Comprehensive Panel- 500 Genes

Test Description

The MolQ Comprehensive Panel includes 500+ key solid tumor genes (for SNV, CNV, TMB, MSI and fusions) that are well characterized in the published literature and associated with oncology drugs that are FDA approved, part of NCCN guidelines, or in clinical trials.

Patient Demographic

Name: Mr. Rajneesh Singh
Sex: Male
Date of Birth/Age: 59 years
Disease: Colon Cancer

Clinician

Clinician Name: Dr Amit Verma
Medical Facility: Dr AV Institute of Personalized Therapy and Cancer Research (IPTCR)
Pathologist: Not Provided

Specimen

Booking ID: 012312140028
Sample Type: FFPE Block ID- S-1612/23
Tumor Content Percentage: 30%
Date of Collection: 14-12-2023
Date of Booking: 14-12-2023

CLINICAL SYNOPSIS

Rajneesh Singh is a known case of colon carcinoma. He has been evaluated for pathogenic variations in the genes listed in Appendix 2.

RESULTS

No clinically relevant alteration was detected.

Tumor Mutation Burden is 8.54 Mut/Mb.

Microsatellite Instability (MSI) is stable.

VARIANT DETECTED AS PER NCCN GUIDELINES

No clinically relevant alteration detected.

OTHER VARIANTS DETECTED

Mutation in *TP53* (p.Gly266*, VAF= 13.80%), *PALB2* (p.Ser518*, VAF= 8.49%) and *CYP2D6* (c.506-1G>A, VAF= 60.12%) are present in the given sample.

Note: RNA QC failed hence, gene fusion cannot be analyzed.

RELEVANT COLON CANCER FINDINGS

Gene	Findings	Gene	Findings
BRAF	None detected	*NTRK1*	None detected
ERBB2	None detected	*NTRK2*	None detected
KRAS	None detected	*NTRK3*	None detected
NRAS	None detected	*RET*	None detected

RELEVANT BIOMARKERS

Gene/ Transcript (Locus)	Variant ID	Variant/ Exon/ Variant Effect	Allele Frequency /Coverage	#ClinVar	*Relevant Therapies (In this cancer type)	*Relevant Therapies (In other cancer type)	Tier[1]
NBN (chr8:90995031)	-	c.89_90insA (p.Asn30Lysfs*7) Exon 2 *Frameshift Insertion*	8.45% / 1928		None	None	IIc
PALB2 (chr16:23646314)	-	c.1553C>G (p.Ser518*) Exon 4 *Nonsense*	8.49% / 1979	Pathogenic	None	None	IIc

*Public data sources included in relevant therapies: FDA[i], NCCN, EMA[ii], ESMO
#Based on Clinvar version 20220709
[1]Li et al. Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer: A Joint Consensus Recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists. J Mol Diagn. 2017 Jan;19(1):4-23.

HRR DETAILS

Gene/Genome Alterations	Findings
LOH percentage	2.86%
Not Detected	Not Applicable

Homologous recombination repair (HRR) genes were defined from published evidence in relevant therapies, clinical guidelines, as well as clinical trials, and include - *BRCA1, BRCA2, ATM, BARD1, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, RAD51B, RAD51C, RAD51D* and *RAD54L*.

VARIANT OF UNKNOWN SIGNIFICANCE (VUS)

Not present

PREVALENT CANCER BIOMARKERS WITHOUT RELEVANT EVIDENCE BASED ON INCLUDED DATA SOURCES

Gene/ (Locus)	Variant	Variant Effect/ Variant ID	Variant Allele Frequency	Location	Coverage	#ClinVar
APC (chr5:112175529)	c.4239_4240delGG (p.Met1413Ilefs*9)	Frameshift Deletion	10.47%	Exon 16	1939	-
SLX4 (chr16:3639977)	c.3661_3662delGCinsT (p.Ala1221Cysfs*67)	Frameshift Block Substitution	23.75%	Exon 12	1103	-
TP53 (chr17:7577142)	c.796G>T (p.Gly266*)	Nonsense	13.80%	Exon 8	2000	Pathogenic
CYP2D6 (chr22:42524947)	c.506-1G>A (p.?)	Unknown/ COSM5019461	60.12%	Exon 4	810	Likely benign/drug response/other

