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INVITED COMMENT

Current and Proposed Biologic Markers in Prostate Cancer

Chemopreventive trials frequently employ intermediate endpoints that predict development of cancer. This approach is more practical than waiting for clinical development of cancer because a shorter time is needed to obtain results, particularly with relatively slow-growing tumors such as prostate cancer. However, the use of intermediate endpoints is limited by their predictive ability; this is a difficult problem with the prostate because we have limited knowledge of many potentially useful markers.

In this report, we outline many of the current and proposed markers in prostate cancer. This list should not be considered all-inclusive, but is presented as an introduction to possible intermediate endpoints which could be considered by those undertaking chemopreventive trials. Many of these markers may be more useful as prognostic factors following the diagnosis of cancer rather than predictive factors for the development of cancer.

Comparative analysis of most of these factors has not been done, so we are unable to recommend the most promising; however, we recognize that the "gold standard" for the diagnosis of prostatic adenocarcinoma remains histopathologic examination. Emphasis is placed on markers useful in tissue preparations, although some of these are useful in serum samples.

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(This list is incomplete, and is meant only as an introduction to these topics.)

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TABLE I. Biologic Markers in Prostate Cancer

Clinical and Pathologic Markers
- Tumor Volume [1]
- Tumor Stage [2–3]
- Tumor Grade (Gleason grade, nuclear grade) [4]
- Prostatic Intraepithelial Neoplasia [5]
- Atypical Adenomatous Hyperplasia [6]
- Hyperplasia/Metaplasia/Atrophy [7]
- Host Inflammatory Response [8]
- Morphologic Variants of Cancer [9–11]

Morphometric Markers
- Nuclear Abnormalities [12–13]
- Nucleolar Abnormalities [14]
- Chromatin Abnormalities [12]
- Nucleolar Organizer Regions [15]

Proliferation Markers
- Ki67 [16]
- PCNA [17]
- Thymidine Labeling [18]
- Bromodeoxyuridine Labeling [19]

Ploidy Analysis and Genetic Markers
- Ploidy Analysis [20]
- Loss of Heterozygosity
- Retinoblastoma Gene (RB-7) [21]
- p21 [22], p53 [23]
- Oncogenes (*ras*, *myc*, *fos*, *abl*, etc.) [24]
- Chromosomal Deletions, Mutations, etc. [25]
- c-*erbB*-2 [23]

Growth Factors
- TGF-ß [26]
- EGF and EGF Receptors [23]
- FGF and FGF Receptors
- IGF, NGF, PDGF, KGF, etc. [24]

Neuroendocrine Markers
- Chromogranin [27]
- Neuron Specific Enolase [27]
- Serotonin [27]
- Somatostatin [27]
- HCG [27]
- TSH [27]
- Glucagon [27]
- Calcitonin [27]
- Prolactin [27]
- Bombesin (GRP) [27]

Other Cytoplasmic Proteins
- Prostate Specific Antigen (PSA) [28]
- Prostatic Acid Phosphatase (PAP) [28]
- Leu-7 [29]
- Pepsinogen II (PG II) [29]
- Tissue Plasminogen Activator [29]
- Type IV Collagenase [30]
- Tissue Inhibitor Metalloproteinases
- Inhibin [31]
- Cathepsin B
- Polyamines
- Ornithine Decarboxylase
- 5'-Nucleotidase
- PD-41 Cancer-Associated Antigen [32]
- Glutathione S-Transferase π [33]

Hormone Receptors
- Androgen Receptors [34]
- Estrogen/Progesterone Receptors

Intermediate Filaments
- Cytokeratins [35]

Lectins
- *Ulex europaeus* (UEA-1) [36]
- *Concavalia ensiformis* (Con-A) [36]
- *Arachis hypogea* (PNA) [36]
- *Bandeirea simplificifolia* (BS-1) [36]
- *Dolichos biflorus* (DBA) [36]
- *Glycine maximus* (SBA) [36]
- *Triticum vulgaris* (WGA) [36]
- *Lens culinaris* (LCA) [36]
- *Ricinus communis* (RCA-1) [36]

Blood Group Antigens
- A and B [37]
- $Lewis^X$ Antigen [37]

Mucins
- Neutral Mucin [38]
- Acidic Mucin (Nonsulfated) [38]

Stromal Factors
- Neovascularity [39]
- Type IV Collagen [40]
- Laminin and Laminin Receptors [40]
- Fibronectin
- Heparin Sulfate Proteoglycan
- Other Extracellular Matrix Proteins (Integrins, Cadherins, etc.)

Other
- Cell Culture Characteristics [41]

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