Blueprint Genetics

Hereditary Pancreatic Cancer Panel

Test code: ON0301

Is ideal for patients with a clinical suspicion of an inherited susceptibility to pancreatic cancer. This panel is designed to detect heritable germline mutations and should not be used for the detection of somatic mutations in tumor tissue.

The Panel is suited for detecting heritable germline mutations and may not be used for the detection of somatic mutations in tumor tissue. This panel is included in the Hereditary Gastrointestinal Cancer Panel and Comprehensive Hereditary Cancer Panel.

About Hereditary Pancreatic Cancer

Pancreatic ductal carcinoma makes up the vast majority (90%) of all pancreatic neoplasms and remains a disease with very poor prognosis and high morbidity. Familial aggregation has been recognized in approximately 10% of pancreatic cancers. Familial pancreatic cancer is defined as a family with at least one pair of first-degree relatives (parent-child or sibling pair) with pancreatic cancer without an identifiable syndrome in the family. Inherited pancreatic cancer is genetically highly heterogenous and has been associated with germline mutations in *ATM, BRCA2, CDKN2A*, and *PALB2*, among others (PMID: 26658419). Increased susceptibility to pancreatic cancer may also be associated with different cancer syndromes such as hereditary breast and ovarian cancer syndrome, Lynch syndrome, ataxia telangiectasia, and familial adenomatous polyposis (PMID: 23187834). Genetic diagnosis of familial pancreatic cancer offers opportunities for personalized therapies (PMID: 25719666).

Availability

Results in 3-4 weeks

Gene set description

Genes in the Hereditary Pancreatic Cancer Panel and their clinical significance

Gene	Associated phenotypes	Inheritance	ClinVar	HGMD
APC	Gardner syndrome, Desmoid disease, hereditary, Familial adenomatous polyposis	AD	773	1926
ATM	Breast cancer, Ataxia-Telangiectasia	AD/AR	1047	1109
BMPR1A*	Polyposis, juvenile intestinal	AD	110	140
BRCA1*	Pancreatic cancer, Breast-ovarian cancer, familial	AD	2997	2631
BRCA2	Fanconi anemia, Medulloblastoma, Glioma susceptibility, Pancreatic cancer, Wilms tumor, Breast-ovarian cancer, familial	AD/AR	3369	2659
BUB1B	Mosaic variegated aneuploidy syndrome, Premature chromatid separation trait	AD/AR	14	28
CDKN2A	Melanoma, familial, Melanoma-pancreatic cancer syndrome	AD	87	232
EPCAM	Diarrhea 5, with tufting enteropathy, congenital, Colorectal cancer, hereditary nonpolyposis	AD/AR	38	80
FANCC	Fanconi anemia	AR	94	64
MEN1	Hyperparathyroidism, familial primary, Multiple endocrine neoplasia	AD	263	730

MLH1	Muir-Torre syndrome, Endometrial cancer, Mismatch repair cancer syndrome, Colorectal cancer, hereditary nonpolyposis	AD/AR	873	1191
MSH2	Muir-Torre syndrome, Endometrial cancer, Colorectal cancer, hereditary nonpolyposis,, Mismatch repair cancer syndrome	AD/AR	933	1249
MSH6	Endometrial cancer, Mismatch repair cancer syndrome, Colorectal cancer, hereditary nonpolyposis	AD/AR	672	586
NF1*	Watson syndrome, Neurofibromatosis, Neurofibromatosis-Noonan syndrome	AD	1157	2901
PALB2	Fanconi anemia, Pancreatic cancer, Breast cancer	AD/AR	495	406
PMS2*	Mismatch repair cancer syndrome, Colorectal cancer, hereditary nonpolyposis	AD/AR	319	342
SMAD4	Juvenile polyposis/hereditary hemorrhagic telangiectasia syndrome, Polyposis, juvenile intestinal, Myhre dysplasia, Hereditary hemorrhagic telangiectasia	AD	179	143
STK11	Peutz-Jeghers syndrome	AD	173	460
TP53	Colorectal cancer, Li-Fraumeni syndrome, Ependymoma, intracranial, Choroid plexus papilloma, Breast cancer, familial, Adrenocortical carcinoma, Osteogenic sarcoma, Hepatoblastoma, Non-Hodgkin lymphoma	AD	393	505
TSC1	Lymphangioleiomyomatosis, Tuberous sclerosis	AD	177	372
TSC2	Lymphangioleiomyomatosis, Tuberous sclerosis	AD	396	1195
VHL	Erythrocytosis, familial, Pheochromocytoma	AD/AR	206	614

*Some regions of the gene are duplicated in the genome. Read more.

