**Supplementary materials**

Supplemental table 1. Targeted hotspot gene panel

|  |  |
| --- | --- |
| **kit name** | **genes** |
| capture-based 8-gene panel named LungCore (Burning RockBiotech, Guangzhou, China) |

|  |  |  |  |
| --- | --- | --- | --- |
| *ALK* | *EGFR* | *KRAS* | *RET* |
| *BRAF* | *ERBB2* | *MET* | *ROS1* |

 |
| capture-based 168-gene panel named LungPlasma (Burning RockBiotech, Guangzhou, China) |

|  |  |  |  |
| --- | --- | --- | --- |
| *AKT1* | *EPHA3* | *KIT* | *PPP2R1A* |
| *ALK* | *EPHA5* | *KMT2D* | *PRKDC* |
| *APC* | *EPHA7* | *KRAS* | *PTEN* |
| *AR* | *EPHB1* | *LRP1B* | *PTPRD* |
| *ARID1A* | *ERBB2* | *MAP2K1* | *PTPRT* |
| *ATM* | *ERBB3* | *MAP3K13* | *RAD50* |
| *ATR* | *ERBB4* | *MAX* | *RAD51B* |
| *B2M* | *ESR1* | *MCL1* | *RAD51C* |
| *BARD1* | *FANCA* | *MEN1* | *RAD51D* |
| *BCL2L11* | *FANCI* | *MET* | *RAD54L* |
| *BCOR* | *FAT3* | *MLH1* | *RAF1* |
| *BLM* | *FBXW7* | *MRE11* | *RARA* |
| *BRAF* | *FGF19* | *MSH2* | *RB1* |
| *BRCA1* | *FGF3* | *MSH6* | *RBM10* |
| *BRCA2* | *FGF4* | *MTOR* | *RET* |
| *BRINP3* | *FGFR1* | *MUTYH* | *RNF43* |
| *BRIP1* | *FGFR2* | *MYC* | *ROS1* |
| *CARD11* | *FGFR3* | *MYCN* | *RUNX1* |
| *CASP8* | *FLT1* | *NAV3* | *SETD2* |
| *CBL* | *FLT3* | *NBN* | *SMAD4* |
| *CCND1* | *FLT4* | *NF1* | *SMARCA4* |
| *CCNE1* | *GATA2* | *NFE2L2* | *SOX2* |
| *CD274* | *GATA3* | *NOTCH1* | *SOX9* |
| *CD74* | *GRIN2A* | *NRAS* | *SPOP* |
| *CDH18* | *H3F3C* | *NRG1* | *SPTA1* |
| *CDK4* | *HGF* | *NTRK1* | *SRC* |
| *CDK6* | *HIST1H1C* | *NTRK2* | *STAG2* |
| *CDKN1A* | *HIST1H3B* | *NTRK3* | *STK11* |
| *CDKN1B* | *HIST1H3G* | *PAK5* | *TBX3* |
| *CDKN2A* | *HRAS* | *PALB2* | *TERT* |
| *CHEK1* | *IDH1* | *PARP1* | *TGFBR2* |
| *CHEK2* | *IDH2* | *PDGFRA* | *TP53* |
| *CREBBP* | *IGF2* | *PDGFRB* | *TP63* |
| *CSMD3* | *IKZF1* | *PIK3C2G* | *TRIM58* |
| *CTNNB1* | *IL7R* | *PIK3C3* | *TRPC5* |
| *CYP2D6* | *INHBA* | *PIK3CA* | *U2AF1* |
| *DIS3* | *JAK1* | *PIK3CG* | *UGT1A1* |
| *DNMT3A* | *JAK2* | *PIK3R1* | *VEGFA* |
| *DPYD* | *KDM5A* | *PMS2* | *VEGFB* |
| *EGFR* | *KDM6A* | *POLD1* | *VEGFC* |
| *EMSY* | *KDR* | *POLE* | *VHL* |
| *EP300* | *KEAP1* | *POM121L12* | *YES1* |

 |
| capture-based 520-gene panel named Oncoscreen Plus (Burning RockBiotech, Guangzhou, China) |

