Familial Cancer Genetic (CGx) Testing Panel

Express Gene™ Familial Cancer (CGx) Panel:

This panel identifies the risk of genetic factors for various cancers such as breast cancer, ovarian cancer, colon cancer, colon polyps, prostate cancer, melanoma, and others that run in a family. The test looks for inherited genetic variations (germline mutations) associated with an increased risk of cancer. With knowledge of genetic risk factors, physicians would be able to personalize patient healthcare plans.

Definition of cancer risk factor:

Familial cancer genetic tests provide lifetime risk of cancer development. They cannot state if a patient will develop cancer for sure. But they can determine whether an individual has a higher risk than most people.

Only some people with a gene mutation will develop cancer. Nathanson et al. (2001) reported lifetime breast cancer risk of 60 to 80% for female BRCA1 mutation carriers, although lifetime risk estimates as low as 36% had been reported in other studies.

Conversely, sporadic cases of breast cancer happen in patient that do not carry any mutation.

Purpose of the CGx test:

Genes are instructions, written in DNA, for building protein molecules. Different people can have different versions of the same gene. Each version has a slightly different DNA sequence. Some of these variants affect health, such as those gene variants linked to increased risk of cancers. These cancer-related variants can run in families.

Several genes involved in many known inherited cancers have been identified. Testing whether someone carries a harmful (pathogenic) variant in one of these genes can confirm whether a condition is, indeed, the result of an inherited syndrome. Genetic testing is also done to determine whether family members who have not (yet)

developed a cancer have inherited the same variant as a family member who is known to carry a harmful (predisposing cancer susceptibility) variant.

More than 50 hereditary cancer syndromes have been described. Most of these are caused by harmful variants that are inherited in an autosomal dominant fashion—that is, a single altered copy of the gene inherited from one parent is enough to increase a person's chance of developing cancer.

Method:

CGx genetic test investigates a panel of genes (listed below) for the presence of genetic changes compared to human reference (variants) that are linked to increased lifetime risk of cancers.

Express Gene Comprehensive Familial Cancer (Cancer) Panel is a Laboratory Developed Tests (LDT) validated at Express Gene Molecular Diagnostics Laboratory, using Twist Exome 2.0 and Illumina NovaSeq6000 Next Generation Sequencing (NGS) Platform. This test has not been cleared or approved by the FDA.

What is the outcome of familial cancer test results:

A. Positive Result. A positive test result indicates a variant linked to cancer has been identified. This knowledge provides the patient and health care provider an opportunity to understand and, in some cases, manage their cancer risks.

For people who are already diagnosed with a cancer, results of genetic testing may help them make decisions about their treatment and understand their risk for other cancers.
Genetic testing provides an opportunity for family members to learn about their own cancer risks.

B. Variation of uncertain significance (VUS). If genetic testing shows a change that has not been previously associated with cancer, the person's test result may report a VUS. This result may be interpreted as uncertain, which is to say that the information does not help to clarify their risk and is typically not considered in making health care decisions.

Some gene variants may be reclassified as researchers learn more about variants linked to

cancer. Most often, variants that were initially classified as variants of uncertain significance are reclassified as being benign (not clinically important), but sometimes a VUS may eventually be found to be associated with increased risks for cancer. Therefore, it is important for the person who is tested to keep in touch with the health care provider to ensure that they receive updates if any new information on the variant is learned.

C. Negative result. A negative test result means that the laboratory did not find the specific cancer-linked variant on list of genes that the test was designed to detect. Therefore, patient does not have a genetic variation associated with cancer in the genes tested by the CGx panel.

Limitations of Testing

This test is designed to detect individuals with a germline pathogenic variant. Repeat expansion disease, large deletion, duplication and copy number variations, are not detectable by next generation sequencing (NGS) and require different test methodologies. Mutations in the upstream and downstream regulatory regions and mutations outside exons of protein-coding genes are not investigated.

Certain types of variants, such as structural rearrangements, inversions, translocations, variants in regions with low complexity, regions with complex architecture, short tandem repeats, or segmental duplications cannot be detected by this method. Additionally, low level mosaicism, phasing, regions with matching pseudogenes causing mapping ambiguity cause incorrect or insufficient variant calling. The CGx test should not be ordered on tumor tissue.

