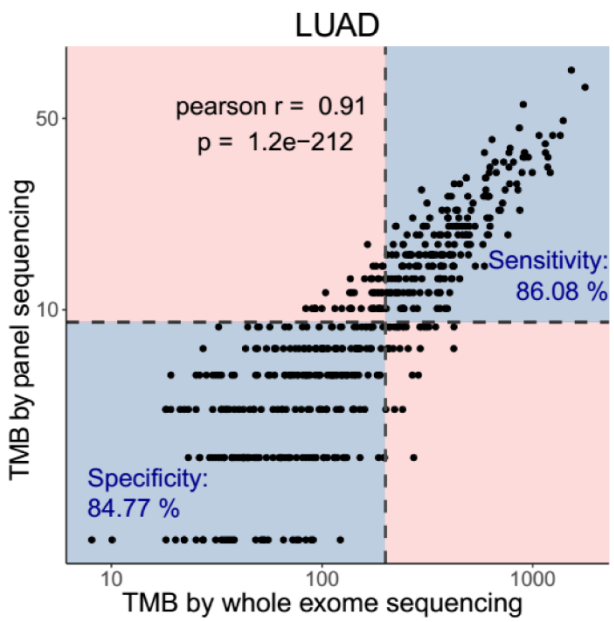
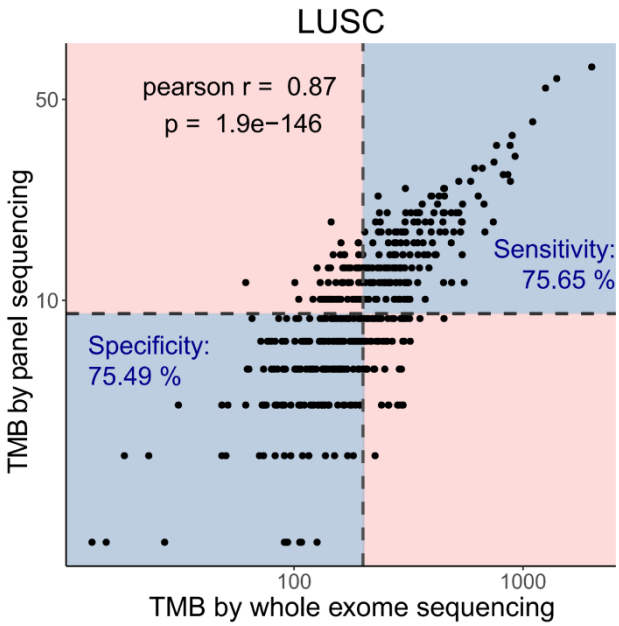
Figure S1. The correlations of TMB value between panel sequencing and WES in published databases.

(**A**) TCGA-LUAD, (**B**) TCGA-LUSC, (**C**) Database from Rizvi H, et al. J Clin Oncol, 2018;36.

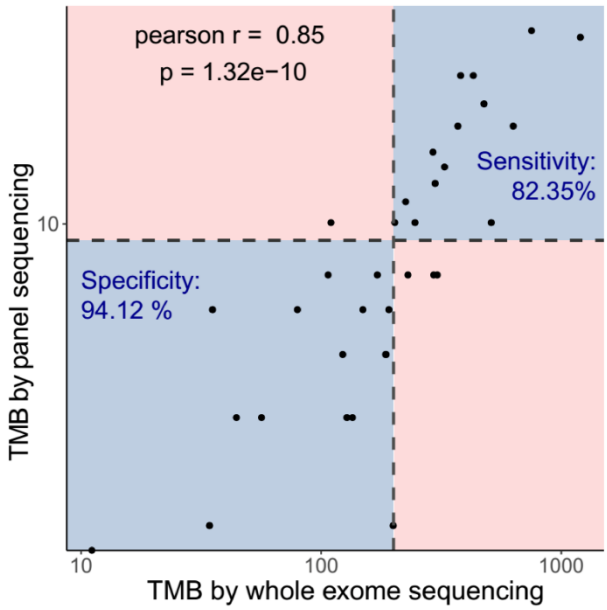
Abbreviations: TMB, tumor mutational burden; TCGA, The Cancer Genome Atlas; LUAD, lung adenocarcinoma; LUSC, lung squamous cell carcinoma; WES, wholeexome sequencing



A



B



C

Figure S2. The comparison of multi-region tTMB among different NSCLC subtypes.

