, by Nagle, and by Slack-Davis and Parsons) are analyzed here from a unique molecular perspective. The focus of the discussion is on the molecular players that allow cancer cells to cope with the absence or presence of androgen, with an abnormal integrin repertoire and with interactions with different extracellular matrices.

Additional molecular mechanisms' abnormalities are examined within the context of cancer cells' ability to circumvent a hostile environment. The emerging concepts that fatty acid metabolism contributes to prostate cancer cell proliferation and apoptosis and that cholesterol accumulation in lipid rafts modulates prostate cancer cell functions are reviewed by Baron et al. and by Freeman and Solomon, respectively. The Prospect by Guseva et al. focuses on aberrant apoptotic pathways in prostate cancer with emphasis on NF $\kappa$ B signaling; this timely topic is also extensively reviewed from a different viewpoint by Suh and Rabson. It should be stressed that the hypothesis that new therapeutic targets can be generated by studying the above mentioned pathways already has won wide appeal and also is rigorously discussed in these articles.

Novel aspects of alterations of role and expression of galectin as well as of growth factor pathways, specifically VEGF and BMP, are covered by Oka et al., by Nicholson and Theodorescu and by Brubaker et al., respectively. Nicholson and Theodorescu also offers an extensive overview of the molecular mechanisms of tumor angiogenesis in prostate cancer.

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Taken together, these articles establish a firm molecular connection between dysregulated expression of soluble factors, extracellular and intracellular proteins and accelerated prostate cancer progression.

Furthermore, a potential association between BPH and prostate cancer, a problem that remains to be completely solved, is addressed by Shah and Getzenberg using gene expression analysis, and the significance of changes in the nucleolar and nuclear envelopes in prostate cancer is discussed by Fischer et al.

Part I concludes with an analysis of an important technical issue in prostate cancer research: the need to characterize at a molecular level primary cultures from human prostate tissues (see Prospects by Peehl, and by Uzgare et al.).

Overall, these Prospect articles highlight the advances made in prostate cancer research and carefully describe the blackholes of this area of study. Several questions arise and are

addressed by the Authors: how does a neoplastic prostate cell cope with a hostile environment? How can we circumvent the insidious ability of prostate cancer cells to invade and grow in distant sites? Can a unifying hypothesis be formulated on prostate cancer etiology based on our current knowledge? Are the basic and clinical aspects of this area of research poised for integration? The answers provided in these articles are, in several instances, quite provocative and identify novel areas of interdisciplinary research in prostate cancer. In conclusion, in a series of stimulating discussion sections of their articles, the Authors cast a unique light on new potential therapeutic targets and raise concerns both about current therapeutic modalities and about diagnostic tools.

#### REFERENCE

Nelson WG, DeMarzo AM, Isaacs WB. 2003. Mechanisms of Disease, Prostate Cancer. *New England J Med* 349: 366–381.