#Based on Clinvar version 20220709

CLINICAL CORRELATION AND VARIANT INTERPRETATION

SLX4 **p.Ala1221Cysfs*67**

Gene description: The *SLX4* gene encodes the SLX4 structure-specific endonuclease subunit[1]. *SLX4*, also known as *FANCP*, is a tumour suppressor protein that functions as a scaffold for DNA repair endonucleases[2]. SLX4 functions in DNA repair mechanisms including double-strand break (DSB) repair and interstrand crosslink repair[2-4]. Specifically, SLX4 localizes at DSB sites and recruits and interacts with other repair proteins such as ERCC1-XPF, MUS81-EME1, and SLX1[2-4]. Germline *SLX4* mutations are associated with Fanconi Anemia, a genetic condition characterized by genomic instability and congenital abnormalities, including bone marrow failure and cancer predisposition[3].

Alterations and prevalence: Recurrent somatic mutations in *SLX4* are observed in 11% of uterine corpus endometrial carcinoma, 9% of skin cutaneous melanoma, 6% of stomach adenocarcinoma, and 4% of bladder urothelial carcinoma[5,6].

Potential relevance: Currently, no therapies are approved for SLX4 aberrations.

CYP2D6 **c.506-1G>A**

Gene description: The *CYP2D6* gene encodes cytochrome P450 family 2 subfamily D member 6, a member of the cytochrome P450 superfamily of proteins[1]. The cytochrome P450 proteins are monooxygenases that play important roles in the biotransformation of xenobiotics and carcinogens, and the synthesis of cholesterol, steroids and other lipids1[,7]. CYP2D6 is a key enzyme involved in the biotransformation of the prodrug tamoxifen to its active metabolites, endoxifen and 4-hydroxytamoxifen[8,9]. The *CYP2D6* gene is highly polymorphic, and inherited *CYP2D6* polymorphisms in individuals may result in absent, reduced, normal, or high CYP2D6 enzyme activity leading to poor, intermediate, normal, or ultrarapid metabolism of tamoxifen[8-11]. *CYP2D6* genotype may impact response to tamoxifen treatment and clinical outcomes[10].

Alterations and prevalence: Somatic mutations in *CYP2D6* are observed in 4% of uterine corpus endometrial carcinoma, 3% of stomach adenocarcinoma and cholangiocarcinoma, and 2% of colorectal adenocarcinoma, skin cutaneous melanoma, and kidney chromophobe[5,6]. Biallelic loss of *CYP2D6* is observed in 2% of ovarian serous cystadenocarcinoma[5,6]. Amplification of *CYP2D6* is observed in 4% of skin cutaneous melanoma, 3% of cholangiocarcinoma, and 2% of pancreatic adenocarcinoma[5,6].

Potential relevance: Currently, no therapies are approved for CYP2D6.

PALB2 **p.Ser518***

Gene description: The *PALB2* gene encodes the partner and localizer of BRCA2 protein that binds to and promotes intranuclear localization of the breast cancer 2 early onset (BRCA2) protein[12]. Also known as FANCN, PALB2 belongs to the Fanconi Anemia (FA) complementation group of proteins that also include FANCA, FANCB, FANCC, FANCD1 (BRCA2), FANCD2, FANCE, FANCF, FANCG, FANCI, FANCJ (BRIP1), FANCL, and FANCM. FA genes are tumour suppressors that play a role in interstrand cross-link (ICL) DNA repair through homologous recombination repair (HRR) of double-strand breaks (DSB) and nucleotide excision repair (NER)[13]. Loss of function mutations of genes in the FA family and HRR pathway, including *PALB2*, can result in the BRCAness phenotype, characterized by a defect in the HRR pathway, mimicking BRCA1 or BRCA2 loss[14,15]. Germline mutations in FA genes lead to Fanconi Anemia, a condition characterized by chromosomal instability and congenital abnormalities including bone marrow failure and cancer predisposition[16,17]. Specifically, biallelic germline mutations resulting in PALB2 loss of function confer a predisposition to paediatric malignancies[18,19]. Additionally, monoallelic germline mutations in *PALB2* have been associated with an increased risk of developing breast cancer[18,20].

