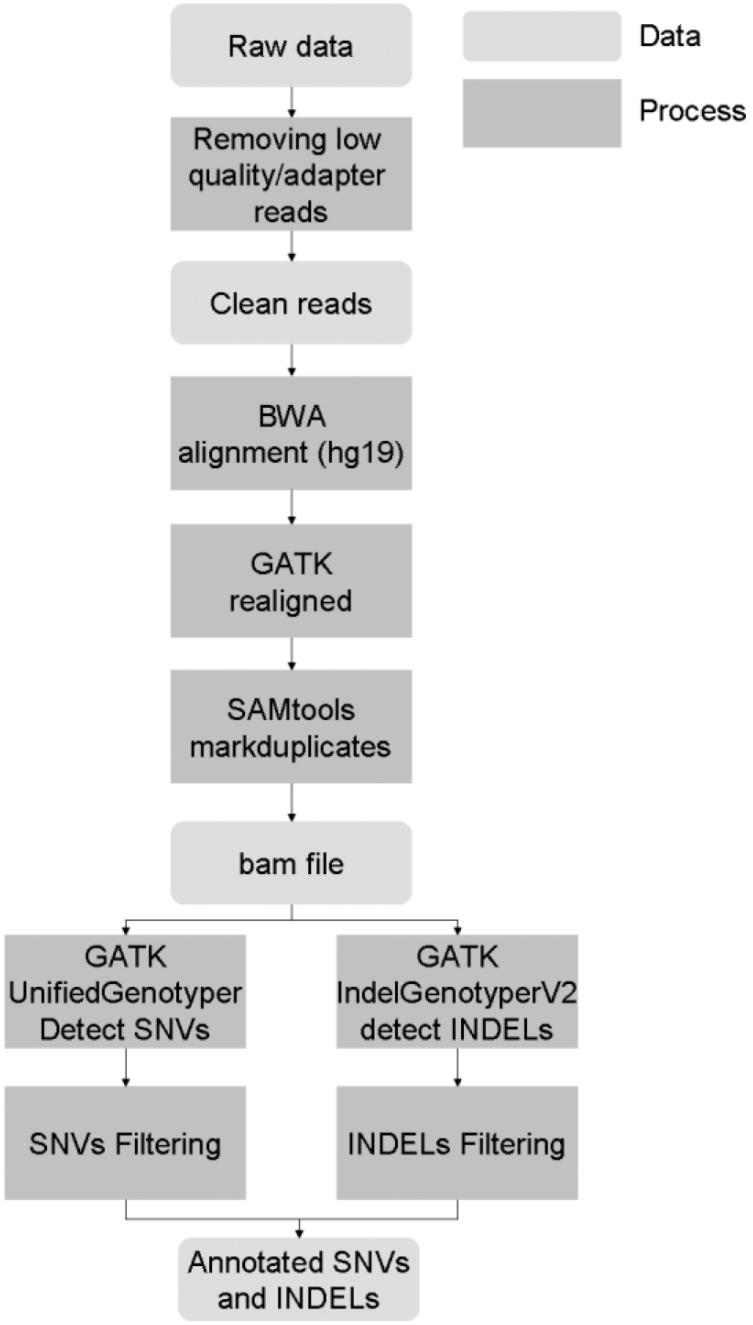
# Intratumoral KIT mutational heterogeneity and recurrent KIT/PDGFRA mutations in KIT/PDGFRA wild-type gastrointestinal stromal tumors

## Supplementary Materials

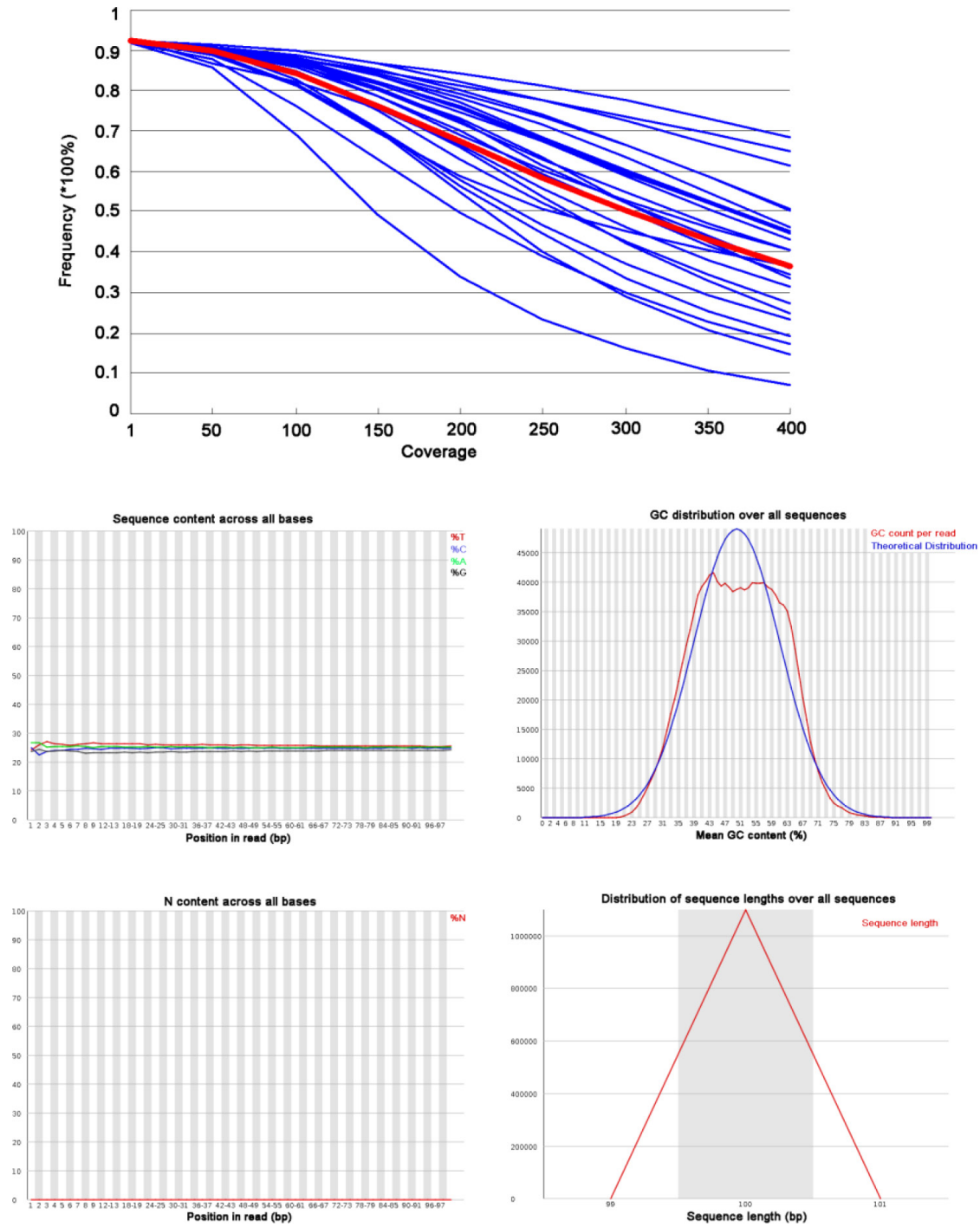
**Supplementary Table S1: The list of 48 genes**

