free PSA

infinosis™

Free Prostate-specific Antigen (FIA)

REF: IN067704 Σ 25

Intended use
The infinosis™ free PSA is a fluorescence immunoassay for the in vitro quantitative determination of free prostate-specific antigen (fPSA) in Human Serum or Plasma.

Summary
Reference[1-5]
PSA is a 32 kDa single chain glycoprotein serine protease with a chymotrypsin like speci city produced by the secretory epithelium of the prostate gland. PSA is normally secreted into the seminal uid and plays a functional role in the cleavage of the seminal vesicle proteins and the liquefaction of the seminal coagulum. Only low levels of PSA are normally present in the blood stream, and increasing serum concentrations indicate prostatic pathology, including benign prostatic hyperplasia and cancer of the prostate. Determination of PSA is now widely used for detection and management of patients with prostatic cancer and considered as the superior serological marker for cancer of the prostate. PSA has been shown to form stable complexes with different antiproteases and the dominating portion of PSA in patient serum occurs in complex with α_1-antichymotrypsin (PSA-ACT). However there are large variations in the relation between Free PSA and PSA-ACT complex between different individuals. A number of studies have found that the proportion of Free PSA is higher in benign prostatic disease as compared to prostatic cancer.

Test principle
Sandwich principle. Total duration of assay: **15 minutes**
Sample is added to the sample well of the test, then the fluorescence-labeled detector anti-fPSA antibody binds to fPSA antigen in blood specimen. As the sample mixture migrates on the nitrocellulose matrix of test strip by capillary action, the complexes of detector antibody and fPSA are captured to anti-fPSA antibody that has been immobilized on test strip. More antigens in the sample will form more antigen-antibody complexes which lead to stronger fluorescence signal by detector antibodies, which is processed by instrument for infinosis™ tests to show fPSA concentration in the sample.

Reagents
Materials provided
- **Test Cartridge**, 25 pcs, individually packaged
- **ID Chip** or **QR code of Calibration Curve**, 1 pcs
- **Sample Buffer,** 25 tubes
- **IFU**, 1 copy

Materials required (but not provided)
- Infinosis™ FIA analyzer
- Single use disposable lancing device
- Transfer pipette set (100 µL size)
- Alcohol pads
- Timer

Precautions and warnings
- For in vitro diagnostic use only.
- Carefully follow the instructions and procedures described in this instructions before testing.
- The Test cartridge should remain in its original sealed pouch until ready to use. Do not use it if the pouch is damaged or the seal is broken.
- Do not use reagents beyond the labeled expiry date.
- Do not mix or use components from kits with different Lots.
- Don't use Test cartridge if its Lot does not match with ID Chip that is inserted onto the instrument.
- The Infinosis™ fPSA assay should be used only in conjunction with the instrument for infinosis™ tests.
- The tests should be applied by professionally trained staff working in certified laboratories at some remove from the patient and clinic at which the sample is taken by qualified medical personnel.
- infinosis™ fPSA assay is single use only. Do not re-use it.
- The Test cartridge and Analyzer should be used away from vibration and magnetic field. During normal usage, the Test cartridge may introduce minute vibration, which should be regarded as normal.
- Use separate clean pipette tips and detector buffer vials for different specimens. The pipette tips and detector buffer vials should be used for one specimen only.
- Do not smoke, eat, or drink in areas in which specimens or kit reagents are handled.
- Blood specimens, used Test cartridges, pipette tips and detector buffer vials are potentially infectious. Proper laboratory safety techniques, handing and disposal methods should be followed in accordance with standard procedures and relevant regulations observed by microbiological hazard materials.
- The results should be interpreted by the physician along with clinical findings and other laboratory test results.

Storage and stability
- Store the test kit at 2-30°C, the stability is up to the expiration date printed on package.
- Test cartridge and sample buffer should be used within 1 hour after opening the pack.

