Precision Panel- 1000 Genes

Disease: Metastatic Lung adenocarcinoma

Test Description

Precision panel is a comprehensive cancer genomic NGS assay to accurately and rapidly identify key actionable biomarkers and provide precision treatment options including Chemotherapy, Targeted Therapy and Immunotherapy. This assay screens both exonic and selected intronic regions of >1000 genes with known genomic alterations with high coverage depth. The assay can detect all classes of genomic alterations, including SNVs, small Indels, CNVs and selected translocations. In addition, TMB, MSI and HRD are analyzed to help guide immunotherapy decisions.

Clinician

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

Patient Demographic

Name: Mr. Lee Kien On Yee
Sex: Male
Date of Birth/Age: 64 years

Specimen

Booking ID: 012405280256
Sample Type: FFPE Block No. H/5865/23 B
Specimen Site: Left lung lesion biopsy
Tumor Content Percentage: NA
Date of Collection: 28-05-2024
Date of Booking: 28-05-2024

CLINICAL SYNOPSIS

Lee Kien On Yee, is a known case of metastatic lung adenocarcinoma. He has been evaluated for pathogenic variations in the genes listed in Appendix 2.

RESULT SUMMARY

Potential clinically significant alteration.
Tier I alterations in *EGFR* (p.Leu858Arg and Amplification) and *TP53* (p.Ser90Valfs*55) genes were observed.

EGFR alterations are found to activate multiple downstream signaling pathways such as PI3K/AKT/MTOR and RAS/RAF/MAPK pathways that lead to cancer cell proliferation and cell cycle progression. Moreover, studies have confirmed EGFR amplification as an independent resistance mechanism to EGFR TKIs.

TP53 gene mutations are associated with an unfavorable prognosis, increased likelihood of metastatic progression and suboptimal response to chemotherapy. The loss of function mutation in TP53 may exacerbate the aggressive nature of this tumor.

Moreover, studies have indicated TP53 mutations as an unfavorable prognostic factor in patients receiving first-, second- and third-generation EGFR-TKI therapy with EGFR mutant advanced NSCLC. Thus, with concomitant concurrence of EGFR and TP53 mutations, the duration of PFS has been reported to be significantly longer with EGFR-TKI treatment combined with antiangiogenic drugs or chemotherapy than with EGFR-TKIs only.

Other Markers

Immunotherapy markers: **TMB is high** and MSI is low, while PD-L1 is positive on tissue (TPS is 20%). The overall **HRD score is intermediate**.
High TMB correlates with genomic instability and immunotherapy response. Intermediate HRD score indicates aberration of the HRR pathway and may show potential response to PARP inhibitors.

RESULTS

Potential clinically significant alterations were observed in *EGFR* and *TP53* genes.

Gene (Transcript ID)	Variant	Allele Frequency	Exon	Mutation Effect	Variant Effect	Tier
EGFR (NM_005228.5)	c.2573T>G p.Leu858Arg	81%	21	Gain of Function	Missense	Ia
EGFR (NM_005228.5)	Amplification	-	-	Gain-of-function	CNV	Ia
TP53 (NM_000546.6)	c.267_277del p.Ser90Valfs*55	20%	4	Unknown	Frameshift	Ib

As per guidelines of the ACMG/AMP/ASCO/CAP

VARIANT OF UNKNOWN SIGNIFICANCE (VUS)

None

IMMUNO-ONCOLOGY FINDINGS

MSI/MMR Status NGS Based	TMB (Tissue / Blood)	PDL-1 IHC on tissue (TBx), Dako clone 22C3 or CTC (LBx)
1.5% Low	**15.6 Muts/Mb High**	PD-L1 Positive on Tissue (TPS 20%)

HOMOLOGOUS RECOMBINANT DEFICIENCY (HRD) FINDINGS

Overall HRD Scoring	HRR Gene	LOH (Loss of Heterozygosity)	TAI & LST (Telomeric Allelic Instability & Large State Transitions)
42% Intermediate	None	12% Low	TAI: 26% LST: 04%

Note: LOH score is calculated based on the genome wide LOH markers present in gene panel.