| | | | |
|---|---|---|---|
| AKT1 | DDR2 | KIT | RET |
| AKT2 | DEPDC5 | KRAS | ROS1 |
| ALK | DPYD | LKB1 | TERT |
| ATRX | EGFR | MEK1 | TP53 |
| BIM | F2 | MEK2 | TPMT |
| BRAF | F5 | MET | TSC1 |
| BRCA1 | FGFR1 | NF1 | TSC2 |
| BRCA2 | FUBP1 | NPRL2 | UGT1A1 |
| CDKN2A | HER2 | NRAS | VEGFA |
| CDKN2B | HRAS | PDGFRA | VEGFR1 |
| CIC | IDH1 | PIK3CA | VEGFR2 |
| DAXX | IDH2 | PTEN | VEGFR3 |

**Supplementary Table S2: KRAS and BRAF variations identified in this study by next-generation sequencing**

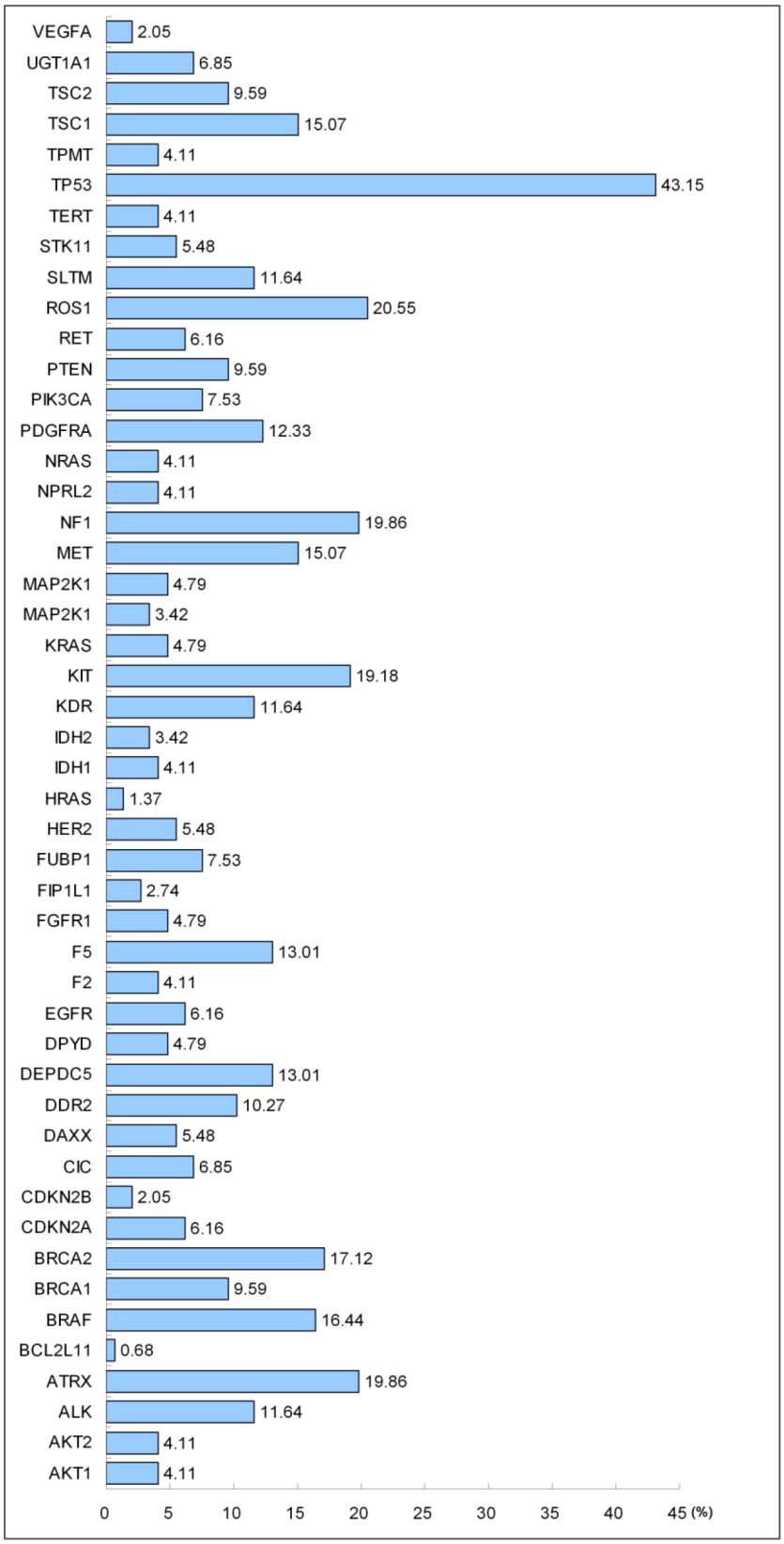