|  |  |  |  |
| --- | --- | --- | --- |
| *ABL1* | *EPHA3* | *KAT6A* | *PRSS8* |
| *ABL2* | *EPHA5* | *KDM5A* | *PTCH1* |
| *ABRAXAS1* | *EPHA7* | *KDM5C* | *PTEN* |
| *ACVR1* | *EPHB1* | *KDM6A* | *PTK2* |
| *ACVR1B* | *ERBB2* | *KDR* | *PTPN11* |
| *ADGRA2* | *ERBB3* | *KEAP1* | *PTPRD* |
| *AKT1* | *ERBB4* | *KEL* | *PTPRS* |
| *AKT2* | *ERCC1* | *KIT* | *PTPRT* |
| *AKT3* | *ERCC2* | *KLF4* | *QKI* |
| *ALK* | *ERCC3* | *KLHL6* | *RAB35* |
| *ALOX12B* | *ERCC4* | *KMT2A* | *RAC1* |
| *AMER1* | *ERCC5* | *KMT2C* | *RAD21* |
| *ANKRD11* | *ERG* | *KMT2D* | *RAD50* |
| *APC* | *ERRFI1* | *KRAS* | *RAD51* |
| *APCDD1* | *ESR1* | *LATS1* | *RAD51B* |
| *AR* | *EWSR1* | *LATS2* | *RAD51C* |
| *ARAF* | *EZH2* | *LMO1* | *RAD51D* |
| *ARFRP1* | *FANCA* | *LRP1B* | *RAD52* |
| *ARID1A* | *FANCC* | *LYN* | *RAD54L* |
| *ARID1B* | *FANCD2* | *LZTR1* | *RAF1* |
| *ARID2* | *FANCE* | *MAGI2* | *RANBP2* |
| *ARID5B* | *FANCF* | *MALT1* | *RARA* |
| *ASXL1* | *FANCG* | *MAP2K1* | *RASA1* |
| *ASXL2* | *FANCI* | *MAP2K2* | *RB1* |
| *ATF1* | *FANCL* | *MAP2K4* | *RBM10* |
| *ATM* | *FANCM* | *MAP3K1* | *RECQL4* |
| *ATR* | *FAS* | *MAP3K13* | *REL* |
| *ATRX* | *FAT1* | *MAP3K14* | *RET* |
| *AURKA* | *FAT3* | *MAPK1* | *RHEB* |
| *AURKB* | *FBXW7* | *MAPK3* | *RHOA* |
| *AXIN1* | *FCGR2B* | *MAX* | *RICTOR* |
| *AXIN2* | *FGF10* | *MCL1* | *RIT1* |
| *AXL* | *FGF12* | *MDC1* | *RNF43* |
| *B2M* | *FGF14* | *MDM2* | *ROS1* |
| *BACH1* | *FGF19* | *MDM4* | *RPA1* |
| *BAP1* | *FGF23* | *MED12* | *RPS6KA4* |
| *BARD1* | *FGF3* | *MEF2B* | *RPS6KB2* |
| *BBC3* | *FGF4* | *MEN1* | *RPTOR* |
| *BCL10* | *FGF6* | *MET* | *RUNX1* |
| *BCL2* | *FGF7* | *MGA* | *RUNX1T1* |
| *BCL2L1* | *FGFR1* | *MITF* | *RYBP* |
| *BCL2L11* | *FGFR2* | *MLH1* | *SDHA* |
| *BCL2L2* | *FGFR3* | *MLH3* | *SDHAF2* |
| *BCL6* | *FGFR4* | *MPL* | *SDHB* |
| *BCOR* | *FH* | *MRE11* | *SDHC* |
| *BCORL1* | *FLCN* | *MSH2* | *SDHD* |
| *BCR* | *FLT1* | *MSH3* | *SETD2* |
| *BIRC3* | *FLT3* | *MSH6* | *SF3B1* |
| *BLM* | *FLT4* | *MST1* | *SH2B3* |
| *BMPR1A* | *FOXA1* | *MST1R* | *SH2D1A* |
| *BRAF* | *FOXL2* | *MTOR* | *SHQ1* |
| *BRCA1* | *FOXO1* | *MUTYH* | *SLIT2* |
| *BRCA2* | *FOXP1* | *MYC* | *SLX4* |
| *BRD4* | *FRS2* | *MYCL* | *SMAD2* |
| *BRIP1* | *FUBP1* | *MYCN* | *SMAD3* |
| *BTG1* | *FYN* | *MYD88* | *SMAD4* |
| *BTK* | *GABRA6* | *MYOD1* | *SMARCA4* |
| *CALR* | *GALNT12* | *NBN* | *SMARCB1* |
| *CARD11* | *GATA1* | *NCOA3* | *SMARCD1* |
| *CASP8* | *GATA2* | *NCOR1* | *SMO* |
| *CBFB* | *GATA3* | *NEB* | *SNCAIP* |
| *CBL* | *GATA4* | *NEGR1* | *SOCS1* |
| *CCND1* | *GATA6* | *NF1* | *SOX10* |
| *CCND2* | *GID4* | *NF2* | *SOX17* |
| *CCND3* | *GLI1* | *NFE2L2* | *SOX2* |
| *CCNE1* | *GNA11* | *NFKBIA* | *SOX9* |
