nature portfolio

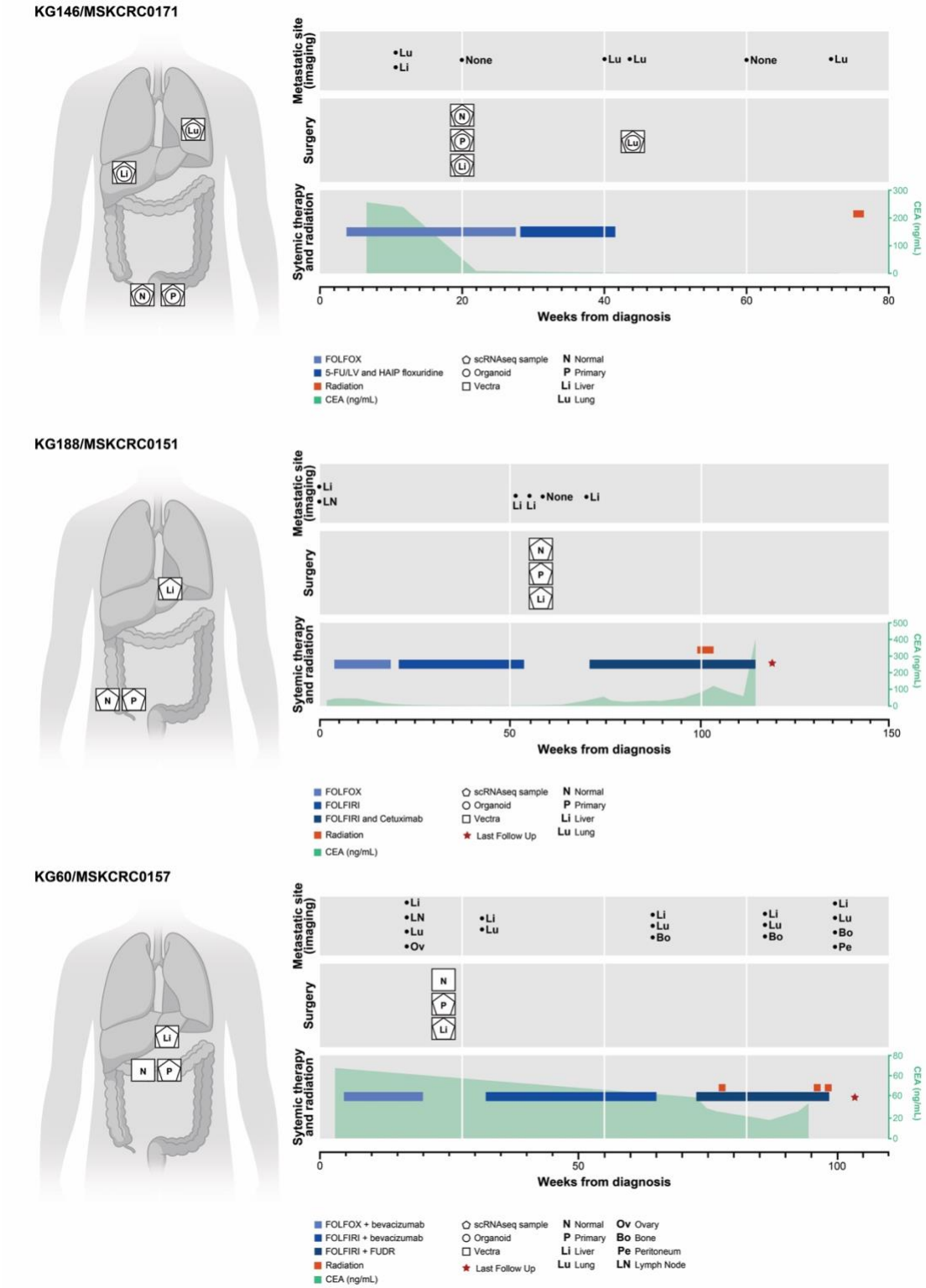
https://doi.org/10.1038/s41586-024-08150-0

Supplementary information

Progressive plasticity during colorectal cancer metastasis

In the format provided by the authors and unedited

Supplementary Data Figures



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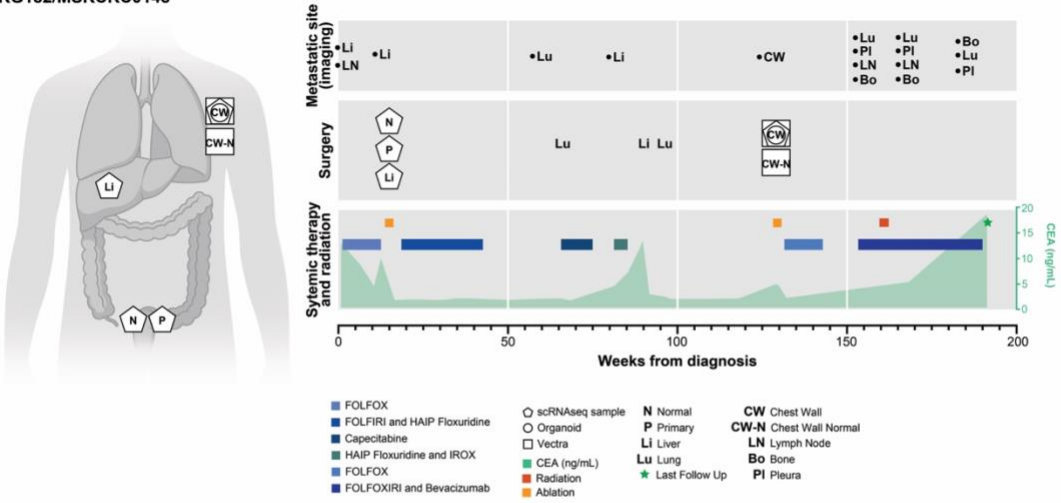

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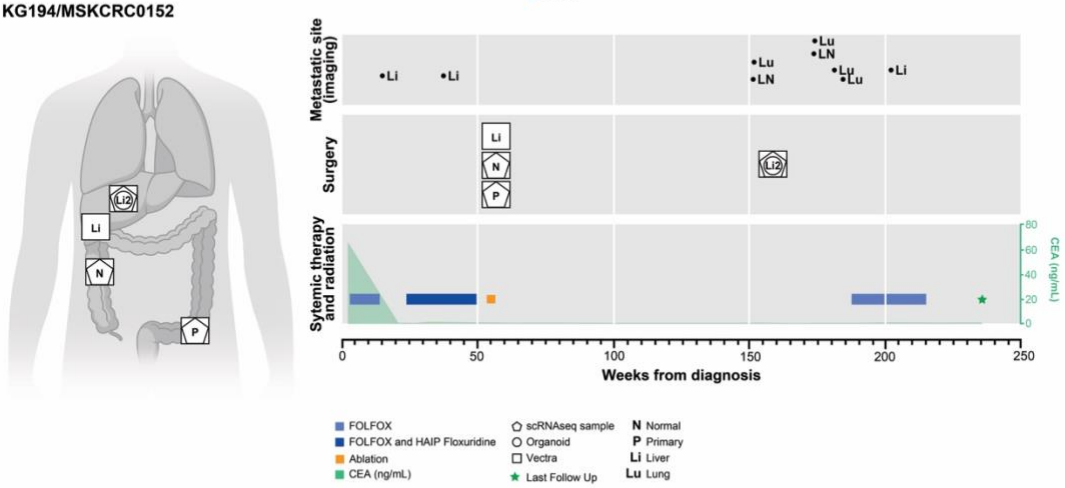

