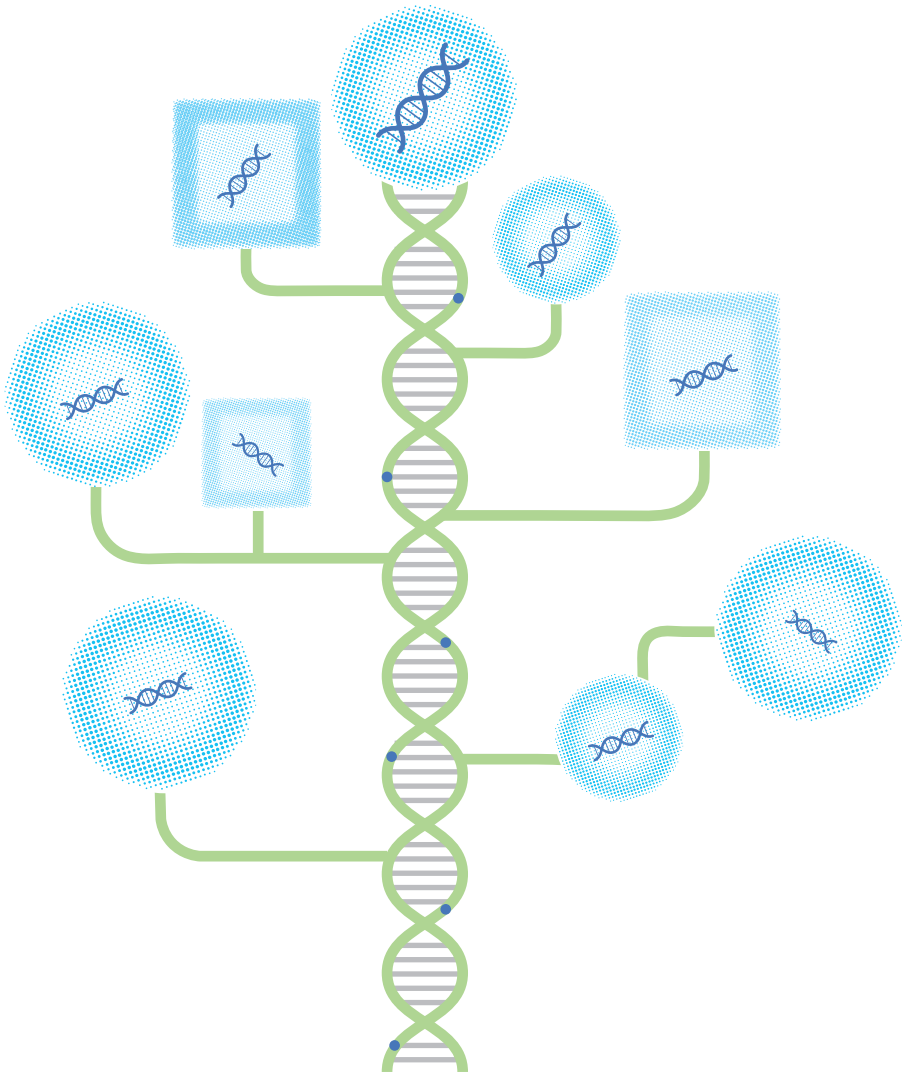
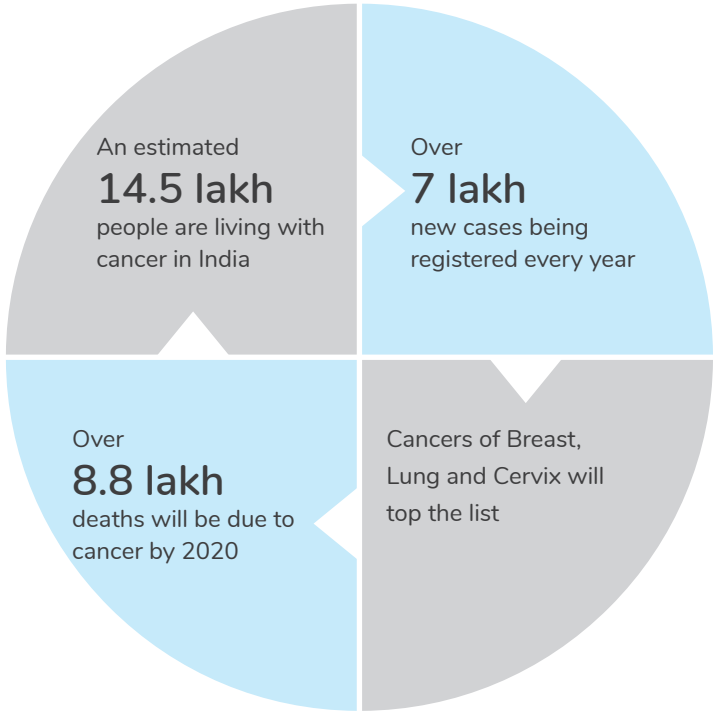
Prima
Cancer Genetics

