

Table S1 Gene panel

341 tumor-related genes

<i>ABL1</i>	<i>CASP8</i>	<i>E2F3</i>	<i>FOXA1</i>	<i>KDM5A</i>	<i>MYOD1</i>	<i>PMAIP1</i>	<i>SDHA</i>	<i>TP63</i>
<i>AKT1</i>	<i>CBFB</i>	<i>EED</i>	<i>FOXL2</i>	<i>KDM5C</i>	<i>NBN</i>	<i>PMS1</i>	<i>SDHAF2</i>	<i>TRAF7</i>
<i>AKT2</i>	<i>CBL</i>	<i>EGFL7</i>	<i>FOXP1</i>	<i>KDM6A</i>	<i>NCOR1</i>	<i>PMS2</i>	<i>SDHB</i>	<i>TSC1</i>
<i>AKT3</i>	<i>CCND1</i>	<i>EGFR</i>	<i>FUBP1</i>	<i>KDR</i>	<i>NF1</i>	<i>PNRC1</i>	<i>SDHC</i>	<i>TSC2</i>
<i>ALK</i>	<i>CCND2</i>	<i>EIF1AX</i>	<i>GATA1</i>	<i>KEAP1</i>	<i>NF2</i>	<i>POLE</i>	<i>SDHD</i>	<i>TSHR</i>
<i>ALOX12B</i>	<i>CCND3</i>	<i>EP300</i>	<i>GATA2</i>	<i>KIT</i>	<i>NFE2L2</i>	<i>PPP2R1A</i>	<i>SETD2</i>	<i>U2AF1</i>
<i>APC</i>	<i>CCNE1</i>	<i>EPCAM</i>	<i>GATA3</i>	<i>KLF4</i>	<i>NKX2-1</i>	<i>PRDM1</i>	<i>SF3B1</i>	<i>VHL</i>
<i>AR</i>	<i>CD274</i>	<i>EPHA3</i>	<i>GNA11</i>	<i>KRAS</i>	<i>NKX3-1</i>	<i>PRKAR1A</i>	<i>SH2D1A</i>	<i>VTCN1</i>
<i>ARAF</i>	<i>CD276</i>	<i>EPHA5</i>	<i>GNAQ</i>	<i>LATS1</i>	<i>NOTCH1</i>	<i>PTCH1</i>	<i>SHQ1</i>	<i>WT1</i>
<i>ARID1A</i>	<i>CD79B</i>	<i>EPHB1</i>	<i>GNAS</i>	<i>LATS2</i>	<i>NOTCH2</i>	<i>PTEN</i>	<i>SMAD2</i>	<i>XIAP</i>
<i>ARID1B</i>	<i>CDC73</i>	<i>ERBB2</i>	<i>GREM1</i>	<i>LMO1</i>	<i>NOTCH3</i>	<i>PTPN11</i>	<i>SMAD3</i>	<i>XPO1</i>
<i>ARID2</i>	<i>CDH1</i>	<i>ERBB3</i>	<i>GRIN2A</i>	<i>MAP2K1</i>	<i>NOTCH4</i>	<i>PTPRD</i>	<i>SMAD4</i>	<i>YAP1</i>
<i>ARID5B</i>	<i>CDK12</i>	<i>ERBB4</i>	<i>GSK3B</i>	<i>MAP2K2</i>	<i>NPM1</i>	<i>PTPRS</i>	<i>SMARCA4</i>	<i>YES1</i>
<i>ASXL1</i>	<i>CDK4</i>	<i>ERCC2</i>	<i>H3F3C</i>	<i>MAP2K4</i>	<i>NRAS</i>	<i>PTPRT</i>	<i>SMARCB1</i>	
<i>ASXL2</i>	<i>CDK6</i>	<i>ERCC3</i>	<i>HGF</i>	<i>MAP3K1</i>	<i>NSD1</i>	<i>RAC1</i>	<i>SMARCD1</i>	
<i>ATM</i>	<i>CDK8</i>	<i>ERCC4</i>	<i>HIST1H1C</i>	<i>MAP3K13</i>	<i>NTRK1</i>	<i>RAD50</i>	<i>SMO</i>	
<i>ATR</i>	<i>CDKN1A</i>	<i>ERCC5</i>	<i>HIST1H2BD</i>	<i>MAPK1</i>	<i>NTRK2</i>	<i>RAD51</i>	<i>SOCS1</i>	
<i>ATRX</i>	<i>CDKN1B</i>	<i>ERG</i>	<i>HIST1H3B</i>	<i>MAX</i>	<i>NTRK3</i>	<i>RAD51B</i>	<i>SOX17</i>	
<i>AURKA</i>	<i>CDKN2A</i>	<i>ESR1</i>	<i>HNF1A</i>	<i>MCL1</i>	<i>PAK1</i>	<i>RAD51C</i>	<i>SOX2</i>	