OTHER BIOMARKERS

Gene	Findings	Gene	Findings
EGFR	Amplification	*NTRK*	None detected
ALK	None detected	*RET*	None detected
ERBB2	None detected	*ROS1*	None detected
KRAS	None detected		
MET	None detected		

LONGITUDINAL MONITORING MARKERS

Circulating Tumor Cells (CTC)	CTC Cluster	Highest Mutant Allele Frequency	Tumor DNA Fraction (%)
NA	NA	*TP53*: p.Ser90Valfs*55 (VAF: 20%)	29

Note: EDTA blood sample for CTS is not provided.
AI-powered probabilistic model is used to calculate the tumor fraction, enabling the simultaneous segmentation of the genome and accurate prediction of large-scale copy number variations. The model takes into consideration variations in clonality and copy number at each locus, ensuring a comprehensive analysis.

CLINICAL CORRELATION AND VARIANT INTERPRETATION

EGFR **p.Leu858Arg and Amplification**

Gene description: EGFR (HER1), epidermal growth factor receptor, is a tyrosine kinase receptor, which activates RAS/RAF/MEK and PI3K/AKT/Mtor pathways, leading to increased cell proliferation and growth (Domvri K, Zarogoulidis P, et al. 2013). EGFR activating mutations, amplification, and overexpression are found in a variety of tumors, including non-small cell lung cancer (Midha A, Dearden S, McCormack R., et al. 2015, Ruiz-Patiño A, Castro CD., et al. 2018) and colorectal cancer (Ben Brahim E, Ayari I., et al. 2018). According to AACR Genie cases, *EGFR* is altered in 26.09% of lung adenocarcinoma patients with *EGFR* Mutation present in 25.24% of all lung adenocarcinoma patients.

Variant description: *EGFR* activating mutations, amplification, and overexpression are found in a variety of tumors, including non-small cell lung cancer (Midha A, Dearden S, McCormack R., et al. 2015; Ruiz-Patiño, Alejandro et al. 2018). About 15% of Caucasian and close to 50% of Asian individuals with advanced NSCLC had somatic, activating mutations in the EGFR tyrosine kinase domain. Exon 19 deletions or exon 21 L858R point mutations make up around 90% of these alterations. These genetic alterations function as oncogenic drivers that activate EGFR downstream signaling without the need for ligands, boosting cell proliferation, survival, and migration. Thus, since EGFR mutations are found to activate PI3K/PDK1/AKT as well as RAS/RAF/MAPK pathways and therefore, suggestive of potential therapeutic benefit from EGFR inhibitors.

Potential relevance: EGFR TKIs such as Osimertinib, Afatinib, Dacomitinib, Erlotinib and Gefitinib have been approved as therapy options for patients with non-small-cell lung cancer (NSCLC) who have tumors that contain EGFR exon 19 deletions or exon 21 (L858R) mutations. EGFR TKIs such as Osimertinib, Afatinib, Dacomitinib, Erlotinib and Gefitinib have been approved as therapy options for patients with non-small-cell lung cancer (NSCLC) who have tumors that contain EGFR exon 19 deletions or exon 21 (L858R) mutations. However, studies have shown that the presence EGFR amplification/overexpression are associated with cancer aggressiveness (Lu, Zhimin, et al.2001; Citri, Ami, and Yosef Yarden., et al.2006) and unfavorable factor when patients are treated with EGFR TKIs (Cheng, Ying, et al.2020; Yang, Hainan, et al. 2022).

TP53 **p.Ser90Valfs*55**

Gene description: TP53, tumor protein p53, is a tumor suppressor (Wang, Li-Hui et al. 2018) and oncogene (Yamamoto, Satomi, and Tomoo Iwakuma.2018) involved in cell cycle arrest and apoptosis, and is the most frequently mutated gene in cancer (Oren, M, and V Rotter.1999; Freed-Pastor, William A, and Carol Prives.2012). Somatic missense mutations are frequent in almost all cancer types (Giacomelli, Andrew O et al. 2018) and are also implicated in chemoresistance (Blandino, G et al.1999; Brachova, Pavla et al. 2013; Ferraiuolo, Maria et al. 2016).

Variant description: *TP53* p.S90Vfs*55 indicates a shift in the reading frame starting at amino acid 90 and terminating 55 residues downstream causing a premature truncation of TP53 protein.