Alterations and prevalence: Somatic alterations in *PALB2* include missense or truncating mutations and are observed in 2-6% of melanoma, uterine, bladder, breast, lung, stomach and colorectal cancers[5].

Potential relevance: The PARP inhibitor, olaparib[21] is approved (2020) for metastatic castration-resistant prostate cancer (mCRPC) with deleterious or suspected deleterious, germline or somatic mutations in HRR genes that includes PALB2. Additionally, talazoparib[22] in combination with enzalutamide is approved (2023) for mCRPC with mutations in HRR genes that includes *PALB2*. In a phase II trial of patients with metastatic, castration-resistant prostate cancer, one patient exhibiting a

somatic *PALB2* frameshift mutation exhibited durable response to olaparib for 39 weeks[23,24]. However, olaparib resistance was observed following 9-months of treatment due to the emergence of a secondary deletion which restored the *PALB2* reading frame, a resistance mechanism similar to that observed in PARPi treated BRCA mutated patients[24,25]. In 2022, the FDA granted fast track designation to the small molecule inhibitor, pidnarulex[26], for BRCA1/2, PALB2, or other homologous recombination deficiency (HRD) mutations in breast and ovarian cancers. Rucaparib is recommended as a maintenance therapy for germline or somatic *PALB2* mutations in metastatic pancreatic cancer[27].

TP53 p.Gly266*

Gene description: The *TP53* gene encodes the p53 tumour suppressor protein that binds to DNA and activates transcription in response to diverse cellular stresses to induce cell cycle arrest, apoptosis, or DNA repair. In unstressed cells, TP53 is kept inactive by targeted degradation via MDM2, a substrate recognition factor for ubiquitin-dependent proteolysis. Alterations in *TP53* is required for oncogenesis as they result in loss of protein function and gain of transforming potential[28]. Germline mutations in *TP53* are the underlying cause of Li-Fraumeni syndrome, a complex hereditary cancer predisposition disorder associated with early-onset cancers[29,30].

Alterations and prevalence: *TP53* is the most frequently mutated gene in the cancer genome with approximately half of all cancers experiencing *TP53* mutations. Ovarian, head and neck, esophageal, and lung squamous cancers have particularly high *TP53* mutation rates (60-90%)[5,6,31-34]. Approximately two-thirds of *TP53* mutations are missense mutations and several recurrent missense mutations are common including substitutions at codons R158, R175, Y220, R248, R273 and R282[5,6]. Invariably, recurrent missense mutations in *TP53* inactivate its ability to bind DNA and activate transcription of target genes[35-38].

Potential relevance: The small molecule p53 reactivator, PC14586, received a fast track designation (2020) by the FDA for advanced tumours harbouring a *TP53* Y220C mutation[39]. The FDA has granted fast track designation (2019) to the p53 reactivator, eprenetapopt[40] and breakthrough designation[41] (2020) in combination with azacitidine or azacitidine and venetoclax for acute myeloid leukemia patients (AML) and myelodysplastic syndrome (MDS) harbouring a *TP53* mutation, respectively. In addition to investigational therapies aimed at restoring wild-type TP53 activity, compounds that induce synthetic lethality are also under clinical evaluation[42,43]. *TP53* mutations confer poor prognosis and poor risk in multiple blood cancers including AML, MDS, myeloproliferative neoplasms (MPN), and chronic lymphocytic leukemia (CLL), and acute lymphoblastic leukemia (ALL)[44-49]. In mantle cell lymphoma, *TP53* mutations are associated with poor prognosis when treated with conventional therapy including hematopoietic cell transplant[50]. Mono- and bi-allelic mutations in *TP53* confer unique characteristics in MDS, with multi-hit patients also experiencing associations with complex karyotype, few co-occurring mutations, and high-risk disease presentation as well as predicted death and leukemic transformation independent of the IPSS-R staging system[51].