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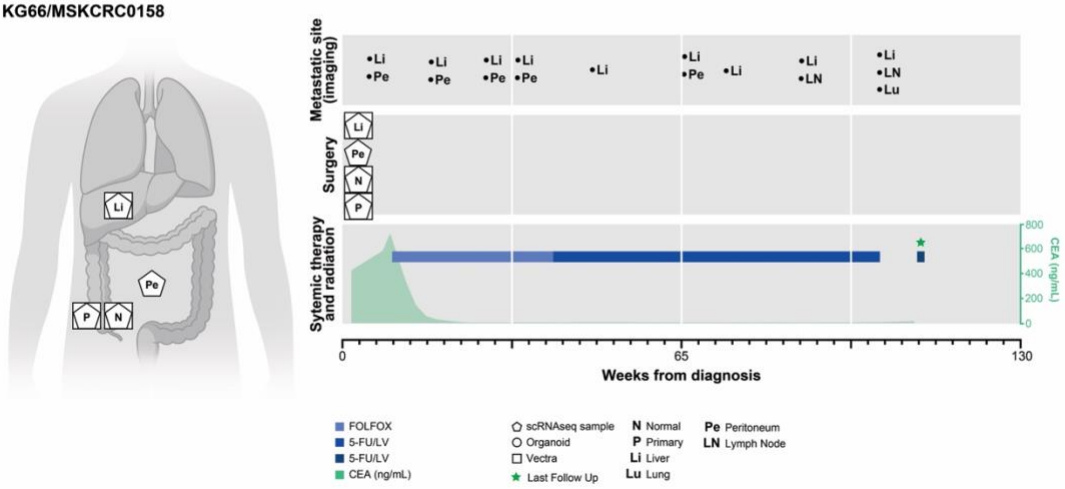

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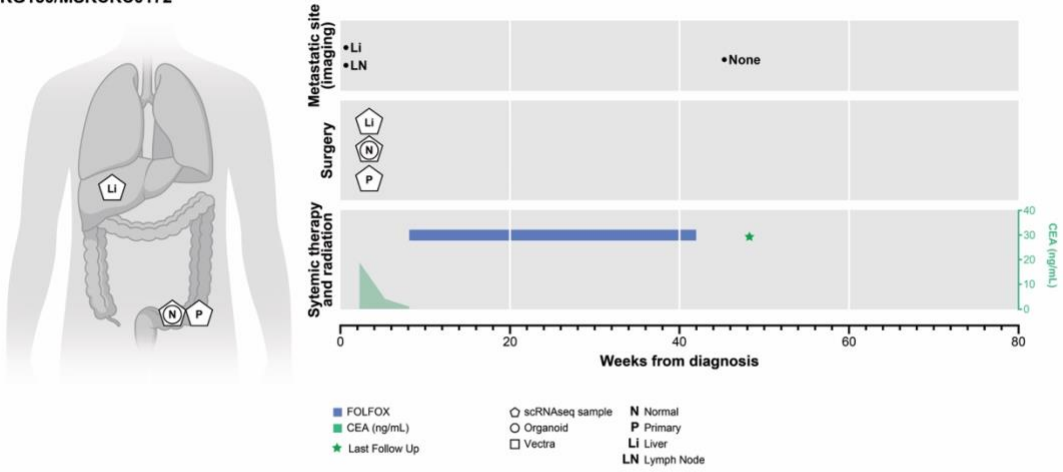

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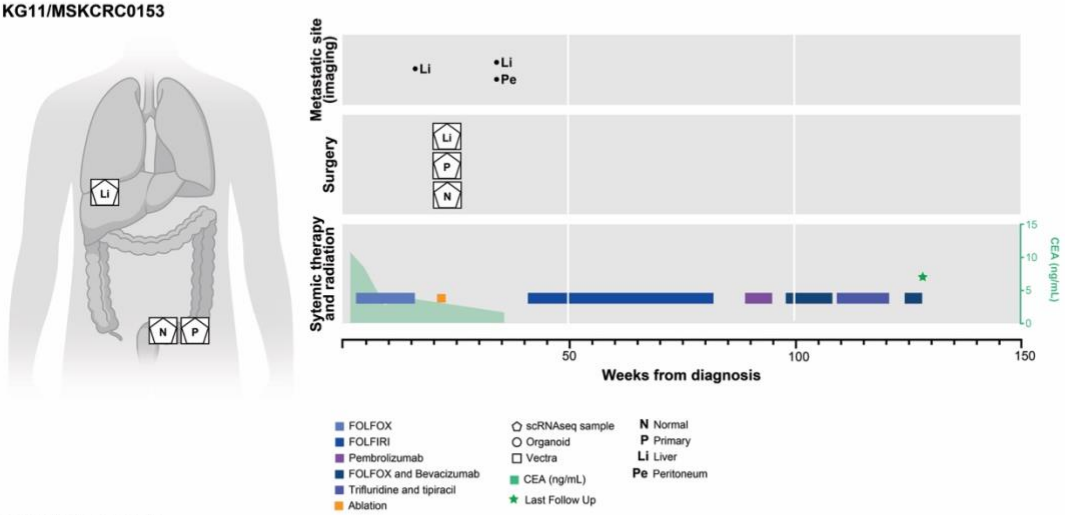

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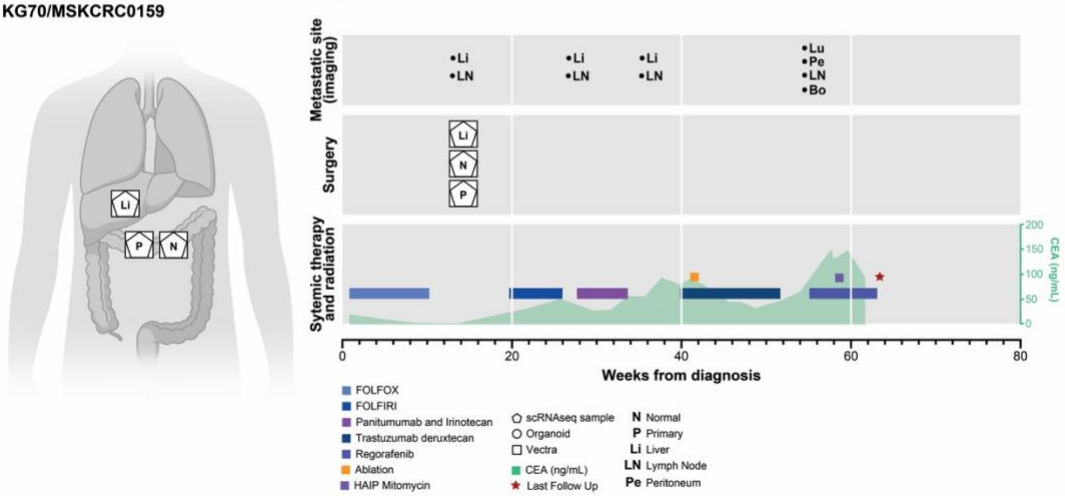

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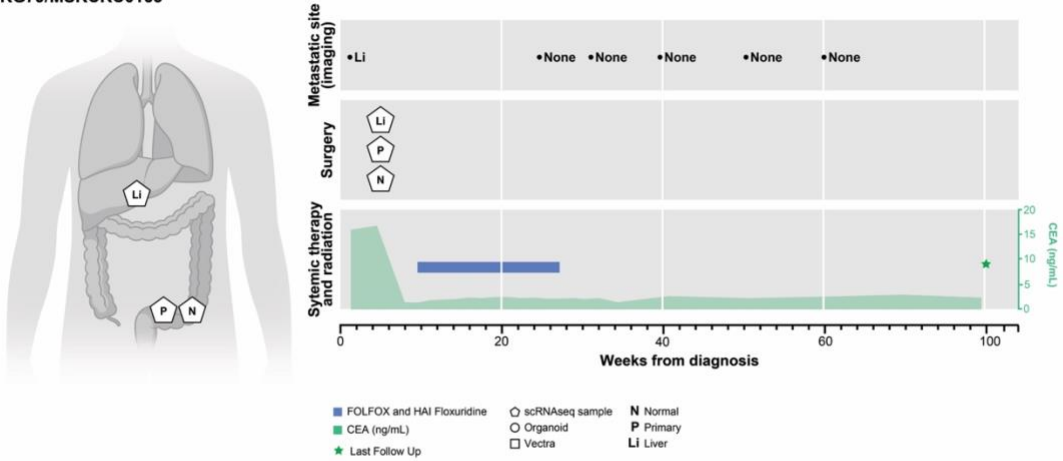