Potential relevance: According to AACR GENIE studies, *TP53* is altered in 39.52% of all cancers with lung adenocarcinoma, colon adenocarcinoma, breast invasive ductal carcinoma, pancreatic adenocarcinoma and high grade ovarian serous adenocarcinoma having the greatest prevalence of alterations. Moreover, it is reported that in general *TP53* alterations are associated with a worse prognosis and relatively more resistance to chemotherapy and radiation.

DESCRIPTION OF PERTINENT BIOMARKERS

Tumor mutational burden (TMB) is defined as the number of somatic mutations per megabase of the coding region in the genome. TMB is a clinical biomarker associated with response to immune checkpoint inhibitors in various cancers, including NSCLC, bladder cancer, and melanoma (Rizvi, Naiyer A., et al. 2015; Carbone, David P et al. 2017; Hellmann, Matthew D et al. 2018; Kowanetz, Marcin, et al. 2017; Rizvi, Hira et al. 2018). High tumor mutational burden (TMB-H) is defined by >10 mutations/megabase [mut/Mb] can be seen frequently in cancers linked to mutagens, such as exposure to ultraviolet light in melanoma and smoking in non–small- cell lung cancer. Other tumor forms, such as mesothelioma, sarcomas and prostate cancers have been reported to have a TMB-H prevalence of less than 5% (Shao C, Li G, Huang L, et al. 2020). TMB is also affected by mutations in the proofreading domains of DNA polymerases encoded by the *POLE* and *POLD1* genes and microsatellite

instability (MSI). (Cancer Genome Atlas Research Network et al. 2013; Briggs, Sarah and Ian Tomlinson.2013; Heitzer, Ellen and Ian Tomlinson.2014; Cancer Genome Atlas Network.2012; Roberts, Steven A. and Dmitry A. Gordenin. 2014).

Pembrolizumab is a monoclonal antibody that binds to the PD-1 receptor and disrupts its interaction with PD-L1 and PD-L2, resulting in PD-1 pathway-mediated immune response suppression, including antitumor immunity. Antibodies to PD-1 or its ligands have been used to block this pathway in patients with a variety of cancers, including melanomas, non–small-cell lung cancer, renal cell carcinoma, bladder cancer and Hodgkin lymphoma. (Marcus, Leigh et al. 2019). The FDA approved for the treatment of adult and pediatric patients with unresectable or metastatic tumor mutational burden-high solid tumors and for patients with unresectable or metastatic, MSI-H/dMMR solid tumors with progression on prior treatment with no satisfactory alternative treatment options. FDA granted the approval based on a clinically important overall response rate (29%; 95% confidence interval, 21-39) and duration of response (57% of responses lasting ≥ 12 months) in the subset of patients with TMB-H solid tumors (n = 102) spanning nine different tumor types enrolled in a multicenter single-arm trial (KEYNOTE- 158, Marcus, Leigh et al. 2021).

Genomic instability is one of the most common primary aspects of tumorigenesis and defective DNA repair. Homologous recombination deficiency (HRD) is a phenotype that is characterized by the inability of a cell to effectively repair DNA double-strand breaks using the homologous recombination repair (HRR) pathway. Loss-of-function genes involved in this pathway can sensitize tumors to PARP inhibitors and platinum-based chemotherapy, which target the destruction of cancer cells by working in concert with HRD through synthetic lethality.

The loss of heterozygosity (LOH) score is a profile of the percentage of the tumor genome that is under focal loss of one allele (Swisher, Elizabeth M et al. 2017); focal LOH events accumulate as genomic "scars" as a result of incorrect DNA double-strand break repair when the homologous recombination pathway is deficient (HRD) (Wang, Zhigang C et al. 2012; Abkevich, V et al. 2012; Watkins, Johnathan A et al. 2014; Vanderstichele, Adriaan et al. 2017). HRD and consequent genomic LOH occur because of genetic or epigenetic inactivation of one or more of the homologous recombination pathway proteins, including BRCA1, BRCA2, RAD51C, ATM, PALB2 and BRIP1 (Watkins, Johnathan A et al. 2014; Vanderstichele, Adriaan et al. 2017; Cancer Genome Atlas Research Network. 2011; Venkitaraman, Ashok R. 2003).

