Short Communications

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The Clinical Utility of Y-PSMA2 Monoclonal Antibody in the Detection of Primary and Peripheral Blood Metastatic Prostate Cancer

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Prostate-specific membrane antigen (PSMA) is a 100 Kd transmembrane glycoprotein originally defined by the murine IgG monoclonal antibody (mAb) **7E11-C5.3** with a type of prostate cancer cell line known as LNCap cells and is highly expressed in all forms of prostate tissue including benign secretory acinar epithelium, high grade prostatic intra-epithelial neoplasia (PIN), and prostate cancer.[1-6] The PSMA glycoprotein consists of three domains: a 19-amino acid intracellular domain, a 24-amino acid transmembrane region, and a 707-amino acid extracellular domain making up the bulk of the molecule. [1, 5]

PSMA is located on the short arm of chromosome 11 in a region that is not commonly deleted in prostate cancer.[1] It functions both as a folate hydrolase and a neuropeptidase that acts as a glutamate-preferring carboxypeptidase.[1]

Over the past two decades, monoclonal antibody technology has had an increasing impact on clinical diagnostic and therapeutic options, and this is true in the realm of managing prostate cancer. [2, 3]

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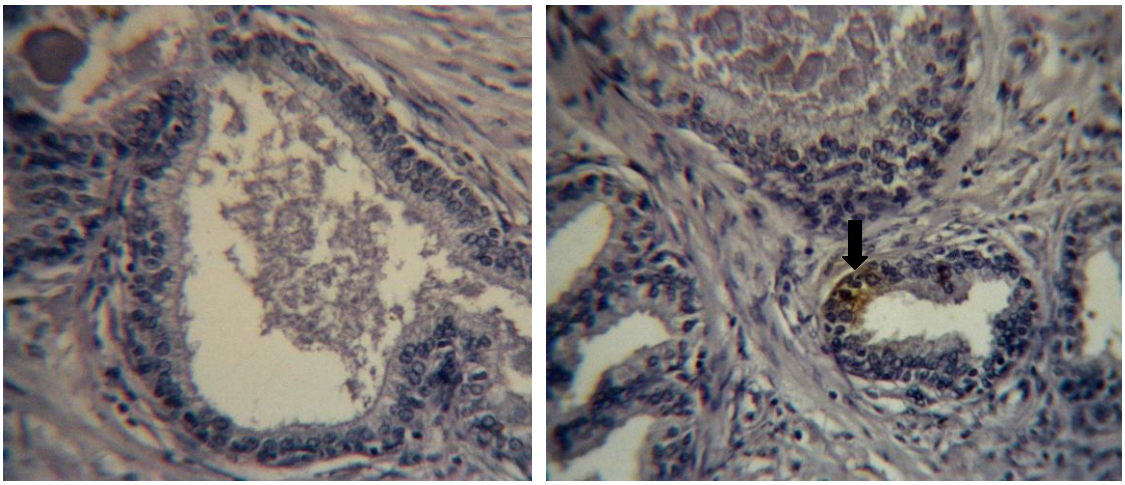
The monoclonal antibody **Y-PSMA2** is a primary IgG2bκ mouse anti-human PSMA recently developed by Abazyme LCC (MA, USA). The antibody is reactive with PSMA expressed prostate cancer LNcap cell lines

In the present study the immunohistochemical properties of Y-PSMA2 clone with primary prostate cancer tissue and its utility in the detection of hematogenous prostate cancer cell dissemination have been examined.

The Y-PSMA2 clone showed undetectable to extremely weak PSMA immunoreactivity with the 16 cases of benign prostatic hyperplasia (BPH, negative controls) examined but had consistent PSMA immunoreactivity with 14 of 16 cases (87.5%) of prostate adenocarcinoma showing the greatest extent and intensity with poorly differentiated prostate tumors (Figs.1&2). The antibody did not react with peripheral blood mononuclear and $CD34^{+}$ progenitor cells from healthy individuals (25 negative controls) indicating the absence of ectopic membrane PSMA expression in blood and eliminating false positives from such cells, but it detected circulating prostate cancer cells in all 10 cases of stage IV patients examined (Fig.3) thereby increasing its specificity for prostate cancer cells.

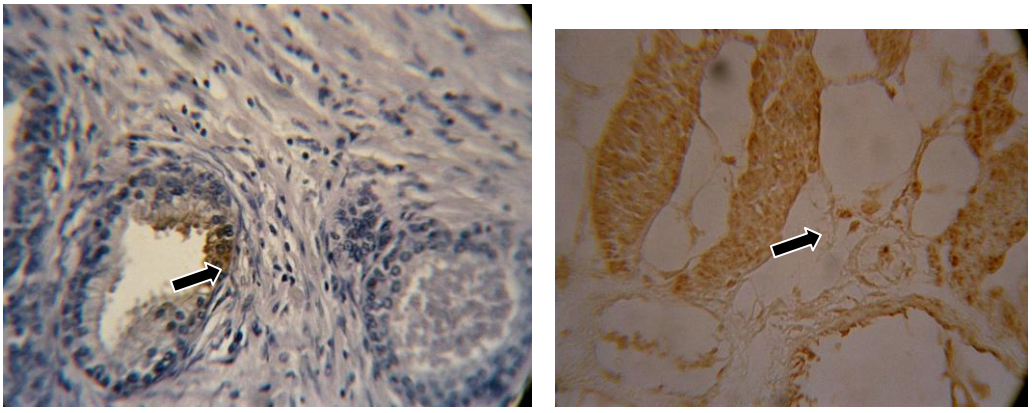
This study demonstrates the potential utility of Y-PSMA2 monoclonal antibody in the early detection of localized prostate cancer and in the detection of occult peripheral blood metastasis after radical prostatectomy allowing it to be useful as a tissue-based prostate carcinoma marker and as a peripheral blood metastatic surveillance marker during or after therapy.



