Hereditary Breast and Ovarian Cancer

Precision Panel

Overview

Breast cancer is the most common malignancy among females and the second most common cause of death from a neoplastic disease affecting women. Up to 5%-10% of breast cancer cases are hereditary and are caused by pathogenic mutations in genes such as BRCA1 and BRCA2 as well as germline mutations in other high penetrant genes. Nonetheless, some of these genes have been associated with other cancers, such as ovarian, pancreatic and colorectal cancer.

Hereditary cancer syndromes are encountered in all medical specialties. Although they account for about 5% of all malignancies, it is of special importance to identify these patients because, unlike patients with sporadic cancers, they require special, long-term care as their predisposition can cause them to develop certain tumors at a relatively early age. These cancers can arise in the lungs, kidneys, liver, pancreas, skin, eyes, heart. Most hereditary cancers are associated with a "germline mutation" that will be present in every cell of the human body. Identification of patients at risk of inherited cancer susceptibility is dependent upon the ability to characterize genes and alterations associated with increased cancer risk as well as gathering a detailed personal and family history aiding in the identification of the mode of inheritance as well as other family members at risk of suffering from this susceptibility. Most of these genes are inherited in an autosomal dominant fashion.

The Igenomix Hereditary Breast and Ovarian Cancer Precision Panel can be used as a screening and diagnostic tool ultimately leading to a better management and prognosis of the disease. It provides a comprehensive analysis of the genes involved in this disease using next-generation sequencing (NGS) to fully understand the spectrum of relevant genes involved, and their high or intermediate penetrance.

Indications

The Igenomix Hereditary Breast and Ovarian Cancer Precision Panel is indicated in those cases where there are:

- Individuals with personal history of breast/ovarian cancer and one of the following
    - Breast and/or ovarian or pancreatic cancer in at least two blood relatives.
    - Multiple primary breast cancers or bilateral breast cancer first diagnosed before the age of 50 years.
    - Premenopausal triple negative breast cancer diagnosed at a young age (<45 years).
    - Male breast cancer in a blood relative.

- Ethnicities with high BRCA mutation frequency, such as Ashkenazi Jews, should be tested, even in the absence of family history.

Clinical Utility

The clinical utility of this panel is:

- The genetic and molecular diagnosis for an accurate clinical diagnosis of a patient with personal or family history suggestive of hereditary breast cancer.
- Early initiation of treatment with a multidisciplinary team for appropriate surveillance, chemoprevention and risk-reducing mastectomy (RRM) or risk-reduction salpingo-oophorectomy.
- Risk assessment of asymptomatic family members according to the mode of inheritance
- Reduce morbidity related to breast cancer or morbidity secondary to complications of surveillance and treatment.
- Improved pathways from diagnosis to treatment in susceptible populations.

Genes & Diseases

List of genes included in the Hereditary Breast and Ovarian Cancer Precision Panel.
Most relevant genes have been classified according to:

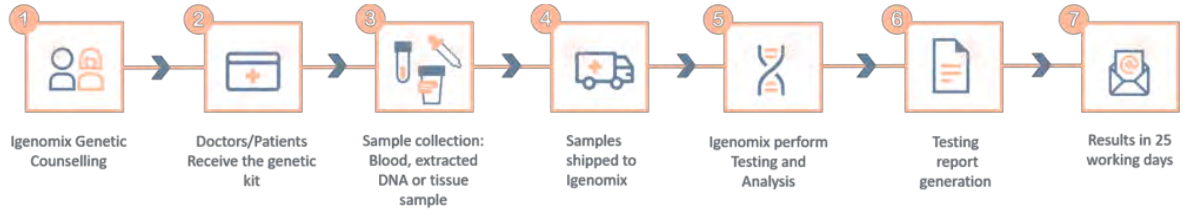
High Risk	Well studied Greater than 4-fold risk of developing one or more cancers Can cause a moderate risk for other cancers Guidelines or expert opinion for cancer screening and prevention
Moderate Risk	Well-studied 2- to 4-fold risk of developing one or more cancers May increase risk for other cancers Limited guidelines for screening and prevention
Research	Not as well-studied Precise lifetime risks and tumor spectrum not yet determined Guidelines for screening and prevention are limited or not available