NBN p.Asn30Lysfs*7

Gene description: The *NBN* gene encodes nibrin, a nuclear protein that is part of the multisubunit MRE11/RAD50/NBN (MRN) protein complex, which is necessary for the maintenance of genomic stability[52,53]. The MRN complex is involved in repair of double-stranded breaks (DSB) by homologous recombination repair (HRR) and non-homologous end joining (NHEJ)[54-56]. Specifically, NBN contains a nuclear localization signaling motif responsible for translocation of the MRN complex into the nucleus and contributes to DNA repair by mediating protein-protein interactions at the site of DNA damage[52]. *NBN* is a tumour suppressor gene. Loss of function mutations in *NBN* are implicated in the BRCAness phenotype, which is characterized by a defect in the HRR pathway, mimicking BRCA1 or BRCA2 loss[14,57]. Germline mutations in *NBN* are associated with Nijmegen breakage syndrome, an autosomal recessive disorder resulting in microcephaly at birth, immunodeficiency, radiosensitivity, and cancer predisposition[58,59].

Alterations and prevalence: Somatic mutations in *NBN* are observed in 7-8% of uterine cancer and 2-4% of melanoma, colorectal, esophageal, bladder and stomach cancers[5].

Potential relevance: The PARP inhibitor, talazoparib22 in combination with enzalutamide is approved (2023) for metastatic castration resistant prostate cancer (mCRPC) with mutations in HRR genes that includes *BRCA2*. Loss of function mutations in

one or more HRR genes, including NBN, may confer sensitivity to platinum agents and PARP inhibitors[14,57,60]. NBN overexpression has been shown to be associated with poor prognosis in uveal melanoma, head and neck cancer, and ovarian cancer[61-64].

APC **p.Met1413Ilefs*9**

Gene description: The *APC* gene encodes the adenomatous polyposis coli tumour suppressor protein that plays a crucial role in regulating the β-catenin/WNT signalling pathway which is involved in cell migration, adhesion, proliferation, and differentiation[65]. APC is an antagonist of WNT signalling as it targets β-catenin for proteasomal degradation[66,67]. Germline mutations in *APC* are predominantly inactivating and result in an autosomal dominant predisposition for familial adenomatous polyposis (FAP) which is characterized by numerous polyps in the intestine[65,68]. Acquiring a somatic mutation in *APC* is considered to be an early and possibly initiating event in colorectal cancer[69].

Alterations and prevalence: Somatic mutations in *APC* are observed in up to 65% of colorectal cancer, and in up to 15% of stomach adenocarcinoma and uterine corpus endometrial carcinoma[5,6,70]. In colorectal cancer, ~60% of somatic *APC* mutations have been reported to occur in a mutation cluster region (MCR) resulting in C-terminal protein truncation and APC inactivation[71,72].

Potential relevance: Currently, no therapies are approved for APC aberrations.

RECOMMENDATIONS

- Genetic counselling is advised for interpretation on the consequences of the variant(s).

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APPENDIX 1: TEST METHODOLOGY

METHOD

Pathology Assessment

The FFPE block is reviewed for presence of tumor cells and tumor percentage by histopathologists through screening of H & E staining slides.

Assay Methods

The test was performed using the Oncomine Comprehensive Assay Plus targeted, amplicon based next-generation sequencing assay that analyses 500+ unique genes for SNV, CNV, TMB, MSI and fusions. The minimum of 20ng of DNA isolated by Qiagen nucleic acid isolation kit is amplified using Oncomine Comprehensive assay plus as per the instruction manual. The amplicon libraries are prepared from 4 pools of primer which includes 2 pools of DNA based targets. The amplified primer pools are enzyme fragmented and Ion adapter barcodes are added. Amplified library is purified followed by quantitation using Ion Library TaqManTM Quantitation Kit. The quality of amplified libraries having 150-200bp sizes are confirmed by Agilent TapeStation. The quantified pooled library is loaded on Ion 550 Chip using Ion Chef and sequencing is performed on the Ion GeneStudio S5 prime system. For the current report RNA was not included.

Secondary Analysis Methods

The sequence data is processed using Ion Torrent server and the Ion reporter software 5.20.2.0. TMB is reported as High (>10 mutations/Mb), Intermediate (>3 to 10 mutations/Mb) and Low (<3 mutations/Mb). All the reported alterations are manually curated using Integrative Genomics Viewer (IGV). The Final report is generated using oncomine knowledgebase which includes contextual investigations of sample-specific variants with respect to labels, guidelines (AMP, ASCO, CAP), current clinical trials and peer-reviewed literature which is frequently updated.