Deficiency in one or more HR genes increases the risk of many malignancies. Another conserved mechanism involved in the repair of DNA single-strand breaks (SSBs) is base excision repair, in which poly (ADP-ribose) polymerase (PARP) enzymes play an important role (Mekonnen, Negesse et al. 2022). Poly (ADP-ribose) polymerase (PARP) inhibitors (PARPi) are a novel class of anti-cancer therapies that compete with NAD+ for the catalytically active site of PARP molecules. PARPi has been shown to be effective in the treatment of homologous recombination repair (HR) deficient tumors (Rose, Maddison et al.2020). The use of PARPIs in non-BRCA mutation carrier patients can be expanded to sporadic cancers that display “BRCAness” (cancers that have defective HR without germline *BRCA1* and *2* mutations) (Mekonnen, Negesse et al.2022). HRD-positive tumors are being evaluated for clinical efficacy in different solid tumors including lung cancers.

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RECOMMENDATIONS

- A follow-up liquid biopsy after 3 months may be recommended to explore markers for immunotherapy.
- Validation of the variant(s) by Sanger sequencing is recommended to rule out false positives.
- Genetic counselling is advised for interpretation on the consequences of the variant(s).
- If results obtained do not match the clinical findings, additional testing should be considered as per referring clinician's recommendations.

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APPENDIX 1: TEST METHODOLOGY

Test Description & Methodology

Nucleic acids were isolated from samples and after quality check was directly loaded on Next Generation Sequencer and subjected to automated library preparation and template preparation followed by sequencing.
Analysis is done and the data is visualized on Integrative Genomics Viewer (IGV) and analyzed. The final report is generated using curated knowledgebase reporter. The assay has been optimized to enable rapid and accurate detection of true somatic alterations by effective sequencing of both tissue and ctDNA based blood samples with high sensitivity and specificity for supporting reliable treatment decisions. The assay can detect all classes of genomic alterations, including Single Nucleotide Variants (SNVs), Small Insertions and Deletions (Indels), Copy Number Alterations (Amplifications) and selected translocations with minimal amounts of routine clinical samples (including core or fine-needle biopsies). In addition, all samples are simultaneously profiled for Tumor Mutation Burden (TMB), Microsatellite Instability (MSI) status and Homologous Recombination Deficiency (HRD) to help guide immunotherapy decisions. MSI status is reported as MSI-High, MSI-Intermediate or MSI-Stable (MSS). TMB status is reported for all cancer types as TMB-High (≥10 Muts/Mb), or TMB-Low (<10 Muts/Mb).

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 witFhout 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.