The gene has suboptimal coverage (means <90% of the gene's target nucleotides are covered at >20x with mapping quality score (MQ>20) reads), and/or the gene has exons listed under Test limitations section that are not included in the panel as they are not sufficiently covered with high quality sequence reads.

The sensitivity to detect variants may be limited in genes marked with an asterisk (*) or number sign (#)

Gene refers to the HGNC approved gene symbol; Inheritance refers to inheritance patterns such as autosomal dominant (AD), autosomal recessive (AR), X-linked (XL), X-linked dominant (XLD) and X-linked recessive (XLR); ClinVar refers to the number of variants in the gene classified as pathogenic or likely pathogenic in this database (ClinVar); HGMD refers to the number of variants with possible disease association in the gene listed in Human Gene Mutation Database (HGMD). The list of associated, gene specific phenotypes are generated from CGD or Orphanet databases.

Non-coding disease causing variants covered by the panel

Gene	Genomic location HG19	HGVS	RefSeq	RS-number
APC	Chr5:112043009–112043595			
APC	Chr5:112043220	c.-195A>C	NM_001127511.2	
APC	Chr5:112043223	c.-192A>G/T	NM_001127511.2	
APC	Chr5:112043223	c.-192A>G	NM_001127511.2	rs879253784
APC	Chr5:112043223	c.-192A>T	NM_001127511.2	
APC	Chr5:112043224	c.-191T>C	NM_001127511.2	

APC	Chr5:112043225	c.-190G>A	NM_001127511.2	
APC	Chr5:112043289	c.-125delA	NM_001127511.2	
APC	Chr5:112072710–112073585			
APC	Chr5:112111314	c.423-12A>G	NM_000038.5	
APC	Chr5:112111315	c.423-11A>G	NM_000038.5	
APC	Chr5:112115546	c.532-941G>A	NM_000038.5	rs730881227
APC	Chr5:112151175	c.835-17A>G	NM_000038.5	
APC	Chr5:112158419	c.1408+731C>T	NM_000038.5	
APC	Chr5:112158423	c.1408+735A>T	NM_000038.5	
ATM	Chr11:108093770	c.-174A>G	NM_000051.3	
ATM	Chr11:108094508	c.-31+595G>A	NM_000051.3	
ATM	Chr11:108098321	c.-30-1G>T	NM_000051.3	rs869312754
ATM	Chr11:108138753	c.2639-384A>G	NM_000051.3	
ATM	Chr11:108141209	c.2839-579_2839-576delAAGT	NM_000051.3	
ATM	Chr11:108151710	c.3403-12T>A	NM_000051.3	rs201370733
ATM	Chr11:108158168	c.3994-159A>G	NM_000051.3	rs864622543
ATM	Chr11:108164028	c.4612-12A>G	NM_000051.3	
ATM	Chr11:108179837	c.5763-1050A>G	NM_000051.3	rs774925473
ATM	Chr11:108214779	c.8418+681A>G	NM_000051.3	rs748635985
BRCA1	Chr17:41196352	c.*1340_*1342delTGT	NM_007294.3	rs1281551853
BRCA1	Chr17:41196424	c.*1271T>C	NM_007294.3	
BRCA1	Chr17:41197167	c.*528G>C	NM_007294.3	rs1060504556
BRCA1	Chr17:41197588	c.*103_*106delTGTC	NM_007294.3	rs431825382
BRCA1	Chr17:41197637	c.*58C>T	NM_007294.3	rs137892861
BRCA1	Chr17:41197859	c.5468-40T>A	NM_007294.3	rs80358151
BRCA1	Chr17:41199745	c.5407-25T>A	NM_007294.3	rs758780152
BRCA1	Chr17:41201232	c.5333-36_5333-22delTACTGCAGTGATTTT	NM_007294.3	
BRCA1	Chr17:41206122	c.5277+2916_5277+2946delAAATTCTAGTGCTTTGGATTTTTTCCTCCATinsGG	NM_007294.3	
BRCA1	Chr17:41209164	c.5194-12G>A	NM_007294.3	rs80358079
BRCA1	Chr17:41215994	c.5075-27delA	NM_007294.3	
BRCA1	Chr17:41251909	c.442-22_442-13delTGTTCTTTAC	NM_007294.3	rs879254224
BRCA1	Chr17:41256984	c.213-11T>G	NM_007294.3	rs80358061
BRCA1	Chr17:41256985	c.213-12A>G	NM_007294.3	rs80358163
BRCA1	Chr17:41256988	c.213-15A>G	NM_007294.3	
BRCA1	Chr17:41276134	c.-19-2A>G	NM_007294.3	
BRCA2	Chr13:32889805	c.-40+1G>A	NM_000059.3	
BRCA2	Chr13:32890469	c.-39-89delC	NM_000059.3	
BRCA2	Chr13:32890556	c.-39-1_-39delGA	NM_000059.3	rs758732038
BRCA2	Chr13:32890558	c.-39-1G>A	NM_000059.3	rs1060499566
BRCA2	Chr13:32900222	c.426-12_426-8delGTTTT	NM_000059.3	rs276174844
BRCA2	Chr13:32945079	c.8488-14A>G	NM_000059.3	
BRCA2	Chr13:32953872	c.8954-15T>G	NM_000059.3	