Specimen collection and preparation
- The test can be performed with either Serum or Plasma.
- Collect serum samples in accordance with correct medical practices.
- Using standard phlebotomy procedure, collect a venipuncture whole blood specimen using a blood collection tube. If collecting plasma use a blood collection tube containing suitable anticoagulant (EDTA recommended).
- Separate the serum/plasma from blood as soon as possible to avoid hemolysis.
- Test should be performed immediately after the specimens have been collected. Do not leave the specimens at room temperature for prolonged periods. Specimens may be stored at 2-8°C for up to 3 days. For long-term storage, specimens should be kept below -20°C.

Calibration
The instrument automatically reads in the lot-specific calibration data from the QR code information printed on the Test cartridge.

Quality control
- Quality control tests are a part of the good testing practice to confirm the expected results and validity of the assay and should be performed at regular intervals.
- The control tests should be performed immediately after opening a new test lot to ensure the test performance is not altered.
- Quality control tests should also be performed whenever there is any question concerning the validity of the test results.
- Control materials are provided on demand with infinosis™ tests. For more information regarding obtaining the control materials, contact DiaSino Laboratories Co., Ltd for assistance.

Test setup
- Ensure that the lot number of the cartridge matches that of the sample buffer, and the ID Chip or calibration curve.
- If the sealed cartridge and sample buffer have been stored in refrigerator, place them at room temperature (18-25 °C) at least 30 minutes before measurement.
- Turn on the instrument for infinosis™ tests.
  Refer to the *'instrument for infinosis™ tests Operation Manual'* for the complete information and operating instructions.

Test procedure
1. Insert ID Chip into the instrument for infinosis™ tests or Scan the QR code to read the calibration curve.
2. Using a pipette to transfer **50 µL** of sample (Human plasma/serum) to the **sample buffer tube** provided in the kit.
3. Close the lid of the sample mixing tube and mix the sample thoroughly for **5-10 seconds** by tapping or inverting the tube.
4. Pipette out **100 µL** of **sample mixture** and load it onto the sample well on the cartridge.
5. Leave the sample-loaded cartridge at room temperature for **15 minutes.**
6. Insert the sample-loaded cartridge into the cartridge holder of instrument for infinosis™ tests.
   Ensure proper orientation of the cartridge before pushing it all the way inside the cartridge holder.
7. Press **"Test"** button on the instrument for infinosis™ tests.
8. Instrument for infinosis™ tests will start scanning the sample-loaded cartridge immediately.
9. Read the test result on the display screen of the instrument for infinosis™ tests.
10. Print out the testing results when press **"Print"** button on the instrument for infinosis™ tests.

Limitations - interference

IVD

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- The assay is unaffected by icterus (bilirubin < 1000 µmol/L or < 58 mg/dL), hemolysis (Hb < 1.0 mmol/L or < 1.61 g/dL), lipemia (Intralipid < 1500 mg/dL) and biotin (< 200 nmol/L or < 49 ng/mL).
- Criterion: Recovery within ± 10 % of initial value.
- No interference was observed from rheumatoid factors up to a concentration of 1500 IU/mL.
- There is no high-dose hook effect at tPSA concentrations up to 8000 ng/mL.
- In vitro tests were performed on 28 commonly used pharmaceuticals. No interference with the assay was found.
- Patients who have received mouse monoclonal antibodies for either diagnosis or therapy can develop HAMA (human Anti- mouse antibodies). HAMA can produce either falsely high or falsely low values in immunoassays which use mouse monoclonal antibodies. Additional information may be required for diagnosis.
- For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

Measuring range
0.02-20 ng/mL (defined by the lower detection limit and the maximum of the master curve). Values below the detection limit are reported as < 0.02 ng/mL. Values above the measuring range are reported as > 20 ng/mL

Lower detection limit
0.02 ng/mL
The detection limit represents the lowest analyte level that can be distinguished from zero. It is calculated as the value lying two standard deviations above that of the lowest standard (master calibrator, standard 1+2 SD, repeatability study, n = 21).