MEDGENOME

Germline Mutation Testing for
Hereditary Cancers



Alarming scenario of Cancer in India*



*National Cancer Registry Program - ICMR

MedGenome's comprehensive offering of the most advanced Genetic and Molecular Tests for Cancer Management

Advanced testing techniques in Prima

Next Generation Sequencing (NGS)	Sanger Sequencing	Microarray
Immunohistochcmistry IHC	Cytogenetics	Multiplex Ligation-dependent Probe Amplification (MLPA)
Fluorescence In-Situ Hybridization (FISH)	Flow Cytometry	Droplet Digital PCR (DD-PCR)
Fragment Analysis	Real Time PCR	Reverse Transcriptase Polymerase Chain Reaction (RT-PCR)

How Molecular and Genetic Testing Helps?

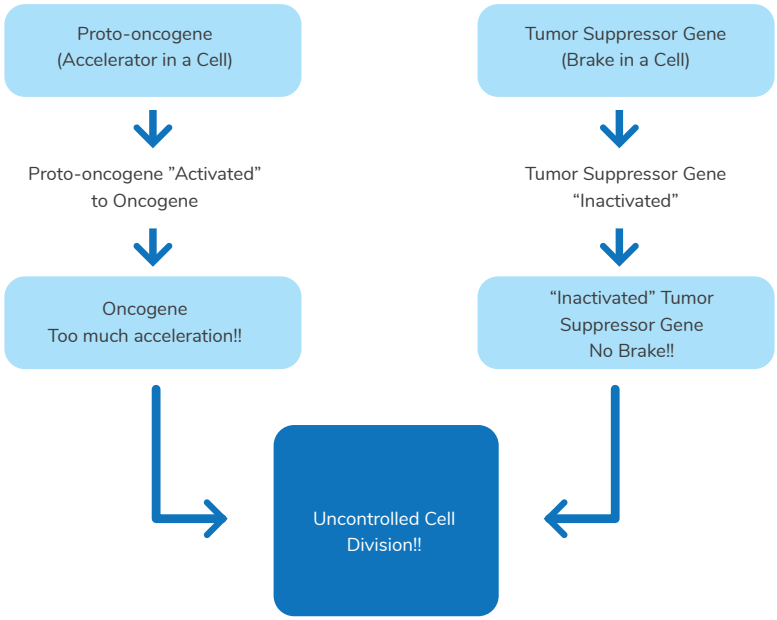
- Ability to sub-classify the type of cancer
- Disease prognostication (assessment of survival and response to treatment)
- Theranostic chemotherapy Value and (Finding radiation) the best fit targeted drugs -alleviating unnecessary
- Hereditary Cancer risk assessment

Clinical Background of Hereditary Cancers

- About 5% of cancer patients have genetic preponderance which would be passed on to next generation.
- People who have inherited a mutation (pathogenic variant) in a cancer-susceptibility gene are at significantly greater risk of developing certain types of cancer compared with those without the mutation.
- For example, a woman with a BRCA1 mutation has a 65% lifetime risk of develop-ing breast cancer, whereas a woman without a mutation has a lifetime risk of only 12%.

