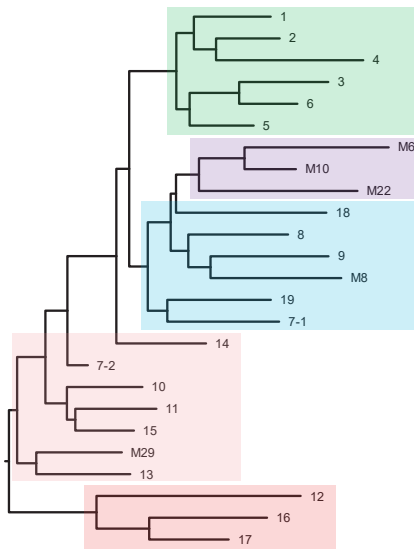
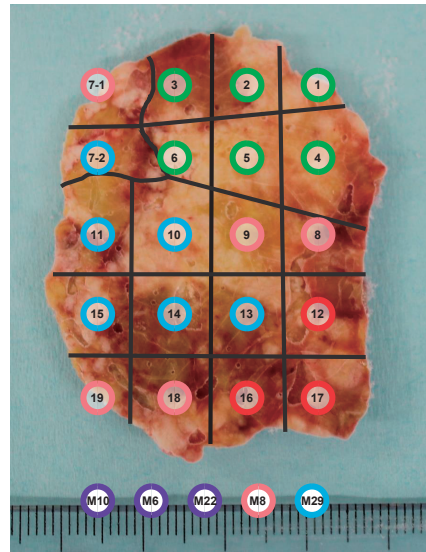


Supplementary Figure S20. Multi-region analysis using multi-omics data in the autopsied Panc-NEC.

