

deCODE ProstateCancer™ Genetic Risk Assessment

*TO ACCESS GENETIC RISK FOR DEVELOPING PROSTATE
CANCER IN CAUCASIAN MEN*

Test Highlights

- The deCODE ProstateCancer™ genetic screen analyzes 25 DNA variants to provide a personalized risk for developing prostate cancer. Risk values are reported as genetic risk relative to the general population and lifetime risk for prostate cancer development.
- Genetic risk for prostate cancer is independent from family history of prostate cancer; thus, this test may help assess risk in men without a family history of early onset prostate cancer.
- The screen can provide a more sensitive and specific risk for prostate cancer than serum prostate-specific antigen (PSA) levels alone.

Disease Overview

- Prostate cancer is the second leading cause of cancer deaths in men, and is nearly as common as breast cancer is in women.
- The median age of prostate cancer diagnosis in the United States is 67 years.
- As 80 percent of prostate cancer is localized at the time of diagnosis, prognosis is often good, with a five-year survival of 99 percent.
- Approximately 5 percent of men have a family history of early-onset prostate cancer (diagnosis at <65 years of age); therefore, the majority of men in the United States are considered to be at population risk.
- Current screening of blood PSA levels has poor specificity and sensitivity for prostate cancer. Of prostate biopsies performed in the United States after an elevated PSA result, 80 percent are negative; conversely, many men with aggressive prostate cancer have normal PSA values.
- Results from the deCODE ProstateCancer genetic screen may help provide a more accurate assessment of risk, which can help guide management and treatment strategies to facilitate early cancer diagnoses and avoid unnecessary biopsies.

Epidemiology

- The age-adjusted incidence of prostate cancer in the United States for all ethnicities is estimated at 160:100,000 men.
- Approximately 2.3 million men in the United States are living with prostate cancer or have a personal history of prostate cancer.
- The lifetime risk for developing prostate cancer for Caucasian men of European ancestry in the United States is approximately 16 percent.¹

Genetics

- The 25 DNA variants tested are single nucleotide polymorphisms (SNPs), each representing a single base change in the DNA sequence.
- The risk for prostate cancer development contributed by each SNP is independent of the other SNPs tested and also independent of family history. The genetic variants tested are not associated with benign prostatic hyperplasia (BPH), a common source for false-positive PSA results.

- Two SNPs tested, rs2710646 and rs1447295, are associated with more aggressive and advanced prostate cancer (based on Gleason score and staging) at the time of diagnosis.

DNA VARIANTS TESTED		
Includes chromosome location, reference SNP number (rs number), and number of patients and controls used to validate the risk conferred by each variant		
Chromosome/Gene	SNP	Number of Cases/Controls
2p15	rs2710646	10,000/29,000
8q24	rs16901979	2,600/5,500
8q24	rs1447295	2,000/5,000
8q24	rs6983267	4,300/4,300
11q13.3	rs7947353	5,000/5,000
17q24	rs1859962	3,500/14,000
17q12	rs4430796	3,500/14,000
Xp11.22	rs5945572	10,000/29,000
MBMB	rs10993994	5,000/5,000
SLC22A3	rs9364554	7,370/5,742
LMTK2	rs6465657	7,370/5,742
3p12	rs2660753	7,370/5,742
TERT	rs401681	9,473/37,901
JAZF1	rs10486567	5,200/5,133
KLK2/KLK3	rs2735839	7,370/5,742
3q21.3	rs10934853	13,774/4,7614
8q24.21	rs16902104	1,201/16,913
19q13.2	rs8102476	13,173/47,198
22q13	rs5759167	16,229/14,821
8p21	rs1512268	16,229/14,821
8q24	rs10086908	5,504/5,834
2q31	rs10207654	16,229/1,4821
4q24	rs7679673	16,229/14,821
11p15	rs7127900	16,229/14,821
8q24.21	rs445114	8,234/4,3651

Indication for Ordering

- To assess genetic risk for prostate cancer development in men with or without a family history of early onset prostate cancer.
 - Genetic screening may be ordered prior to or in conjunction with PSA monitoring to help guide health management.