**Supplementary Figure S1: The work flow of gene variation analysis.**

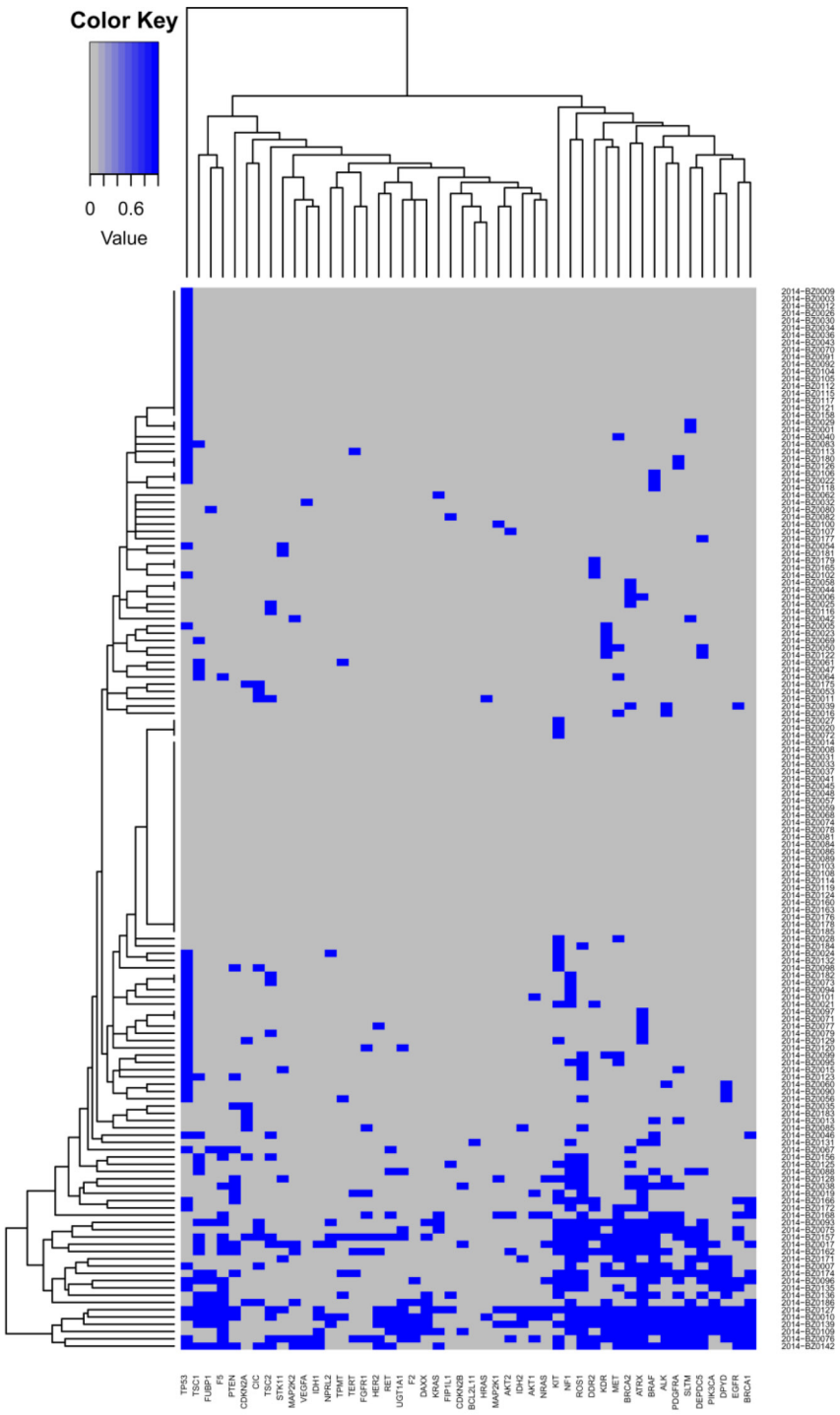


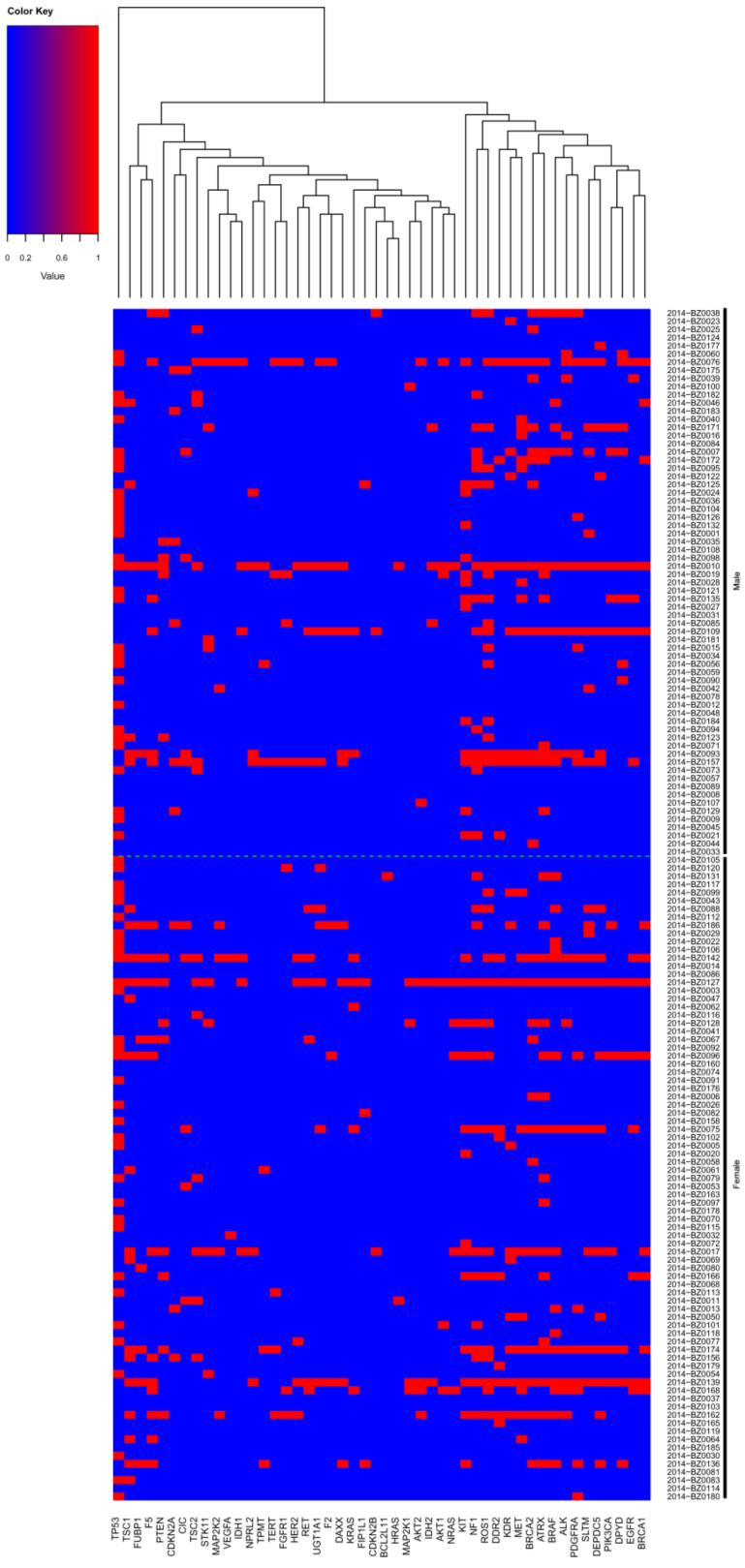

**Supplementary Figure S2: Quality control of next-generation sequencing.** All parameters (including average coverage of sequencing, sequence content of four bases, actual GC distribution, the proportion of N appearing, and the distribution of fragment sizes) guaranteed the accuracy of sequencing and established the foundation for data elucidation.

