OVERVIEW

Molecular profiling of tumors is performed to identify mutations that accumulate in cancer cells, in particular driver mutations that can serve as treatment targets. Mutations identified in tumors usually include single nucleotide variants (SNVs), deletions and duplications. Fusion genes were originally associated with hematologic cancers; however, more than 300 gene fusions have been identified in almost every kind of solid tumor (sarcomas, carcinomas and tumors of the central nervous system). Identifying and characterizing the mutations in tumors therefore can have both diagnostic and therapeutic applications. The advent of next generation sequencing has enabled high-throughput, accurate molecular profiling across many tumor types.
The JAX Cancer Treatment Profile™ is a targeted panel of 358 cancer-related genes and 53 genes known to form fusions associated with various carcinomas, sarcomas, and hematologic malignancies, analyzed using next-generation sequencing. The panel assesses all identified functional variants for clinical relevance, based on associations in the biomedical literature with response or resistance to FDA-approved therapies or new drugs in development. The gene targets are selected for their known association with cancer types in over 20 different cancer primary sites, enabling detection of mutations present in as few as 10% of the cells in the tumor specimen. Evidence of association between genomic variants and potential response to therapy or availability of clinical trials is curated from the peer-reviewed literature, publicly available databases, and The Jackson Laboratory Clinical Knowledgebase (CKB).

**Methods**

For the 358 gene panel, genomic DNA is extracted from macro dissection-enriched FFPE tissue sections, followed by cDNA synthesis and amplification to generate a minimum of 1.5 million reads per sample. The LOD for variant detection is 10% allele frequency, however, due to the high specificity of this assay; variants detected at 5% allele frequency are also reported. Mutational analysis is performed using the Clinical Genomics Analytical (CGA) pipeline, developed at The Jackson Laboratory (JAX).

**Specimen Requirements**

- Formalin-fixed, paraffin-embedded (FFPE) tissue only.
- One representative hematoxylin and eosin (H&E) stained slide and 5 to 10 adjacent unstained 5 μm sections on uncoated, unbaked slides. We also accept tumor blocks.
- Any solid tumor, primary or metastatic tissue. The area of highest tumor cell content should be a minimum of 3 x 3 mm.