BRCA2	Chr13:32971007	c.9502-28A>G	NM_000059.3	rs397508059
BRCA2	Chr13:32971023	c.9502-12T>G	NM_000059.3	rs81002803
BUB1B	Chr15:40409289	c.-44133G>A	NM_001211.5	rs576524605
BUB1B	Chr15:40504689	c.2386-11A>G	NM_001211.5	rs751421137
CDKN2A	Chr9:21968346	c.458-105A>G	NM_000077.4	
CDKN2A	Chr9:21972311	c.151-1104C>G	NM_000077.4	
CDKN2A	Chr9:21973573	c.150+1104C>A	NM_000077.4	rs756102261
CDKN2A	Chr9:21974401	c.*73+2T>G	NM_058197.4	
CDKN2A	Chr9:21974847	c.-21C>T	NM_000077.4	
CDKN2A	Chr9:21974875	c.-49C>A	NM_000077.4	rs1064797383
CDKN2A	Chr9:21974882	c.-56G>T	NM_000077.4	
CDKN2A	Chr9:21974916	c.-93_-91delAGG	NM_000077.4	
EPCAM	Chr2:47606078	c.556-14A>G	NM_002354.2	rs376155665
FANCC	Chr9:98011653	c.-78-2A>G	NM_000136.2	rs587779898
FANCC	Chr9:98079807	c.-79+1G>A	NM_000136.2	
MEN1	Chr11:64571394	c.*412G>A	NM_000244.3	
MEN1	Chr11:64575165	c.670-15_670-14delTC	NM_000244.3	
MEN1	Chr11:64577602	c.-23-11_-22delTTGCCTTGCAGGC	NM_000244.3	
MEN1	Chr11:64577603	c.-23_-22insT	NM_000244.3	
MEN1	Chr11:64577626	c.-23-22C>A	NM_000244.3	
MLH1	Chr3:37034619	c.-413_-411delGAG	NM_000249.3	rs953169437
MLH1	Chr3:37034932	c.-107C>G	NM_000249.3	rs587778886
MLH1	Chr3:37034976	c.-63_-58delGTGATTinsCACGAGGCACGAGCACGA	NM_000249.3	
MLH1	Chr3:37034997	c.-42C>T	NM_000249.3	rs41285097
MLH1	Chr3:37035012	c.-27C>A	NM_000249.3	rs587779001
MLH1	Chr3:37035260	c.116+106G>A	NM_000249.3	
MLH1	Chr3:37038099	c.117-11T>A	NM_000249.3	rs267607711
MLH1	Chr3:37050292	c.454-13A>G	NM_000249.3	rs267607749
MLH1	Chr3:37061788	c.885-9_887dupTCCTGACAGTTT	NM_000249.3	rs63751620
MLH1	Chr3:37070436	c.1558+13T>A	NM_000249.3	rs267607834
MSH2	Chr2:47630106	c.-225G>C	NM_000251.2	rs138068023
MSH2	Chr2:47630150	c.-181G>A	NM_000251.2	rs786201698
MSH2	Chr2:47630249	c.-81dupA	NM_000251.2	rs560991330,rs587779187
MSH2	Chr2:47630251	c.-78_-77delTG	NM_000251.2	rs587779182
MSH2	Chr2:47698086	c.1662-17dupG	NM_000251.2	rs587779099
MSH6	Chr2:48018295	c.457+33_457+34insGTGT	NM_000179.2	
MSH6	Chr2:48030536	c.3173-16_3173-5delCCCTCTCTTTTA	NM_000179.2	
MSH6	Chr2:48034014	c.*15A>C	NM_000179.2	
MSH6	Chr2:48034047	c.*49_*68dupTTCAGACAACATTATGATCT	NM_000179.2	rs777409019
NF1	Chr17:29422055	c.-273A>C	NM_001042492.2	
NF1	Chr17:29422056	c.-272G>A	NM_001042492.2	
NF1	Chr17:29431417	c.60+9031_60+9035delAAGTT	NM_001042492.2	