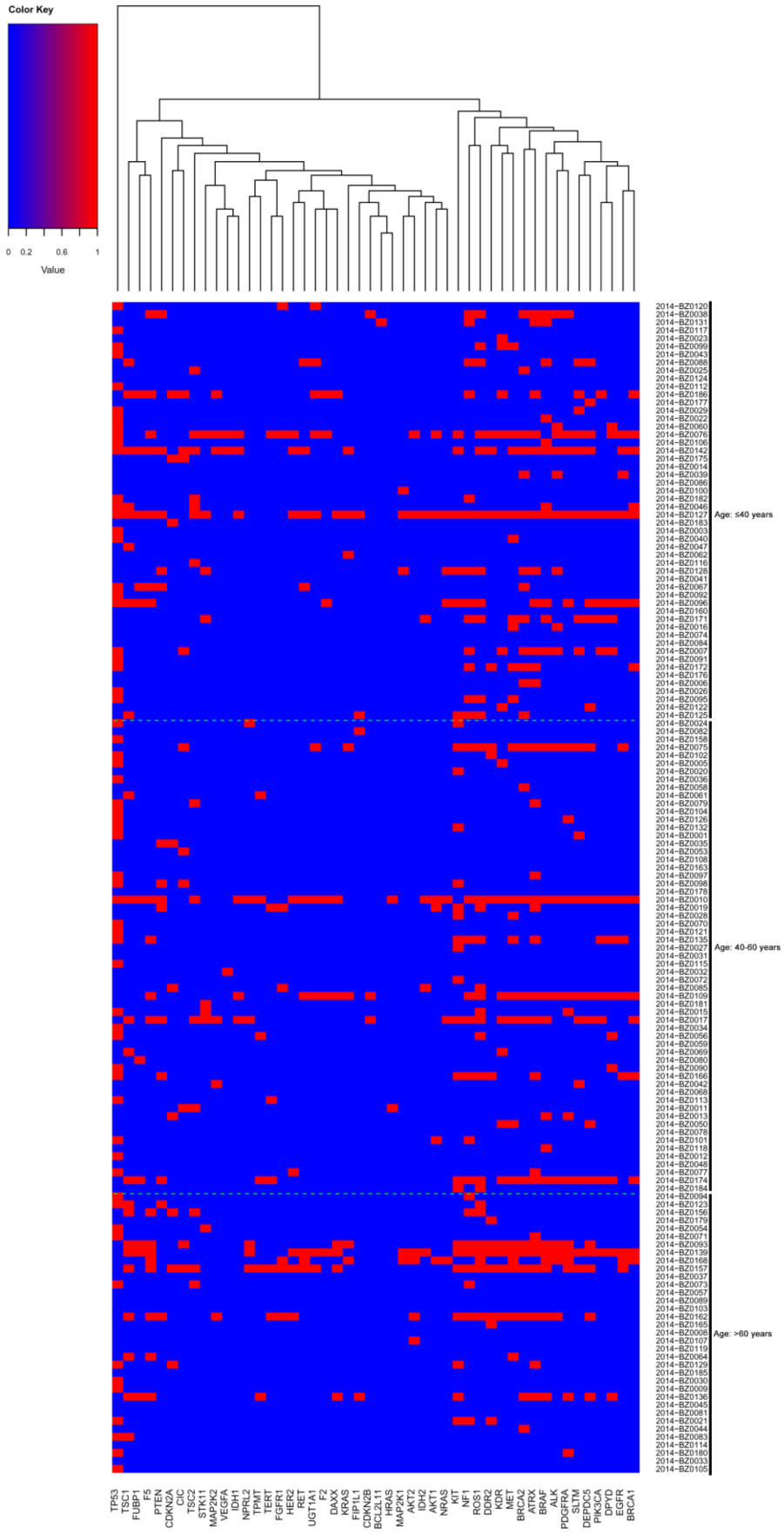

**Supplementary Figure S3: The number of variants in 146 patients.** Among all patients, 119 cases had at least one nonsynonymous or deletion variant in the captured gene set. The number of variants in all patients ranged from 0 to 34 with a median of 2.