APPENDIX 2: GENE LIST WITH COVERAGE

DNA Hotspots										
ABCB1	*CARD11*	*CYP19A1*	*FANCA*	*H2BC12*	*IRS2*	*MIB1*	*PAX3*	*QKI*	*SHQ1*	*TNFAIP3*
ABL1	*CARM1*	*CYP2D6*	*FANCB*	*H2BC17*	*IRS4*	*MIDEAS*	*PAX5*	*RAB35*	*SIN3A*	*TNFRSF11A*
ABL2	*CASP8*	*CYSLTR2*	*FANCC*	*H2BC4*	*ITGAM*	*MIR142*	*PAX7*	*RABEP1*	*SIRPA*	*TNFRSF14*
ABRAXAS1	*CBFA2T3*	*DACH1*	*FANCD2*	*H2BC5*	*ITK*	*MITF*	*PAX8*	*RAC1*	*SLC26A3*	*TNFRSF17*
ACTA2	*CBFB*	*DAXX*	*FANCE*	*H3-3A*	*ITPKB*	*MKI67*	*PAXIP1*	*RAC2*	*SLC34A2*	*TNFRSF18*
ACTB	*CBL*	*DAZAP1*	*FANCF*	*H3-3B*	*JAK1*	*MKNK1*	*PBRM1*	*RAD21*	*SLFN11*	*TNFRSF4*
ACVR1	*CBLB*	*DCSTAMP*	*FANCG*	*H3-4*	*JAK2*	*MLH1*	*PC*	*RAD50*	*SLIT2*	*TNFRSF9*
ACVR1B	*CBLC*	*DCUN1D1*	*FANCI*	*H3-5*	*JAK3*	*MLH3*	*PCBP1*	*RAD51*	*SLX4*	*TOP1*
ACVR2A	*CBWD3*	*DDB2*	*FANCL*	*H3C1*	*JARID2*	*MLLT1*	*PCLO*	*RAD51B*	*SMAD2*	*TOP2A*
ADGRA2	*CCDC6*	*DDR1*	*FANCM*	*H3C10*	*JAZF1*	*MLLT10*	*PDCD1*	*RAD51C*	*SMAD3*	*TP53*
ADGRB1	*CCL2*	*DDR2*	*FAS*	*H3C11*	*JUN*	*MLLT3*	*PDCD11*	*RAD51D*	*SMAD4*	*TP53BP1*
AGO1	*CCN6*	*DDX3X*	*FASLG*	*H3C12*	*KANSL1*	*MPL*	*PDCD1LG2*	*RAD52*	*SMARCA1*	*TP63*
AGO2	*CCNB3*	*DDX41*	*FAT1*	*H3C13*	*KAT6A*	*MR1*	*PDGFB*	*RAD54B*	*SMARCA2*	*TPMT*
AJUBA	*CCND1*	*DEK*	*FBXO11*	*H3C14*	*KAT6B*	*MRE11*	*PDGFRA*	*RAD54L*	*SMARCA4*	*TPTE2*
AKT1	*CCND2*	*DHX9*	*FBXO31*	*H3C15*	*KBTBD4*	*MRTFA*	*PDGFRB*	*RAF1*	*SMARCAL1*	*TRAF2*
AKT2	*CCND3*	*DIAPH2*	*FBXW7*	*H3C2*	*KDM2B*	*MRTFB*	*PDK1*	*RANBP17*	*SMARCB1*	*TRAF3*
AKT3	*CCNE1*	*DICER1*	*FCGR2A*	*H3C3*	*KDM4C*	*MSH2*	*PDPK1*	*RANBP2*	*SMARCD1*	*TRAF5*
ALB	*CCR2*	*DIS3*	*FCGR3A*	*H3C4*	*KDM5A*	*MSH3*	*PDS5B*	*RARA*	*SMARCE1*	*TRAF7*
ALK	*CCR4*	*DIS3L2*	*FGF1*	*H3C6*	*KDM5C*	*MSH6*	*PGBD5*	*RASA1*	*SMC1A*	*TRIP13*
ALOX12B	*CCR5*	*DKC1*	*FGF10*	*H3C7*	*KDM6A*	*MSI2*	*PGR*	*RASGEF1A*	*SMC3*	*TRPA1*
AMER1	*CCT6B*	*DKK4*	*FGF12*	*H3C8*	*KDM6B*	*MSMB*	*PHF6*	*RB1*	*SMO*	*TSC1*
ANKRD11	*CD19*	*DMD*	*FGF14*	*HAVCR2*	*KDR*	*MST1*	*PHOX2B*	*RBM10*	*SMYD3*	*TSC2*
ANKRD26	*CD22*	*DNAJB1*	*FGF19*	*HDAC1*	*KEAP1*	*MST1R*	*PICALM*	*RBM15*	*SNCAIP*	*TSHR*
APC	*CD27*	*DNM2*	*FGF2*	*HDAC2*	*KEL*	*MT1JP*	*PIGA*	*RBM38*	*SOCS1*	*TSLP*
APH1A	*CD274*	*DNMT1*	*FGF23*	*HDAC4*	*KIF1A*	*MTAP*	*PIK3C2B*	*RECQL*	*SOCS2*	*TUSC3*
APLNR	*CD276*	*DNMT3A*	*FGF3*	*HDAC7*	*KIF1B*	*MTOR*	*PIK3C2G*	*RECQL4*	*SOCS3*	*TXNIP*
APOB	*CD28*	*DNMT3B*	*FGF4*	*HDAC9*	*KIF5B*	*MUC17*	*PIK3C3*	*REL*	*SOS1*	*TYK2*
AR	*CD33*	*DOCK8*	*FGF5*	*HGF*	*KIR3DL1*	*MUC6*	*PIK3CA*	*RELA*	*SOX10*	*TYRO3*