<i>AURKB</i>	<i>CDKN2B</i>	<i>ETV1</i>	<i>HRAS</i>	<i>MDC1</i>	<i>PAK7</i>	<i>RAD51D</i>	<i>SOX9</i>	
<i>AXIN1</i>	<i>CDKN2C</i>	<i>ETV6</i>	<i>ICOSLG</i>	<i>MDM2</i>	<i>PALB2</i>	<i>RAD52</i>	<i>SPEN</i>	
<i>AXIN2</i>	<i>CHEK1</i>	<i>EZH2</i>	<i>IDH1</i>	<i>MDM4</i>	<i>PARK2</i>	<i>RAD54L</i>	<i>SPOP</i>	
<i>AXL</i>	<i>CHEK2</i>	<i>FAM123B</i>	<i>IDH2</i>	<i>MED12</i>	<i>PARP1</i>	<i>RAF1</i>	<i>SRC</i>	
<i>B2M</i>	<i>CIC</i>	<i>FAM175A</i>	<i>IFNGR1</i>	<i>MEF2B</i>	<i>PAX5</i>	<i>RARA</i>	<i>STAG2</i>	
<i>BAP1</i>	<i>CREBBP</i>	<i>FAM46C</i>	<i>IGF1</i>	<i>MEN1</i>	<i>PBRM1</i>	<i>RASA1</i>	<i>STK11</i>	
<i>BARD1</i>	<i>CRKL</i>	<i>FANCA</i>	<i>IGF1R</i>	<i>MET</i>	<i>PDCD1</i>	<i>RB1</i>	<i>STK40</i>	
<i>BBC3</i>	<i>CRLF2</i>	<i>FANCC</i>	<i>IGF2</i>	<i>MITF</i>	<i>PDGFRA</i>	<i>RBM10</i>	<i>SUFU</i>	
<i>BCL2</i>	<i>CSF1R</i>	<i>FAT1</i>	<i>IKBKE</i>	<i>MLH1</i>	<i>PDGFRB</i>	<i>RECQL4</i>	<i>SUZ12</i>	
<i>BCL2L1</i>	<i>CTCF</i>	<i>FBXW7</i>	<i>IKZF1</i>	<i>MLL</i>	<i>PDPK1</i>	<i>REL</i>	<i>SYK</i>	
<i>BCL2L11</i>	<i>CTLA4</i>	<i>FGF19</i>	<i>IL10</i>	<i>MLL2</i>	<i>PHOX2B</i>	<i>RET</i>	<i>TBX3</i>	
<i>BCL6</i>	<i>CTNNB1</i>	<i>FGF3</i>	<i>IL7R</i>	<i>MLL3</i>	<i>PIK3C2G</i>	<i>RFWD2</i>	<i>TERT</i>	
<i>BCOR</i>	<i>CUL3</i>	<i>FGF4</i>	<i>INPP4A</i>	<i>MPL</i>	<i>PIK3C3</i>	<i>RHOA</i>	<i>TET1</i>	
<i>BLM</i>	<i>DAXX</i>	<i>FGFR1</i>	<i>INPP4B</i>	<i>MRE11A</i>	<i>PIK3CA</i>	<i>RICTOR</i>	<i>TET2</i>	
<i>BMPR1A</i>	<i>DCUN1D1</i>	<i>FGFR2</i>	<i>INSR</i>	<i>MSH2</i>	<i>PIK3CB</i>	<i>RIT1</i>	<i>TGFBR1</i>	
<i>BRAF</i>	<i>DDR2</i>	<i>FGFR3</i>	<i>IRF4</i>	<i>MSH6</i>	<i>PIK3CD</i>	<i>RNF43</i>	<i>TGFBR2</i>	
<i>BRCA1</i>	<i>DICER1</i>	<i>FGFR4</i>	<i>IRS1</i>	<i>MTOR</i>	<i>PIK3CG</i>	<i>ROS1</i>	<i>TMEM127</i>	
<i>BRCA2</i>	<i>DIS3</i>	<i>FH</i>	<i>IRS2</i>	<i>MUTYH</i>	<i>PIK3R1</i>	<i>RPS6KA4</i>	<i>TMPRSS2</i>	
<i>BRD4</i>	<i>DNMT1</i>	<i>FLCN</i>	<i>JAK1</i>	<i>MYC</i>	<i>PIK3R2</i>	<i>RPS6KB2</i>	<i>TNFAIP3</i>	
<i>BRIP1</i>	<i>DNMT3A</i>	<i>FLT1</i>	<i>JAK2</i>	<i>MYCL1</i>	<i>PIK3R3</i>	<i>RPTOR</i>	<i>TNFRSF14</i>	
<i>BTK</i>	<i>DNMT3B</i>	<i>FLT3</i>	<i>JAK3</i>	<i>MYCN</i>	<i>PIM1</i>	<i>RUNX1</i>	<i>TOP1</i>	
<i>CARD11</i>	<i>DOT1L</i>	<i>FLT4</i>	<i>JUN</i>	<i>MYD88</i>	<i>PLK2</i>	<i>RYBP</i>	<i>TP53</i>	