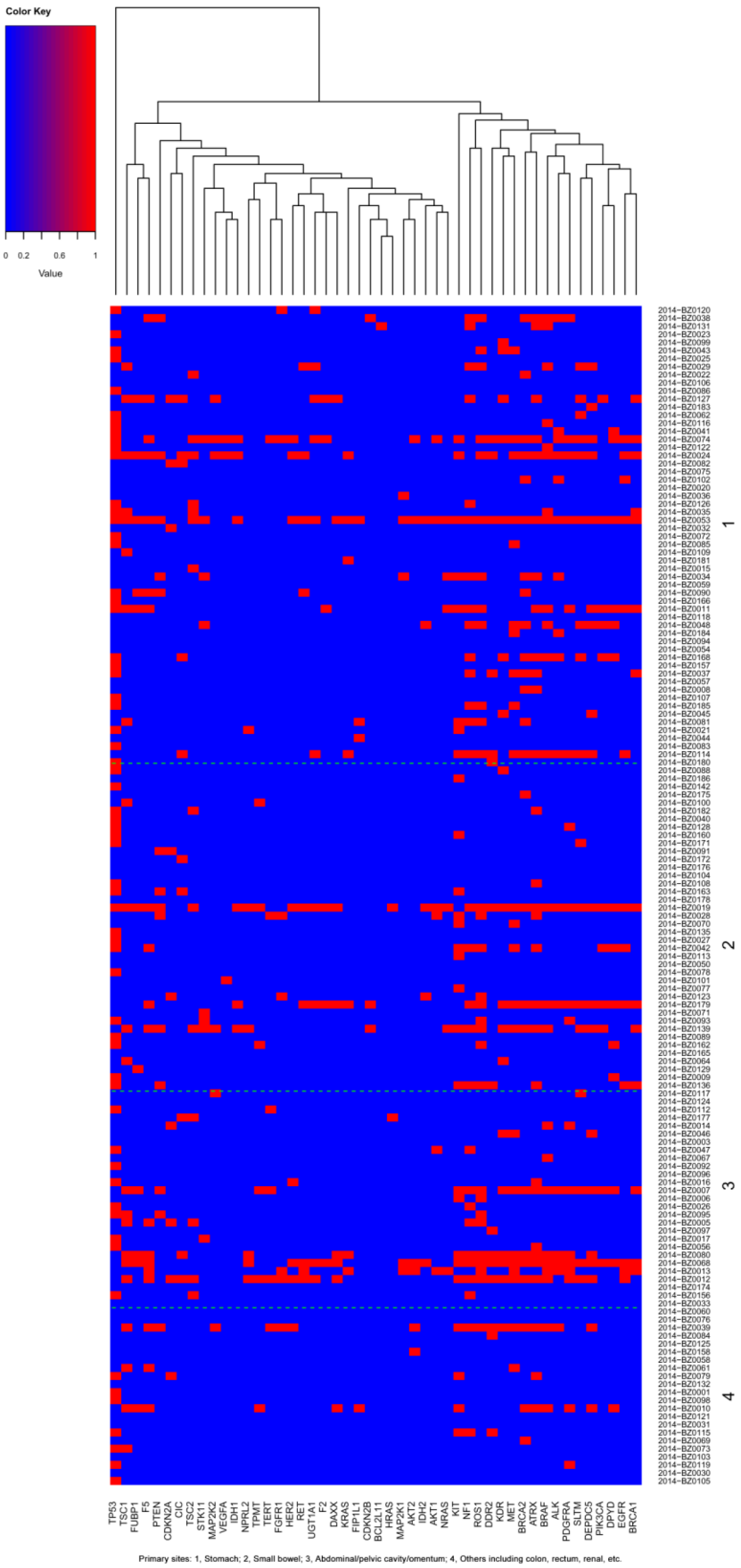



**Supplementary Figure S4: The frequency of variants in our cohort.** Whether these variants participated in tumorigenesis of GISTs need to be further investigated.

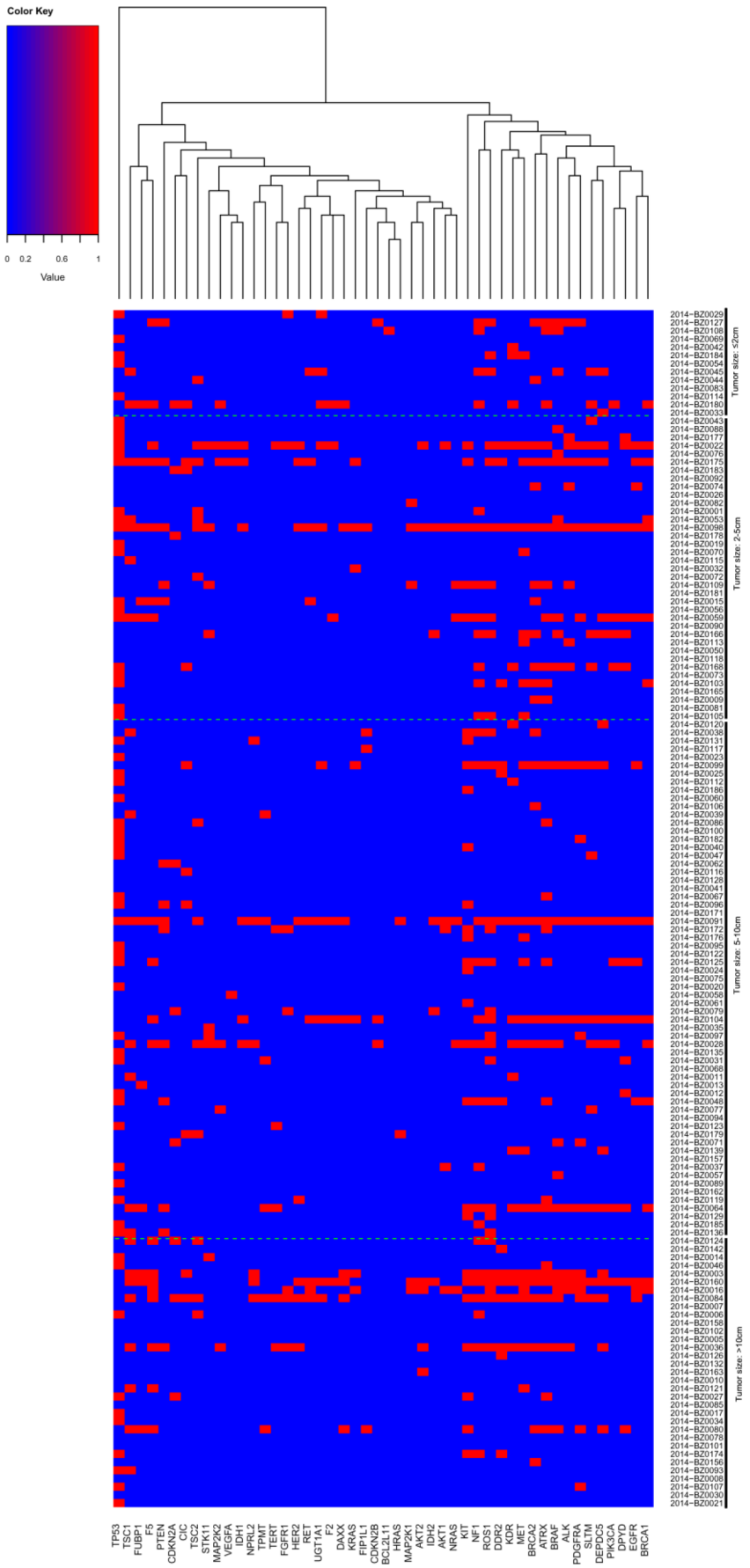

Color Key
0
0.6
Value
TP53
TSC1
FGFR3
PIK3
PTEN
CDKN2A
CIC
TSC2
STK11
MAP2K2
VEGFA
IDH1
NPRL2
TPMT
TERT
FGFR1
HER2
RET
UGT1A1
F2
DAXX
KRAS
FIP1L1
CDKN2B
BCL2L11
HRAS
MAP2K1
AKT2
IDH2
AKT1
NRAS
KIT
NF1
ROS1
DDR2
KDR
MET
BRCA2
ATRX
BRAF
ALK
PDGFRA
SLTM
DEPDC5
PIK3CA
DPYD
EGFR
BRCA1