Abbreviations: TMB, tumor mutational burden; tTMB, tissue TMB

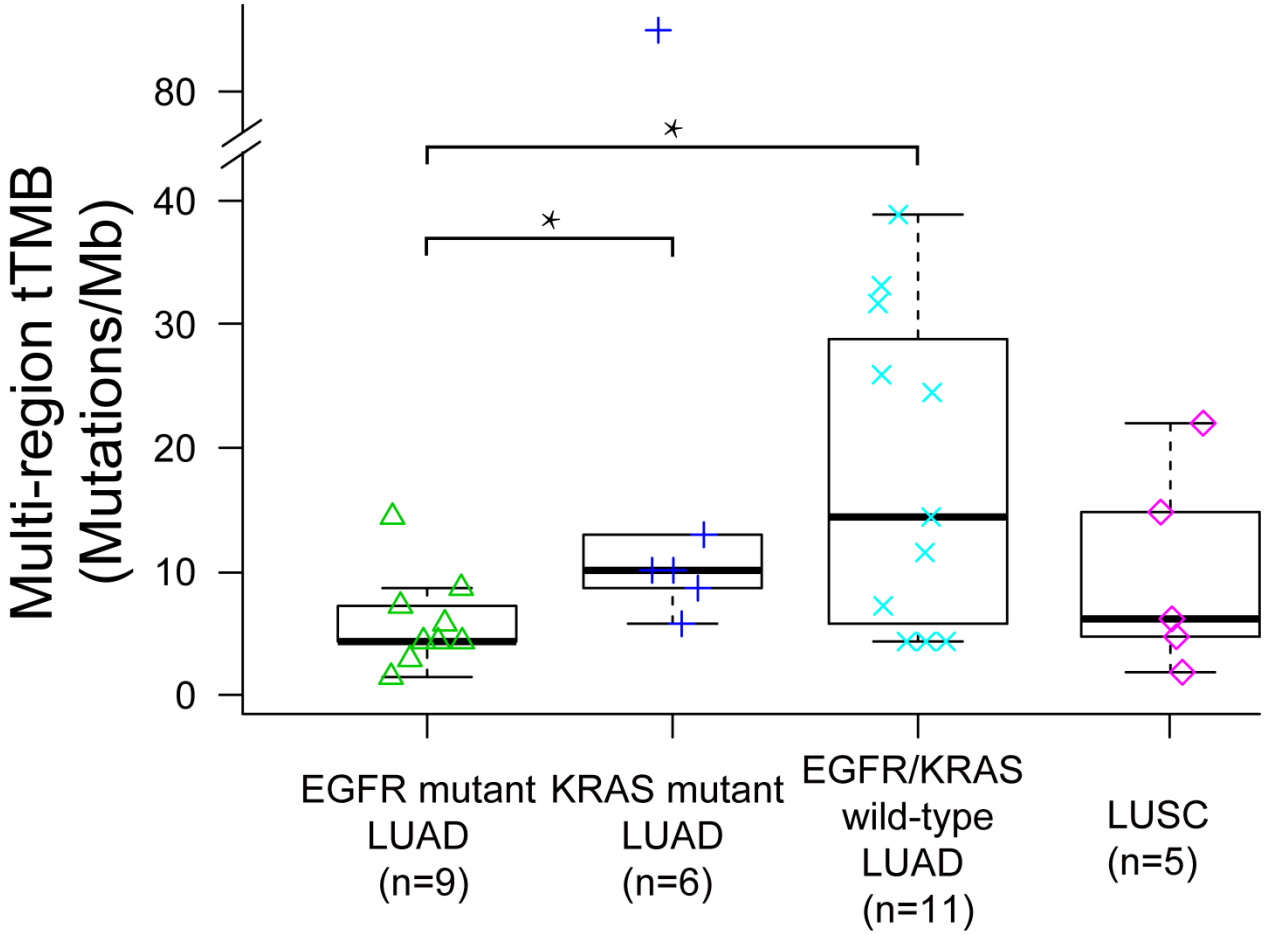
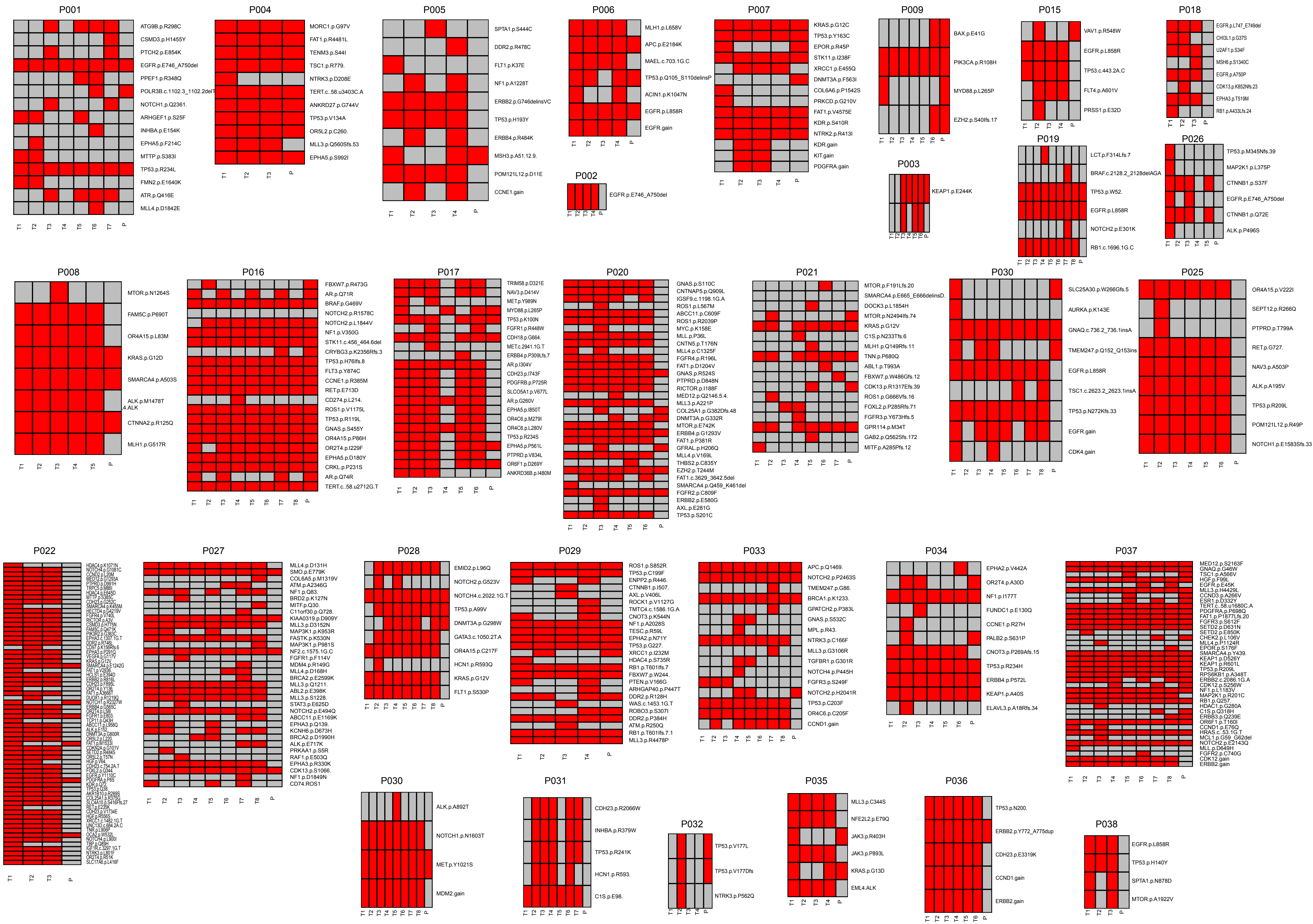