Table S2 Clinicopathological characteristics of pNET patients

Parameters	N=29
Age at pNET resection, years, median [IQR]	51 [42–54]
Sex, n (%)	
Male	15 (51.7)
Female	14 (48.3)
Genetic syndrome, n (%)	
MEN1	4 (13.8)
Sporadic	25 (86.2)
Primary tumor	
Location, n (%)	
Head/neck	7 (24.1)
Body/tail	21 (72.4)
Both	1 (3.4)
Operation, n (%)	
Pancreaticoduodenectomy	3 (10.3)
Distal pancreatectomy	20 (69.0)
Total pancreatectomy	1 (3.4)
Enucleation	3 (10.3)
Segmental resection	1 (3.4)
No resection	1 (3.4)
Number, n (%)	
Solitary	26 (89.7)
Multiple	3 (10.3)
Diameter of the largest lesion, cm, median [IQR]	3.4 [2.0–5.0]
Necrosis, n (%)	
Yes	3 (10.3)
No	25 (86.2)
NA	1 (3.4)
Margin status, n (%)	
Negative	27 (93.1)
Positive	1 (3.4)
NA	1 (3.4)
Perineural invasion, n (%)	
Yes	11 (37.9)
No	17 (58.6)
NA	1 (3.4)
Microvascular invasion, n (%)	
Yes	7 (24.1)
No	21 (72.4)
NA	1 (3.4)
2019 WHO grade, n (%)	
G1	5 (17.2)
G2	22 (75.9)
G3	2 (6.9)
Liver metastasis	n=19
Number, n (%)	
Solitary	5 (26.3)
Multiple	14 (73.7)
Synchronous metastasis, n (%)	
Yes	17 (89.5)
No	2 (10.5)
Diameter of the largest lesion, cm, median [IQR]	2.5 [1.6–3.0]

pNET, pancreatic neuroendocrine tumor; MEN1, multiple endocrine neoplasia type 1; WHO, World Health Organization; IQR, interquartile range; NA, not available.