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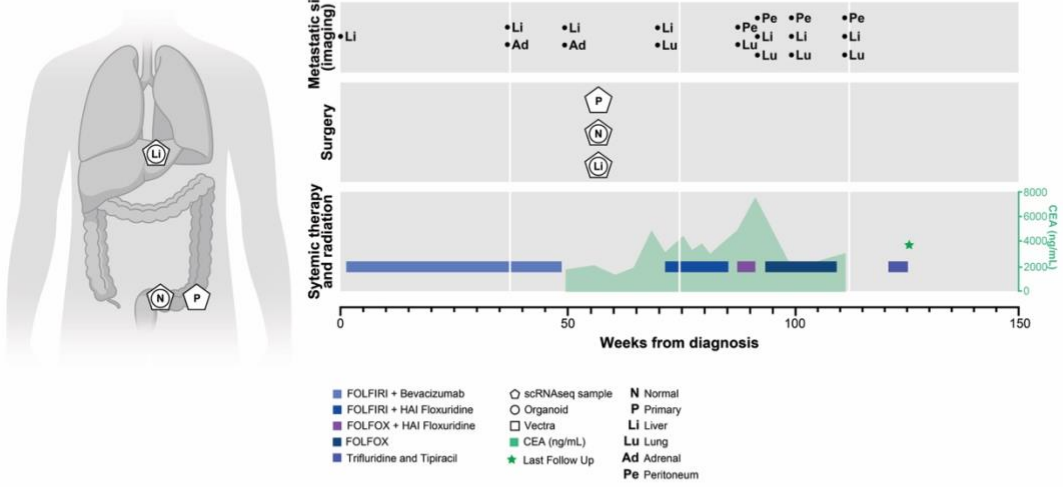

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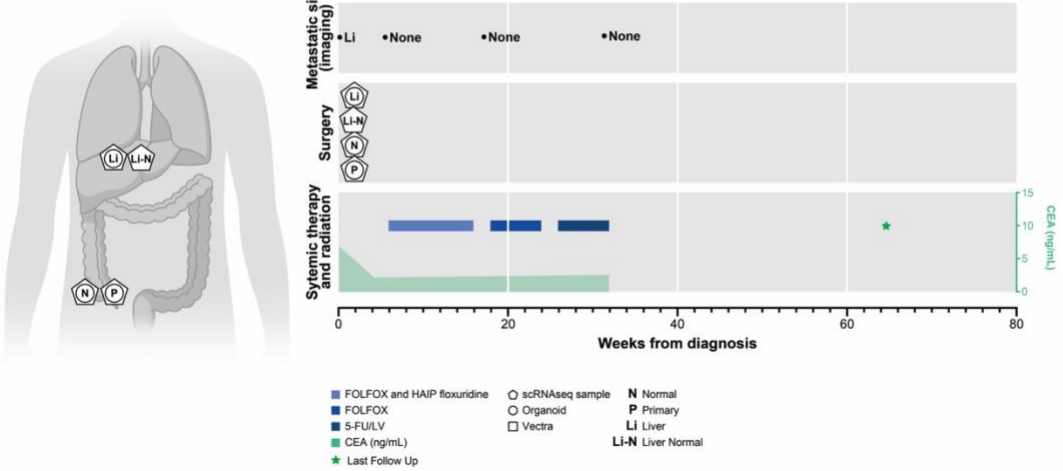

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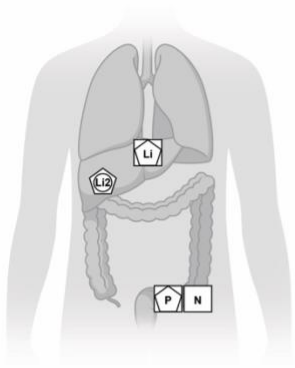
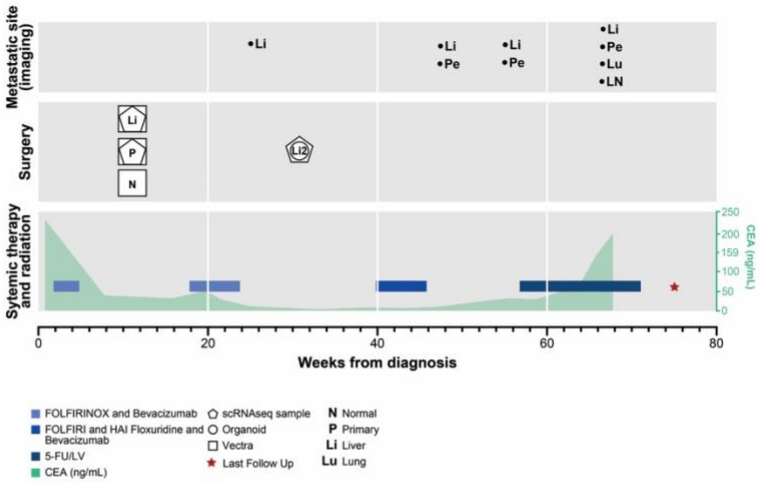
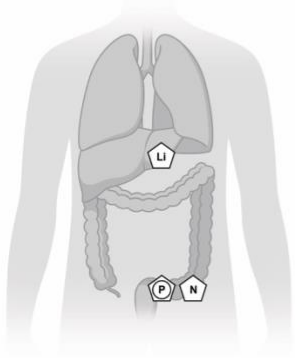
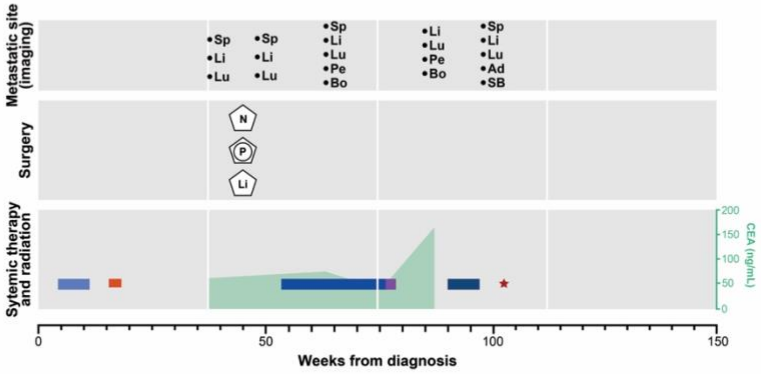




FOLFIRINOX and Bevacizumab
FOLFIRI and HAI Floxuridine and Bevacizumab
5-FU/LV
CEA (ng/mL)
scRNAseq sample
Organoid
Vectra
Last Follow Up
N Normal
P Primary
Li Liver
Lu Lung

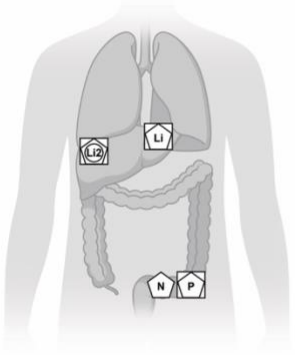
KG156/MSKCRC0174

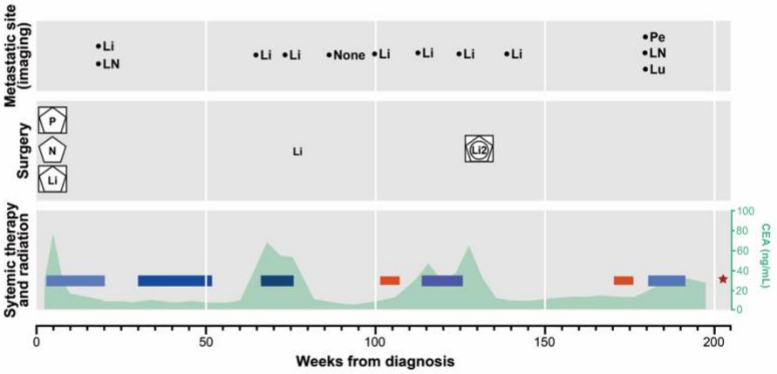




FOLFOX
Irinotecan + HAI Floxuridine
FOLFIRI + HAI Floxuridine
Trastuzumab + Lapatinib
Radiation
scRNAseq sample
Organoid
Vectra
CEA (ng/mL)
Last Follow Up
N Normal
P Primary
Li Liver
Lu Lung
Sp Spleen
Ad Adrenal
Pe Peritoneum
Bo Bone
SB Small Bowel