Genetic counseling:

Genetic counseling is recommended to explain the results, risks, and potential pitfalls of the CGx cancer testing panel. Genetic testing can have potential emotional, and social, harms. Psychological stress can arise from learning that one has a genetic variant that increases cancer risk, as well as from making decisions regarding whether to share test finding with blood relatives. Survivor's guilt can also occur upon learning that one does not have a harmful variant present in other family members.

Sources: Breast cancer genetics, PubMed: 11329055
https://www.cancer.gov/about-cancer/

Express Gene™ Comprehensive Familial Cancer (CGx) Panel

The Express Gene™ Familial Cancer (CGx) Panel examines 193 genes associated with hereditary cancers. This panel includes both well-established genes that increase a person's risk for cancer, but also includes candidate genes that may have only been recently discovered or for which additional research is needed.

Familial Cancer CGx Panel

EXPRESS GENE MOLECULAR DIAGNOSTICS LABORATORY
9000 SW 152 Street Ste. 209
Miami • FL • 33157
Tel: 786.250.3419 • Fax: 786.250.3074
Email: info@expressgene.us

Row	Gene name	Condition	Row	Gene name	Condition	Row	Gene name	Condition
1	ABL1	Leukemia	66	FANCC	Fanconi anemia	131	POT1	Melanoma
2	ABL2	Leukemia	67	FANCD2	Fanconi anemia	132	PRF1	Leukemia
3	ABRAXAS1	Breast Cancer	68	FANCE	Fanconi anemia	133	PRKAR1A	Adrenocortical tumor
4	ACVR1B	Pancreatic	69	FANCF	Fanconi anemia	134	PRSS1	Pancreatic cancer
5	AIP	Pituitary adenoma	70	FANCG	Fanconi anemia	135	PTCH1	Basal cell Carcinoma
6	AKT1	Breast Colorectal	71	FANCI	Fanconi anemia	136	PTCH2	Basal cell Carcinoma
7	ALK	Neuroblastoma	72	FANCL	Fanconi anemia	137	PTEN	Endometrial Cancer
8	ANKRD26	Leukemia	73	FANCM	Multiple cancer	138	PTPN11	Leukemia
9	APC	Pituitary adenoma	74	FGFR1	Leukemia	139	RAD50	Multiple cancer
10	ARMC5	Adrenal hyperplagia	75	FGFR3	Colon cancer	140	RAD51C	Breast Cancer
11	ASXL1	Leukemia	76	FGFR4	Multiple cancer	141	RAD51D	Breast Cancer
12	ATM	Breast Cancer	77	FH	Renal Carcinoma	142	RARA	Leukemia
13	ATR	Multiple cancer	78	FLCN	Colon cancer	143	RARG	Leukemia
14	AXIN2	Colon cancer	79	FLT3	Leukemia	144	RB1	Bladder Cancer
15	BAP1	Multiple cancer	80	FLT4	Breast Cancer	145	RECQL	Breast Cancer
16	BARD1	Breast Cancer	81	GALNT12	Colon cancer	146	RECQL4	Multiple cancer
17	BLM	Multiple cancer	82	GATA2	Leukemia	147	REST	Wilms tumor
18	BMPR1A	Colon cancer	83	GPC3	Renal Carcinoma	148	RET	Thyroid cancer
19	BRAF	Colon cancer	84	GREM1	Colon cancer	149	RHBDF2	Esophageal cancer
20	BRCA1	Breast Cancer	85	HNF1A	Renal Carcinoma	150	RPL5	Leukemia
21	BRCA2	Breast Cancer	86	HOXB13	Prostate cancer	151	RPS20	Colon cancer
22	BRIP1	Breast Cancer	87	HRAS	Thyroid cancer	152	RUNX1	Leukemia
23	BUB1B	Colon cancer	88	IDH1	Brain tumor	153	SAMD9L	Leukemia
