

GST-P1 and APC Gene Methylation

Diagnostic and prognostic information for prostate cancer

Prostate cancer is the most common cancer among men in the US.¹ Prostate-specific antigen (PSA) is the primary screening test, but a prostate biopsy is required for a definitive diagnosis. The pathology findings, including tumor grade and the extent of the cancer (Gleason score), determine patient prognosis and also influence therapeutic considerations. Biopsy techniques (including number of samples taken and areas sampled) can vary greatly.² Histopathology shows considerable inter-observer and intra-observer variability and may also be affected by sampling error, particularly as smaller core biopsies are used. In addition, a growing number of patients present with elevated PSA but no evidence of malignancy on biopsy findings. New markers for prostate cancer may provide the needed additional diagnostic and prognostic information.

Studies indicate that epigenetic alterations, such as DNA methylation, are significant events in prostate cancer. These changes can lead to cancer initiation, progression, invasion, or metastasis.³ Among those genes that most commonly demonstrate an aberrant methylation pattern in prostate cancer are glutathione S-transferase pi (GST-P1) and adenomatous polyposis coli (APC).

Attributes of GST-P1

- GST-P1 is the most frequently methylated gene in prostate cancer, occurring in as many as 95% of cases.⁴
- GST-P1 hypermethylation occurs at distinctly different frequencies within diagnosis categories, such as prostate cancer, high-grade prostatic intraepithelial neoplasia (HPIN), and benign prostatic hyperplasia (BPH).⁵
- Because GST-P1 methylation occurs at different frequencies within diagnosis categories, it is a useful adjunct to histopathology, providing additional and complementary information.

Combination of Gene Methylation Markers (GST-P1 with APC)

- APC is hypermethylated in as many as 90% of prostate cancers.⁶
- When both GST-P1 and APC are used on tissue samples, results are correlated with prognostic indicators, such as pathologic stage and Gleason score.^{2,5}
- Studies have shown that hyper-methylation of the promoter regions of the GSTP1 and APC genes occur at a significantly higher frequency in prostate cancer samples than in benign conditions of the prostate gland.
- When both GST-P1 and APC are used, the test provides increased sensitivity compared to either marker alone while maintaining high specificity,^{2,5} making the gene markers useful in cases where there is a clinical suspicion of prostate cancer.⁵⁻⁷

GST-P1 and APC Clinical Application

- **Potential application for “prostate dilemma” prognosis**
In men with elevated PSA and a negative biopsy, the use of a GST-P1 and APC combined assay may be useful in the assessment of a patient’s risk for prostate cancer.^{7,8} A positive result may indicate an elevated risk that a lesion was not sampled during the biopsy process and may be detected on a subsequent repeat biopsy; a negative result, because of the high negative predictive value associated with this assay, provides reasonable assurance that there is not an underlying lesion.
- **Added information for difficult histopathology cases**
GST-P1 and APC gene methylation provides high sensitivity and specificity for changes associated with prostate cancer, and it thus may be a useful adjunctive procedure for cases in which the pathology has atypical findings, although not definitive for prostate cancer. A positive gene methylation result is associated with an elevated risk of prostate cancer.
- **Prognostic information**
When used in conjunction with other tumor features, it may provide additional prognostic information in prostate cancer patients.



The methylation status of GST-P1 and APC provides an important tissue biomarker for prostate cancer.

DIANON Systems
A LabCorp Company

U S L A B S

Glutathione S-transferase Gene (GSTP1, pi-class) Methylation Assay

Special Instructions Please provide a copy of the pathology report. Please direct any questions regarding this test to Customer Service at 800-533-0567.

Specimen Formalin-fixed, paraffin-embedded tissue (FFPE)

Use Prostate cancer is the most common cancer in men and the second leading cause of cancer-related deaths in the United States. Due to the reportedly high false negative rate of initial biopsy results after an elevated PSA level, new approaches for improved detection in prostate cancer are needed. Several studies have shown that hyper-methylation of the promoter regions of the GSTP1 and APC genes occur at a significantly higher frequency in prostate cancer samples than in benign conditions of the prostate gland. For that reason, gene methylation assays may be used as an adjunct to histopathology for patients where prostate disease is considered. It has been shown that the methylation levels for genes, such as GSTP1, may increase with patient age. Therefore, age should be considered along with other clinical features in the interpretation of test results.

Limitations Preparation of DNA from tissue samples is dependent upon the quality of the provided specimen. Inadequate DNA extraction may occur in a significant number of paraffin-embedded samples.

Methodology Quantitative methylation-specific PCR

Please call DIANON client services at 800-328-2666 or US LABS client services at 800-710-1800, option 2 for the most current test information, including CPT codes, patient preparation, specimen collection information, and storage instructions.

DIANON also offers

- **TriView Pro IHC Stain**

Immunohistochemistry stain combining p63, CK903, and p504s on one slide to aid in the diagnosis of small foci of prostate cancer.

- **CaPDetect: PCA3™**

A noninvasive molecular amplification assay that detects and quantifies both PCA3 and PSA mRNA levels, providing a PCA3/PSA ratio score that can assist in determining whether a patient is at increased risk for developing prostate cancer.

Additional prostate cancer assays from DIANON include

- Circulating Tumor Cells
- Biomarkers/Hormones
- PSA Velocity

References

1. American Cancer Society. Cancer Facts & Figures 2008. Atlanta, Ga: American Cancer Society; 2008
2. Bastian PJ, Ellinger J, Wellmann A, et al. Diagnostic and prognostic information in prostate cancer with the help of a small set of hypermethylated gene loci. *Clin Can Res.* 2005;11:4097-4015.
3. Li LC, Carroll PR, Dahiya, R. Epigenetic changes in prostate cancer: implication for diagnosis and treatment. *J Natl Cancer Inst.* 2005;97:103-115.
4. Shulz WA, Hatina J. Epigenetics of prostate cancer. *J Cell Mol Med.* 2006; 10:100-125.
5. Jeronimo C, Henrique R, Hoque MO, et al. A quantitative promoter methylation profile of prostate cancer. *Clin Can Res.* 2004;10:8472-8478.
6. Yegnasubramanian S, Kowalski J, Gonzalgo ML, et al. Hypermethylation of CpG islands in primary and metastatic human prostate cancer. *Can Res.* 2004;64:1975-1986.
7. Kwabi-Addo B, Chung W, Shen L, et al. Age-related DNA methylation changes in normal human prostate tissues. *Clin Can Res.* 2007;13:3796-3802.
8. Trock B, Epstein J, McLeod D, et al. Use of DNA methylation to predict the absence of prostate cancer in men with high-risk and initially negative prostate biopsy. Abstract presented at: American Society of Clinical Oncology (ASCO) 2008 Genitourinary Cancers Symposium; February 14-16, 2008; San Francisco, Calif.

DIANON Systems
A LabCorp Company

US LABS

For more information, call your DIANON representative at 800-328-2666 or your US LABS representative at 800-710-1800.