GENE	RISK	OMIM DISEASES	INHERITANCE*	% GENE COVERAGE (20X)	HGMD**
AKT1		Breast Cancer, Colorectal Cancer, Cowden Syndrome, Meningioma, Proteus Syndrome	AD	100%	6 of 6
ATM	Moderate risk	Ataxia-Telangiectasia, Breast Cancer, Mantle Cell Lymphoma	AD,AR	99.93%	1608 of 1632
BARD1	Moderate risk	Breast Cancer, Hereditary Breast And Ovarian Cancer Syndrome	AD	99.86%	195 of 195
BRCA1	High risk	Breast Cancer, Familial Breast-Ovarian Cancer, Familial Pancreatic Carcinoma, Fanconi Anemia Complementation Group S, Hereditary Breast And Ovarian Cancer Syndrome, Primary Peritoneal Carcinoma	AD,AR,MU	98.97%	2783 of 2894
BRCA2	High risk	Breast Cancer, Familial Breast-Ovarian Cancer, Familial Pancreatic Carcinoma, Fanconi Anemia Complementation Group D1, Glioma, Hereditary Breast And Ovarian Cancer Syndrome, Medulloblastoma, Nephroblastoma, Pancreatic Cancer, Prostate Cancer, Wilms Tumor	AD,AR,MU	98.51%	3343 of 3451
BRE		Brain Glioma, Synchronous Bilateral Breast Carcinoma		98.20%	NA of NA
BRIP1	Moderate risk	Breast Cancer, Fanconi Anemia Complementation Group J, Hereditary Breast And Ovarian Cancer Syndrome	AD,AR	94.97%	235 of 237
CDH1	High risk	Blepharo-Cheilo-Odontic Syndrome, Breast Cancer, Cleft Lip/Palate, Endometrial Carcinoma, Gastric Cancer, Prostate Cancer	AD	100%	361 of 363
CHEK2	Moderate risk	Breast Cancer, Hereditary Breast And Ovarian Cancer Syndrome, Li-Fraumeni Syndrome, Osteosarcoma, Prostate Cancer	AD	99.47%	307 of 310

