GENETRACK Diagnostics

Prostate Specific Antigen (PSA)

WHAT IS PROSTATE SPECIFIC ANTIGEN (PSA)?
Prostate specific antigen (PSA) is a serine protease glycoprotein, which is predominantly produced in the prostate. Blood levels of PSA are a useful indicator of prostatic pathology, to evaluate men at risk of prostate cancer, and for assessment after treatment.

PURPOSE OF A PSA TEST
Prostate cancer is the most frequently diagnosed cancer and second leading cause of cancer deaths in men in the United States. Early diagnosis of small tumors that are confined to the prostate provides the best prognosis for recovery from prostate cancer. However, there are often no symptoms in the early stages of prostate cancer. Analyses of blood PSA levels are the most accurate and non-invasive way to detect prostate cancer, particularly in the early stages. These analyses are usually combined with, or followed up by, digital rectal examination.

ROLES OF PSA
In normal healthy individuals, PSA is secreted into the seminal fluid in high concentrations to liquefy seminal gel by proteolytic cleavage of gel-forming proteins. This helps to increase sperm mobility. A small amount of PSA is also normally found in the blood as a result of leakage from the prostate gland (1).

FORMS OF PSA
There are three major forms of PSA in the blood, two of which are detectable on current immunoassays. The predominant detectable form is PSA complexed with a serine protease inhibitor (alpha-1-antichymotrypsin). Free PSA is also present and detectable, and generally appears to be in an inactive form. The third form is complexed with alpha-2-macroglobulin, but it is not detectable with current immunoassays (1).

PSA AND PROSTATIC PATHOLOGY
High levels of PSA in the blood are associated with prostatic pathology, including prostatitis, benign prostatic hyperplasia (BPH), and prostate cancer (2). The differing levels of the two detectable forms of PSA are useful for distinguishing between individuals with BPH and prostate cancer, particularly in men with PSA levels between 4.1 and 10 ng/mL (3). Although both abnormalities result in increased blood PSA, the proportion of free PSA is much higher in individuals with BPH compared to prostate cancer patients (4).

PROSTATE CANCER
The prostate is a small walnut shaped gland in the pelvis of men. Prostate cancer is the most frequently diagnosed cancer and second leading cause of cancer deaths in men in the United States (5). There are often no symptoms in the early stages of prostate cancer. When symptoms do appear, they can include pain the lower pelvic area, lower back, hips, or upper thighs, frequent urination which can be painful, hematuria, loss of appetite and weight, and painful ejaculation (6).

Early diagnosis of small tumours that are confined to the prostate provides the best prognosis for recovery from prostate cancer. Analyses of blood PSA levels are the most accurate way to detect prostate cancer, particularly in the early stages (7). These analyses are usually combined with, or followed up by, digital rectal examination (8).

REFERENCE RANGES FOR PSA
Healthy males should have blood total PSA levels less than 4 ng/mL. Higher levels occur in individuals with BPH, prostatitis, and prostate cancer (4 – 30 ng/mL), with very high levels (>30 ng/mL) occurring at higher frequencies in men with advanced stages of prostate cancer.

TEST PROCEDURE
Correct specimen collection and handling is required for optimal assay performance.

This test requires a blood sample from a finger prick. All supplies for sample collection are provided in this kit. First wash and dry hands. Warm hands aid in blood collection. Clean the finger prick site with the alcohol swab and allow to air dry. Use the provided lancet to puncture the skin in one quick, continuous and deliberate stroke. Wipe away the first drop of blood (as it may be contaminated with tissue fluid or skin debris). Massage finger to increase blood flow at the puncture site and hold in a position that gravity facilitates the collection of blood on the fingertip. Transfer the blood to the blood collection card or blood collection tube (microtainer).

Avoid squeezing or 'milking' the finger excessively. If blood flow stops, perform a second skin puncture on another finger if more blood is required.

Dispose of all sharps safely and return sample to the laboratory in the provided prepaid return shipping envelope.