A B

Fig. 1: A*. Undetectable prostate-specific membrane antigen (PSMA) immunoreactivity by immunohistochemistry (IHC) in a 72-year-old man with benign prostatic hyperplasia (BPH) [Y-PSMA2 antibody, immunoperoxidase with hematoxylin counterstain, 40X]. The same result with absent PSMA immunostaining was obtained without incubating the BPH tissue section with the primary antibody.*

B. *Prostate-specific membrane antigen (PSMA) immunoreactivity (Black arrow) detected by IHC in an 84-year old man with well-differentiated prostate adenocarcinoma [Y-PSMA2 antibody, immunoperoxidase with hematoxylin counterstain, 40X].*



A **B**

Fig. 2: A. *Positive PSMA immunostaining (Black arrow) detected by IHC in a 75-year-old man with well-differentiated prostate adenocarcinoma [Y-PSMA2 monoclonal antibody, immunoperoxidase with hematoxylin counterstain, 40X].*

B. *Intense PSMA immunoreactivity (Black arrow) detected by IHC in a 72-year-old man with poorly differentiated prostatic adenocarcinoma [Y-PSMA2 monoclonal antibody, immunoperoxidase, 40X].*

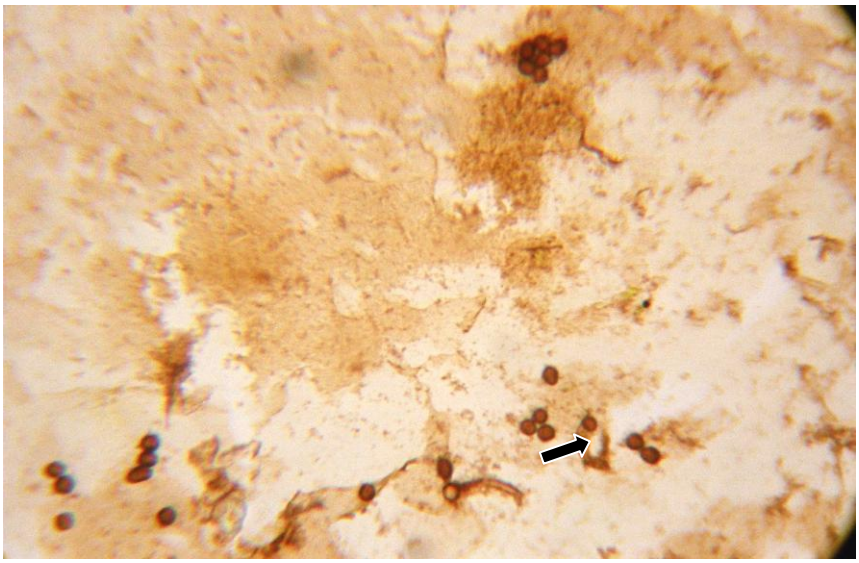


Fig. 3: *Detection of Hematogenous prostate cancer cell dissemination using Y-PSMA2 monoclonal antibody. In this peripheral blood mononuclear cell smear taken from a patient with Stage IV prostate cancer (Total PSA, 150 ng/ml), prostate carcinoma cells express PSMA and are clearly stained brown (Black arrow) by the indirect immunoperoxidase [ABComplex] method with Y-PSMA2 monoclonal antibody, 40X.*

References:

1. Chang S. (2004). Overview of prostate-specific membrane antigen. Reviews in Urology; 6 (Suppl 10): 13-18.

2. Chang S, N. Bander, W. Heston. (2000). Monoclonal antibodies: Will they become an integral part of the evaluation and treatment of prostate cancer? Curr. Opin. Urol., 9:391-395

3. Horoszewicz J, E. Kawinski, G. Murphy. (1987). Monoclonal antibodies to a new antigenic marker in epithelial cells and serum of prostatic cancer patients. Anticancer Res.; 7:927-936.

4. Israeli, R., C. Powel, J. Corr, W. Fair, and W. Heston, (1994). Expression of the prostate-specific membrane antigen. Cancer Res., 54:1807-1811.

5. Murphy, G.P., A. Elgamal, S. Su, D. Bostwick, and E. Holmes, (1998). Current evaluation of the tissue localization and diagnostic utility of prostate-specific membrane antigen. Cancer (Phila.), 83:2259-2269.

6. Wright, G.L., C. Haley, M. Beckett, and P. Schelhammer. (1995). Expression of prostate-specific membrane antigen in normal, benign and malignant prostate tissues. Urol. Oncol., 1:18-28.