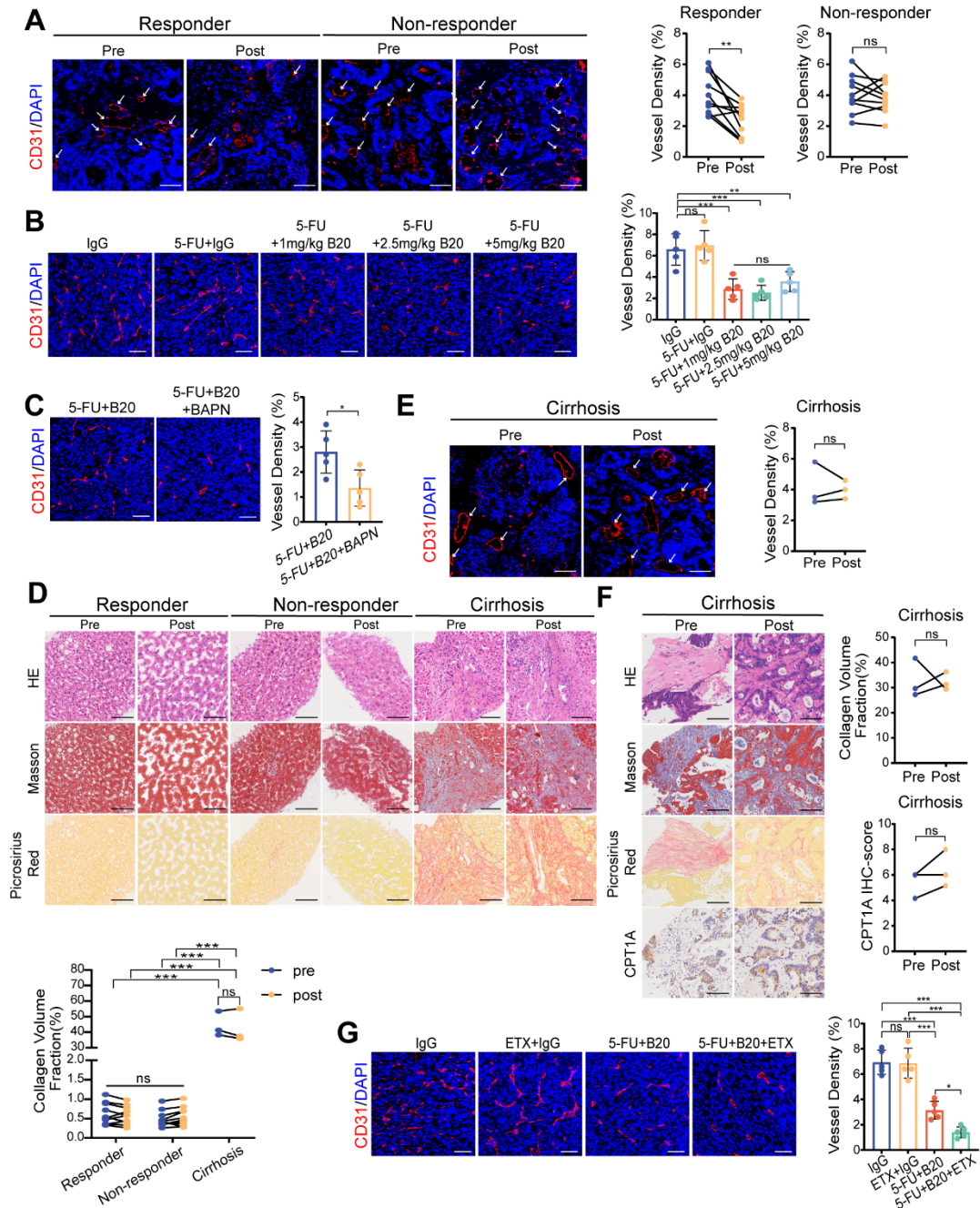


Supplementary Fig. S1



Supplementary Figure. S1 Increased ECM deposition and active FAO metabolism induce Bevacizumab resistance in liver metastases. (A) Representative immunofluorescence images (left) showing tumor vessels (stained for CD31) in liver metastases from CRC patients before and after receiving chemotherapy and bevacizumab treatment. Quantification of intraindividual comparisons of vessel density (right) in paired samples (two-tailed paired t-test, n=10 per group). Scale bar: 50 μ m. (B) Representative immunofluorescence images (left) and quantification of vessel density (right) showing tumor vessels (stained for CD31) in liver metastases in mice with indicated treatment (one-way ANOVA, n=5 per group). Scale bar: 50 μ m. (C) Representative immunofluorescence images (left) and quantification of vessel density (right) showing tumor vessels (stained for CD31) in liver metastases in mice with indicated treatment

(two-tailed unpaired t-test, n=5 per group). Scale bar: 50 μ m. (D) Representative HE, Masson, picrosirius red images (upper) showing ECM deposition in normal liver tissues from CRC patients before and after receiving chemotherapy and bevacizumab treatment. Quantification of intraindividual comparisons of collagen volume fraction (lower) in paired samples (two-way ANOVA, n=10, 10, 3). Scale bar: 100 μ m. (E) Representative immunofluorescence images (left) showing tumor vessels (stained for CD31) in liver metastases from CRC patients, who had been diagnosed with cirrhosis, before and after receiving chemotherapy and bevacizumab treatment. Quantification of intraindividual comparisons of vessel density (right) in paired samples (two-tailed paired t-test, n=3 per group). Scale bar: 50 μ m. (F) Representative HE, Masson, picrosirius red and IHC images (left) on serial sections showing ECM deposition change and CPT1A expression in liver metastases from CRC patients, who had been diagnosed with cirrhosis, before and after receiving chemotherapy and bevacizumab treatment. Quantification of collagen volume fraction and IHC scores of CPT1A (right) of intraindividual comparisons in paired samples (two-tailed paired t-test, n=3 per group). Scale bar: 100 μ m. (G) Representative immunofluorescence images (left) and quantification of vessel density (right) showing tumor vessels (stained for CD31) in liver metastases in mice with indicated treatment (one-way ANOVA, n=5 per group). Scale bar: 50 μ m. Data are graphed as the mean \pm SD. ns, not significant, $P > 0.05$; * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$.