Genes Assayed

The panel covers 1.50M bases of DNA region, including 1.06M bases of exonic regions. It includes a total of 500+ genes covering 165 hotspot genes, 333 genes with focal CNV gains and loss, 227 genes with full coding sequence (CDS), >1 Mb exonic regions for TMB evaluation and 76 MSI markers for Microsatellite Instability (MSI) and Microsatellite stable (MSS). It also covers 46 genes (SNVs, Indels, CNVs) for homologous recombination deficiency (HRD) including *BRCA1* and *BRCA2*. A subset of these (20 genes) were assessed for determining Loss of Heterozygosity (LOH) at gene level. Details available on request.

AMP/ASCO/CAP Classification

Tier I: Variants of Strong Clinical Significance	1A	Biomarkers that predict response or resistance to US FDA-approved therapies for a specific type of tumor or have been included in **professional guidelines** as **therapeutic, diagnostic, and/or prognostic biomarkers** for specific types of tumors.
	1B	Biomarkers that predict response or resistance to a therapy based on well-powered studies with consensus from experts in the field, or have diagnostic and/or prognostic significance of certain diseases based on **well- powered studies with expert consensus**.
Tier II: Variants of Potential Clinical Significance	2C	Biomarkers that predict response or resistance to therapies approved by FDA or professional **societies for a different tumor type (ie, off-label use of a drug)**, serve as inclusion criteria for clinical trials, or have diagnostic and/or prognostic significance based on the results of multiple small studies.
	2D	Biomarkers that show plausible therapeutic significance based on preclinical studies, or may assist disease diagnosis and/or prognosis themselves or along with other biomarkers based on **small studies or multiple case reports** with no consensus.
Tier III: Variants of Unknown Clinical Significance		Not observed at a significant allele frequency in the general or specific subpopulation databases, or pan-cancer or tumor-specific variant databases No convincing published evidence of cancer association.
Tier IV: Benign or Likely Benign Variants		Observed at significant allele frequency in the general or specific subpopulation databases.

DISCLAIMER

- This report was generated using the materials and methods as recommended which required the use of quality reagents, protocols, instruments, software, databases and other items, some of which were provided or made accessible by third

parties. A defect or malfunction in any such reagents, protocols, instruments, software, databases and/or other items may compromise the quality or accuracy of the report.

- The report has been created based on, or incorporated inferences to, various scientific manuscripts, references, and other sources of information, including without limitation manuscripts, references, and other sources of information that were prepared by third parties that describe correlations between certain genetic mutations and particular diseases (and/or certain therapeutics that may be useful in ameliorating the effects of such diseases). Such information and correlations are subject to change over time in response to future scientific and medical findings. MolQ Laboratory makes no representation or warranty of any kind, expressed or implied, regarding the accuracy of the information provided by or contained in such manuscripts, references, and other sources is later determined to be inaccurate, the accuracy and quality of the Report may be adversely impacted. MolQ Laboratory is not obligated to notify you of any of the impact that future scientific or medical findings may have on the report.
- The report must always be interpreted and considered within the clinical context, and a physician should always consider the report along with all other pertinent information and data that a physician would prudently consider prior to providing a diagnosis or developing and implementing a plan of care for the patient. The report should never be considered or relied upon alone in making any diagnosis or prognosis. The manifestations of many diseases are caused by more than one gene variant, a single gene variant may be relevant to more than one disease, and certain relevant gene variants may not have been considered in the report. In addition, many diseases are caused or influenced by modifier genes, epigenetic factors, environmental factors, and other variables that are not addressed by the report. This report is based on a Next Generation Assay which does not distinguish between a somatic and a germline variant. If germline variant is in question, further testing is recommended. The report provided by MolQ Laboratory is on a "as is" basis. MolQ Laboratory makes no representation or warranty of any kind, expressed or implied, regarding the report. In no event will MolQ Laboratory be liable for any actual damages, indirect damages, and/or special or consequential damages arising out of or in any way connected with the Report, your use of the report, your reliance on the report, or any defect or inaccurate information included within the report.
- Medical knowledge and annotation are constantly updated and reflects the current knowledge at the time.
- Due to inherent technology limitations of the assay, not all bases of the exome can be covered by this test. Accordingly, variants in regions of insufficient coverage may not be identified and/or interpreted. Therefore, it is possible that certain variants are present in one or more of the genes analyzed, but have not been detected. The variants not detected by the assay that was performed may/ may not impact the phenotype.
- It is also possible that a pathogenic variant is present in a gene that was not selected for analysis and/or interpretation in cases where insufficient phenotypic information is available.
- The report shall be generated within turnaround time (TAT), however, such TAT may vary depending upon the complexity of test(s) requested. MolQ Laboratory under no circumstances will be liable for any delay beyond afore mentioned TAT.
- It is hereby clarified that the report(s) generated from the test(s) do not provide any diagnosis or opinion or recommends any cure in any manner. MolQ Laboratory hereby recommends the patient and/or the guardians of the patients, as the case may be, to take assistance of the clinician or a certified physician or doctor, to interpret the report(s) thus generated. MolQ Laboratory hereby disclaims all liability arising in connection with the report(s).
- In a very few cases genetic test may not show the correct results, e.g. because of the quality of the material provided to MolQ Laboratory. In case where any test provided by MolQ Laboratory fails for unforeseeable or unknown reasons that cannot be influenced by MolQ Laboratory in advance, MolQ Laboratory shall not be responsible for the incomplete, potentially misleading or even wrong result of any testing if such could not be recognized by MolQ Laboratory in advance.
- This is a laboratory developed test and the development and the performance characteristics of this test was determined by reference laboratory as required by the CLIA 1988 regulations. The report, and the tests used to generate the Report have not been cleared or approved by the US Food and Drug Administration (FDA). The FDA has determined that such clearance or approval is not necessary. The test results have scientifically shown to be clinically useful.

