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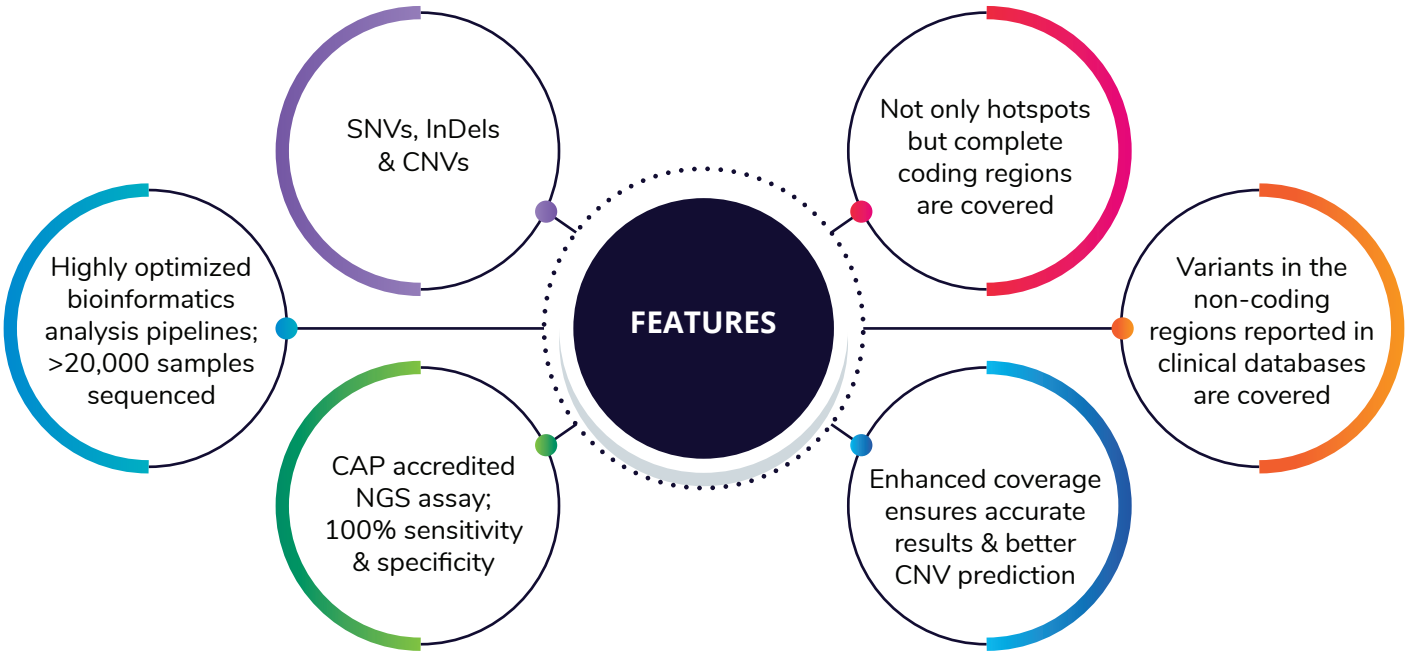
# Cancer Risk and Hereditary Cancer Genetic Test

NGS based comprehensive analysis of cancer predisposing genes (SNVs, InDels & CNVs)




## Indications

- Hereditary Breast & Ovarian Cancer Syndrome
- Paragangliomas
- MEN Syndrome
- Lynch Syndrome
- Nervous System Cancer
- Endocrine Cancer
- Pancreatic Cancer
- Renal Cancer
- Hereditary Nonpolyposis Colorectal Cancer
- Von-Hippel Lindau syndrome
- Prostate Cancer
- Thyroid Cancer
- Gynaecological Cancer
- Li-Fraumeni Syndrome
- Juvinile Polyposis
- Peutz-Jeghers
- Retinoblastoma

## Testing criteria

- Personal medical and/or family cancer history meets criteria for more than one hereditary cancer syndrome
- Family cancer history does not meet established testing guidelines, but consideration of inherited cancer risk persists and an appropriate panel is available
- Individuals with multiple cancer diagnoses
- Individuals concerned about cancer predisposition for whom family cancer history is limited or unknown
- Second-line workup for inherited cancer risk when first-line evaluation has been inconclusive