| *CD274* | *GNA13* | *NKX2-1* | *SPEN* |
| *CD276* | *GNAQ* | *NKX3-1* | *SPOP* |
| *CD79A* | *GNAS* | *NOTCH1* | *SPTA1* |
| *CD79B* | *GPS2* | *NOTCH2* | *SRC* |
| *CDC73* | *GREM1* | *NOTCH3* | *SRSF2* |
| *CDH1* | *GRIN2A* | *NOTCH4* | *STAG2* |
| *CDK12* | *GRM3* | *NPM1* | *STAT3* |
| *CDK4* | *GSK3B* | *NR4A3* | *STAT4* |
| *CDK6* | *GSTM1* | *NRAS* | *STAT5A* |
| *CDK8* | *GSTT1* | *NRG1* | *STAT5B* |
| *CDKN1A* | *H3F3A* | *NSD1* | *STK11* |
| *CDKN1B* | *H3F3B* | *NTHL1* | *STK40* |
| *CDKN1C* | *H3F3C* | *NTRK1* | *SUFU* |
| *CDKN2A* | *HDAC1* | *NTRK2* | *SUZ12* |
| *CDKN2B* | *HDAC2* | *NTRK3* | *SYK* |
| *CDKN2C* | *HDAC4* | *NUP93* | *TACC3* |
| *CEBPA* | *HGF* | *PAK1* | *TAF1* |
| *CENPA* | *HIST1H1C* | *PAK3* | *TBX3* |
| *CHD1* | *HIST1H2BD* | *PAK5* | *TCF3* |
| *CHD2* | *HIST1H3A* | *PALB2* | *TCF7L2* |
| *CHD4* | *HIST1H3B* | *PARP1* | *TENT5C* |
| *CHEK1* | *HIST1H3C* | *PARP2* | *TERC* |
| *CHEK2* | *HIST1H3D* | *PARP3* | *TERT* |
| *CHUK* | *HIST1H3E* | *PARP4* | *TET1* |
| *CIC* | *HIST1H3F* | *PAX5* | *TET2* |
| *COP1* | *HIST1H3G* | *PBRM1* | *TGFBR1* |
| *CRBN* | *HIST1H3H* | *PDCD1* | *TGFBR2* |
| *CREBBP* | *HIST1H3I* | *PDCD1LG2* | *TIPARP* |
| *CRKL* | *HIST1H3J* | *PDGFRA* | *TMEM127* |
| *CRLF2* | *HIST2H3C* | *PDGFRB* | *TMPRSS2* |
| *CSF1R* | *HIST2H3D* | *PDK1* | *TNFAIP3* |
| *CSF3R* | *HIST3H3* | *PDPK1* | *TNFRSF14* |
| *CTCF* | *HLA-A* | *PGR* | *TNFSF11* |
| *CTLA4* | *HNF1A* | *PHOX2B* | *TOP1* |
| *CTNNA1* | *HNF1B* | *PIK3C2B* | *TOP2A* |
| *CTNNB1* | *HOXB13* | *PIK3C2G* | *TP53* |
| *CUL3* | *HRAS* | *PIK3C3* | *TP63* |
| *CUL4A* | *HSD3B1* | *PIK3CA* | *TRAF2* |
| *CUL4B* | *HSP90AA1* | *PIK3CB* | *TRAF7* |
| *CXCR4* | *ICOSLG* | *PIK3CD* | *TRRAP* |
| *CYLD* | *ID3* | *PIK3CG* | *TSC1* |
| *CYP17A1* | *IDH1* | *PIK3R1* | *TSC2* |
| *DAXX* | *IDH2* | *PIK3R2* | *TSHR* |
| *DCUN1D1* | *IFNGR1* | *PIK3R3* | *U2AF1* |
| *DDR2* | *IGF1* | *PIM1* | *VEGFA* |
| *DICER1* | *IGF1R* | *PLCG2* | *VEGFB* |
| *DIS3* | *IGF2* | *PLK2* | *VEGFC* |
| *DNAJB1* | *IKBKE* | *PMAIP1* | *VHL* |
| *DNMT1* | *IKZF1* | *PMS1* | *VTCN1* |
| *DNMT3A* | *IL10* | *PMS2* | *WISP3* |
| *DNMT3B* | *IL7R* | *PNRC1* | *WRN* |
| *DOT1L* | *INHA* | *POLD1* | *WT1* |
| *E2F3* | *INHBA* | *POLE* | *XIAP* |
| *EED* | *INPP4A* | *POM121L12* | *XPO1* |
| *EGFL7* | *INPP4B* | *PPM1D* | *XRCC2* |
| *EGFR* | *INSR* | *PPP2R1A* | *XRCC3* |
| *EIF1AX* | *IRF2* | *PPP2R2A* | *YAP1* |
| *EIF4A2* | *IRF4* | *PPP6C* | *YES1* |
| *EIF4E* | *IRS1* | *PRDM1* | *ZBTB2* |
| *ELOC* | *IRS2* | *PREX2* | *ZFHX3* |
| *EMSY* | *JAK1* | *PRKAR1A* | *ZNF217* |
| *EP300* | *JAK2* | *PRKCI* | *ZNF703* |
| *EPCAM* | *JAK3* | *PRKDC* | *ZNRF3* |
| EPHA2 | JUN | PRKN | ZRSR2 |