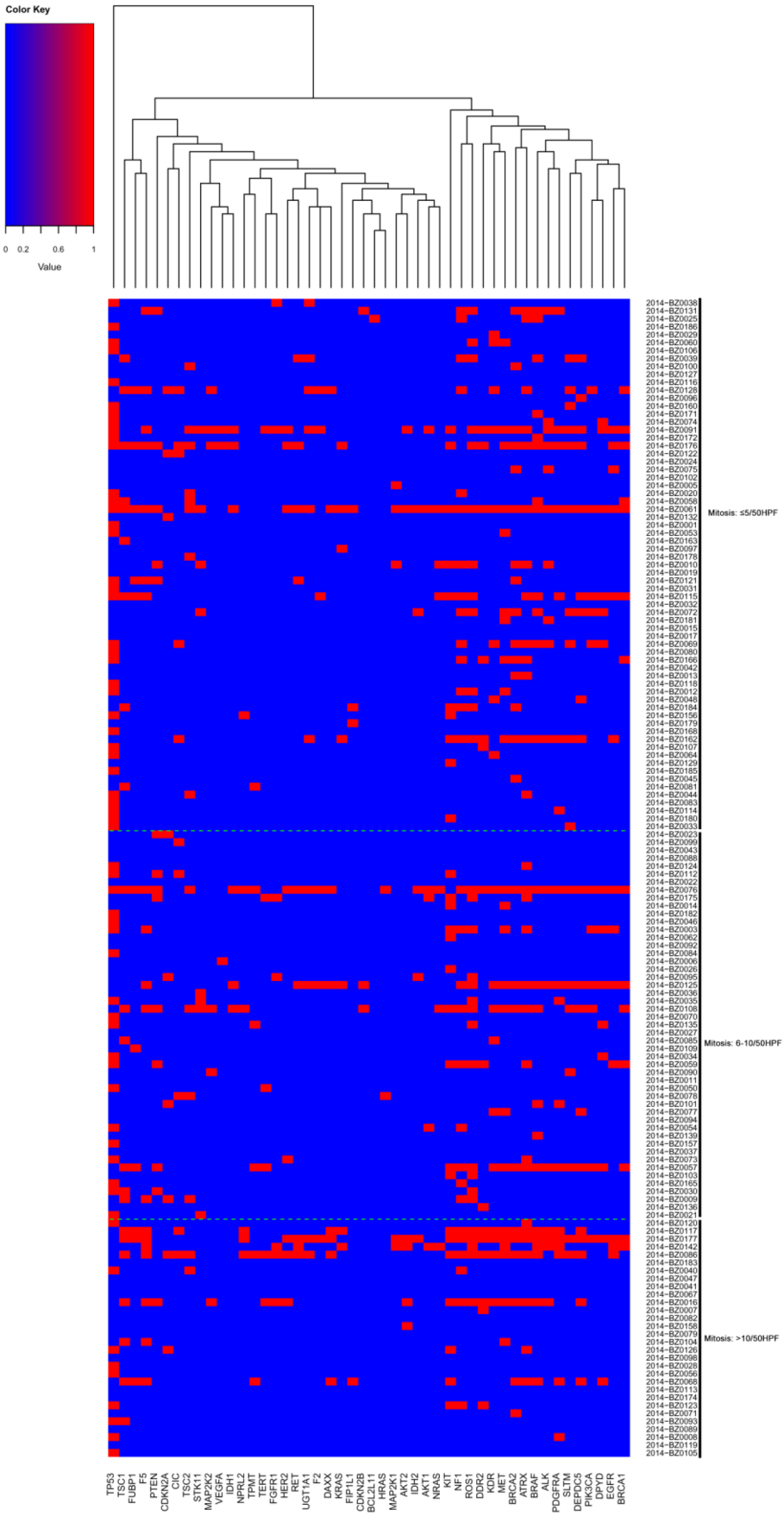

Color Key
0 0.2 0.6 1
Value
Male
Female
TP53
TSC1
FUBP1
F5
PTEN
CDKN2A
CIC
TSC2
STK11
MAP2K2
VEGFA
IDH1
NPRL2
TPMT
TERT
FGFR1
HER2
RET
UGT1A1
F2
DAX
KRAS
FIP1L1
CDKN2B
BCL2L11
HRAS
MAP2K1
AKT2
IDH2
AKT1
NRAS
KIT
NF1
ROS1
DDR2
KDR
MET
BRCA2
ATRX
BRAF
ALK
PDGFRA
SUFU
DEPDC5
PIK3CA
DPYD
EGFR
BRCA1