NF1	Chr17:29475515	c.61-7486G>T	NM_001042492.2	
NF1	Chr17:29488136	c.288+2025T>G	NM_001042492.2	
NF1	Chr17:29508426	c.587-14T>A	NM_001042492.2	
NF1	Chr17:29508428	c.587-12T>A	NM_001042492.2	
NF1	Chr17:29510334	c.888+651T>A	NM_001042492.2	
NF1	Chr17:29510427	c.888+744A>G	NM_001042492.2	
NF1	Chr17:29510472	c.888+789A>G	NM_001042492.2	
NF1	Chr17:29527428	c.889-12T>A	NM_001042492.2	
NF1	Chr17:29530107	c.1260+1604A>G	NM_001042492.2	
NF1	Chr17:29533239	c.1261-19G>A	NM_001042492.2	
NF1	Chr17:29534143	c.1392+754T>G	NM_001042492.2	
NF1	Chr17:29540877	c.1393-592A>G	NM_001042492.2	
NF1	Chr17:29542762	c.1527+1159C>T	NM_001042492.2	rs878853868
NF1	Chr17:29548419	c.1642-449A>G	NM_001042492.2	
NF1	Chr17:29549489	c.*481A>G	NM_001128147.2	
NF1	Chr17:29553439	c.2002-14C>G	NM_001042492.2	
NF1	Chr17:29554225	c.2252-11T>G	NM_001042492.2	
NF1	Chr17:29556025	c.2410-18C>G	NM_001042492.2	
NF1	Chr17:29556027	c.2410-16A>G	NM_001042492.2	
NF1	Chr17:29556028	c.2410-15A>G	NM_001042492.2	
NF1	Chr17:29556031	c.2410-12T>G	NM_001042492.2	
NF1	Chr17:29556839	c.2851-14_2851-13insA	NM_001042492.2	
NF1	Chr17:29557267	c.2991-11T>G	NM_001042492.2	
NF1	Chr17:29558777	c.3198-314G>A	NM_001042492.2	
NF1	Chr17:29563299	c.3974+260T>G	NM_001042492.2	
NF1	Chr17:29577082	c.4110+945A>G	NM_001042492.2	
NF1	Chr17:29580296	c.4173+278A>G	NM_001042492.2	
NF1	Chr17:29588708	c.4578-20_4578-18delAAG	NM_001042492.2	
NF1	Chr17:29588715	c.4578-14T>G	NM_001042492.2	
NF1	Chr17:29654479	c.5269-38A>G	NM_001042492.2	
NF1	Chr17:29656858	c.5610-456G>T	NM_001042492.2	
NF1	Chr17:29657848	c.5812+332A>G	NM_001042492.2	rs863224491
NF1	Chr17:29661577	c.5813-279A>G	NM_001042492.2	
NF1	Chr17:29664375	c.6428-11T>G	NM_001042492.2	
NF1	Chr17:29664618	c.6642+18A>G	NM_001042492.2	
NF1	Chr17:29676126	c.7190-12T>A	NM_001042492.2	
NF1	Chr17:29676127	c.7190-11_7190-10insGTTT	NM_001042492.2	
NF1	Chr17:29685177	c.7971-321C>G	NM_001042492.2	
NF1	Chr17:29685481	c.7971-17C>G	NM_001042492.2	
NF1	Chr17:29685665	c.8113+25A>T	NM_001042492.2	
PALB2	Chr16:23649285	c.109-12T>A	NM_024675.3	rs774949203
PMS2	Chr7:6027263	c.1145-31_1145-13delCTGACCCTCTTCTCCGTCC	NM_000535.5	rs751973268