Figure S3. The comparisons and overlaps of tumor-derived mutational profiles among tumor tissues in each region and the corresponding ctDNA.

The P0XX was the patient No. shown at the top. Each tumor region (T1, T2, T3…) with plasma (P) were arranged in the x axis. ctDNA was isolated from plasma (more details in Supplementary Methods). Right y axis displayed tumor-derived mutational profiles in detail. The detected mutations were shown in red, while undetected cases were shown in gray.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CSMD3.p.H1455Y
PTCH2.p.E854K
EGFR.p.E746_A750del
PPEF1.p.R348Q
POLR3B.c.1102.3_1102.2delT
NOTCH1.p.Q2361.
ARHGEF1.p.S25F
INHBA.p.E154K
EPHA5.p.F214C
MTTP.p.S383I
TP53.p.R234L
FMN2.p.E1640K
ATR.p.Q416E
MLL4.p.D1842E
P004
MORC1.p.G97V
FAT1.p.R4481L
TENM3.p.S44I
TSC1.p.R779.
NTRK3.p.D208E
TERT.c..58.u3403C.A
ANKRD27.p.G744V
TP53.p.V134A
OR5L2.p.C260.
MLL3.p.Q560Sfs.53
EPHA5.p.S992I
P005
SPTA1.p.S444C
DDR2.p.R478C
FLT1.p.K37E
NF1.p.A1228T
ERBB2.p.G746delinsVC
TP53.p.H193Y
ERBB4.p.R484K
MSH3.p.A51.12.9.
POM121L12.p.D11E
CCNE1.gain
P006
MLH1.p.L658V
APC.p.E2184K
MAEL.c.703.1G.C
TP53.p.Q105_S110delinsP
ACIN1.p.K1047N
EGFR.p.L858R
EGFR.gain
P002
EGFR.p.E746_A750del
P007
KRAS.p.G12C
TP53.p.Y163C
EPOR.p.R45P
STK11.p.I238F
XRCC1.p.E455Q
DNMT3A.p.F563I
COL6A6.p.P1542S
PRKCD.p.G210V
FAT1.p.V4575E
KDR.p.S410R
NTRK2.p.R413I
KDR.gain
KIT.gain
PDGFRA.gain
P009
BAX.p.E41G
PIK3CA.p.R108H
MYD88.p.L265P
EZH2.p.S40Ifs.17
P003
KEAP1.p.E244K
P015
VAV1.p.R548W
EGFR.p.L858R
TP53.c.443.2A.C
FLT4.p.A601V
PRSS1.p.E32D
P019
LCT.p.F314Lfs.7
BRAF.c.2128.2_2128delAGA
TP53.p.W52.
EGFR.p.L858R
NOTCH2.p.E301K
RB1.c.1696.1G.C
P018
EGFR.p.L747_E749del
CHI3L1.p.G37S
U2AF1.p.S34F
MSH6.p.S1340C
EGFR.p.A750P
CDK13.p.K852Nfs.23
EPHA3.p.T519M
RB1.p.A433Lfs.24
P026
TP53.p.M345Nfs.39
MAP2K1.p.L375P
CTNNB1.p.S37F
EGFR.p.E746_A750del
CTNNB1.p.Q72E
ALK.p.P496S
P008
MTOR.p.N1264S
FAM5C.p.P690T
OR4A15.p.L83M
KRAS.p.G12D
SMARCA4.p.A503S
ALK.p.M1478T
CTNNA2.p.R125Q
MLH1.p.G517R
P016
FBXW7.p.R473G
AR.p.Q71R
BRAF.p.G469V
NOTCH2.p.R1578C
NOTCH2.p.L1844V
NF1.p.V350G
STK11.c.456_464.6del
CRYBG3.p.K2356Rfs.3
TP53.p.H76Ifs.8
FLT3.p.Y874C
CCNE1.p.R385M
RET.p.E713D
CD274.p.L214.
ROS1.p.V1175L
TP53.p.R119L
GNAS.p.S455Y
OR4A15.p.P86H
OR2T4.p.I229F
EPHA5.p.D180Y
CRKL.p.P231S
AR.p.Q74R
TERT.c..58.u2712G.T
P017
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NAV3.p.D414V
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MYD88.p.L265P
TP53.p.K100N
FGFR1.p.R448W
CDH18.p.G664.
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CDH23.p.I743F
PDGFRB.p.P725R
SLCO5A1.p.V677L
AR.p.G260V
EPHA5.p.I850T
OR4C6.p.M279I
OR4C6.p.L280V
TP53.p.R234S
EPHA5.p.P561L
PTPRD.p.V834L
OR6F1.p.D269Y
ANKRD36B.p.I480M
P020
GNAS.p.S110C
CNTNAP5.p.Q909L
IGSF9.c.1198.1G.A
ROS1.p.L567M
ABCC11.p.C609F
ROS1.p.R2039P
MYC.p.K158E
MLL.p.P36L
CNTN5.p.T176N
MLL4.p.C1325F
FGFR4.p.R196L
FAT1.p.D1204V
GNAS.p.R524S
PTPRD.p.D848N
RICTOR.p.I188F
MED12.p.Q2146.5.4.
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FAT1.p.P381R
GFRAL.p.H206Q
MLL4.p.V169L
THBS2.p.C835Y
EZH2.p.T244M
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FGFR2.p.C809F
ERBB2.p.E580G
AXL.p.E281G
TP53.p.S201C
P021
MTOR.p.F191Lfs.20
SMARCA4.p.E665_E666delinsD.
DOCK3.p.L1854H
MTOR.p.N2494Ifs.74
KRAS.p.G12V
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TNN.p.P680Q
ABL1.p.T993A
FBXW7.p.W486Gfs.12
CDK13.p.R1317Efs.39
ROS1.p.G666Vfs.16
FOXL2.p.P285Rfs.71
FGFR3.p.Y673Hfs.5
GPR114.p.M34T
GAB2.p.Q562Sfs.172
MITF.p.A285Pfs.12
P030
SLC25A30.p.W266Gfs.5
AURKA.p.K143E
GNAQ.c.736.2_736.1insA
TMEM247.p.Q152_Q153ins
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TSC1.c.2623.2_2623.1insA
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CDK4.gain
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PTPRD.p.T799A
RET.p.G727.
NAV3.p.A503P
ALK.p.A195V
TP53.p.R209L
POM121L12.p.R49P
NOTCH1.p.E1583Sfs.33
P022
P027
MLL4.p.D131H
SMO.p.E779K
COL6A5.p.M1319V
ATM.p.A2346G
NF1.p.Q83.
BRD2.p.K127N
MITF.p.Q30.
C11orf30.p.Q728.
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MAP3K1.p.K953R
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FGFR3.p.S249F
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PALB2.p.S631P
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KEAP1.p.A40S
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