The Genetic Mutations impacting occurrence of Hereditary Cancers

- Numerous cancer-susceptibility genes have been identified
- Many of these genes are associated with multiple cancer types
- Conversely, a single cancer type can be linked to mutations in several genes



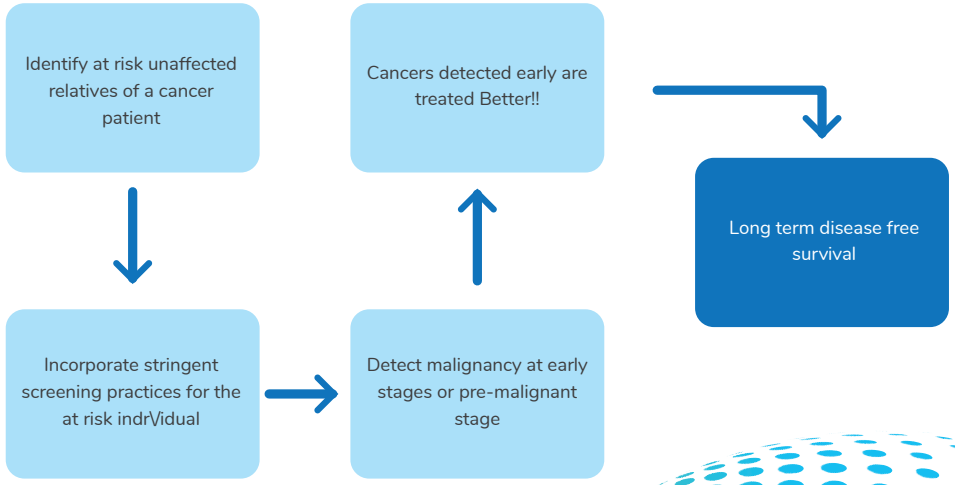
GERMLINE Mutation testing is empowering the Oncologist to change the trend of Cancer care for the First time in History

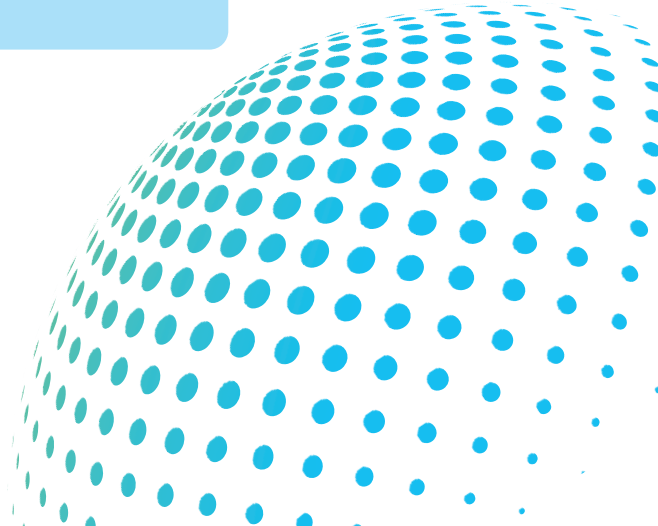
Positive BRCA Mutation

- Upto 87% increased risk of Ca Breast
- Upto 44% increased risk of Ca Ovarian
- Upto 10% increased risk of other Cancers (Pancreas, Prostate)

Positive FAP/MAP/AFAP

- Upto 99% increased risk of Colorectal Cancer





GERMLINE Mutation tests for Hereditary Cancers

A simple blood sample to answer the most complex questions of Cancer Inheritance

The decision between single gene and panel testing?

Next Generation Sequencing (NGS) is the answer

- NGS based test panels analyse multiple genes simultaneously
- Advantage - Genes and Molecular Pathways that were not anticipated to be involved may be detected
- It is done at a much lower cost than traditional sequencing methods
- Has a higher likelihood of identifying a causative mutation
- Reduces the need for multiple follow-ups and additional testing