## Universal genetic testing vs Guideline-based testing for patients with Hereditary Cancer Syndrome

A multicenter cohort study of

**2984 patients**

with cancer was carried out

1

**13.3%**

of patients had **pathogenic germline variant**

2

**28.2% of patients**

with **pathogenic variants** in high penetrance genes **could have treatment modification**

3

**6.4% of patients**

had incremental **clinically actionable** findings that would not have been identified **by phenotype or family history**- based testing criteria

4

The commonest genes found to be mutated were:

***BRCA1, BRCA2, MUTYH, CHEK2, ATM*** and **Lynch syndrome genes *(MLH1, MSH2, PALB2)***

5

**Early onset**

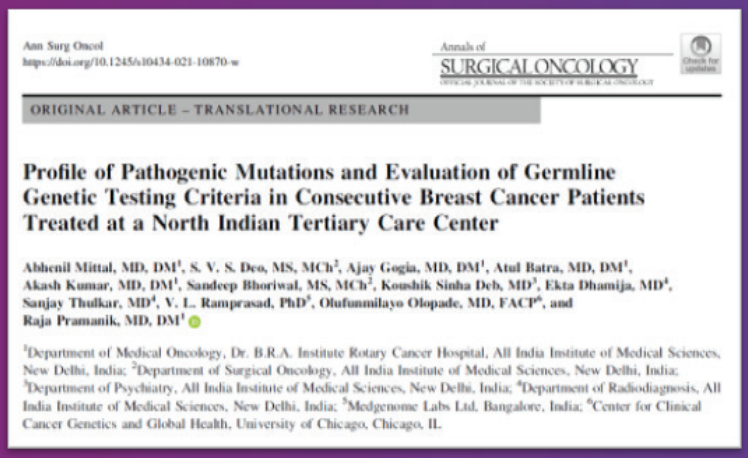
of disease was associated with **higher probability** of finding a **pathogenic variant**

6

**Universal testing among patients with solid tumor was associated with an increased detection of heritable variants over the predicted yield of targeted testing based on guidelines**

Reference: Samadder NJ, Riegert-Johnson D, Boardman L, et al. Comparison of Universal Genetic Testing vs Guideline-Directed Targeted Testing for Patients With Hereditary Cancer Syndrome [published online ahead of print, 2020 Oct 30]. JAMA Oncol. 2020;e206252. doi:10.1001/jamaoncol.2020.6252

# North Indian *BRCA* germline testing data (n=236)



Ann Surg Oncol
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Annals of SURGICAL ONCOLOGY

ORIGINAL ARTICLE – TRANSLATIONAL RESEARCH

**Profile of Pathogenic Mutations and Evaluation of Germline Genetic Testing Criteria in Consecutive Breast Cancer Patients Treated at a North Indian Tertiary Care Center**

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**Results**

Overall, 275 breast cancer patients were screened and 236 patients were included (median age 45 years); 30 patients did not consent and 9 patients previously underwent genetic testing. Thirty-four (14%) women had a positive family history and 35% had triple-negative breast cancer. P/LP mutations were found in 44/236 (18.64%) women; mutations in BRCA1 (22/47, 46.8%) and BRCA2 (9/47, 19.1%) were the most common, with 34% of mutations present in non-BRCA genes. Patients qualifying the testing criteria had a higher risk of having a P/LP mutation (NCCN: 23.6% vs. 7.04%, p = 0.03; MCG plus: 24.8% vs. 7.2%, p = 0.01). The sensitivity of the NCCN criteria was 88.6% (75.4–96.2) and 86.36% (72.65–94.83) for MCG plus. More than 95% sensitivity was achieved if all women up to 60 years of age were tested. Cascade testing was performed in 31 previous (16/44 families), with 23 testing positive.