Upon receipt at the laboratory, the blood sample is analyzed by the fully automated Alinity i Total PSA and Alinity i Free PSA chemiluminescent microparticle immunoassays on the Alinity ci series analyzer.

The total PSA assay measures total PSA levels (both free PSA and PSA complexed to alpha-1-antichymotrypsin) by binding to anti-PSA coated microparticles. The free PSA assay measures free PSA levels by binding to anti-free PSA coated microparticles. The amount of total and free PSA in the blood sample is measured in relative light units by a chemiluminescent reaction.

The PSA Ratio is calculated by:
PSA Ratio = 100 x (Free PSA / Total PSA)

This ratio is useful for distinguishing between men with benign prostatic hypertrophy (BPH) and those at increased risk of early prostate cancer, as PSA values between 4 and 10 ng/mL are difficult to interpret.

TEST INTERPRETATION
This assay will provide accurate total PSA and free PSA values for the tested specimen, along with the calculated PSA ratio. This value is to be used in conjunction with other clinical and laboratory information for the identification of men with increased risk of prostate cancer. Prostatic biopsy is required for the diagnosis of cancer.

NOTE: Total and free PSA values determined with assays from different manufacturers can vary due to differences in assay methods and reagent specificity. Values obtained with different assay methods cannot be used interchangeably during patient monitoring.

DISCLAIMERS/LIMITATIONS

These results should be interpreted in conjunction with other laboratory and clinical information.

Assay interference may occur in specimens from individuals routinely exposed to animals or to animal serum products. Additional clinical or diagnostic information may be required for these specimens.

Additional testing is recommended if PSA results are inconsistent with clinical evidence.

False results may occur in specimens from individuals that have received preparations of mouse monoclonal antibodies for diagnosis or therapy. Additional clinical or diagnostic information may be required for these specimens.

Hormonal therapy may affect PSA expression.

Digital rectal examination, prostatic massage, ultrasonography, needle biopsy, and ejaculation may cause clinically significant PSA increases. Blood for PSA analyses should be collected prior to prostatic manipulations.

Total and free PSA values determined with assays from different manufacturers can vary due to differences in assay methods and reagent specificity. Values obtained with different assay methods cannot be used interchangeably during patient monitoring.

Correct specimen collection and handling is required for optimal assay performance. The assay is unaffected (≤10% interference) by hemoglobin (500 mg/dL), bilirubin (20 mg/dL), triglycerides (3000 mg/dL), prostatic acid phosphatase (1000 ng/mL), protein (12 g/dL), hytrin (10 µg/mL), proscar (25 µg/mL), and Flomax (1 µg/mL). Several chemotherapeutic agents also do not cause any interference with this assay.

REFERENCES

(1) McCormack RT, et al. (1995). Molecular Forms of Prostate-Specific Antigen and the Human Kallikrein Gene Family: A New Era. *Urology*, 45, 729-744.

(2) Partin AW, Oesterling JE. (1994). The Clinical Usefulness of Prostate Specific Antigen: Update 1994. *J Urol*, 152, 1358-1368.

(3) Ito K, et al. (2003). Free/total PSA ratio is a powerful predictor of future prostate cancer morbidity in men with initial PSA levels of 4.1 to 10.0 ng/mL. *Urology*. 61(4), 760-4.

(4) Christensson A, et al. (1993). Serum Prostate Specific Antigen Complexed to a-Antichymotrypsin as an Indicator of Prostate Cancer. *J Urol,* 150, 100-105.

(5) Parker SL, et al. (1997). Cancer Statistics, 1997. *CA Cancer J Clin*, 47, 5-27.

(6) What is Prostate Cancer? *Urology Care Foundation*. Updated August 2018. https://www.urologyhealth.org/urology-a-z/p/prostate-cancer

(7) Crawford ED, et al. (1996). Serum Prostate-Specific Antigen and Digital Rectum Examination for Early Detection of Prostate Cancer in a National Community-Based Program. *Urology,* 47, 863-869.

(8) American Urological Association - Early Detection of Prostate Cancer Policy Statement. Board of Directors Minutes 1992.