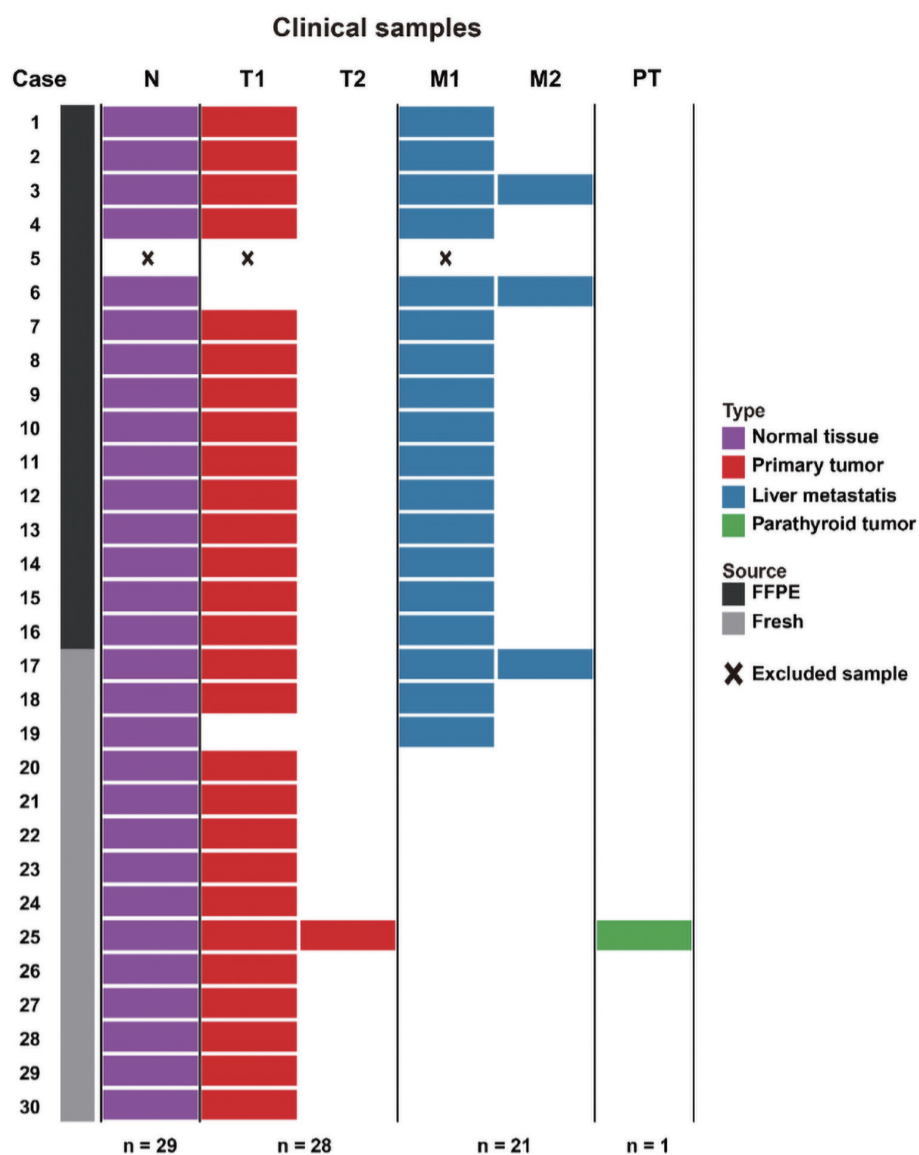


Figure S1 Detailed information of the collected samples for sequencing. N, normal tissue; T, primary tumor; T1, primary tumor 1; T2, primary tumor 2; M, liver metastasis; M1, liver metastasis 1; M2, liver metastasis 2; PT, parathyroid tumor; FFPE, formalin-fixed, paraffin-embedded.