LIMITATIONS

- Testing has been performed assuming that the sample received belongs to the above-named individual(s) and any stated relationships between individuals are accepted as true.
- Due to inherent technology limitations, coverage is not uniform across all regions. Hence pathogenic variants present in areas of insufficient coverage may not be analyzed/ reported.
- The classification and interpretation of all the variants in this assay reflects the current state of scientific understanding at the time this report was issued. In some instances, the classification and interpretation of such variants may change as new scientific information comes to light.
- Test results should be interpreted in context of clinical findings, tumor sampling, histopathology, and other laboratory data.

- If results obtained do not match other clinical laboratory findings, please contact the laboratory for possible. Misinterpretation of results may occur if the information provided is inaccurate or incomplete.
- Genetic testing is highly accurate. Rarely, inaccurate results may occur for various reasons. These reasons include, but are not limited to mislabelled samples, inaccurate reporting of clinical/medical information, rare technical errors or unusual circumstances such as bone marrow transplantation, blood transfusion; or the presence of change(s) in such a small percentage of cells that may not be detectable by the test (mosaicism).

APPENDIX 2: GENE LIST

Gene	Gene	Gene	Gene	Gene	Gene	Gene
ABL1	*CDKN2A*	*FANCF*	*HIST3H3*	*MEN1*	*PIK3R3*	*SMAD3*
ABL2	*CDKN2B*	*FANCG*	*HLA-A*	*MET*	*PIM1*	*SMAD4*
ACVR1	*CDKN2C*	*FANCI*	*HLA-B*	*MGA*	*PLCG2*	*SMARCA4*
ACVR1B	*CEBPA*	*FANCL*	*HLA-C*	*MITF*	*PLK2*	*SMARCB1*
AKT1	*CENPA*	*FAS*	*HNF1A*	*MLH1*	*PMAIP1*	*SMARCD1*
AKT2	*CHD2*	*FAT1*	*HNRNPK*	*MLL*	*PMS1*	*SMC1A*
AKT3	*CHD4*	*FBXW7*	*HOXB13*	*MLLT3*	*PMS2*	*SMC3*
ALK	*CHEK1*	*FGF1*	*HRAS*	*MPL*	*PNRC1*	*SMO*
ALOX12B	*CHEK2*	*FGF10*	*HSD3B1*	*MRE11A*	*POLD1*	*SNCAIP*