Contraindication for Ordering

Genetic risk assessment for men from ethnic groups other than European Caucasian.

Interpretation

- Genotype results for each of the 25 SNPs tested will be provided. Genetic risk for prostate cancer development will be reported as relative genetic risk, lifetime risk, and risk for tumor pathological aggressiveness. In addition, a patient handout will be provided that summarizes and visually represents the risk data.
- Relative genetic risk:
 - A man's relative genetic risk for prostate cancer (i.e., risk compared to the general Caucasian population risk of 1.0 in the United States) is determined by multiplying the risks conferred by each SNP.
 - Reported relative risk of prostate cancer ranges from 0.2-fold to 5.6-fold risk compared to the general population. Caution should be applied in assigning a very high-risk genotype to the results of this test, as such genotype combinations are extremely rare.
 - Approximately 40 percent of the population has an increased relative risk (>1.0) over the general population risk.
 - An estimated 6 percent of the population has a relative risk above 2.0.
 - About 1 percent of the population has a relative risk above 3.0.
- Lifetime risk for prostate cancer:

A man's lifetime risk estimate of developing prostate cancer is calculated by multiplying relative genetic risk (as determined by the deCODE ProstateCancer test) by the lifetime population risk for prostate cancer (16 percent for Caucasian men in the United States). This estimate assumes the man has a prior risk of prostate cancer similar to the general population.
- Absolute risk for pathologically advanced/aggressive cancer at diagnosis:

A man's risk for advanced/aggressive cancer (based on Gleason score and grading at time of diagnosis), assuming he were to actually be diagnosed with prostate cancer, is estimated based on results from the rs2710646 and rs1447295 SNPs.
- Overall risk for developing prostate cancer:

Overall risk is NOT directly estimated by this genetic screen, and all results should be interpreted within the context of all available information, including family history, other identifiable risk factors (e.g., ethnicity, age, etc.), serology and other clinical data.

Limitations

- A diagnosis or confirmation of prostate cancer cannot be made using this test alone. Diagnosis of prostate cancer is based on physical examination, ultrasound detection, and biopsy.
- This test is NOT a determinative diagnostic test for prostate cancer. Men with a high genetic risk as determined by this test may never develop prostate cancer, while men with low genetic risk could still develop prostate cancer.
- Family history is not incorporated into the results of this test. Any clinical assessment of a man's overall risk for prostate cancer should incorporate family history and other risk factors not measured by this screen.
- Only the 25 targeted DNA variants will be used to assess genetic risk for prostate cancer. Genetic variants that have yet to be discovered or incorporated into this test will not be measured.
- The DNA variants tested have not been validated for ethnicities other than European Caucasians.
- Rare diagnostic errors may occur due to primer- or probe-site mutations.

Methodology

- PCR followed by fluorescent primer/probe hybridization and Centaurus™ method of genotyping (Nanogen, Inc.) to assess 25 SNPs associated with increased likelihood of developing prostate cancer.
- Analytical sensitivity and specificity are 99 percent.

Related Tests

- [Prostate Specific Antigen, Total \(0070121\)](#)
- [Prostate Specific Antigen, Total with Reflex to Free PSA \(Includes Free Percentage\) \(0080264\)](#)
- [Prostate Specific Antigen, Free Percentage \(Includes Free PSA & Total PSA\) \(0080206\)](#)
- [Prostate Specific Antigen, Ultrasensitive \(0098581\)](#)
- [PCA3 - Prostate Cancer Biomarker \(2001999\)](#)

References

1. National Cancer Institute. Surveillance epidemiology and end results. <http://seer.cancer.gov/statfacts/html/prost.html#incidence-mortality> (accessed on June 24, 2010).
2. deCODE Diagnostic Laboratory. www.decodediagnostics.com (accessed on September 14, 2010).

Test Information

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[deCODE ProstateCancer™ \(Genetic Risk Assessment\)](#)

For specific collection, transport, and testing information, refer to the ARUP website at www.aruplab.com.

For information on test selection, ordering, and interpretation, refer to ARUP Consult® at www.arupconsult.com.