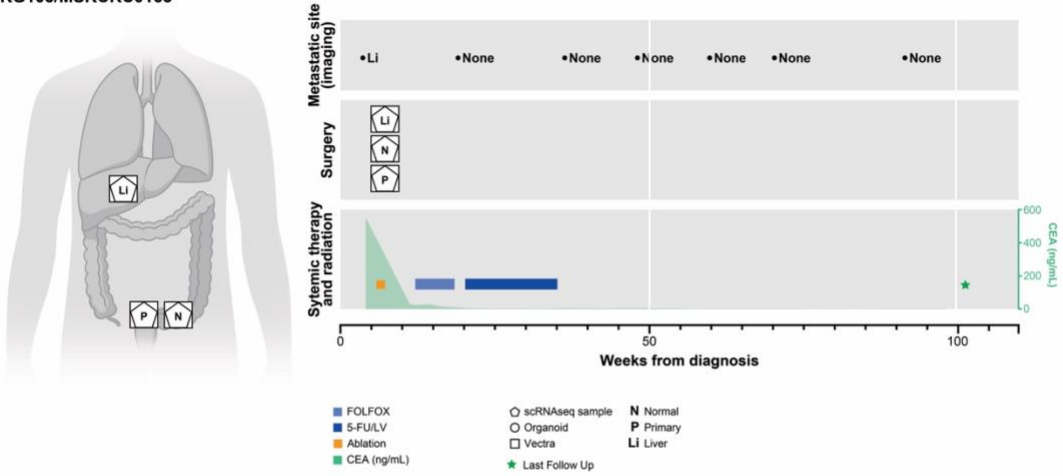
KG183/MSKCRC0149





FOLFOX
5-FU/LV and HAIP Floxuridine
FOLFIRI
HAIP Floxuridine
FOLFIRI and Bevacizumab
scRNAseq sample
Organoid
Vectra
CEA (ng/mL)
Radiation
Last Follow Up
N Normal
P Primary
Li Liver
Lu Lung
LN Lymph Node
Pe Peritoneum

KG103/MSKCRC0165



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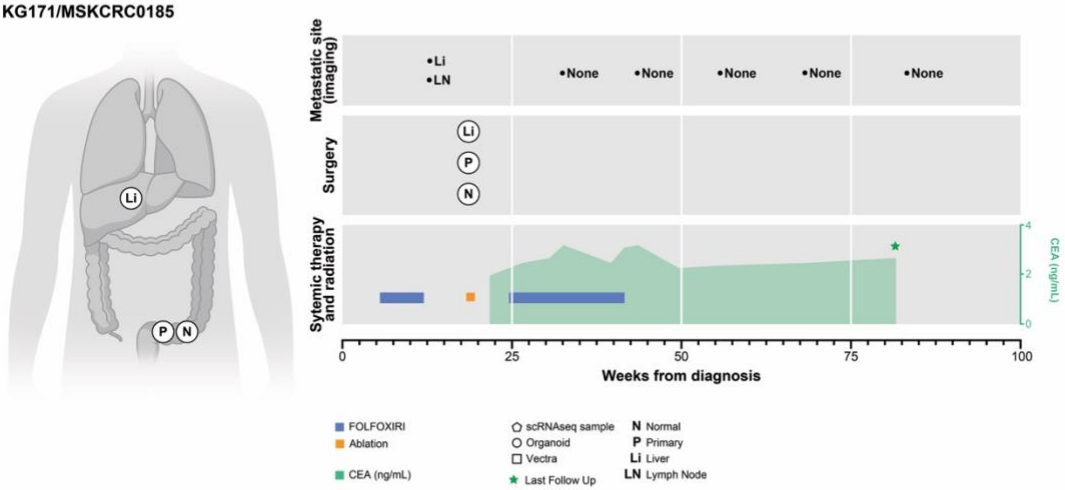

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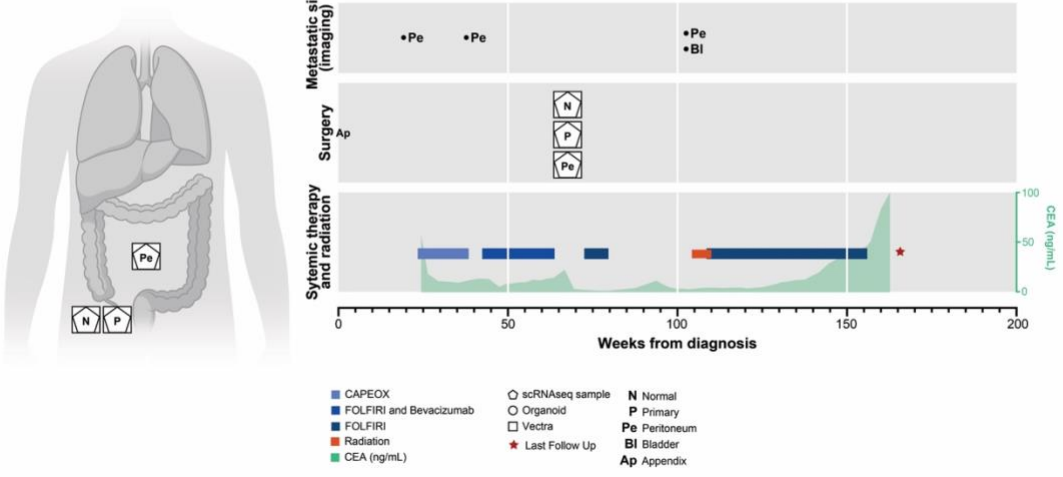

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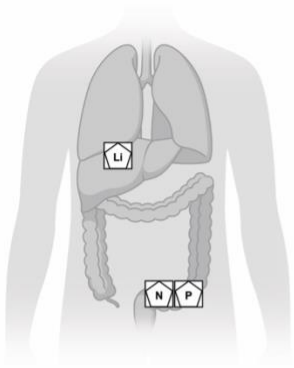
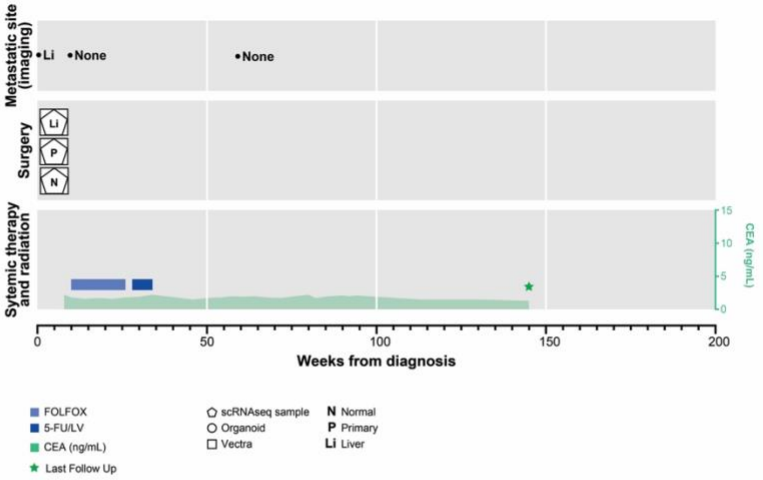
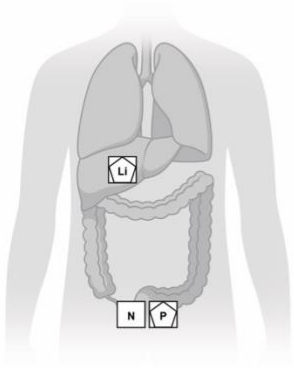
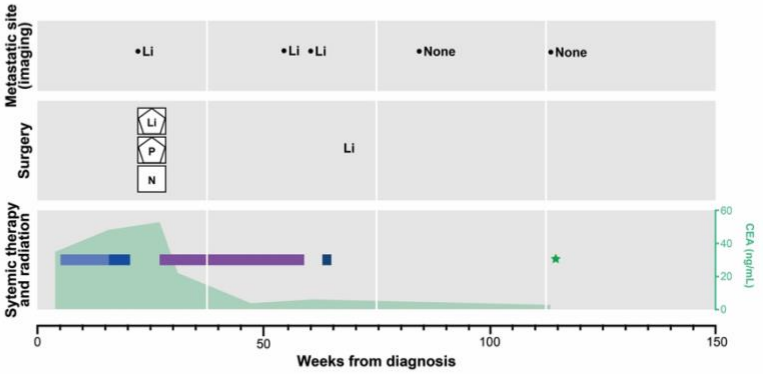