ARAF	*CD36*	*DOT1L*	*FGF6*	*HIF1A*	*KIT*	*MUSK*	*PIK3CB*	*RELN*	*SOX17*	*U2AF1*
ARFRP1	*CD40*	*DROSHA*	*FGF7*	*HLA-A*	*KLF2*	*MUTYH*	*PIK3CD*	*REST*	*SOX2*	*U2AF2*
ARHGAP26	*CD58*	*DTX1*	*FGF8*	*HLA-B*	*KLF3*	*MYB*	*PIK3CG*	*RET*	*SOX9*	*UBE2T*
ARHGAP35	*CD70*	*DUSP2*	*FGF9*	*HLA-C*	*KLF4*	*MYBL1*	*PIK3R1*	*RFC1*	*SP140*	*UBR5*
ARHGEF10	*CD74*	*DUSP22*	*FGFR1*	*HLA-DMA*	*KLF5*	*MYC*	*PIK3R2*	*RGPD3*	*SPEN*	*UNCX*
ARHGEF12	*CD79A*	*DUSP4*	*FGFR2*	*HLA-DMB*	*KLHL6*	*MYCL*	*PIK3R3*	*RHEB*	*SPOP*	*USP6*
ARID1A	*CD79B*	*DUSP9*	*FGFR3*	*HLA-DOA*	*KLLN*	*MYCN*	*PIM1*	*RHOA*	*SPRED1*	*USP8*
ARID1B	*CD80*	*E2F3*	*FGFR4*	*HLA-DOB*	*KMT2A*	*MYD88*	*PKN1*	*RHOB*	*SPRTN*	*USP9X*
ARID2	*CDC73*	*EBF1*	*FGR*	*HLA-DPA1*	*KMT2B*	*MYH11*	*PLAG1*	*RHPN2*	*SPTA1*	*VAV1*
ARID3A	*CDH1*	*ECT2L*	*FH*	*HLA-DPB1*	*KMT2C*	*MYH9*	*PLCB4*	*RICTOR*	*SPTAN1*	*VEGFA*
ARID4B	*CDH10*	*EED*	*FHIT*	*HLA-DPB2*	*KMT2D*	*MYO18A*	*PLCG1*	*RINT1*	*SRC*	*VHL*
ARID5B	*CDH4*	*EEF1A1*	*FLCN*	*HLA-DQA1*	*KNSTRN*	*MYOD1*	*PLCG2*	*RIT1*	*SRP72*	*VTCN1*
ASMTL	*CDK12*	*EEF2*	*FLI1*	*HLA-DQA2*	*KRAS*	*NADK*	*PLK2*	*RNF111*	*SRSF2*	*WAS*
ASXL1	*CDK4*	*EGFL7*	*FLNA*	*HLA-DQB1*	*KRT222*	*NBN*	*PLXNB2*	*RNF139*	*SS18*	*WDR90*
ASXL2	*CDK6*	*EGFR*	*FLT1*	*HLA-DQB2*	*LAG3*	*NCOA2*	*PMAIP1*	*RNF43*	*SSBP2*	*WEE1*
ATF7IP	*CDK8*	*EGLN1*	*FLT3*	*HLA-DRA*	*LATS1*	*NCOA3*	*PML*	*ROBO1*	*STAG1*	*WIF1*
ATM	*CDKN1A*	*EGR1*	*FLT4*	*HLA-DRB1*	*LATS2*	*NCOR1*	*PMS1*	*ROS1*	*STAG2*	*WNK2*
ATP6AP1	*CDKN1B*	*EGR2*	*FLYWCH1*	*HLA-DRB5*	*LCK*	*NCOR2*	*PMS2*	*RPA1*	*STAT1*	*WRN*
ATP6V1B2	*CDKN1C*	*EGR3*	*FOXA1*	*HLA-DRB6*	*LDB1*	*NCSTN*	*PNRC1*	*RPL10*	*STAT2*	*WT1*
ATR	*CDKN2A*	*EIF1AX*	*FOXA2*	*HLA-E*	*LEF1*	*NECTIN4*	*POLD1*	*RPL22*	*STAT3*	*WWTR1*
ATRX	*CDKN2B*	*EIF3E*	*FOXD4L1*	*HLA-F*	*LEMD2*	*NEGR1*	*POLE*	*RPL5*	*STAT4*	*XBP1*
ATXN3	*CDKN2C*	*EIF4A2*	*FOXL2*	*HLA-G*	*LIFR*	*NEIL2*	*POLH*	*RPS15*	*STAT5A*	*XIAP*
ATXN7	*CEBPA*	*EIF4E*	*FOXO1*	*HLTF*	*LMO1*	*NF1*	*POLQ*	*RPS20*	*STAT5B*	*XPA*
AURKA	*CENPA*	*ELANE*	*FOXO3*	*HMGA2*	*LRP1B*	*NF2*	*POLR2A*	*RPS3A*	*STAT6*	*XPC*
AURKB	*CFTR*	*ELF3*	*FOXP1*	*HNF1A*	*LRP5*	*NFATC2*	*POLRMT*	*RPS6KA3*	*STK11*	*XPO1*
AXIN1	*CHD2*	*ELOC*	*FOXQ1*	*HNRNPK*	*LRP6*	*NFE2*	*POT1*	*RPS6KA4*	*STK19*	*XRCC1*
AXIN2	*CHD3*	*ELP2*	*FRK*	*HOXA11*	*LRRK2*	*NFE2L2*	*POU2F2*	*RPS6KB1*	*STK40*	*XRCC2*
AXL	*CHD4*	*EML4*	*FRS2*	*HOXB13*	*LTB*	*NFKBIA*	*PPARG*	*RPS6KB2*	*SUFU*	*XRCC3*