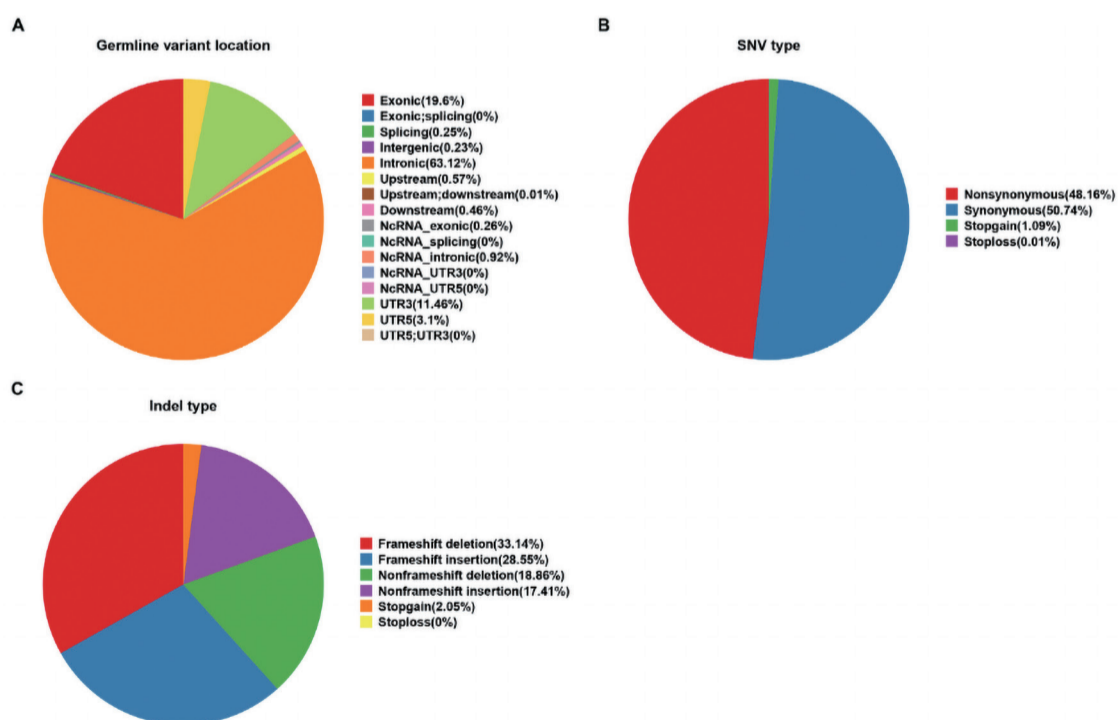


Figure S2 Germline variant classification. The constituent ratios of variant location (A), exonic SNV function (B), and Indel function (C). SNV, single nucleotide variant; Indel, insertion and deletion; NcRNA, non-coding RNA; UTR, untranslated region.