ANKRD11	*CIC*	*FGF14*	*HSP90AA1*	*MSH2*	*POLE*	*SOCS1*
ANKRD26	*CREBBP*	*FGF19*	*ICOSLG*	*MSH3*	*PPARG*	*SOX10*
APC	*CRKL*	*FGF2*	*ID3*	*MSH6*	*PPM1D*	*SOX17*
AR	*CRLF2*	*FGF23*	*IDH1*	*MST1*	*PPP2R1A*	*SOX2*
ARAF	*CSF1R*	*FGF3*	*IDH2*	*MST1R*	*PPP2R2A*	*SOX9*
ARFRP1	*CSF3R*	*FGF4*	*IFNGR1*	*MTOR*	*PPP6C*	*SPEN*
ARID1A	*CSNK1A1*	*FGF5*	*IGF1*	*MUTYH*	*PRDM1*	*SPOP*
ARID1B	*CTCF*	*FGF6*	*IGF1R*	*MYB*	*PREX2*	*SPTA1*
ARID2	*CTLA4*	*FGF7*	*IGF2*	*MYC*	*PRKAR1A*	*SRC*
ARID5B	*CTNNA1*	*FGF8*	*IKBKE*	*MYCL1*	*PRKCI*	*SRSF2*
ASXL1	*CTNNB1*	*FGF9*	*IKZF1*	*MYCN*	*PRKDC*	*STAG1*
ASXL2	*CUL3*	*FGFR1*	*IL10*	*MYD88*	*PRSS8*	*STAG2*
ATM	*CUX1*	*FGFR2*	*IL7R*	*MYOD1*	*PTCH1*	*STAT3*
ATR	*CXCR4*	*FGFR3*	*INHA*	*NAB2*	*PTEN*	*STAT4*
ATRX	*CYLD*	*FGFR4*	*INHBA*	*NBN*	*PTPN11*	*STAT5A*
AURKA	*DAXX*	*FH*	*INPP4A*	*NCOA3*	*PTPRD*	*STAT5B*
AURKB	*DCUN1D1*	*FLCN*	*INPP4B*	*NCOR1*	*PTPRS*	*STK11*
AXIN1	*DDR2*	*FLI1*	*INSR*	*NEGR1*	*PTPRT*	*STK40*
AXIN2	*DDX41*	*FLT1*	*IRF2*	*NF1*	*QKI*	*SUFU*
AXL	*DHX15*	*FLT3*	*IRF4*	*NF2*	*RAB35*	*SUZ12*
B2M	*DICER1*	*FLT4*	*IRS1*	*NFE2L2*	*RAC1*	*SYK*
BAP1	*DIS3*	*FOXA1*	*IRS2*	*NFKBIA*	*RAD21*	*TAF1*
BARD1	*DNAJB1*	*FOXL2*	*JAK1*	*NKX2-1*	*RAD50*	*TBX3*
BBC3	*DNMT1*	*FOXO1*	*JAK2*	*NKX3-1*	*RAD51*	*TCEB1*
BCL10	*DNMT3A*	*FOXP1*	*JAK3*	*NOTCH1*	*RAD51B*	*TCF3*
BCL2	*DNMT3B*	*FRS2*	*JUN*	*NOTCH2*	*RAD51C*	*TCF7L2*
BCL2L1	*DOT1L*	*FUBP1*	*KAT6A*	*NOTCH3*	*RAD51D*	*TERC*
BCL2L11	*E2F3*	*FYN*	*KDM5A*	*NOTCH4*	*RAD52*	*TERT*
BCL2L2	*EED*	*GABRA6*	*KDM5C*	*NPM1*	*RAD54L*	*TET1*
BCL6	*EGFL7*	*GATA1*	*KDM6A*	*NRAS*	*RAF1*	*TET2*
BCOR	*EGFR*	*GATA2*	*KDR*	*NRG1*	*RANBP2*	*TFE3*
BCORL1	*EIF1AX*	*GATA3*	*KEAP1*	*NSD1*	*RARA*	*TFRC*
BCR	*EIF4A2*	*GATA4*	*KEL*	*NTRK1*	*RASA1*	*TGFBR1*
BIRC3	*EIF4E*	*GATA6*	*KIF5B*	*NTRK2*	*RB1*	*TGFBR2*
BLM	*EML4*	*GEN1*	*KIT*	*NTRK3*	*RBM10*	*TMEM127*
BMPR1A	*EP300*	*GID4*	*KLF4*	*NUP93*	*RECQL4*	*TMPRSS2*
BRAF	*EPCAM*	*GLI1*	*KLHL6*	*NUTM1*	*REL*	*TNFAIP3*