FOLFOX
5-FU/LV
CEA (ng/mL)
Last Follow Up
scRNAseq sample
Organoid
Vectra
N Normal
P Primary
Li Liver

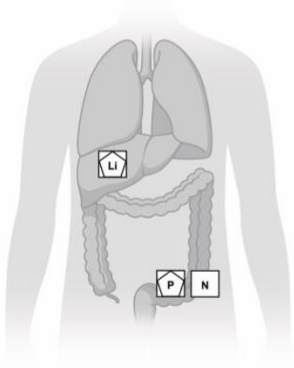
KG71/MSKCRC0160

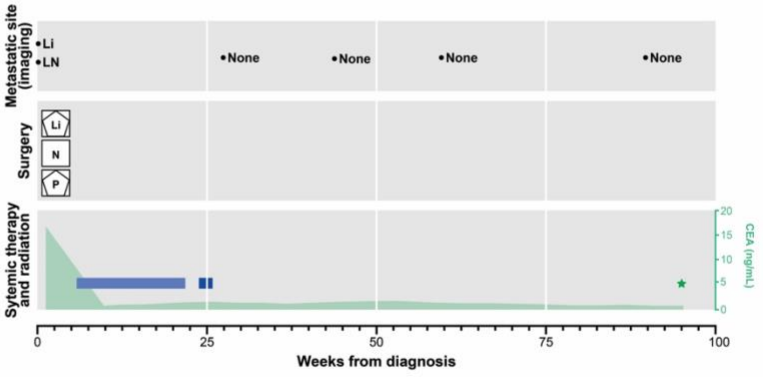




CAPEOX
Capecitabine
HAI Floxuridine and Irinotecan
Panitumumab and Irinotecan
scRNAseq sample
Organoid
Vectra
CEA (ng/mL)
Last Follow Up
N Normal
P Primary
Li Liver

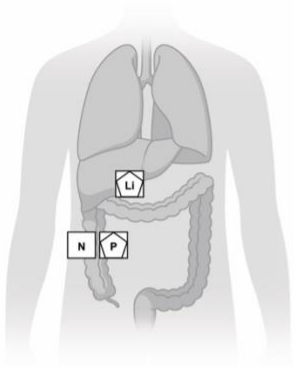
KG105/MSKCRC0166

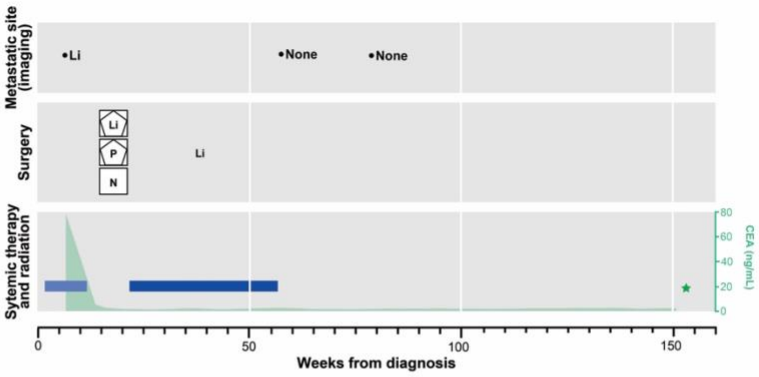




FOLFOX + HAI Floxuridine
5-FU/LV + HAI Floxuridine
CEA (ng/mL)
scRNAseq sample
Organoid
Vectra
Last Follow Up
N Normal
P Primary
Li Liver
Lu Lung

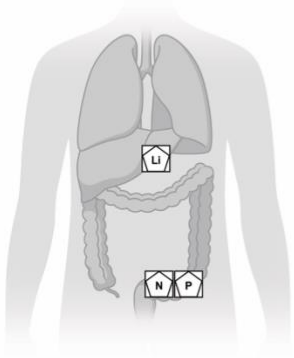
KG35/MSKCRC0155

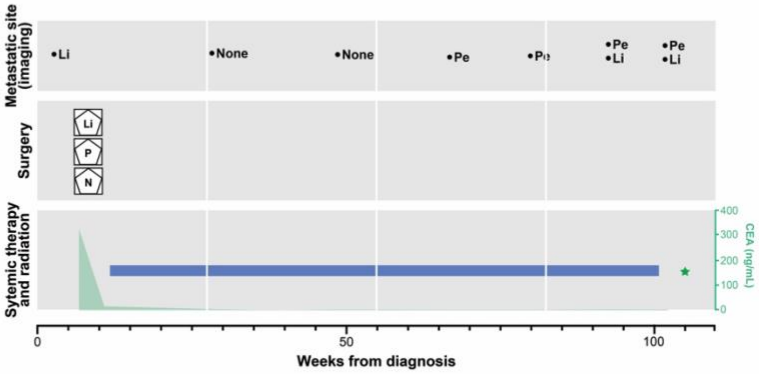




FOLFOX
FOLFIRI
CEA (ng/mL)
Last Follow Up
scRNAseq sample
Organoid
Vectra
N Normal
P Primary
Li Liver

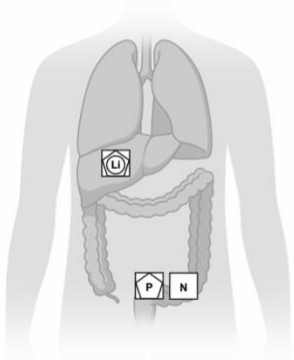
KG74/MSKCRC0161

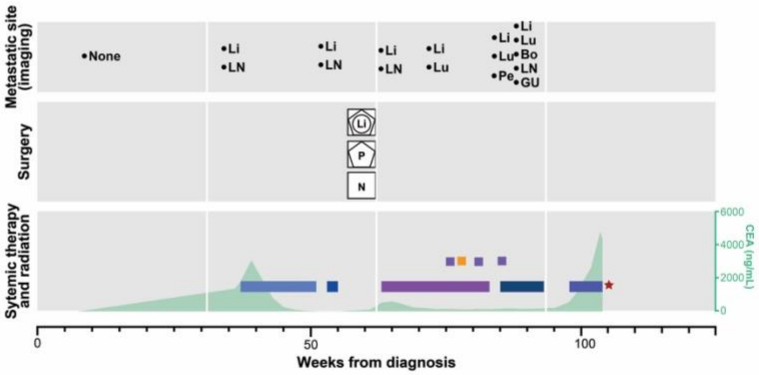




FOLFOX + HAI Floxuridine
CEA (ng/mL)
Last Follow Up
scRNAseq sample
Organoid
Vectra
N Normal
P Primary
Li Liver
Pe Peritoneum