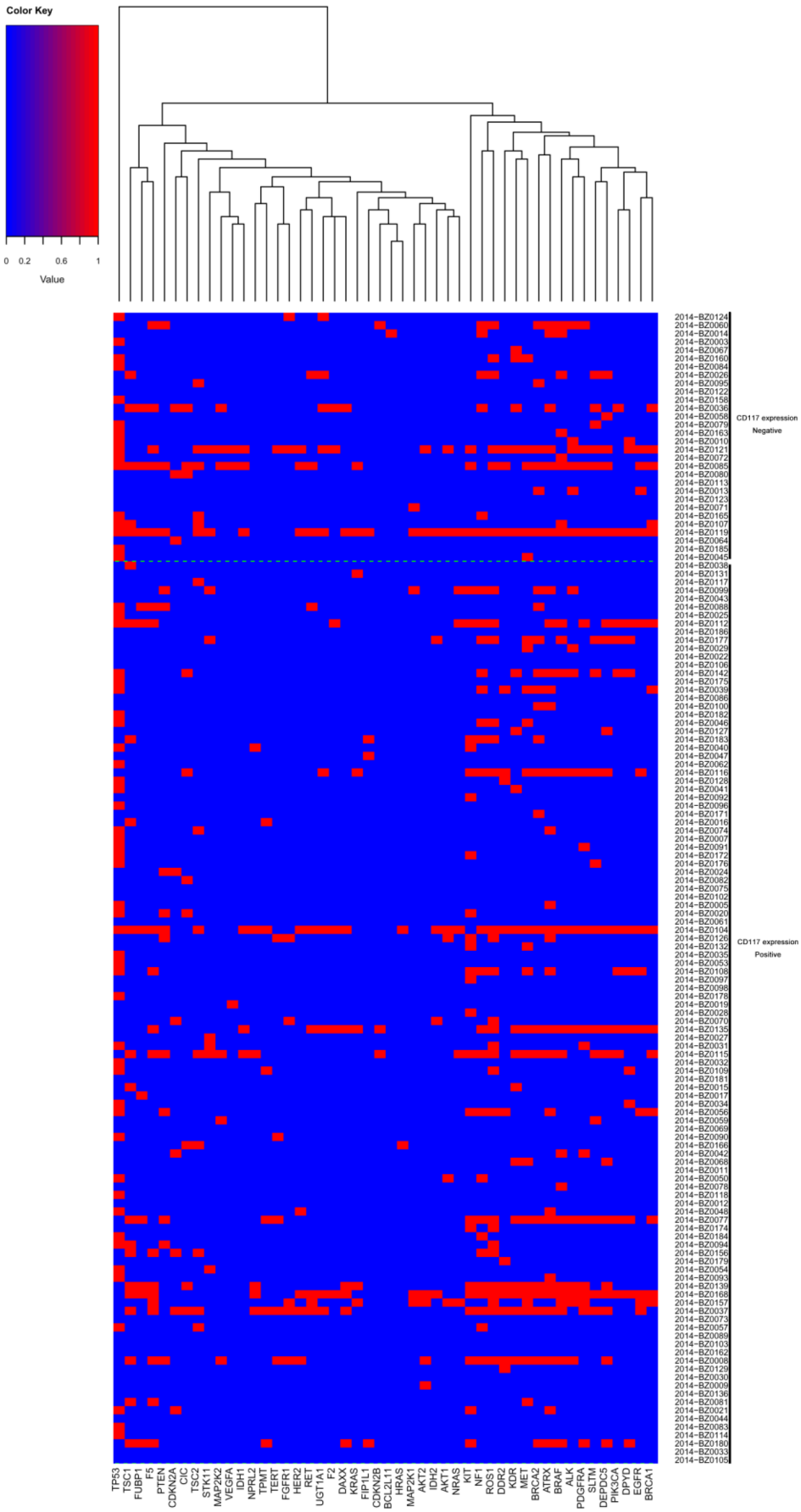

Color Key
0 0.2 0.6 1
Value
Age: ≤40 years
Age: 40-60 years
Age: >60 years
TP53
TSC1
FUBP1
F5
PTEN
CDKN2A
CIC
TSC2
STK11
MAP2K2
VEGFA
IDH1
NPRL2
TPMT
TERT
FGFR1
HER2
RET
UGT1A1
F2
DAXX
KRAS
FIP1L1
CDKN2B
BCL2L11
HRAS
MAP2K1
AKT2
IDH2
AKT1
NRAS
KIT
NF1
ROS1
DDR2
FGFR
MET
BRCA2
ATRX
BRAF
ALK
PDGFRA
SLTM
DEPDC5
PIK3CA
DDR2
EGFR
BRCA1

