ACTIONSEQ™

MOLECULAR PROFILING OF TUMORS TO IDENTIFY MUTATIONS THAT ACCUMULATE IN CANCER CELLS.

TEST 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. 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.

TEST DESCRIPTION
The JAX ActionSeq™ test is a targeted panel of 212 cancer related genes 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 targeted therapies. The gene targets are selected for their known association with cancer types in over 20 different cancer primary sites. 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**

Genomic DNA is extracted from macro dissection-enriched FFPE tissue sections, followed by enrichment of target exons by followed by enrichment of target exons and introns by hybrid-capture (Roche NimbleGen). Illumina sequencers generate 150bp paired-end sequence reads with a mean coverage of ≥500X, with a required minimum coverage of 130X for reporting variants. The LOD (limit of detection) was determined to be 3% for SNVs and 8% for indels. For copy number variants (CNVs), the LOD was determined to be 6 copies for amplifications and 0 copies (homozygous deletions) for losses. Mutational analysis is performed using the ActionSeq Genome Analytics (AGA) pipeline, developed at The Jackson Laboratory (JAX).

**SPECIMEN REQUIREMENTS**

- Formalin-fixed, paraffin-embedded (FFPE) material only.
- One representative hematoxylin and eosin (H&E) stained slide and 5 to 10 adjacent unstained 5 um 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.

**PLEASE SHIP SAMPLES TO:**
The Jackson Laboratory for Genomic Medicine, 10 Discovery Drive, Farmington, CT 06032, USA.

**GENE LIST**

212 Gene panel (SNPs, CNVs and micro InDels):

- ABL1, ABL2, AIM2, AKT1, AKT2, AKT3, ALK, APC, AR, ARAF, ARID1A, ATM, ATR, AURKA, AURKB, AXIN1, AXL, BAP1, BARD1, BCL2, BIRC5 (Survivin), BRAF, BRCA1, BRCA2, BRD3, BRD4, BRIP1, BTK, CALR, CBL, CCND1, CCND2, CCND3, CCNE1, CD274, CD79A, CD79B, CDK12, CDK4, CDK6, CDK8, CDKN1A, CDKN2A, CHEK1, CHEK2, CREBBP, CRKL, CSF1R, CSF3R, CTNNB1, CXXC4, DDR1, DDR2, DDX11, DNMT3A, DNMT3B, DYSK1B, EGFR, EP300, EPHA2, EPHB4, ERBB2, ERBB3, ERBB4, ERG, ESR1, ETV1, EZH1, EZH2, FANCA, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCL, FANCN, FBXW7, FES, FGF19, FGF3, FGFR1, FGFR2, FGFR3, FGFR4, FH, FLCN, FLT1, FLT3, FLT4, FRK, FRS2, GLI1, GLI2, GNA11, GNAQ, GNAS, GRM3, HGF, HRAS, HSP90AA1, ID1, ID2, ID3, IDH1, IDH2, IGF1R, IKBKE, IL7R, IR52, JAK1, JAK2, JAK3, JUN, KDM4C, KDR, KEAP1, KIAA1524 (CIP2A), KIT, KRAS, LTK, MAP2K1, MAP2K2, MAP3K9, MAPK1, MCL1, MD2, MDM2, MDM4, MEF2, MET, MFL, MRE11A, MSH2, MSH6, MSTR1 (RON), MTO1, MYC, MLYC, MKN, MYD88, NBN, NOA3, NF1, NF2, NFE2L2, NISCH, NOTCH1, NOTCH2, NOTCH3, NOTCH4, NRAS, NTRK1, NTRK2, NUAK2, PAK1, PALB2, PDGFRAl, PDGFRl, PDPK1, PIK3CA, PIK3CB, PIK3CD, PIK3CG, PIK3R1, PIK3R2, PIM1, PLK1, POLB, POLR2A, PPARG, PPP1D1, PPP2R1A, PPP2R1B, PRKAA1, PTCH1, PTEN, PTK2 (FAK), PTPN11, PTPRB, RAD50, RAD51, RAD51C, RAD51D, RAF1, RARB, RAS, RET, RHEB, RICTOR, RIT1, RNF43, ROS1, RSPO2, RSPO3, SHFM1, SMARCB1, SMO, SRC, STAT3, STAT5A, STAT5B, STK11 (LKB1), SYK, TGIFBR2, TNK2 (ACK1), TP53, TP63, TSC1, TSC2, TTK (MPS1), VEGFA, VHL

**REFERENCES**
