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VIEW POINT

Advances in Prostate Cancer Research Part-II

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We present here the second in a series of three groups of "Prospect" articles on Prostate Cancer focusing on the translational and clinical aspects of prostate cancer research.

As mentioned in Part I, the Prospect articles on prostate cancer have been compiled in three groups to be published in three separate issues: Part I (see *Journal of Cellular Biochemistry, Volume 91(1), January 2004*) emphasized new discoveries in the area of the basic mechanisms of Prostate Cancer; Part II, in this issue, elucidates the translational and clinical aspects concerning the disease. Part III, in a forthcoming issue, will highlight our current knowledge about the cross-talk between the bone microenvironment and prostate cancer bone metastases.

Part II covers a broad range of translational and clinical topics that reflect the current status of prostate cancer research. The authors elucidate recent progress in diagnostic and therapeutic areas; they point out the strengths and the weaknesses of individual targets and suggest alternative approaches and areas of improvement. These outstanding Prospect articles provide aficionado and non-aficionado scientists with a roadmap into the translational and clinical understanding of the genetic as well as the environmental factors that contribute to prostate cancer. Basic scientists as well as clinician scientists will benefit from the stimulating discussions provided here.

The Prospect article by FitzGerald and colleagues highlights new ideas for translational research and thoroughly reviews current therapeutic modalities for prostate cancer. Surgery, radiation therapy and hormone therapy are carefully analyzed in this article. In the following Prospect, Meuillet and colleagues center their discussion on the potential of selenium for cancer prevention and provide an update on preclinical findings and current clinical trials including the SELECT NCI trial, scheduled to be completed in 2013.

The emerging concept that a "chronic epithelial injury" is responsible for prostate cancer is reviewed by DeMarzo and colleagues. Implications of this hypothesis with regard to diagnosis, detection, prevention and treatment are discussed in this article.

The Prospects by Rubin and Kantoff, and Taplin and Balk review two important aspects of the role of androgen and androgen receptor in prostate cancer progression. Rubin and Kantoff analyze the implications of the Prostate Cancer Prevention Trial results, where finasteride, a drug that blocks conversion of testosterone to dihydrotestosterone, was shown to prevent or delay the detection of prostate cancer but also to increase the risk of high-grade tumors; the authors raise concerns about treatments that aim to inhibit androgen-activated pathways. Taplin and Balk review the androgen receptor alterations that occur and are responsible for androgen- independent prostate cancer progression. This Prospect provides a broad range perspective of this issue from the molecular basis of these alterations to their clinical significance.

The Prospect articles that follow focus on the translational aspects of the molecular players that contribute to prostate cancer progression. These articles establish a firm molecular connection between prostate cancer progression and deregulated expression and/or function of

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each of the following: estrogens; the pro-apoptotic molecule, Par-4 (prostate apoptosis response-4); the differentiation regulator PPAR (peroxisome proliferator-activated receptor)-gamma; the cell surface protein, PSMA (prostate specific membrane antigen; see Prospects by Ho, Gurumurthy and Rangnekar, Jiang et al., Ghosh and Heston). In some instances the Authors examine the relevance of these molecules to imaging; in other instances, to therapy. 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 this, too, is rigorously discussed in these articles.

An elegant overview of the literature on GST (glutathione S-transferase) P1 hypermethylation due to epigenetic alterations as a molecular biomarker for prostate cancer screening, detection and diagnosis is presented by Nakayama and colleagues.

Part II concludes with a timely topic: a critical analysis of the epidemiological parameters used in prostate cancer studies in the "PSA (prostate specific antigen) era" (see Prospect by Platz et al.). The article also highlights the controversy about the use of appropriate controls in these studies and the problems generated by the "enriched" number of prostate cancer cases diagnosed in the PSA era, and offers solutions to cancer misclassification.

In conclusion, in Part II, the authors highlight new potential therapeutic targets and raise concerns both about current therapeutic modalities and about diagnostic tools. As mentioned in the previous Viewpoint (see Part I), several questions arise and are addressed. In Part II, the most important issue for discussion—"Are the basic and clinical aspects of this area of research poised for integration?"—receives provocative answers and points to novel areas of interdisciplinary research in prostate cancer.