Expected values
Free PSA measurements may be used in conjunction with an equimolar test such as Porria tPSA for total PSA in order to generate the ratio of Free PSA/ Total PSA. Serum specimens from 45 men objectively diagnosed with benign prostate hyperplasia (BPH) and 67 men diagnosed with prostate cancer (PCa) were analysed using Porrima tPSA and Porrima Free PSA:

Diagnosis (n)	fPSA/tPSA			fPSA/tPSA	
	Median	Max.	Min.	Mean	95% confidence interval
BPH (54)	0.18	0.05	0.43	0.20	(0.17-0.23)
PCa(87)	0.09	0.02	0.55	0.11	(0.09-0.15)

The choice of a cut-off to be used in clinical practice depends upon the clinical application, i.e. whether optimised sensitivity or speci city is desired. Sensitivities (% PCa correctly detected) and Speci cities (% BPH correctly detected) for different FPSA/TPSA ratio cut-offs are shown below:

fPSA/ tPSA	Clinical specificity (BPH>cut-off)			Clinical specificity (PCa ≤ cut-off)		
cut-off	n	%	95% confidence interval	n	%	95% confidence interval)
0.25	16 (54)	29.6	(17-45)	80(87)	92.0	(84-96)
0.15	40 (54)	74.0	(55-86)	76(87)	87.3	(75-90)
0.09	50 (54)	92.6	(83-98)	39(87)	44.8	(30-52)

Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference ranges.

Specific performance data
Representative performance data are given below. Results obtained in individual laboratories may differ.

Analytical specificity
For the monoclonal antibodies used, the following cross-reactivities were found: PAP and ACT: none; PSA and PSA-ACT are recognized on an equimolar basis.

Functional sensitivity
0.07 ng/mL
The functional sensitivity is the lowest analyte concentration that can be reproducibly measured with an intermediate precision CV of 20 %.

Method comparison
A comparison of the Infinosis™ fPSA assay (y) with the Elecsys fPSA assay (x) using 171 clinical samples gave the following correlations:

Linear regression

y = 1.0149x + 0.051

r = 0.9512

Analytical specificity
The infinosis fPSA is based on two mouse monoclonal antibodies, directed against two distinct epitopes exposed in Free PSA. This antibody combination provides an assay specific for Free PSA showing <1% cross-reactivity to the PSA-ACT complex.

Functional sensitivity
0.05 ng/mL
The functional sensitivity is the lowest analyte concentration that can be reproducibly measured with an intermediate precision CV of ≤ 20 %.

References

1. Wang MC, Valenzuela LA, Murphy GP, Chu TM (1979). Puri cation of a human prostate speci c antigen. *Invest Urol* 17: 159–163.
2. Lilja H. (1985). A kallikrein-like serine protease in prostatic uid cleavesthe predominant seminal vesicle protein. *J Clin Invest* 76: 1899–1903.
3. Haese A., Becker C., Diamandis E., and Lilja H., (2002) Adenocarcinoma of the Prostate In: „Tumor Markers. Phusiology, Pathobiology, Technology, and Clinical applications". Eds. Diamandis et al., AACC Press, Washington, pp. 193-238.
4. Lilja H., Christensson A., Dahlén U., Matikainen M-T., Nilsson O., Pettersson K., Lövgren T. (1991). Prostate-speci c antigen in serum occurs predominantly
in complex with α1-antichymotrypsin. *Clin Chem* 37: 1618–1625.
5. Christensson A., Björk T., Nilsson O., Dahlén U., Matikainen M-T., Cockett ATK, Abrahamsson PA, Lilja H. (1993). Serum prostate speci c antigen complexed to α1-antichymotrypsin as an indicator of prostate cancer. *J Urology* 150: 100–105.

Symbols

IVD In vitro diagnostic medical device	2°C 30°C Temperature limit	Consult instructions for use	REF Catalog number
LOT Batch code	Date of manufacture	Use-by date	Contains sufficient for <n> tests
Manufacturer	Do not re-use	Do not use if package is damaged and consult instructions for use	

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