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Supplemental table 2. Co-occurring driver oncogenes with KRAS

|  |  |  |
| --- | --- | --- |
| Patient number | KRAS mutation | Other driver oncogenes mutation |
| NO.2 | KRAS G12D | RET R694Q |
| NO.15 | KRAS Q61L | - |
| NO.41 | KRAS G12A; KRAS CAN | - |
| NO.51 | KRAS G12A | RET A420S |
| NO.57 | KRAS Q61L | - |
| NO.101 | KRAS CAN | - |
| NO.115 | KRAS G13E | - |
| NO.122 | KRAS Q61H | - |
| NO.139 | KRAS G12A | - |
| NO.143 | KRAS G12V | - |
| NO.148 | KRAS G12A | - |
| NO.163 | KRAS G12D | - |
| NO.175 | KRAS G12S | ALK G1054R |
| NO.189 | KRAS G12F | - |
| NO.236 | KRAS G13C | - |
| NO.245 | KRAS G12V | - |
| NO.257 | KRAS G12V | - |
| NO.288 | KRAS Q61L | - |
| NO.315 | KRAS G12D | - |
| NO.333 | KRAS G12D | - |
| NO.343 | KRAS G12D | EGFR 19del |
| NO.361 | KRAS G12D | - |
| NO.362 | KRAS CAN | EGFR 19del |
| NO.371 | KRAS G12V | - |
| NO.381 | KRAS G12D | - |
| NO.402 | KRAS G12D | - |
| NO.412 | KRAS G12C | EGFR V1097I |
| NO.413 | KRAS G12C | - |
| NO.414 | KRAS G12C | - |
| NO.415 | KRAS G12C | - |
| NO.416 | KRAS G12C | BRAF G466A; ERBB2 CAN |
| NO.417 | KRAS G12C | - |
| NO.418 | KRAS G12C | - |
| NO.419 | KRAS G12C |  |
| NO.420 | KRAS G12C | EGFR CAN |
| NO.421 | KRAS G12C | MET CAN |
| NO.422 | KRAS G12C |  |
| NO.423 | KRAS G12C |  |
| NO.424 | KRAS G12C |  |
| NO.425 | KRAS G12C |  |
| NO.426 | KRAS G12C | ROS1 6133del |
| NO.427 | KRAS G12C | ROS1 M1111K, |
| NO.428 | KRAS G12C | ALK L1195M |
| NO.429 | KRAS G12C | MET M1250T |
| NO.430 | KRAS G12C | - |
| NO.431 | KRAS G12C | - |

CAN: Copy Number Amplification