PMS2	Chr7:6048599	c.23+21_23+28delTCCGGTGT	NM_000535.5	
STK11	Chr19:1220520	c.597+16_597+33delGGGGGGCCCTGGGGCGCCinsTG	NM_000455.4	
STK11	Chr19:1220530	c.598-32_597+31delGCCCCCTCCCGGGC	NM_000455.4	
TP53	Chr17:7571520		NM_000546.5	
TP53	Chr17:7577647	c.673-39G>A	NM_000546.5	
TP53	Chr17:7579601	c.97-11C>G	NM_000546.5	
TP53	Chr17:7590694	c.-29+1G>T	NM_000546.5	
TSC1	Chr9:135800306	c.363+668G>A	NM_000368.4	
TSC2	Chr16:2098067	c.-30+1G>C	NM_000548.3	rs587778004
TSC2	Chr16:2106052	c.600-145C>T	NM_000548.3	
TSC2	Chr16:2107460	c.848+281C>T	NM_000548.3	
TSC2	Chr16:2110656	c.976-15G>A	NM_000548.3	rs45517150
TSC2	Chr16:2127477	c.2838-122G>A	NM_000548.3	
TSC2	Chr16:2138031	c.5069-18A>G	NM_000548.3	rs45484794
VHL	Chr3:10183453	c.-75_-55delCGCACGCAGCTCCGCCCCGCG	NM_000551.3	rs727503744
VHL	Chr3:10183471	c.-54_-44dupTCCGACCCGCG	NM_000551.3	
VHL	Chr3:10191719	c.*70C>A	NM_000551.3	
VHL	Chr3:10191719	c.*70C>T	NM_000551.3	rs552290225

Test Strengths

The strengths of this test include:

- CAP accredited laboratory
- CLIA-certified personnel performing clinical testing in a CLIA-certified laboratory
- Powerful sequencing technologies, advanced target enrichment methods and precision bioinformatics pipelines ensure superior analytical performance
- Careful construction of clinically effective and scientifically justified gene panels
- Our Nucleus online portal providing transparent and easy access to quality and performance data at the patient level
- Our publicly available analytic validation demonstrating complete details of test performance
- ~2,000 non-coding disease causing variants in our clinical grade NGS assay for panels (please see 'Non-coding disease causing variants covered by this panel' in the Panel Content section)
- Our rigorous variant classification scheme
- Our systematic clinical interpretation workflow using proprietary software enabling accurate and traceable processing of NGS data
- Our comprehensive clinical statements

Test Limitations

This panel may not detect inversions, including the inversion of exons 1-7 of *MSH2*. Genes with partial, or whole gene, segmental duplications in the human genome are marked with an asterisk (*) if they overlap with the UCSC pseudogene regions. The technology may have limited sensitivity to detect variants in genes marked with these symbols (please see the Panel content table above).

This test does not detect the following:

- Complex inversions
- Gene conversions
- Balanced translocations
- Mitochondrial DNA variants

- Repeat expansion disorders unless specifically mentioned
- Non-coding variants deeper than ±20 base pairs from exon-intron boundary unless otherwise indicated (please see above Panel Content / non-coding variants covered by the panel).