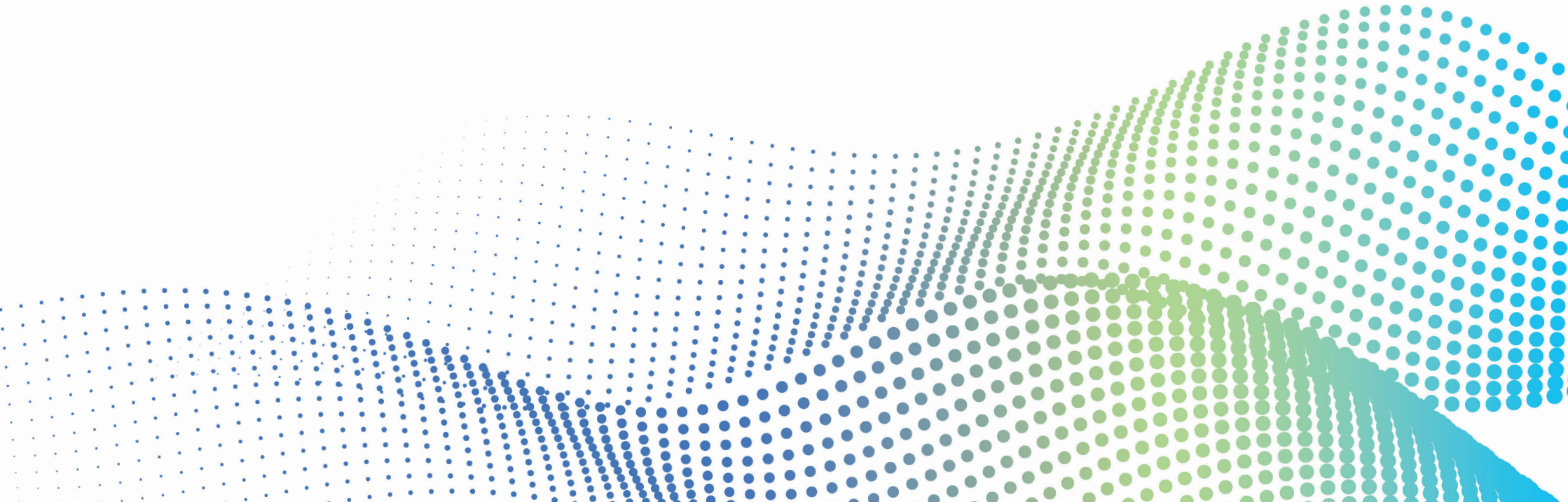
Why Panel testing?

Many solution's to Multigene Panel testing

High Penetrant Cancer Susceptibility Genes in Common Cancers[2,8,9]	
Malignancy	High Penetrant Cancer Susceptibility Genes
Breast Cancer	BRACA1, BRCA2. p53, PTEN, COH1
Colon & Colorectal Cancer	MLH1, MSH2,MSH6,PMS2, MYH, APC, STK11, MSI
Uterine cancer	MLH1, MSH2, MSH6, PMS2, PTEN
Ovarian Cancer	BRCA1, BRCA2, MLH1, MSH2, MSH6, PMS2, p53
Prostate Cancer	BRCA2, RNASEL ELAC2, MSR1
Pancreatic Cancer	BRCA2, STK11/LKB1, PALB2, PRSS1, SPINK1, COKN2A

Julie A. Katz, July 2015, The Impact of BRCA Testing: Research at ASCO and Treatment Implications for Ovarian, Breast, Prostate, and Pancreatic Cancers.

Lu, Karen H MD. Value of Family History in Common Cancers, Epidemiology: From Genetics to Practice Presentation, Health Services Research and Quality of Care Track. ASCO 2015.



Who should be tested for Hereditary Cancers?

1. An individual whose first line blood relative has been detected with a pathogenic or likely pathogenic variant in a cancer susceptibility gene
2. An individual with personal history of ≥1 of the following:
    - Cancer diagnosed at age ≤50 years
    - Bilateral or multiple primary cancers
    - Cancer diagnosed at any age and significant family history
    - Rare cancer (eg, male breast cancer or ovarian cancer)
3. Individuals with family history of cancer with ≥1 of the following:
    - ≥3 Blood relatives on same side of the family with the same or related cancer type
    - ≥2 Blood relatives on same side of the family with the same or related cancer type, at least l of whom was diagnosed at age ≤50 years
    - ≥1 Blood relative on same side of the family with the same or related cancer type and Ashkenazi Jewish ancestry

MedGenome offers Broad Multi-Gene NGS panels for evaluation of Hereditary Cancer predisposition