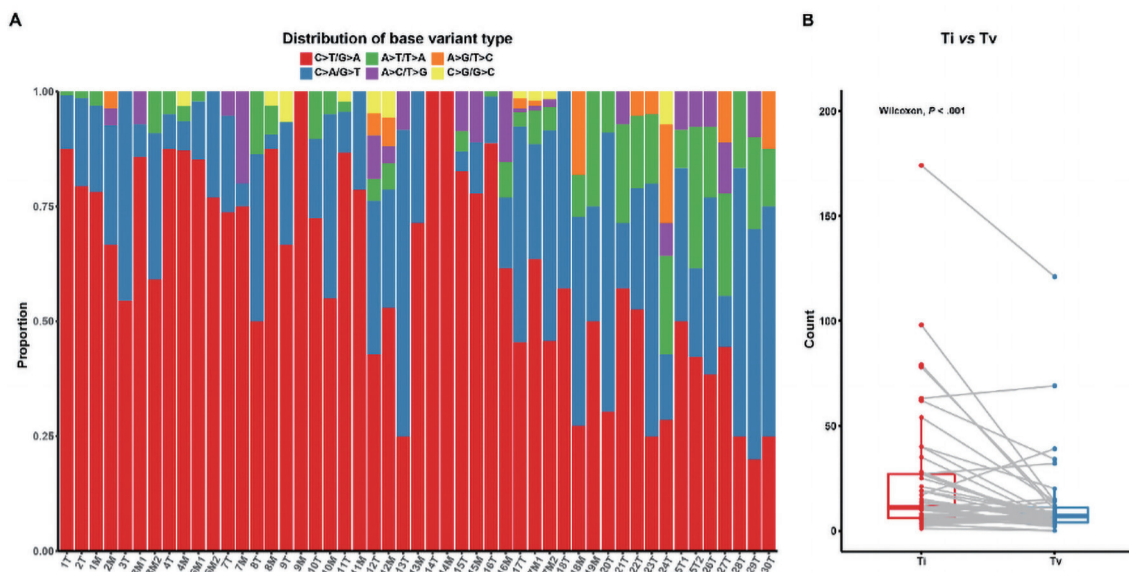


Figure S3 Somatic base alteration type. (A) Distribution of somatic base alteration type in every sample; (B) comparison of transition and transversion. Ti, transition; Tv, transversion; T, primary tumor; T1, primary tumor 1; T2, primary tumor 2; M, liver metastasis; M1, liver metastasis 1; M2, liver metastasis 2.