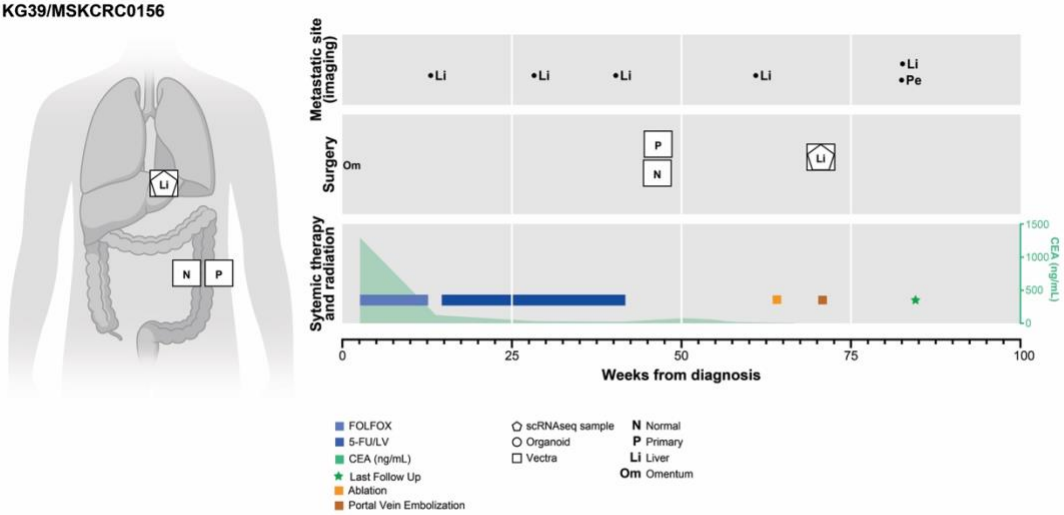
KG119/MSKCRC0168





FOLFOX
5-FU/LV
FOLFIRI + HAI Floxuridine
FOLFOX + HAI Floxuridine
Ipilimumab + Nivolumab
Ablation
scRNAseq sample
Organoid
Vectra
CEA (ng/mL)
Last Follow Up
HAIP Mitomycin
N Normal
P Primary
Li Liver
Lu Lung

KG39/MSKCRC0156



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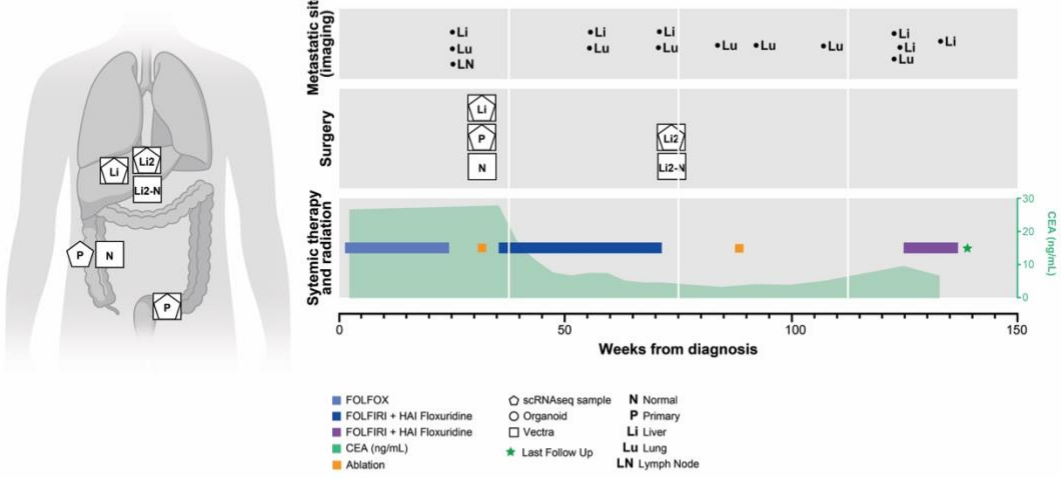

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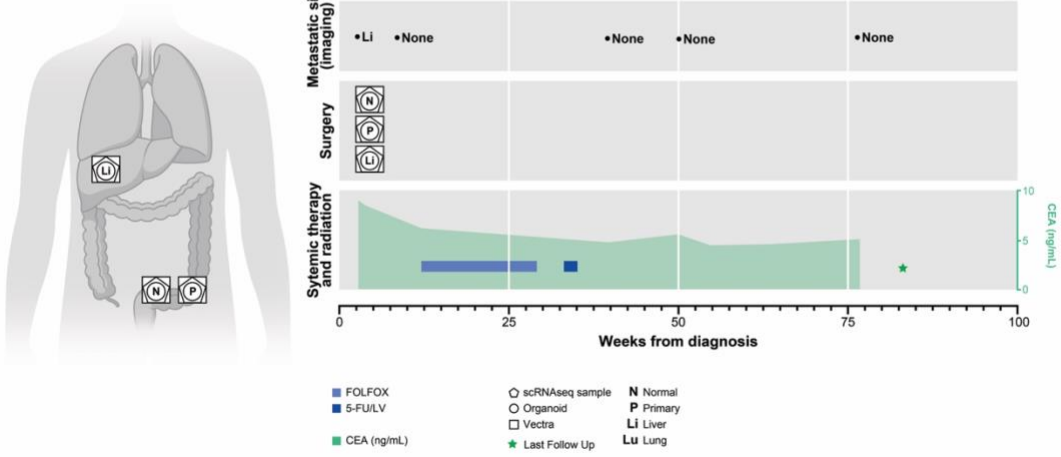

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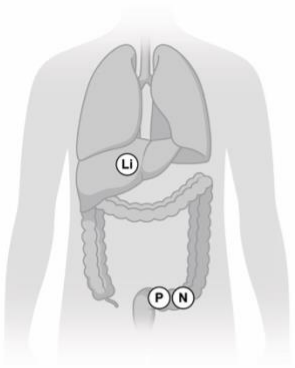
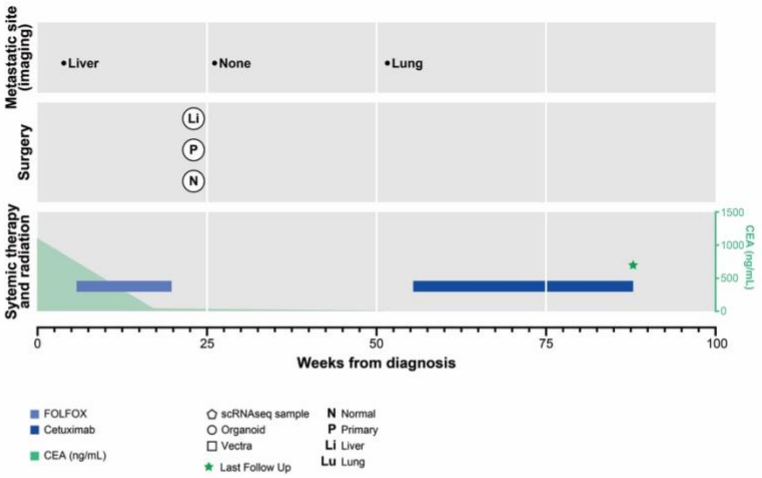