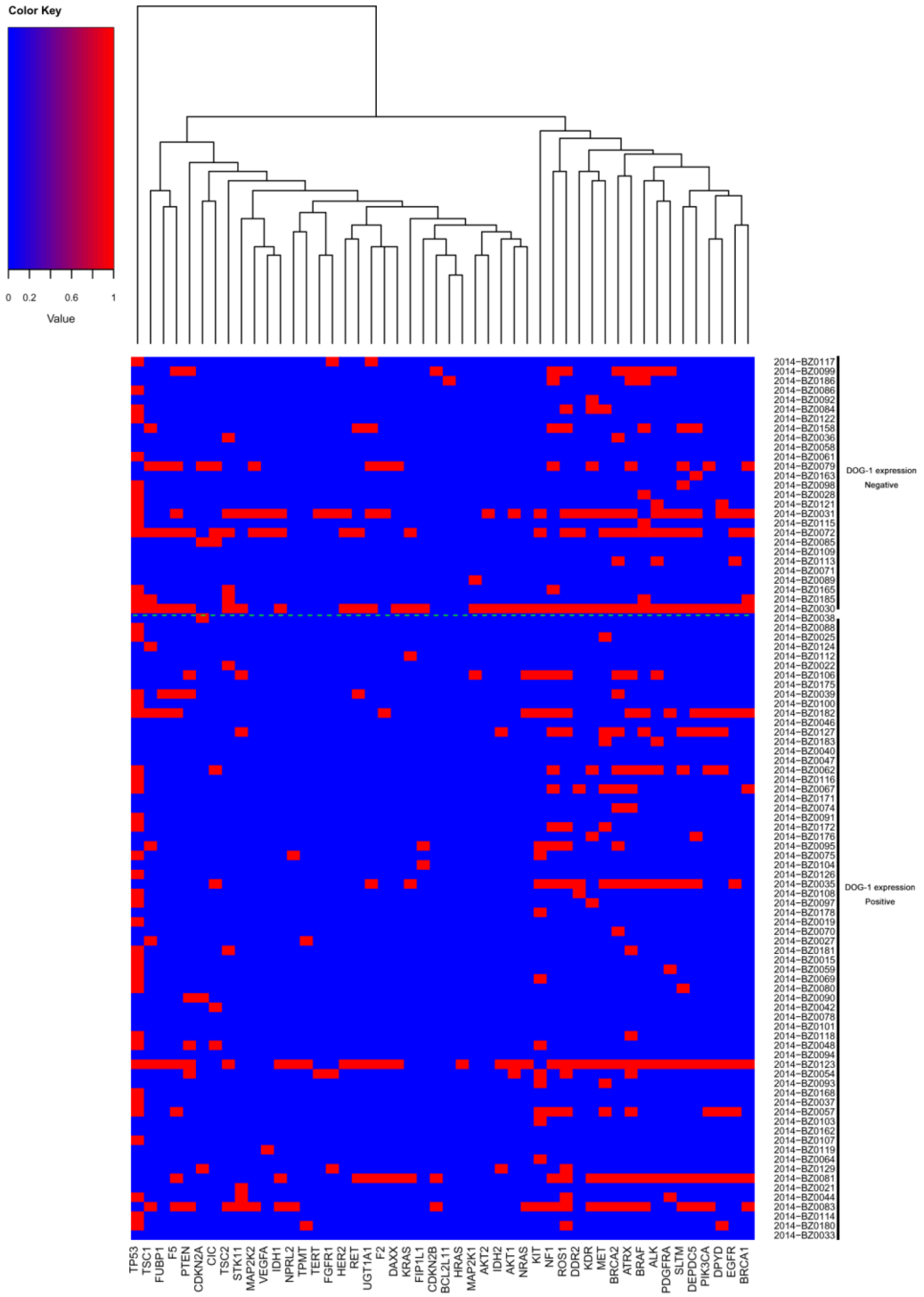


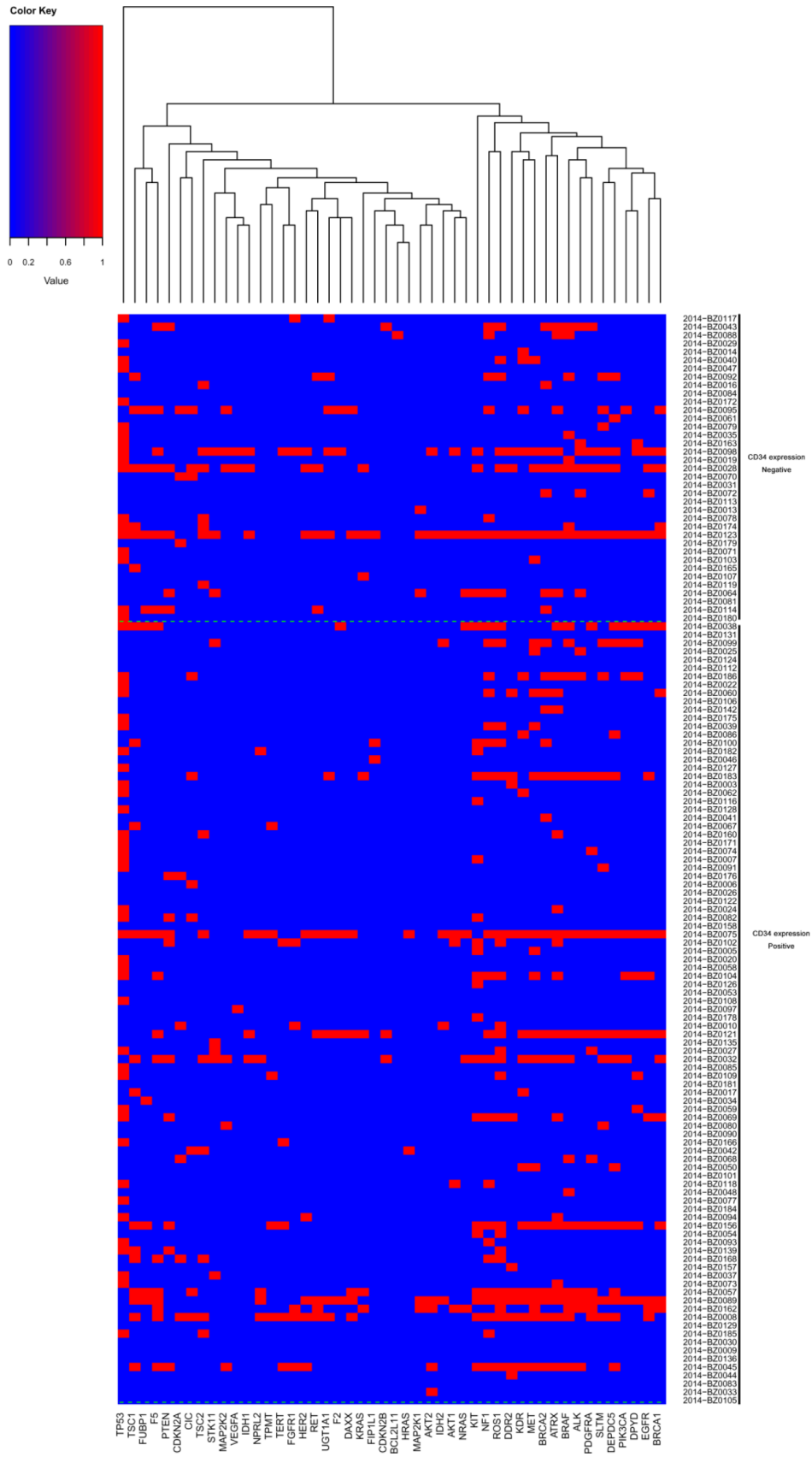

Primary sites: 1, Stomach; 2, Small bowel; 3, Abdominal/pelvic cavity/omentum; 4, Others including colon, rectum, renal, etc.


Color Key
0 0.2 0.6 1
Value
Tumor size: ≤2cm
Tumor size: 2-5cm
Tumor size: 5-10cm
Tumor size: >10cm
TP53
TSC1
FUBP1
F5
PTEN
CDKN2A
ATRX
TSC2
STK11
MAP2K2
VEGFA
IDH1
NPRL2
TPMT
TERT
FGFR1
HER2
RET
UGT1A1
F2
DAXX
KRAS
FIP1L1
CDKN2B
BCL2L11
HRAS
MAP2K1
AKT2
IDH2
AKT1
NRAS
KIT
NF1
ROS1
DDR2
KDR
MET
BRCA2
ATRX
BRAF
ALK
PDGFRA
SLIT4
DEPDC5
PIK3CA
DPYD
EGFR
BRCA1


Color Key
0 0.2 0.6 1
Value
Mitosis: ≤5/50HPF
Mitosis: 6-10/50HPF
Mitosis: >10/50HPF
TP53 TSC1 FUBP1 F5 PTEN CDKN2A CIC TSC2 STK11 MAP2K2 VEGFA IDH1 NPRL2 TPMT TERT FGFR1 HER2 RET UGT1A1 F2 DAXX KRAS FIP1L1 CDKN2B BCL2L11 HRAS MAP2K1 AKT2 IDH2 AKT1 NRAS KIT NF1 ROS1 DDR2 KDR MET BRCA2 ATRX BRAF ALK PDGFRA SLTM DEPDC5 PIK3CA DPYD EGFR BRCA1


Color Key
0 0.2 0.6 1
Value
CD117 expression
Negative
CD117 expression
Positive
TP53
TSC1
FUBP1
F5
PTEN
CDKN2A
CIC
TSC2
STK11
MAP2K2
VEGFA
IDH1
NPRL2
TPMT
TERT
FGFR1
HER2
RET
UGT1A1
F2
DAXX
KRAS
FIP1L1
CDKN2B
BCL2L11
HRAS
MAP2K1
AKT2
IDH2
AKT1
NRAS
ATI
NF1
ROS1
DDR2
KDR
MET
BRCA2
ATRX
BRAF
ALK
PDGFRA
SLTM
DEPDC5
PIK3CA
DPYD
EGFR
BRCA1


Color Key
0 0.2 0.6 1
Value
DOG-1 expression
Negative
DOG-1 expression
Positive
TP53 TSC1 FUBP1 F5 PTEN CDKN2A CIC TSC2 STK11 MAP2K2 VEGFA IDH1 NPRL2 TPMT TERT FGFR1 HER2 RET UGT1A1 F2 DAXX KRAS FIP1L1 CDKN2B BCL2L11 HRAS MAP2K1 AKT2 IDH2 AKT1 NRAS KIT NF1 ROS1 DDR2 KDR MET BRCA2 ATRX BRAF ALK PDGFRA SLTM DEPDC5 PIK3CA DPYD EGFR BRCA1




**Supplementary Figure S5-S13: Variation profile of 48 genes based on clinicopathological features.** Hierarchical cluster analysis result for all patients (S5), and stratified cluster analysis indicated that no obvious differences of variation profile were found between sex (S6), age (S7), tumor sites (S8), tumor sizes (S9), mitosis (S10), CD117 (S11), DOG-1 (S12), and CD34 (S13) expressions.