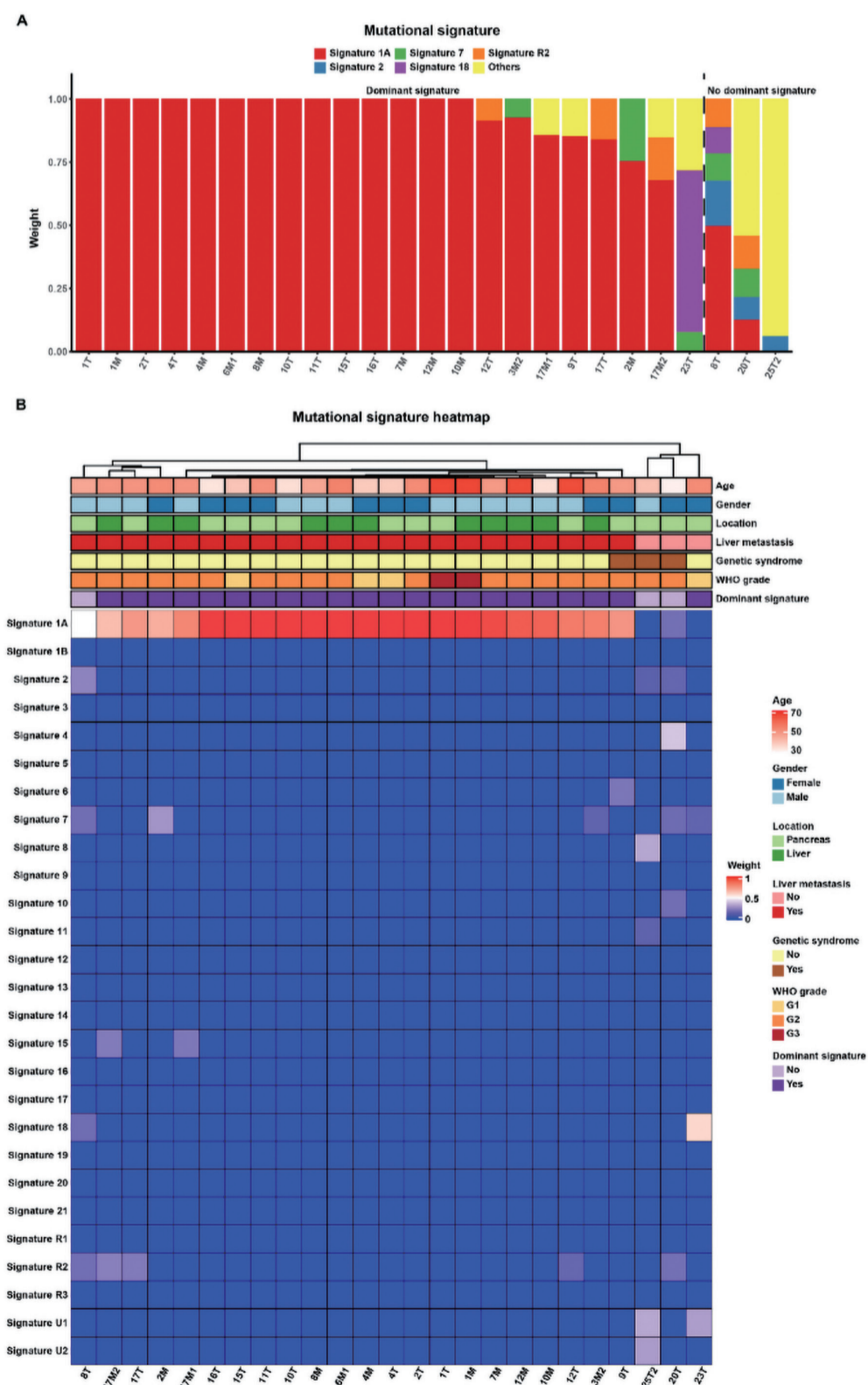


Figure S4 Mutational signatures. (A) Distribution of mutational signatures in the samples harboring ≥ 20 SNVs; (B) clustering analysis. SNVs, single nucleotide variants; WHO, World Health Organization; T, primary tumor; T1, primary tumor 1; T2, primary tumor 2; M, liver metastasis; M1, liver metastasis 1; M2, liver metastasis 2.

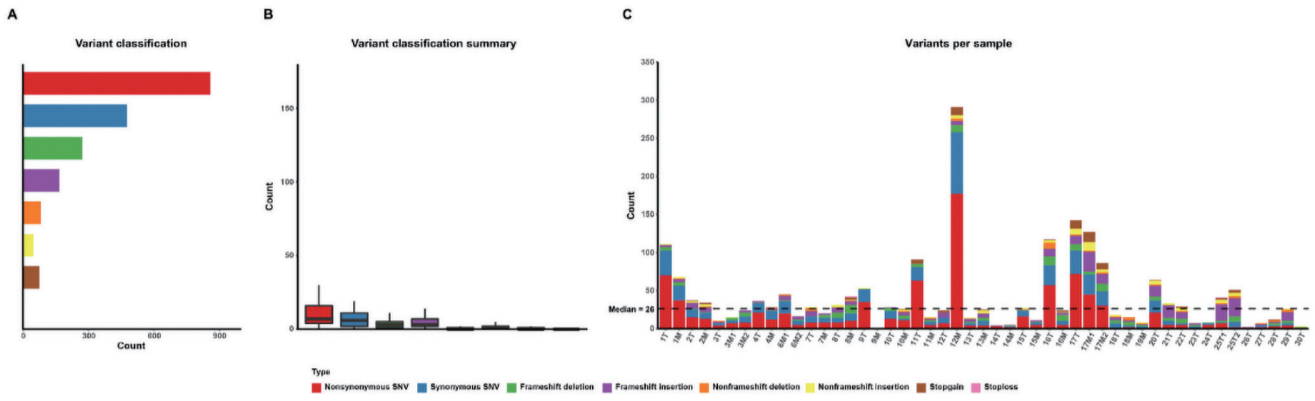


Figure S5 Classification (A,B) and distribution (C) of somatic variants in the exonic regions. SNV, single nucleotide variant; Indel, insertion and deletion; T, primary tumor; T1, primary tumor 1; T2, primary tumor 2; M, liver metastasis; M1, liver metastasis 1; M2, liver metastasis 2.