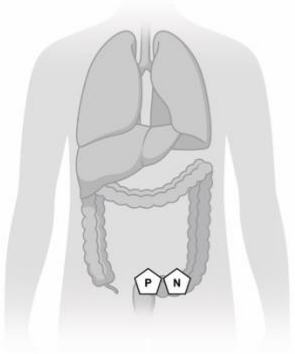


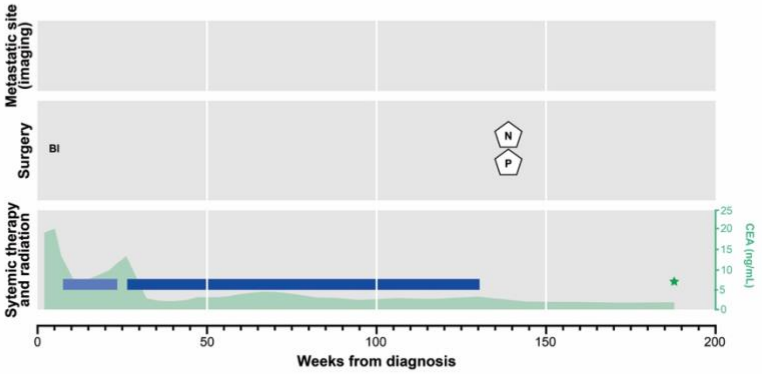
FOLFOX
Cetuximab
CEA (ng/mL)

scRNAseq sample
Organoid
Vectra
Last Follow Up

N Normal
P Primary
Li Liver
Lu Lung

KG203/MSKCRC0232



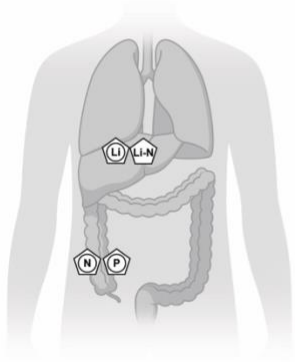


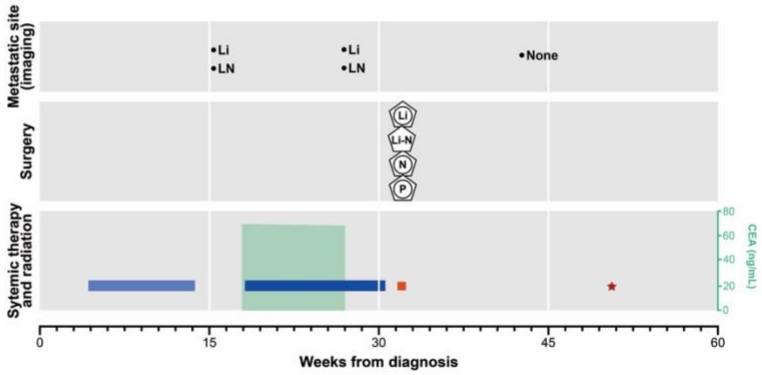
FOLFOX
Pembrolizumab
CEA (ng/mL)

scRNAseq sample
Organoid
Vectra
Last Follow Up

N Normal
P Primary
LN Lymph Node
BI Lung

KG181/MSKCRC0188



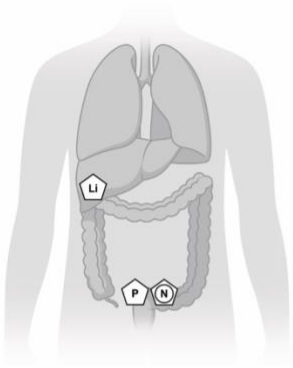


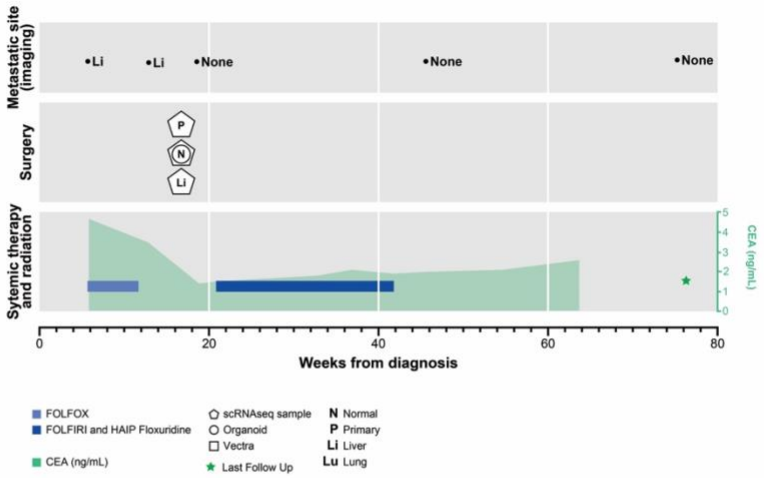
FOLFOX
FOLFIRI
Ablation
CEA (ng/mL)

scRNAseq sample
Organoid
Vectra
Last Follow Up

N Normal
P Primary
Li Liver
Lu Lung

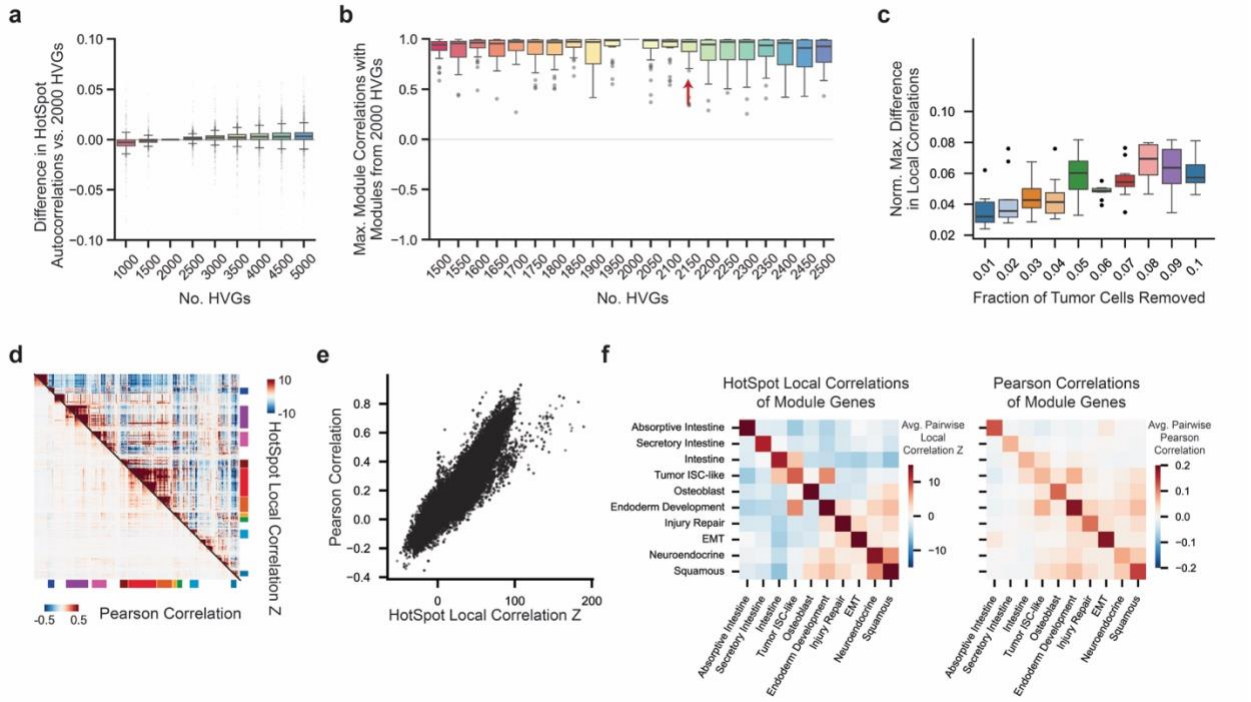
KG190/MSKCRC0231





Supplementary Data 1 | Description of samples, treatment history, carcinoembryonic antigen levels, and metastatic sites for each patient.