24	CASR	Multiple cancer	89	JAK1	Leukemia	154	SBDS	Leukemia
25	CBFB	Leukemia	90	KIF1B	Brain tumor	155	SCG5	Colon cancer
26	CBL	Leukemia	91	KIT	Multiple cancer	156	SDHA	Ganglioma
27	CCND1	Colon cancer	92	KRAS	Multiple cancer	157	SDHAF2	Ganglioma
28	CDC73	Multiple cancer	93	LZTR1	Brain tumor	158	SDHB	Gastrointestinal Tumor
29	CDH1	Breast Cancer	94	MAP2K4	Pancreatic cancer	159	SDHC	Gastrointestinal Tumor
30	CDK4	Melanoma	95	MAX	Renal Carcinoma	160	SDHD	Gastrointestinal Tumor
31	CDKN1B	Multiple cancer	96	MC1R	Melanoma	161	SF3B1	Leukemia
32	CDKN1C	Multiple cancer	97	MEN1	Multiple cancer	162	SLC45A2	Melanoma
33	CDKN2A	Melanoma	98	MET	Renal Carcinoma	163	SLX4	Fanconi anemia
34	CEBPA	Leukemia	99	MIR142	Leukemia	164	SMAD4	Colon cancer
35	CHEK2	Breast Cancer	100	MITF	Leukemia	165	SMARCA4	Rhabdoid Tumor
36	CHIC2	Leukemia	101	MLH1	Colon cancer	166	SMARCB1	Rhabdoid Tumor
37	CPA1	Pancreatic cancer	102	MLH3	Colon cancer	167	SMARCE1	Meningioma
38	CREBBP	Leukemia	103	MPL	Leukemia	168	SMO	Skin cancer
39	CTC1	Multiple cancer	104	MRE11	Breast Cancer	169	SOS1	Fibroma
40	CTNNA1	Multiple cancer	105	MSH2	Colon cancer	170	SRC	Colon cancer
41	CTNNB1	Colon cancer	106	MSH3	Multiple cancer	171	SRP72	Leukemia
42	CYLD	Multiple cancer	107	MSH6	Colon cancer	172	STK11	Melanoma
43	DDB2	Multiple cancer	108	MST1R	Multiple cancer	173	SUFU	Meningioma
44	DDX41	Leukemia	109	MUTYH	Colon cancer	174	TERC	Leukemia
45	DICER1	Multiple cancer	110	MYC	Leukemia	175	TERT	Leukemia
46	DIS3L2	Multiple cancer	111	NBN	Leukemia	176	TET2	Leukemia
47	DKC1	Multiple cancer	112	NF1	Leukemia	177	TGFBR2	Colon cancer
48	EGFR	Lung cancer	113	NF2	Brain tumor	178	TINF2	Multiple cancer
49	EGLN1	Leukemia	114	NHP2	Multiple cancer	179	TLR4	Colon cancer
50	EP300	Colon cancer	115	NOP10	Multiple cancer	180	TMEM127	Renal Carcinoma
51	EPCAM	Colon cancer	116	NPM1	Leukemia	181	TP53	Breast Cancer
52	ERBB2	Lung cancer	117	NRAS	Colon cancer	182	TRIP13	Liver cancer
53	ERCC1	Multiple cancer	118	NSD1	Leukemia	183	TSC1	Multiple cancer
54	ERCC2	Multiple cancer	119	NTHL1	Colon cancer	184	TSC2	Multiple cancer
55	ERCC3	Multiple cancer	120	PALB2	Breast Cancer	185	TYR	Melanoma
56	ERCC4	Fanconi anemia	121	PALLD	Pancreatic cancer	186	U2AF1	Leukemia
57	ERCC5	Multiple cancer	122	PBRM1	Renal Carcinoma	187	VHL	Renal Carcinoma
58	ESR1	Breast Cancer	123	PDGFRA	Gastrointestinal Tumor	188	WRAP53	Multiple cancer
59	ETV6	Leukemia	124	PDGFRB	Leukemia	189	WRN	Multiple cancer
60	EXT1	Multiple cancer	125	PHOX2B	Neuroblastoma	190	WT1	Lung cancer
61	EXT2	Multiple cancer	126	PIK3CA	Breast Cancer	191	XPA	Multiple cancer
62	EZH2	Multiple cancer	127	PMS2	Colon cancer	192	XPC	Multiple cancer
63	FAN1	Multiple cancer	128	POLD1	Colon cancer	193	XRCC2	Fanconi
64	FANCA	Fanconi anemia	129	POLE	Colon cancer			
65	FANCB	Fanconi anemia	130	POLH	Multiple cancer			