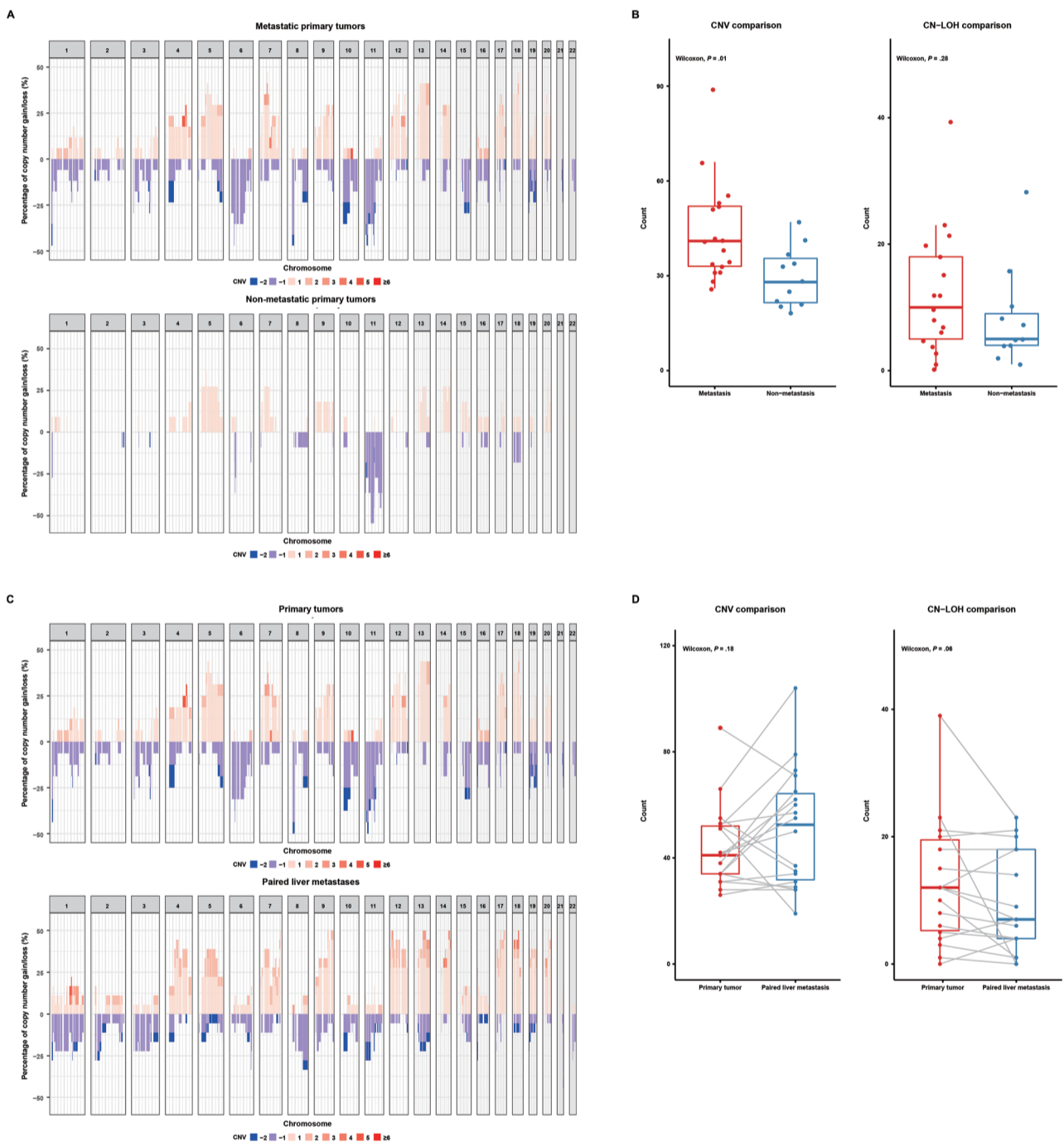


Figure S6 Distribution and comparison of somatic CNVs and CN-LOHs. (A) The proportion of CNVs in the primary pNETs grouped by liver metastasis; (B) comparison of CNVs and CN-LOHs in the primary pNETs; (C) the proportion of CNVs in the paired metastatic pNET cases; (D) comparison of CNVs and CN-LOHs in the paired metastatic pNET cases. pNET, pancreatic neuroendocrine tumor; CNV, copy number variation; CN-LOH, copy neutral loss of heterozygosity.