Hereditary Cancer Panel (HCP) - Focussed

- Provides evaluation of 106 genes

Sample Requirement

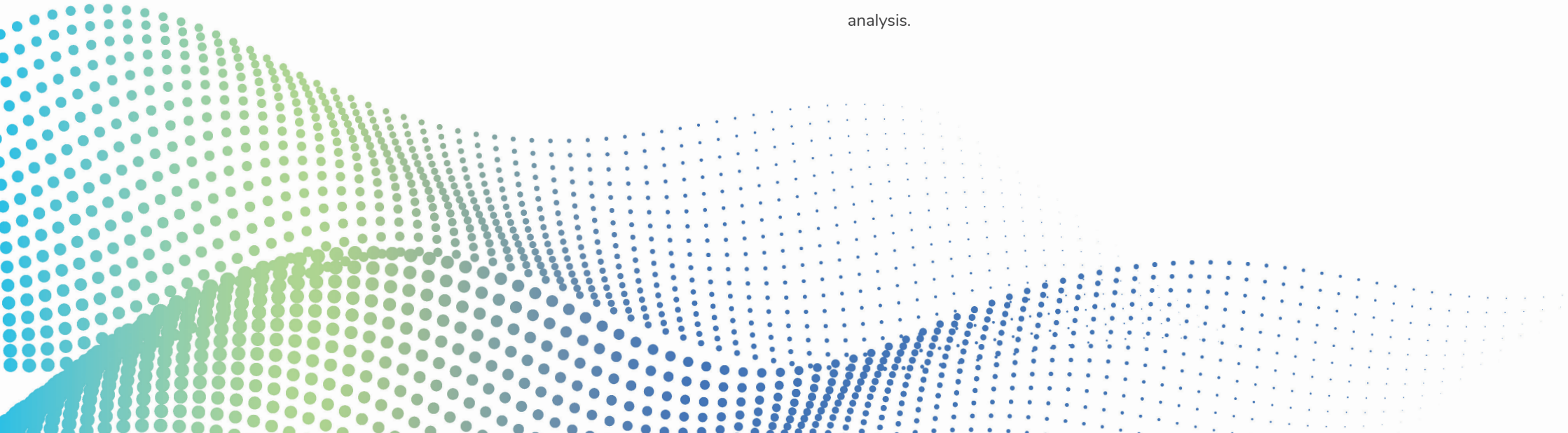
Blood (3-5ml) EDTA Tubes

Turn Around Time

Time taken for the generating a clinical report will be maximum of

- 4 weeks by NGS

In case where the sample quality is poor (sample which fails our QA/QC), the TAT will get prolonged. New batch of sample will need to be submitted for sequencing and analysis.

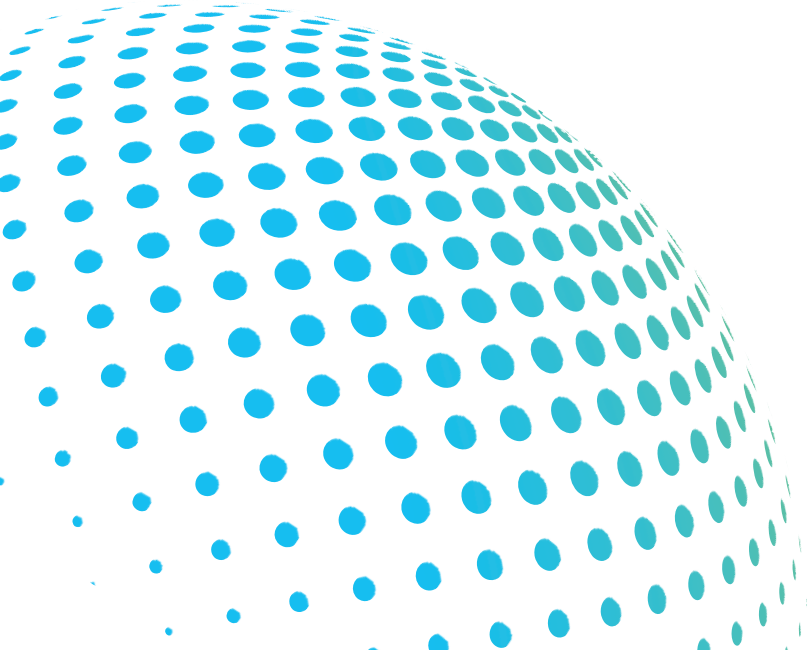


Free Genetic Counselling

In accordance with the latest global cancer management guidelines (NCCN - National Comprehensive Cancer Network) Prima offers FREE Pre and Post-test Genetic Counselling with our expert and certified Genetic Counsellors to all your patients.

