The University of Chicago Genetic Services Laboratories

5841 S. Maryland Ave., Rm. G701, MC 0077, Chicago, Illinois 60637
Toll Free: (888) UC GENES □ (888) 824 3637
Local: (773) 834 0555 □ FAX: (773) 702 9130
ucgslabs@genetics.uchicago.edu □ dnatesting.uchicago.edu
CLIA #: 14D0917593 CAP #: 18827-49

Next Generation Sequencing Panel for Hereditary Prostate Cancer

Clinical Features: Prostate cancer (PC) is the most frequent malignant non-cutaneous cancer and the second leading cause of cancer-related mortality among men over 50 years old. Hereditary PC accounts for about 5% to 10% of all PC cases and is characterized by an early age at onset. First degree relatives of patients with PC have a 2-5-fold increased risk of developing the condition, depending on the number of affected individuals in the family, indicating the existence of prostate-cancer-susceptibility genes [1] . The results of several studies using segregation analyses suggest that about 43-65% of cases of familial PC among men with early-onset disease before age 56 can be best explained by autosomal dominant inheritance [2] and other studies suggested an autosomal recessive mode of inheritance at older ages of diagnoses [3]. PC-susceptibility genes have also been reported in several syndromes associated with tumor growth, including Lynch syndrome and hereditary breast/ovarian cancer. Detection of mutations in such a genes may result in earlier diagnosis and treatment.

Our Hereditary Prostate Cancer Panel includes mutation analysis of all 13 genes listed below.

Hereditary Prostate Cancer Panel				
ATM	BRCA1	BRCA2	CHEK2 (CHK2)	EPCAM
HOXB13	MLH1	MSH2	MSH6	NBN
PALB2 (FANCN)	PMS2	TP53		

Hereditary Prostate Cancer Panel genes and associated cancers

Gene	Prostate Cancer risk	Related Cancer	Associated Syndrome*	References
ATM	Elevated	Breast	Ataxia telangiectasia	[4]
BRCA1	Approximately 20%	Breast/Ovarian cancer, pancreatic cancer.	Fanconi anemia*	[1, 5-7]
BRCA2	Approximately 20%	Breast/Ovarian cancer, adenocarcinoma, CLL	Fanconi anemia*	[1, 5-7]
CHEK2 (CHK2)	Elevated	Osteosarcoma (somatic), Breast cancer, colorectal cancer	Li-Fraumeni syndrome	[1]
EPCAM	Up to 30%	Colorectal cancer, carcinomas of the bladder, pancreas and breast	Lynch syndrome, Congenital tufting enteropathy*	[1, 8, 9]
HOXB13	Up to 60%	Ovarian cancer	Unknown	[1, 10, 11]
MLH1, MSH2, MSH6, PMS2**	Up to 30%	Colorectal, endometrial, ovarian, duodenal cancers	Muir-Torre syndrome, Lynch syndrome, Mismatch repair cancer syndrome*	[1, 5, 8, 9]
NBN	Elevated	Aplastic anemia, leukemia, lymphoma, breast/ovarian cancer, melanoma, medulloblastoma, glioma, rhabdomyosarcoma	Aplastic anemia, ALL, Nijmegen breakage syndrome*	[1, 12]
PALB2 (FANCN)	Elevated	Breast cancer, pancreatic cancer	Fanconi anemia*	[1]
TP53	Elevated	Adrenal cortical carcinoma, Breast cancer, colorectal cancer, choroid plexys papilloma, osteosarcoma, pancreatic cancer	Li Fraumeni syndrome	[13]

*Indicates if the syndrome is recessive

***Please note variations within exons 1-5, 9 and 11-15 of the PMS2 gene may not be analyzed or reported due to homology issues.*

Test methods:

Comprehensive sequence coverage of the coding regions and splice junctions of all genes in this panel is performed. Targets of interests are enriched and prepared for sequencing using the Agilent SureSelect system. Sequencing is performed using Illumina technology and reads are aligned to the reference

sequence. Variants are identified and evaluated using a custom collection of bioinformatic tools and comprehensively interpreted by our team of directors and genetic counselors. All pathogenic and likely pathogenic variants are confirmed by Sanger sequencing. The technical sensitivity of this test is estimated to be >99% for single nucleotide changes and insertions and deletions of less than 20 bp.

Our CNV detection algorithm was developed and its performance determined for the sole purpose of identifying deletions and duplications within the coding region of the gene(s) tested. Partial exonic copy number changes and rearrangements of less than 400 bp may not be detected by this methodology. Regions of high homology and repetitive regions may not be analyzed. This methodology will not detect low level mosaicism, balanced translocations, inversions, or point mutations that may be responsible for the clinical phenotype. The sensitivity of our deletion/duplication assay may be reduced when DNA extracted by an outside laboratory is provided.

Hereditary Prostate Cancer Panel (mutation analysis of 13 genes)

Sample specifications:	3 to10 cc of blood in a purple top (EDTA) tube
Cost:	$3500
CPT codes:	81406. 81407
Turn-around time:	4-6 weeks

Results:

Results, along with an interpretive report, are faxed to the referring physician as soon as they are completed. All abnormal results are reported by telephone.

For more information about our testing options, please visit our website at dnatesting.uchicago.edu or contact us at 773-834-0555.

References:

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