- The prevalence of pathogenic mutations in breast cancer patients is higher in Indian patients compared with most other populations.
- Testing by NGS is recommended at a centralized CAP- and/or CLIA-certified laboratory for all patients followed by reflex MLPA for all patients if negative by NGS
- Pre and post genetic counseling

**Testing by guidelines may miss 11-13% of patients carrying high risk mutations.**

## Clinical benefits

- Risk estimation for secondary cancers and relapse
- Personal & Familial risk assessment
- Early detection for better clinical outcome
- Risk management & disease prevention through active surveillance and prophylactic surgeries
- Determines PARPi eligibility and platinum sensitivity

## Germline test details

| Test Code | Test Name | Technology | Test Information | TAT |
|---|---|---|---|---|
| MGM194 | Hereditary cancer panel (*BRCA1* and *BRCA2* along with other 143 genes) | Next Generation Sequencing | Complete coding regions and intron exon boundaries of 143 genes including *BRCA1* and *BRCA2* genes covered | 21 working days |
| MGM1841 | Comprehensive Hereditary Cancer panel | Next Generation Sequencing | Mutation analysis of 143 genes and deletion/duplication analysis of 30 genes including *BRCA1* and *BRCA2* genes | 21 working days |

**Sample Type: 3-4 ml of Peripheral blood in EDTA tube shipped at room temperature**

# Gene list

| COMPREHENSIVE HEREDITARY CANCER PANEL GENE LIST (143 genes covering SNVs, InDels, CNVs) | | | | | | | |
|---|---|---|---|---|---|---|---|
| ABRAXAS1 | CDK12 | ERCC3 | GALNT12 | MUTYH | PRKAR1A | SBDS | TSC1 |
| AIP | CDK4 | ERCC4 | GATA2 | MXI1 | PRSS1 | SDHA | TSC2 |
| ALK | CDKN1B | ERCC5 | GPC3 | NBN | PTCH1 | SDHAF2 | TYR |
| APC* | CDKN1C | EXT1 | HOXB13 | NF1 | PTCH2 | SDHB | VHL |
| AR | CDKN2A | EXT2 | HRAS | NF2 | PTEN | SDHC | WRN |
| ATM | CEBPA | EZH2 | KIF1B | NSD1 | RAD50 | SDHD | WT1 |
| AXIN2 | CEP57 | FAN1 | KIT | NTHL1 | RAD51B | SLC45A2 | XPA |
| BAP1 | CHEK1 | FANCA | LZTR1 | PALB2 | RAD51C | SLX4 | XPC |
| BARD1 | CHEK2 | FANCB | MAX | PALLD | RAD51D | SMAD4 | XRCC2 |
| BLM | CTNNA1 | FANCC | MEN1 | PAX5 | RAD54L | SMARCA4 | XRCC3 |
| BMPR1A | CYLD | FANCD2 | MET | PDGFRA | RB1 | SMARCB1 | |
| BRCA1 | DDB2 | FANCE | MITF | PHOX2B | RECQL | SMARCE1 | |
| BRCA2 | DICER1 | FANCF | MLH1 | PMS1 | RECQL4 | SRGAP1 | |
| BRIP1 | DIS3L2 | FANCG | MLH3 | PMS2 | RET | STK11 | |
| BUB1B | EGFR | FANCI | MRE11 | POLD1 | RHBDF2 | SUFU | |
| CBL | ELAC2 | FANCL | MSH2 | POLE | RINT1 | TERT* | |
| CD82 | ENG | FANCM | MSH3 | POT1 | RNASEL | TGFBR2 | |
| CDC73 | EPCAM | FH | MSH6 | PPP2R2A | RNF43 | TMEM127 | |
| CDH1 | ERCC2 | FLCN | MSR1 | PRF1 | RUNX1 | TP53 | |

| HEREDITARY CANCER GENES FOR DELETION/DUPLICATION ANALYSIS BY DIGITAL MLPA (30 Genes) | | | | | | | |
|---|---|---|---|---|---|---|---|
| MUTYH | BARD1 | APC | BMPR1A | POLE | CDH1 | RAD51C | CHEK2 |
| EPCAM | MLH1 | PMS2 | PTEN | BRCA2 | TP53 | BRIP1 | GREM1 |
| MSH2 | BAP1 | NBN | ATM | SCG5 | RAD51D | SMAD4 | |
| MSH6 | MITF | CDKN2A | CDK4 | PALB2 | BRCA1 | STK11 | |

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## Talk to the Experts


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