Precision Panel- 1000 Genes

B2M	CHD7	EMSY	FUBP1	HRAS	LTK	NFKBIE	PPM1D	RPTOR	SUSD2	YAP1
BABAM1	CHD8	ENG	FUS	HSD3B1	LUC7L2	NIPBL	PPP2R1A	RRAGC	SUZ12	YEATS4
BAP1	CHEK1	EP300	FYN	HSP90AA1	LYN	NKX2-1	PPP2R2A	RRAS	SYK	YES1
BARD1	CHEK2	EPAS1	GAB1	HSP90AB1	LZTR1	NKX3-1	PPP4R2	RRAS2	TAF1	YWHAE
BBC3	CIC	EPC1	GAB2	HUWE1	MACF1	NOD1	PPP6C	RSPO2	TAF15	YY1AP1
BCL10	CIITA	EPCAM	GABRA6	ICOS	MAD2L2	NOTCH1	PRDM1	RSPO3	TAL1	ZBTB2
BCL11B	CILK1	EPHA2	GADD45B	ICOSLG	MAF	NOTCH2	PRDM14	RTEL1	TAP1	ZBTB20
BCL2	CKS1B	EPHA3	GALNT12	ID3	MAFB	NOTCH3	PREX2	RUNX1	TAP2	ZBTB7B
BCL2L1	CLIP1	EPHA5	GATA1	IDH1	MAGED1	NOTCH4	PRF1	RUNX1T1	TAPBP	ZC3H12A
BCL2L11	CMTR2	EPHA7	GATA2	IDH2	MAGI2	NPM1	PRKACA	RXRA	TBL1XR1	ZCCHC12
BCL2L12	CNBD1	EPHB1	GATA3	IDO1	MALT1	NPRL2	PRKAR1A	RYBP	TBX3	ZFHX3
BCL2L2	CNOT9	EPHB4	GATA4	IFNAR1	MAML2	NR4A3	PRKCA	S1PR2	TCF12	ZFP36L1
BCL6	COL1A1	EGP1	GATA6	IFNGR1	MAMLD1	NRAS	PRKCB	SALL4	TCF3	ZFP36L2
BCL7A	COL5A1	ERBB2	GEM	IFNGR2	MAP2K1	NRG1	PRKCD	SAMD9	TCF7L2	ZMYM2
BCL9	COL7A1	ERBB3	GEN1	IGF1	MAP2K2	NSD1	PRKCI	SAMD9L	TCL1A	ZMYM3
BCLAF1	COP1	ERBB4	GID4	IGF1R	MAP2K4	NSD2	PRKD1	SAMHD1	TCL1B	ZNF133
BCOR	CPS1	ERCC1	GLI1	IGF2	MAP3K1	NSD3	PRKDC	SBDS	TDG	ZNF217
BCORL1	CRBN	ERCC2	GLI2	IKBKE	MAP3K13	NT5C2	PRKN	SCAF4	TEK	ZNF24
BCR	CREB3L3	ERCC3	GLIS2	IKZF1	MAP3K14	NT5E	PRPF40B	SCG5	TENT5C	ZNF384
BIRC3	CREBBP	ERCC4	GNA11	IKZF2	MAP3K4	NTHL1	PRPF8	SDC4	TENT5D	ZNF703
BLM	CRKL	ERCC5	GNA12	IKZF3	MAP3K6	NTRK1	PRPS1	SDHA	TERC	ZNF750
BMPR1A	CRLF1	ERCC6	GNA13	IL10	MAP3K7	NTRK2	PRSS1	SDHAF2	TERF1	ZNRF3
BRAF	CRLF2	ERF	GNAI2	IL2	MAPK1	NTRK3	PRSS8	SDHB	TERT	ZRANB3