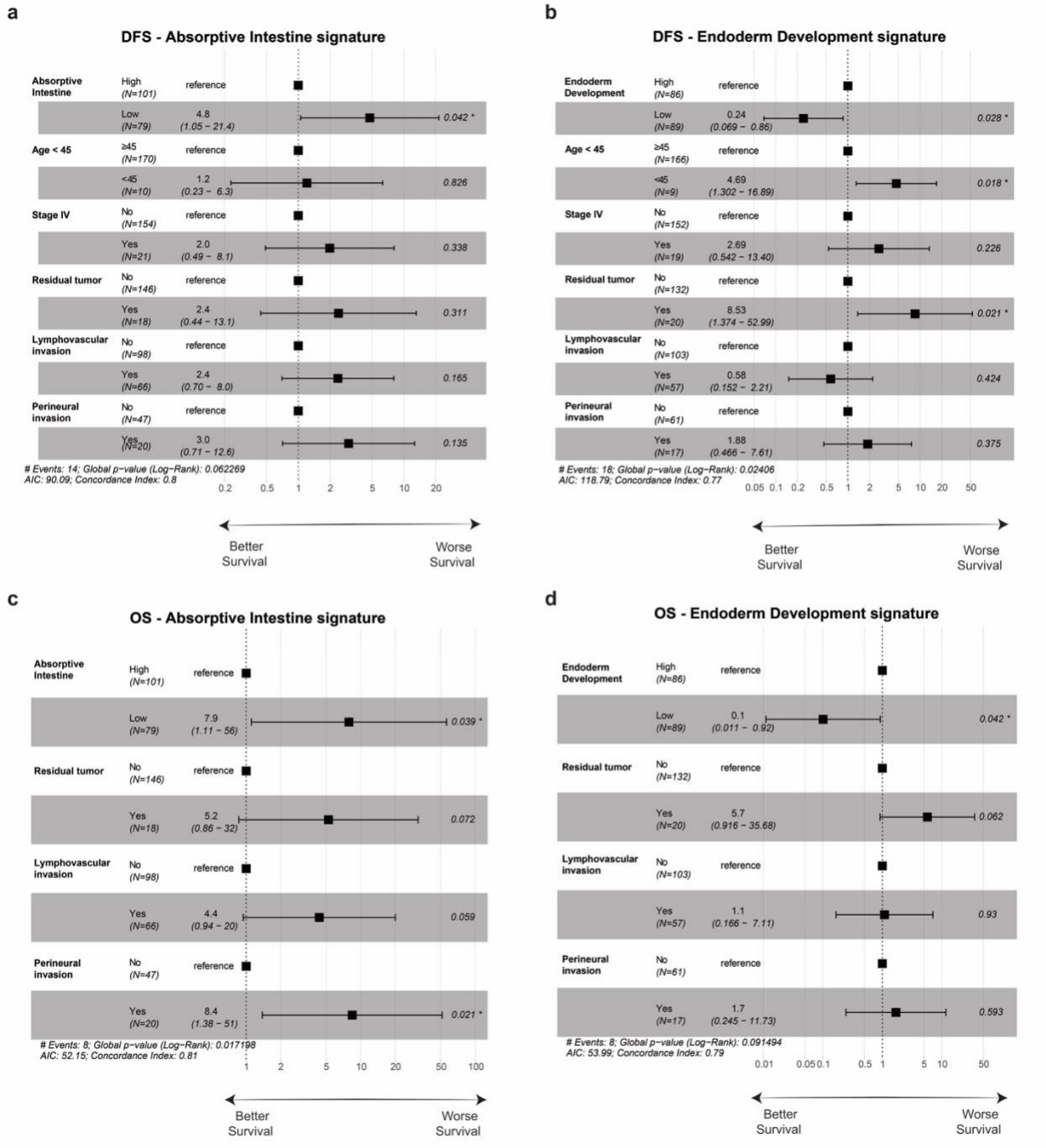
a, Primary and metastatic tumor sites, treatment history (systemic therapy, radiation and surgery), sample data and carcinoembryonic antigen (CEA) levels over time from the date of diagnosis for each patient. Left, schematic indicating the primary and metastatic tumor samples analyzed by scRNA-seq, Vectra multiplexed immunofluorescence, and/or used for organoid derivation. Right, graph of weeks from diagnosis (x-axis), showing metastatic sites that were identified by imaging over time (top third), length of time between diagnosis and surgical resection and biospecimen collection (middle third), and the type of systemic or radiation therapy received (bottom third). Horizontal bars color coded for the type of treatment and superimposed on a graph of levels of the serum tumor marker CEA over time (right axis). The composite figures demonstrate when samples were obtained for analysis in relation to the date of diagnosis, systemic therapies and radiation received, surgical interventions, response to therapy and clinical disease progression.



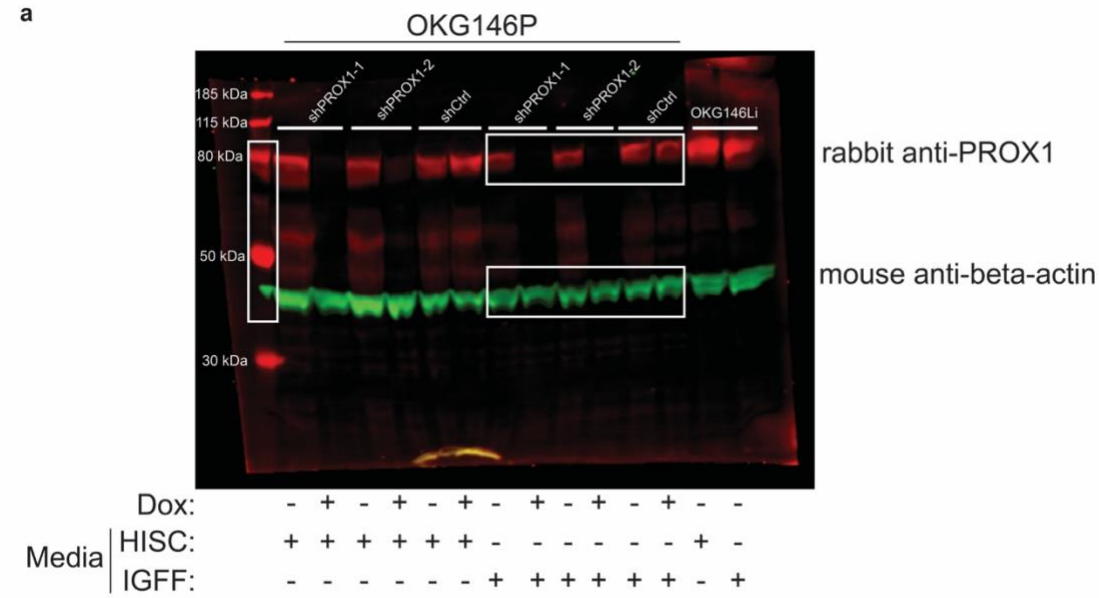
Supplementary Data 2 | Local autocorrelation and detected HotSpot modules are highly robust to varying parameter values

a, Difference in gene autocorrelation score between using 2,000 HVGs (used throughout this manuscript) and varying numbers of HVGs (x-axis, n = 26,145 epithelial cells). **b**, Pearson correlation between the 37 Hotspot gene modules in this study (based on 2,000 HVGs) and the most similar gene modules produced using an alternate number of HVGs (x-axis) (Methods, n = 26,145 epithelial cells). **c**, Maximum difference in local gene-gene correlation, normalized by the maximum local correlation value, for 10 progressively large random downsamples of our tumor scRNA-seq dataset (n = 25,883; 25,624; 25,367; 25,113; 24,861; 24,612; 24,365; 24,121; 23,879, 23,640 cells, respectively). **d**, Gene-gene local correlation in CRC tumors computed with Hotspot (upper triangle), or Pearson correlation (lower triangle), for all 1,962 genes (rows and columns) among the top 2,000 HVGs in the complete CRC tumor dataset, with a false discovery rate (FDR) < 0.01, as determined by Hotspot. **e**, Comparison of Pearson r global correlation and Hotspot z

local correlation values for all Hotspot module genes. **f**, Average Hotspot z and Pearson r correlations between all gene pairs; each pair consists of one gene from each indicated Hotspot module. **a-c**, Boxplots depict median (line), interquartile range (boxes) and 1.5x interquartile range (whiskers).



Supplementary Data 3 | Multivariate analysis of associations between module expression and disease free survival or overall survival
a,b, Disease-free survival (DFS) or (**c,d**) overall survival (OS). Hazard ratios and p values were calculated using a Cox proportional hazards model that included all of the clinical and genomic variables shown in the panel. The numbers in parentheses and the length of the error bars show the 95% confidence interval for each hazard ratio (black square).



Supplementary Data Figure 4 | Western Blot analysis of OKG146P shPROX1
a, Uncropped Western Blot scan related to Extended Figure 12c