

<b>Patient Name:</b> John Doe	<b>Requesting Physician:</b> David A. Smith, M.D.	<b>Collected:</b> 03/13/2009
<b>Sex:</b> Male	<b>Client/Group Facility:</b> Urology Associates, PA	<b>Received:</b> 03/20/2009
<b>Date of Birth (Age):</b> 10/10/1958 (50 years)	<b>Additional Recipient:</b> Mark Howard, M.D.	<b>Reported:</b> 03/23/2009
<b>SSN:</b> 212-22-2234	<b>Submitting Pathologist:</b> Tim Jackson, M.D.	<b>Case #:</b> C09-123445
<b>Patient ID:</b> 23445921	<b>Specimen ID:</b> 232323233	<b>Req #:</b>

## Prostate Cancer Gene 3 (PCA3) Assay

### CLINICAL HISTORY

Abnormal digital rectal examination (DRE). PSA 4.5 ng/mL.

### RESULTS

**PCA3 Score: 48 (POSITIVE)**

### REFERENCE RANGE

**Positive:** PCA3 Score (PCA3/PSA Ratio)  $\geq$  35  
**Negative:** PCA3 Score (PCA3/PSA Ratio)  $<$  35  
**Inconclusive:** Inadequate amount of PSA mRNA

### INTENDED USE

The PCA3 Assay is an *in vitro* nucleic acid amplification test (NAAT) that detects Prostate Cancer Gene 3 (PCA3) messenger ribonucleic acid (mRNA) in male urine specimens to generate a PCA3 Score. The PCA3 Score is intended for use in conjunction with standard-of-care diagnostic algorithms as an aid in the diagnosis and prognosis of prostate cancer.

### SUMMARY AND EXPLANATION OF TEST

The use of the serum prostate-specific antigen (PSA) test for prostate cancer screening has resulted in the biopsy diagnosis of smaller, previously undetected tumors (1), thus creating a new diagnostic dilemma: Only a fraction of men with increased serum PSA levels have detectable prostate cancer. Men with at least one negative biopsy often have persistently increased serum PSA, due primarily to enlarged prostates and benign prostatic hyperplasia (BPH). Yet, a significant proportion of men with slightly increased serum PSA (2.5-4.0 ng/L) either have, or will develop, clinically significant prostate cancer (1). While biopsy remains the gold standard for prostate cancer detection, more accurate tests with better specificity are needed to help guide decisions to biopsy the prostate. PCA3 (also known as "PCA3DD3" or "DD3PCA3") is a non-coding prostate specific mRNA that is highly over-expressed in prostate cancer cells, with a median 66-fold up-regulation compared to adjacent benign tissue (2). In contrast, PSA gene expression is similar in cancerous and benign cells; PSA mRNA levels may therefore be used to normalize for the amount of prostate-specific ribonucleic acid (RNA) in molecular test samples. The feasibility of quantitative PCA3-based molecular testing from urine sediments (2) and from whole urine (3) has been demonstrated. The PCA3 Assay utilizes whole urine collected following a digital rectal examination (DRE) consisting of three strokes per lobe. The DRE releases prostate cells through the prostate duct system into the urinary tract, where they can be collected in the first catch urine. The urine is processed by addition of Urine Transport Medium (UTM), which lyses the cells and stabilizes the RNA. PCA3 and PSA mRNAs are quantified, and the PCA3 Score is determined based on the ratio of PCA3/PSA mRNA. In addition to normalizing PCA3 signal, measurement of PSA mRNA also serves to confirm that the yield of prostate-specific RNA is sufficient to generate a valid result. Higher PCA3 Scores correlate with higher probability of a positive prostate biopsy.

### LIMITATIONS

The PCA3 Assay should not be used for patients who are taking medications known to affect serum PSA levels such as finasteride (e.g. Proscar, Propecia), dutasteride (e.g. Avodart), and anti-androgen therapy (e.g. Lupron, Zoladex). The effect of these medications on PCA3 gene expression has not yet been evaluated.

Certain therapeutic and diagnostic procedures such as prostatectomy, radiation, prostate biopsy, and others may affect the viability of prostatic tissue and subsequently impact the PCA3 Score. The effect of these procedures on assay performance has not yet been evaluated. Samples for PCA3 testing should be collected when the clinician believes prostate tissue has recovered.

Results from the PCA3 Assay should be interpreted in conjunction with other laboratory and clinical data available to the clinician.

### REFERENCES

1. Bussemakers, M., Van Bokhoven, A., Verhaegh, G., Smit, F., Karthaus, H., Schalken, J., Debruyne, F., Ru, N. and Isaacs, W.: DD3: A New Prostate-Specific Gene, Highly Overexpressed in Prostate Cancer. *Cancer Res.*, 59: 5975, 1999.
2. Hessels, D., Klein Gunnewiek, J., van Oort, I., Karthaus, H., van Leenders, G., van Balken, B., Kiemeny, L., Witjes, J., and Schalken, J.: DD3PCA3-based Molecular Urine Analysis for the Diagnosis of Prostate Cancer. *European Urology*, 44: 8, 2003.

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If you have any questions on this report please do not hesitate to contact the BioVantra client support center at (866) 627-8221.

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Pathologist Electronic Signature

03/23/2009  
Date