EPCAM		Hereditary Nonpolyposis Colorectal Cancer Type 8, Congenital Diarrhea With Tufting Enteropathy, Lynch Syndrome	AR	99.94%	52 of 70
FAM175A	Moderate risk	Ovarian Cancer, Breast Cancer, Fanconi Anemia Complementation Group A	-	94.81%	NA of NA
FANCC		Fanconi Anemia Complementation Group C	AR	100%	75 of 75
FANCM		Fanconi Anemia, Male Infertility With Azoospermia Or Oligozoospermia Due To Single Gene Mutation, Premature Ovarian Failure; Spermatogenic Failure	AR	99.73%	59 of 61
GEN1		Xeroderma Pigmentosum Complementation Group G	-	99.71%	6 of 6
MEN1		Familial Isolated Hyperparathyroidism, Insulinoma, Multiple Endocrine Neoplasia Type 1, Pituitary Gigantism, Prolactinoma	AD	99.90%	871 of 876
MLH1		Hereditary Nonpolyposis Colorectal Cancer Type 2, Lynch Syndrome, Mismatch Repair Cancer Syndrome, Muir-Torre Syndrome	AD,AR	99.94%	1079 of 1118
MRE11	Moderate risk	Ataxia-Telangiectasia-Like Disorder, Hereditary Breast And Ovarian Cancer Syndrome	AR	99.95%	NA of NA
MSH2		Lynch Syndrome, Mismatch Repair Cancer Syndrome, Muir-Torre Syndrome	AD,AR	99.99%	1032 of 1057
MSH6		Hereditary Nonpolyposis Colorectal Cancer Type 5, Endometrial Carcinoma, Lynch Syndrome, Mismatch Repair Cancer Syndrome, Muir-Torre Syndrome	AD,AR	99.28%	613 of 641
MUTYH		Familial Adenomatous Polyposis, Gastric Cancer, MUTYH-Related Attenuated Familial Adenomatous Polyposis	AR	100%	183 of 183
NBN	Moderate risk	Aplastic Anemia, Hereditary Breast And Ovarian Cancer Syndrome, Acute Lymphocytic Leukemia, Nijmegen Breakage Syndrome	AR,MU,P	100%	200 of 200
NF1		17q11.2 Microduplication Syndrome, Hereditary Pheochromocytoma-Paraganglioma, Juvenile Myelomonocytic Leukemia, Neurofibromatosis Type 1, Neurofibromatosis-Noonan Syndrome, Familial Spinal Neurofibromatosis Type I, Watson Syndrome	AD	97.97%	3082 of 3166
PALB2		Breast Cancer, Familial Pancreatic Carcinoma, Fanconi Anemia Complementation Group N, Hereditary Breast And Ovarian Cancer Syndrome	AD,AR	98.78%	601 of 617
PIK3CA		Breast Cancer, Capillary Malformation Of The Lower Lip, Lymphatic Malformation Of Face And Neck, Asymmetry Of Face And Limbs And Partial/Generalized Overgrowth, Colorectal Cancer, Congenital Lipomatous Overgrowth, Vascular Malformations And Epidermal Nevi, Cowden Syndrome, Gastric Cancer, Hemihyperplasia-Multiple Lipomatosis Syndrome, Hepatocellular Carcinoma, Seborrheic Keratosis, Lung Cancer, Lynch Syndrome, Macrocephaly-Capillary Malformation, Meningioma	AD	99.58%	54 of 58
PMS2		Hereditary Nonpolyposis Colorectal Cancer Type 4, Lynch Syndrome, Mismatch Repair Cancer Syndrome	AD,AR	97.17%	264 of 285
PTEN	High risk	Bannayan-Riley-Ruvalcaba Syndrome, Cowden Disease, Hereditary Breast And Ovarian Cancer Syndrome, Juvenile Polyposis Of Infancy, Lhermitte-Duclos Disease, Macrocephaly/Autism Syndrome, Familial Meningioma, Prostate Cancer, Proteus Syndrome, Proteus-Like Syndrome, Segmental Outgrowth-Lipomatosis-Arteriovenous Malformation-Epidermal Nevus Syndrome	AD	99.97%	609 of 629
RAD50	Moderate risk	Hereditary Breast And Ovarian Cancer Syndrome, Nijmegen Breakage Syndrome-like Disorder	AR	99.94%	117 of 120
RAD51C	Moderate risk	Familial Breast-Ovarian Cancer, Fanconi Anemia Complementation Group O, Hereditary Breast And Ovarian Cancer Syndrome	AR	100%	130 of 130
RAD51D	Moderate risk	Hereditary Breast And Ovarian Cancer Syndrome	-	100%	97 of 97
RECQL		Inherited Cancer-Predisposing Syndrome	-	99.71%	32 of 34
RINT1		Infantile Liver Failure Syndrome	AR	99.96%	16 of 16
STK11	High risk	Pancreatic Cancer, Peutz-Jeghers Syndrome, Testicular tumor	AD	81.99%	456 of 470
TP53	High risk	Adrenocortical Carcinoma, Basal Cell Carcinoma, Bone Marrow Failure Syndrome, Breast Cancer, Colorectal Cancer, Essential Thrombocythemia, Familial Pancreatic Carcinoma, Glioma, Hepatocellular Carcinoma, Hereditary Breast And Ovarian Cancer Syndrome, Li-Fraumeni Syndrome, Nasopharyngeal Carcinoma, Osteosarcoma, Pancreatic Cancer, Papilloma Of Choroid Plexus	AD,MU,P	98.92%	557 of 563
XRCC2		Fanconi Anemia Complementation Group U, Male Infertility With Azoospermia Or Oligozoospermia Due To Single Gene Mutation	AR	98.39%	28 of 28

*Inheritance: AD: Autosomal Dominant; AR: Autosomal Recessive; X: X linked; XLR: X linked Recessive; Mi: Mitochondrial; Mu: Multifactorial.
**Number of clinically relevant mutations according to HGMD

Methodology



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Call +34 963 905 310 or send an email to supportspain@igenomix.com for any of the following objectives:

- Get more information about the test.
- Request your kit.
- Request a pick up of the kit after collecting the sample.

References

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