Comprehensive Panel- 500 Genes

BRCA1	*EPHA3*	*GNA11*	*KMT2B*	*PAK1*	*RET*	*TNFRSF14*
BRCA2	*EPHA5*	*GNA13*	*KMT2C*	*PAK3*	*RFWD2*	*TOP1*
BRD4	*EPHA7*	*GNAQ*	*KMT2D*	*PAK7*	*RHEB*	*TOP2A*
BRIP1	*EPHB1*	*GNAS*	*KRAS*	*PALB2*	*RHOA*	*TP53*
BTG1	*ERBB2*	*GPR124*	*LAMP1*	*PARK2*	*RICTOR*	*TP63*
BTK	*ERBB3*	*GPS2*	*LATS1*	*PARP1*	*RIT1*	*TRAF2*
C11orf30	*ERBB4*	*GREM1*	*LATS2*	*PAX3*	*RNF43*	*TRAF7*
CALR	*ERCC1*	*GRIN2A*	*LMO1*	*PAX5*	*ROS1*	*TSC1*
CARD11	*ERCC2*	*GRM3*	*LRP1B*	*PAX7*	*RPS6KA4*	*TSC2*
CASP8	*ERCC3*	*GSK3B*	*LYN*	*PAX8*	*RPS6KB1*	*TSHR*
CBFB	*ERCC4*	*H3F3A*	*LZTR1*	*PBRM1*	*RPS6KB2*	*U2AF1*
CBL	*ERCC5*	*H3F3B*	*MAGI2*	*PDCD1*	*RPTOR*	*VEGFA*
CCND1	*ERG*	*H3F3C*	*MALT1*	*PDCD1LG2*	*RUNX1*	*VHL*
CCND2	*ERRFI1*	*HGF*	*MAP2K1*	*PDGFRA*	*RUNX1T1*	*VTCN1*
CCND3	*ESR1*	*HIST1H1C*	*MAP2K2*	*PDGFRB*	*RYBP*	*WISP3*
CCNE1	*ETS1*	*HIST1H2BD*	*MAP2K4*	*PDK1*	*SDHA*	*WT1*
CD274	*ETV1*	*HIST1H3A*	*MAP3K1*	*PDPK1*	*SDHAF2*	*XIAP*
CD276	*ETV4*	*HIST1H3B*	*MAP3K13*	*PGR*	*SDHB*	*XPO1*
CD74	*ETV5*	*HIST1H3C*	*MAP3K14*	*PHF6*	*SDHC*	*XRCC2*
CD79A	*ETV6*	*HIST1H3D*	*MAP3K4*	*PHOX2B*	*SDHD*	*YAP1*
CD79B	*EWSR1*	*HIST1H3E*	*MAPK1*	*PIK3C2B*	*SETBP1*	*YES1*
CDC73	*EZH2*	*HIST1H3F*	*MAPK3*	*PIK3C2G*	*SETD2*	*ZBTB2*
CDH1	*FAM123B*	*HIST1H3G*	*MAX*	*PIK3C3*	*SF3B1*	*ZBTB7A*
CDK12	*FAM175A*	*HIST1H3H*	*MCL1*	*PIK3CA*	*SH2B3*	*ZFHX3*
CDK4	*FAM46C*	*HIST1H3I*	*MDC1*	*PIK3CB*	*SH2D1A*	*ZNF217*
CDK6	*FANCA*	*HIST1H3J*	*MDM2*	*PIK3CD*	*SHQ1*	*ZNF703*
CDK8	*FANCC*	*HIST2H3A*	*MDM4*	*PIK3CG*	*SLIT2*	*ZRSR2*
CDKN1A	*FANCD2*	*HIST2H3C*	*MED12*	*PIK3R1*	*SLX4*	
CDKN1B	*FANCE*	*HIST2H3D*	*MEF2B*	*PIK3R2*	*SMAD2*	