BRCA1	CRTC1	ERG	GNAQ	IL2RB	MAPK3	NUDT15	PSIP1	SDHC	TET1	ZRSR2
BRCA2	CSDE1	ERRFI1	GNAS	IL2RG	MAST1	NUF2	PSMB5	SDHD	TET2	
BRCC3	CSF1R	ESR1	GNB1	IL3	MAST2	NUMBL	PTCH1	SERP2	TET3	
BRD3	CSF3R	ESRRA	GPC3	IL4R	MAX	NUP133	PTCH2	SERPINA1	TFE3	
BRD4	CSNK1A1	ETNK1	GPS2	IL6ST	MBD4	NUP214	PTEN	SERPINB3	TFEB	
BRD7	CTC1	ETS1	GREM1	IL7R	MC1R	NUP93	PTK2	SERPINB4	TFG	
BRINP3	CTCF	ETV1	GRIN2A	ING1	MCL1	NUP98	PTK2B	SESN2	TGFBR1	
BRIP1	CTDNEP1	ETV4	GRIN2D	INHA	MDC1	NUTM1	PTMA	SESN3	TGFBR2	
BRSK1	CTLA4	ETV5	GRM3	INHBA	MDM2	P2RY8	PTP4A1	SETBP1	TGIF1	
BTG1	CTNNA1	ETV6	GSK3B	INO80	MDM4	PABPC1	PTPDC1	SETD1B	THADA	
BTG2	CTNNB1	EWSR1	GTF2I	INPP4A	MEAF6	PAG1	PTPN1	SETD2	THRAP3	
BTK	CTNND1	EXO1	GTSE1	INPP4B	MECOM	PAK1	PTPN11	SETDB1	TIPARP	
BTLA	CTR9	EXOSC6	H1-2	INPP5D	MED12	PAK3	PTPN13	SETDB2	TLL2	
BUB1B	CUL1	EXT1	H1-3	INPPL1	MEF2B	PAK5	PTPN14	SF1	TLR4	
C3orf70	CUL3	EXT2	H1-4	INSR	MEF2C	PALB2	PTPN2	SF3A1	TLR9	
C8orf34	CUL4A	EZH1	H19	IRF1	MEF2D	PARP1	PTPN6	SF3B1	TLX3	
CACNA1A	CUL4B	EZH2	H2AC11	IRF2	MEN1	PARP2	PTPRC	SGK1	TMEM127	
CACNA1D	CUX1	EZHIP	H2AC16	IRF4	MERTK	PARP3	PTPRD	SH2B3	TMEM30A	
CAD	CXCR4	EZR	H2AC17	IRF6	MET	PARP4	PTPRO	SH2D1A	TMPRSS2	
CALR	CYLD	FAF1	H2AC6	IRF8	MGA	PARPBP	PTPRS	SHH	TMSB4X	
CAMTA1	CYP17A1	FAM135B	H2BC11	IRS1	MGMT	PASK	PTPRT	SHOC2	TMSB4XP8	

Fusions/ Translocations

ABL1	BCL6	CIITA	DUSP22	FLI1	JAK2	MLLT10	NTRK3	RBM15	TCF3	TYK2
ABL2	BRAF	CREBBP	EPOR	FOXP1	KMT2A	MYC	PDGFB	RET	TCL1A	
ALK	CBFB	CRLF2	FGFR1	GATA1	MAF	NRG1	PDGFRA	ROS1	TCL1B	
BCL10	CCND1	CSF1R	FGFR2	IL3	MAFB	NTRK1	PDGFRB	RUNX1	TLX3	
BCL2	CCND3	DEK	FGFR3	IRF4	MALT1	NTRK2	RARA	TAL1	TP63	