Best available support for your patients and families via

- Latest technologies
- Helpful customer service
- Clear result interpretation
- Counselling sessions with our Genetic Counsellors



Sample Report

MedGenome Labs Ltd.
3rd Floor, Narayana Nethralaya Building, Narayana Health City,
#258/A, Bommasandra, Hosur Road, Bangalore – 560 099, India.
Tel: +91 (0)80 67154932 / 933 Web: www.medgenome.com

MEDGENOME

DNATEST REPORT– MEDGENOME LABORATORIES

Full Name / Ref No:	XXX	Order ID/Sample ID:	XXX /XXX
Gender:	XX	Sample Type:	Blood
Date of Birth / Age:	XX years	Date of Sample Collection:	XX
Referring Clinician:	Dr. XXX, XXX, XXX.	Date of Sample Receipt:	XX
		Date of Order Booking:	XX
		Date of Report:	XX
Test Requested:	Hereditary cancer gene panel – focussed		

CLINICAL DIAGNOSIS / SYMPTOMS / HISTORY

XXX is diagnosed with carcinoma right breast. XXX has a family history of breast cancer with mother affected. XXX has been evaluated for pathogenic variations in the genes listed in appendix 1.

RESULTS

PATHOGENIC VARIANT CAUSATIVE OF THE REPORTED PHENOTYPE WAS IDENTIFIED

Gene (Transcript) ǂ	Location	Variant	Zygosity	Disease (OMIM)	Inheritance	Classification
BRCA1 (-) (ENST00000471181)	Exon 15	c.4571C>A (p.Ser1524Ter)	Heterozygous	{Breast-ovarian cancer, familial, 1}	Autosomal Dominant	Pathogenic

ADDITIONAL FINDINGS: NO VARIANT(S) OF UNCERTAIN SIGNIFICANCE (VUS) IDENTIFIED

No other variant that warrants to be reported was detected. Variations with high minor allele frequencies which are likely to be benign will be given upon request.

VARIANT INTERPRETATION AND CLINICAL CORRELATION

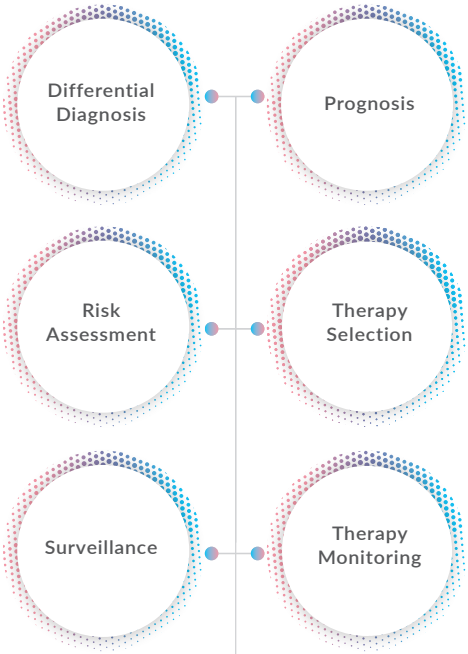
Variant description: A heterozygous nonsense variation in exon 15 of the BRCA1 gene (chr17:41226515G>T; Depth: 171x) that results in a stop codon and premature truncation of the protein at codon 1524 (p.Ser1524Ter; ENST00000471181) was detected (Table). This variation (referred as S1503X) has previously been reported in patients and families withbreast and /or ovarian cancer[23, 24].The Ser1524Ter variant is not reported in the 1000 genomes and our internal database and has a minor allele frequency of 0.0008% in ExAC database. The in-silico predictions# of the variant is damaging by Mutation Taster tool. The reference codon is conserved in primates.

OMIM phenotype: Susceptibility to familial breast-ovarian cancer-1 (OMIM#604370) results from heterozygous germline mutations in the BRCA1 gene (OMIM*113705).

MEDGENOME

Prima by MedGenome offers a wide range of Oncology and Haematology genetic tests, these include:

Molecular Testing for Hematological Malignancies, Comprehensive Leukemia Panel



IGHV Gene Mutation Testing for CLL, Comprehensive Leukemia Panel, BCR-ABL1 gene fusion analysis

Hereditary Cancer Panel, BRCA1 and BRCA2 gene test, Thalassemia Mutation Test

Comprehensive Tumor Gene Panel, Somatic Mutation Panel, Comprehensive Leukemia Panel, Molecular Testing for Lung Cancer

OncoTrack, OncoSelect, OncoFocus (Liquid Biopsy Test)

NGS based IRMA, BCR- ABL1 gene fusion analysis

CAP ACCREDITED
COLLEGE of AMERICAN PATHOLOGISTS

For more information

1800 103 3691

diagnostics@medgenome.com

www.medgenome.com