This test may not reliably detect the following:

- Low level mosaicism (variant with a minor allele fraction of 14.6% is detected with 90% probability)
- Stretches of mononucleotide repeats
- Indels larger than 50bp
- Single exon deletions or duplications
- Variants within pseudogene regions/duplicated segments

The sensitivity of this test may be reduced if DNA is extracted by a laboratory other than Blueprint Genetics.

For additional information, please refer to the Test performance section and see our Analytic Validation.

Test performance

Our panels are sectioned from our high-quality, clinical grade NGS assay. Please see our sequencing and detection performance table for details regarding our ability to detect different types of alterations (Table).

Assays have been validated for various sample types including EDTA-blood, isolated DNA (excluding from formalin fixed paraffin embedded tissue), saliva and dry blood spots (filter cards). These sample types were selected in order to maximize the likelihood for high-quality DNA yield. The diagnostic yield varies depending on the assay used, referring healthcare professional, hospital and country. Plus analysis increases the likelihood of finding a genetic diagnosis for your patient, as large deletions and duplications cannot be detected using sequence analysis alone. Blueprint Genetics' Plus Analysis is a combination of both sequencing and deletion/duplication (copy number variant (CNV)) analysis.

Performance of Blueprint Genetics high-quality, clinical grade NGS sequencing assay for panels.

	Sensitivity % (TP/(TP+FN)	Specificity %
Single nucleotide variants	99.89% (99,153/99,266)	>99.9999%
Insertions, deletions and indels by sequence analysis		
1-10 bps	99.2% (7,745/7,806)	>99.9999%
11-50 bps	99.13% (2,524/2,546)	>99.9999%
Copy number variants (exon level dels/dups)		
1 exon level deletion (heterozygous)	100% (20/20)	NA
1 exon level deletion (homozygous)	100% (5/5)	NA
1 exon level deletion (het or homo)	100% (25/25)	NA
2-7 exon level deletion (het or homo)	100% (44/44)	NA
1-9 exon level duplication (het or homo)	75% (6/8)	NA
Simulated CNV detection		
5 exons level deletion/duplication	98.7%	100.00%

Size range (0.1-47 Mb)	100% (25/25)

The performance presented above reached by Blueprint Genetics high-quality, clinical grade NGS sequencing assay with the following coverage metrics

Mean sequencing depth	143X
Nucleotides with >20x sequencing coverage (%)	99.86%

Bioinformatics

The target region for each gene includes coding exons and ±20 base pairs from the exon-intron boundary. In addition, the panel includes non-coding and regulatory variants if listed above (Non-coding variants covered by the panel). Some regions of the gene(s) may be removed from the panel if specifically mentioned in the 'Test limitations" section above. The sequencing data generated in our laboratory is analyzed with our proprietary data analysis and annotation pipeline, integrating state-of-the art algorithms and industry-standard software solutions. Incorporation of rigorous quality control steps throughout the workflow of the pipeline ensures the consistency, validity and accuracy of results. Our pipeline is streamlined to maximize sensitivity without sacrificing specificity. We have incorporated a number of reference population databases and mutation databases including, but not limited, to 1000 Genomes Project, gnomAD, ClinVar and HGMD into our clinical interpretation software to make the process effective and efficient. For missense variants, *in silico* variant prediction tools such as SIFT, PolyPhen, MutationTaster are used to assist with variant classification. Through our online ordering and statement reporting system, Nucleus, ordering providers have access to the details of the analysis, including patient specific sequencing metrics, a gene level coverage plot and a list of regions with <20X sequencing depth if applicable. This reflects our mission to build fully transparent diagnostics where ordering providers can easily visualize the crucial details of the analysis process.

Clinical interpretation

We provide customers with the most comprehensive clinical report available on the market. Clinical interpretation requires a fundamental understanding of clinical genetics and genetic principles. At Blueprint Genetics, our PhD molecular geneticists, medical geneticists and clinical consultants prepare the clinical statement together by evaluating the identified variants in the context of the phenotypic information provided in the requisition form. Our goal is to provide clinically meaningful statements that are understandable for all medical professionals regardless of whether they have formal training in genetics.

Variant classification is the corner stone of clinical interpretation and resulting patient management decisions. Our classifications follow the Blueprint Genetics Variant Classification Schemes based on the ACMG guideline 2015. Minor modifications were made to increase reproducibility of the variant classification and improve the clinical validity of the report. Our experience with tens of thousands of clinical cases analyzed at our laboratory allowed us to further develop the industry standard.