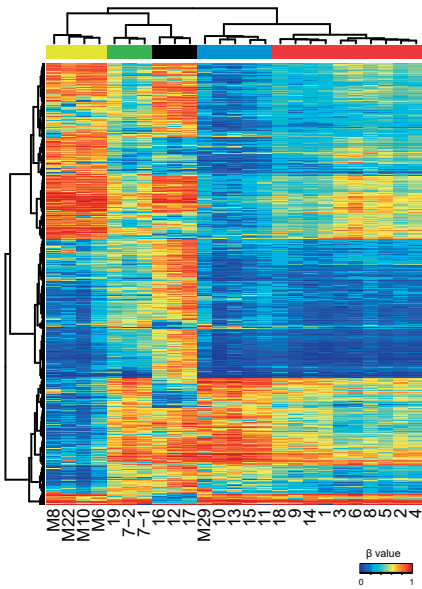
A



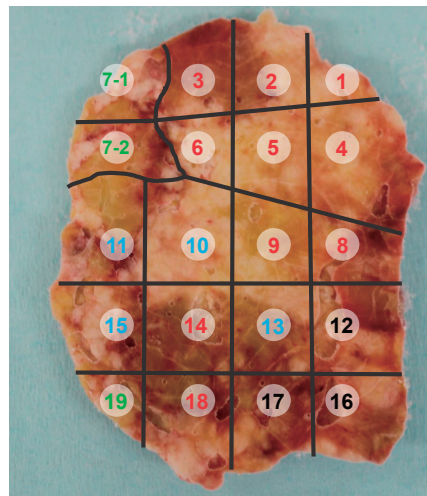
B



C



D

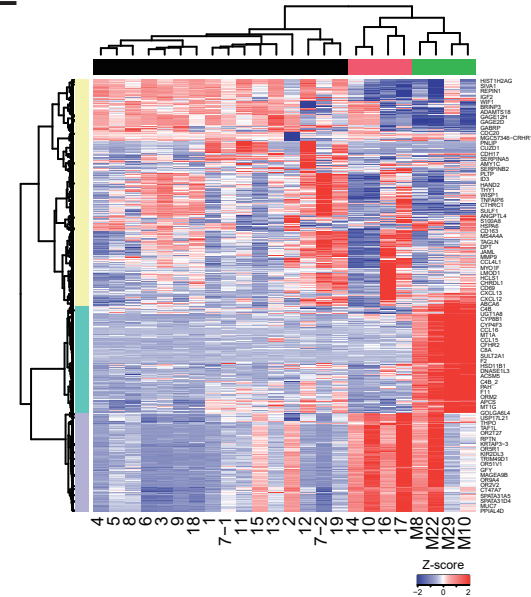


Liver metastasis

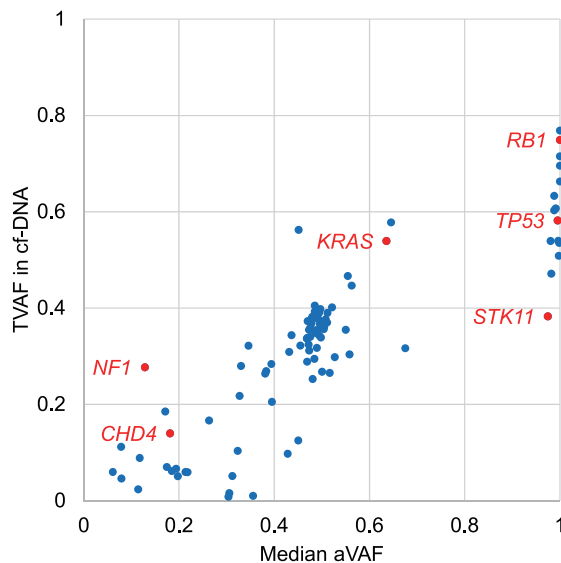
M29

M6 M8 M10 M22

E



F



G

Pattern of sharing mutations	No. of mutation(s)	TVAF in cf-DNA
Common to cf-DNA and all 25 samples	50	0.366
Common to cf-DNA and 24 samples	6	0.330
Common to cf-DNA and 23 samples	6	0.311
Common to cf-DNA and 22 samples	1	0.266
Common to cf-DNA and 21 samples	4	0.409
Common to cf-DNA and 20 samples	1	0.104
Common to cf-DNA and 18 samples	5	0.060
Common to cf-DNA and 17 samples	2	0.064
Common to cf-DNA and 16 samples	1	0.125
Common to cf-DNA and 14 samples	1	0.563
Common to cf-DNA and 8 samples	1	0.304
Common to cf-DNA and 7 samples	2	0.031
Common to cf-DNA and 5 samples	1	0.070
Common to cf-DNA and 3 samples	4	0.147
Common to cf-DNA and 2 samples	1	0.268
Common to cf-DNA and sample 18	4	0.139
Common to cf-DNA and sample M10	1	0.046
Common to cf-DNA and sample M6	2	0.170
Unique to cf-DNA	77	0.035

A, The phylogenetic tree inferred by RAxML (Randomized Axelerated Maximum Likelihood) based on mutations and LOH patterns in the exome sequencing data. Although the algorithm to infer the phylogenetic tree differed from LICHeE (Fig. 6A), the sub-clonal diversity of trees in the cluster is largely consistent. **B**, Sections are marked corresponding to the colors of the predicted subclones based on the phylogenetic tree in A. **C**, Clustering analysis based on DNA methylation assay results. The primary 20 regions and 5 liver metastases formed 5 subgroups. One liver metastasis (M29) located to different branches from the other four liver metastases as well as the lineage and phylogenetic trees based on somatic mutations and LOH status. The regions 12, 16, and 17 (WGD regions) showed clearly separated clusters with methylation data. **D**, Sections are marked corresponding to the colors of the predicted subclones based on methylation data in C. **E**, Unsupervised clustering with 500 high variant genes in multi-region RNA-seq data was performed. **F**, There is a strong correlation between the TVAF of mutations in cf-DNA and median aVAF of the same mutations in tissue samples (Spearman rank correlation, $\rho = 0.850$, $P < 2.2 \times 10^{-16}$). The genes listed in the COSMIC Cancer Gene Census are marked in red. **G**, The relationship between TVAF in cf-DNA and patterns of sharing mutation(s) in tissue samples.