**Cancer types associated with genes selected for use in our cancer panel for the 358 genes**

<table>
<thead>
<tr>
<th>358 GENE PANEL (SNPs, CNVs, and MICRO INDELs):</th>
</tr>
</thead>
</table>
| AICF, ABI1, ACVRIB, ADAR, ADARB1, AFF2, AGO1, AGO2, AGO3, AGD4, AICDA, AKT1, AKT2, AKT3, ALK, AMERI, APCC, APOLI, APOBEC1, APOBEC3A, APOBEC3D, APOBEC3F, APOBEC3G, APOBEC4, AR, ARID1A, ARID2, ASHIL, AXIN1, ATM, ATN1, ATP1B1, ATR, ATRX, AURKA, AURKB, AURKC, AXIN1, B2M, BAP1, BCL2, BCLOR, BCR, BID, BRAF, BRCA1, BRCA2, BRIP1, BTK, CARD11, CARMA, CASP8, CBF, CBL, CCND1, CCNE1, CCR2, CDC73, CDH1, CDK2, CDK4, CDK6, CDKN1B, CDKN2A, CDKN2C, CHEK2, CIC, CIRBP, COL1A1, CReBP, CFL1, CFS1R, CSM3D, CTCF, CTNNB1, CXC4R, CYLD, DAILR3, DAXX, DDI4, DDR2, Dicer, DMTT1, DMTT1A, DMTT3B, DMTT3, DROSHA, DSPP, EGFR, EHM2T, EP100, EPHA10, EPHA3, EPHA5, EPHB6, ERBB2, ERBB3, ERBB4, ESR1, ETV6, EZH1, EZH2, FAM66A, FAT4, FBXO4, FBXW7, FER1L5, FES, FGFR1, FGFR2, FGFR3, FGFR4, FLT3, FOXL1, FUBP1, GATA1, GATA2, GATA3, GLI1, GLI2, GNA11, GNAQ, GNAS, GPR32, GPRIN2, GRIN2A, GRIN2B, GRIP1, GATA3, GLI1, GNA11, GNAQ, GNAS, GPR32, GPRIN2, GRIN2A, GRIN2B, GRIP1, HCEFC1R1, HES1, HES1, HES2, HGF, HIST1H2BC, HIST1H3A, HLA-A, HMCN1, HNFA1, HRS, HSPP1, HSFI, HSFI2, HSFI4, HSFI9, HSPA9A1, ID1, ID2, ID3, IDH2, IFIH1, IKBK, INHBA, INO80C, ITKBP, JAK1, JAK2, JAK3, JMD1D, JMD26, KCNQ2, KDM1A, KDM1B, KDM2A, KDM2B, KDM3A, KDM3B, KDM4A, KDM4B, KDM4C, KDM4D, KDM5A, KDM5B, KDM5C, KDM6B, KDR, KEAP1, KIT, KLF4, LILH, KMT2D, KMT2D, KRAS, LATS1, LATS2, LGL2, LMO1, LRP4N, LRP1B, LTK, LYSMD3, MAPK2, MAPK2, MAPK3, MAPK8, MAPK9, MDM2, MDM4, MEDI, MED21, MED11, MET, MEI, MLH1, MLH4, MSH2, MSH6, MTO1, MUC16, MUC17, MUC18, MUC3B, MYB, MYC, MYCN, MYD88, MYT1L, NCOA3, NCO1, NEK10, NEF1, NEF2L2, NKAIN4, NOTCH1, NOTCH2, NOTCH3, NOTCH4, NPM1, NRAS, NSD1, NTRK1, NTRK2, NTRK3, PAK3, PALB2, PAX5, PB1M, PGCF, PDGFA, PDGFB, PDGFRB, PGR, PHF6, PIK3CA, PIK3R1, PIK3R2, PIK3R3, PIK3R4, PIWIL1, PIK1, PMS1, PMS2, POLB, POLI, PPEF1, PPI2A, PPLQ2, PRMD1, PRMD14M, PRMD2, PRMD9, PRKAA1, PRKAA2, PRKMT1, PRKMT2, PRKMT3, PRKMT5, PRKMT6, PRKX1, PTHC, PTK2B, PTPN11, PTPRD, RAD50, RAD51, RAD51B, RAD51C, RAD51D, RAD54L, RAD54L2, RAF1, RASA1, RASGRF1, RBI, RET, RNF43, ROR2, ROSE1, ROR3, RUNX1, SALL1, SCGBC1, SETBP1, SETD2, SETD7, SF1B1, SKP2, SLCS3A, SMAD2, SMAD4, SMARCA4, SMARCB1, SMO, SMYD3, SOS1, SOX9, SOP, SPC, SRC2F, STAG2, STK11, STK3, STLR2B, TBLR1X, TRP1, TXC1F7, TCF7L2, TEAD1, TEAD2, TEAD4, TGFBR2, TLE6, TMEM22, TNFAIP3, TP53, TP63, TP73, Traf7, TSC1, TSHR, TTB, TTN, U2AF1, UBC, USH2A, VHL, WSC1, WSC1, WNTA, WTTA, WTTW1, XRCC2, XRCC3, XAPI, YES1, ZFP36,2L1, ZMYND19

<table>
<thead>
<tr>
<th>53 FUSION GENE PANEL:</th>
</tr>
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<tbody>
<tr>
<td>AKT3, ALK, ARIKAP26, AXL, BRAF, BRS3, BROY4, EGFR, ERG, ESR1, ETV1, ETV4, ETV5, ETV6, EWSR1, FGFR1, FGFR2, FGFR3, FGFR4, FGR, FGFR, FGFR5, FGR, INSR, MAML2, MAST, MAST2, MET, MDM2, MUSK, MYB, NOTCH1, NOTCH2, NR1, NTR1, NTR1, NTR2, NUM1, NRMT1, PDGFRA, PDGFRB, PIK3CA, PKN1, PPARC, PKR1A, PKR1B, RELA, RET, ROS1, RSPO2, RSPO3, TERT, TFE3, TFE6, THADA, TPMR1S2</td>
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**Gene Targets**

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</tr>
</tbody>
</table>

**REFERENCES:**

Please ship samples to:
The Jackson Laboratory for Genomic Medicine, 10 Discovery Drive, Farmington, CT 06032, USA.

JAX® GENOMIC MEDICINE
800-837-2320
jaxmoleculardx@jax.org

jax.org/ctp