The final step in the analysis is orthogonal confirmation. Sequence variants classified as pathogenic, likely pathogenic and variants of uncertain significance (VUS) are confirmed using bi-directional Sanger sequencing when they do not meet our stringent NGS quality metrics for a true positive call. Reported heterozygous and homo/hemizygous copy number variations with a size <10 and <3 target exons are confirmed by orthogonal methods such as qPCR if the specific CNV has been seen and confirmed less than three times at Blueprint Genetics.

Our clinical statement includes tables for sequencing and copy number variants that include basic variant information (genomic coordinates, HGVS nomenclature, zygosity, allele frequencies, in silico predictions, OMIM phenotypes and classification of the variant). In addition, the statement includes detailed descriptions of the variant, gene and phenotype(s) including the role of the specific gene in human disease, the mutation profile, information about the gene's variation in population cohorts and detailed information about related phenotypes. We also provide links to the references, abstracts and

variant databases used to help ordering providers further evaluate the reported findings if desired. The conclusion summarizes all of the existing information and provides our rationale for the classification of the variant.

Identification of pathogenic or likely pathogenic variants in dominant disorders or their combinations in different alleles in recessive disorders are considered molecular confirmation of the clinical diagnosis. In these cases, family member testing can be used for risk stratification. We do not recommend using variants of uncertain significance (VUS) for family member risk stratification or patient management. Genetic counseling is recommended.

Our interpretation team analyzes millions of variants from thousands of individuals with rare diseases. Our internal database and our understanding of variants and related phenotypes increases with every case analyzed. Our laboratory is therefore well-positioned to re-classify previously reported variants as new information becomes available. If a variant previously reported by Blueprint Genetics is re-classified, our laboratory will issue a follow-up statement to the original ordering health care provider at no additional cost.

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ICD codes

Commonly used ICD-10 codes when ordering the Hereditary Pancreatic Cancer Panel

ICD-10	Disease
C50 C56	Hereditary breast and ovarian cancer syndrome
D48.9	Li-Fraumeni syndrome
Q85.8	Peutz-Jeghers syndrome
C18.0	Lynch syndrome
C25.9	Familial pancreatic cancer
G11.3	Ataxia telangiectasia
Q85.8	Von Hippel-Lindau disease
D12.6	Familial adenomatous polyposis

Accepted sample types

- EDTA blood, min. 1 ml
- Purified DNA, min. 3µg*
- Saliva (Oragene DNA OG-500 kit)

Label the sample tube with your patient's name, date of birth and the date of sample collection.

Note that we do not accept DNA samples isolated from formalin-fixed paraffin-embedded (FFPE) tissue.

Resources

- Ataxia-Telangiectasia Society (UK)
- Becker, AE.et al. Pancreatic ductal adenocarcinoma: risk factors, screening, and early detection. World J Gastroenterol. 2014 Aug 28;20(32):11182-98.
- Bright Pink
- Cancer.Net - Familial Pancreatic Cancer

- Cancer.Net - Peutz-Jeghers Syndrome
- Fighting Hereditary Breast and Ovarian Cancer
- GeneReviews - *BRCA1* and *BRCA2* Hereditary Breast and Ovarian Cancer
- GeneReviews - Ataxia-Telangiectasia
- GeneReviews - BRCA1 and BRCA2 Hereditary Breast and Ovarian Cancer
- GeneReviews - Li-Fraumeni Syndrome
- GeneReviews - Lynch Syndrome
- GeneReviews - Peutz-Jeghers Syndrome
- GeneReviews - Von Hippel-Lindau Syndrome
- GeneReviews - Von-Hippel Lindau Syndrome
- HBOC Society
- Li-Fraumeni Syndrome Association
- Lynch Syndrome International
- NORD - Ataxia Telangiectasia
- NORD - Familial Adenomatous Polyposis
- NORD - Peutz Jeghers Syndrome
- NORD - Von Hippel-Lindau Syndrome
- PALB2Interest Group
- Pan Care Foundation
- Pancreatic Cancer UK
- VHL Alliance