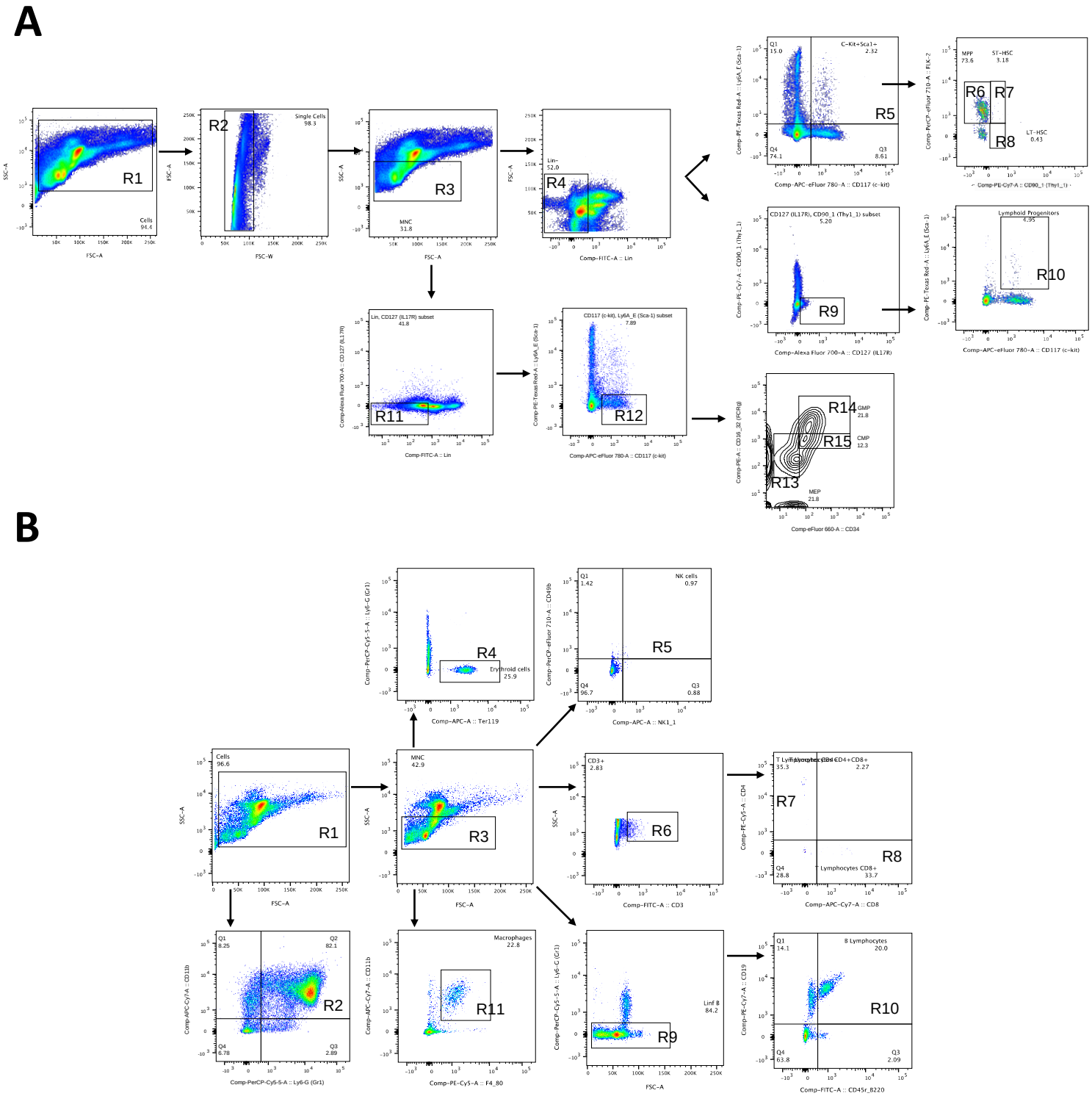
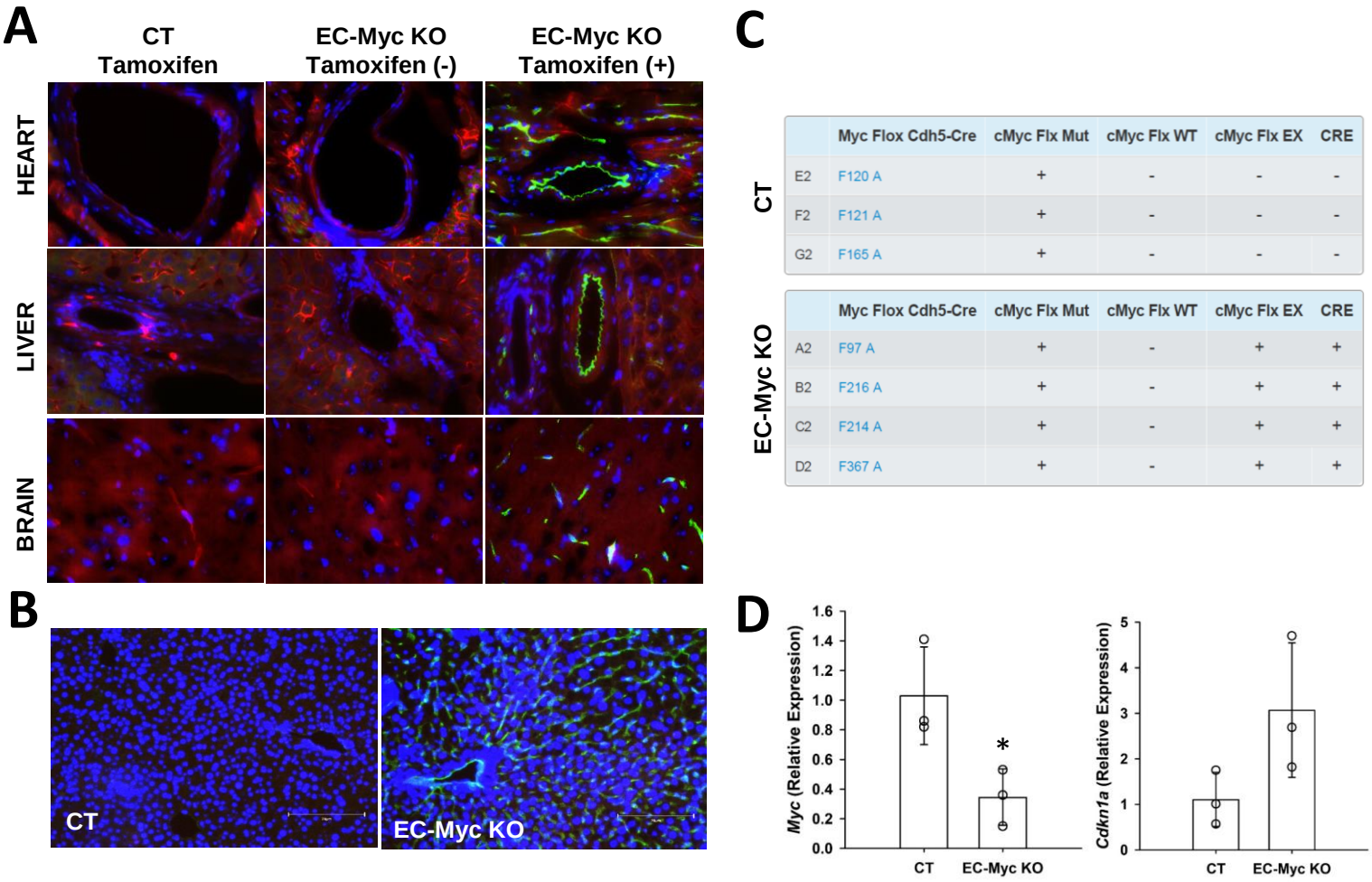
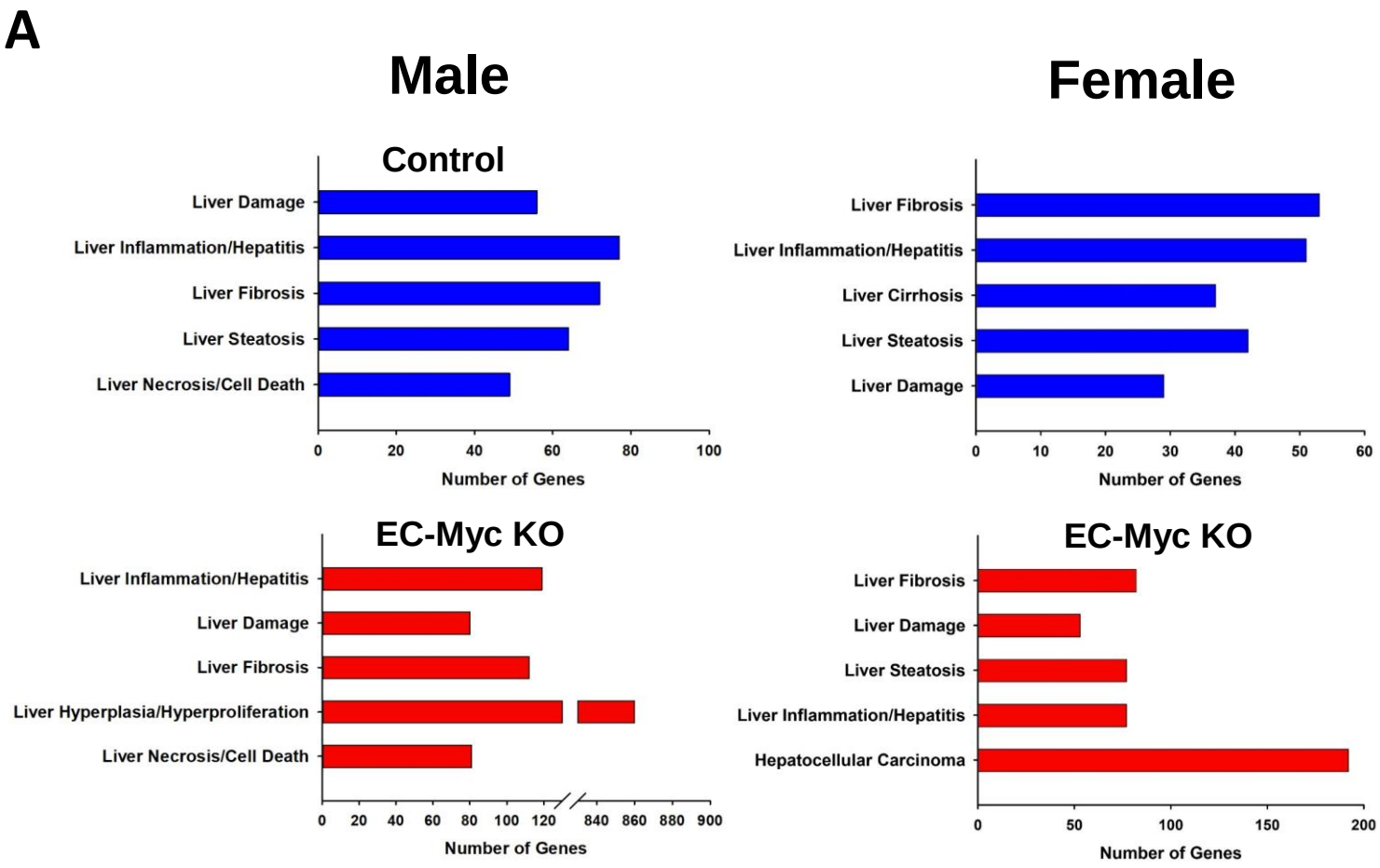
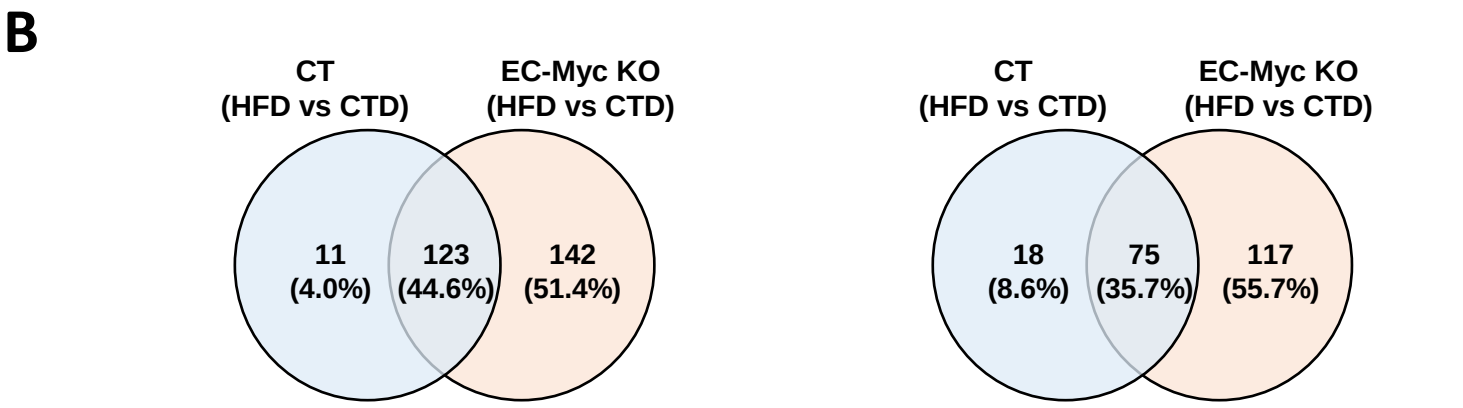


Supplemental Figure 1. Flow cytometry gate strategy. (A) Hematopoietic stem and progenitor cells were analyzed according to the following sequence of gates: cells (R1), single cells (R2) MNC (R3), Lin$^-$ (R4), c-Kit$^+$Sca-1$^+$ (R5), MMP (R6), ST-HSC (R7), LT-HSC (R8), Il7r$^+$Thy1.1$^-$ (R9), LP (R10), Lin$^-$Il7r$^-$ (R11), c-Kit$^+$Sca-1$^-$ (R12), MEP (R13), GMP (R14), and CMP (R15). **(B)** Mature hematopoietic cells were analyzed according to the following sequence of gates: cells, (R1), granulocytes (R2), MNC (R3), erythroid cells (R4), NK cells (R5), CD3$^+$ lymphocytes (R6), CD4$^+$ lymphocytes (R7), CD8$^+$ lymphocytes (R8), GR-1$^-$ cells (R9), B lymphocytes (R10), and monocytes/macrophages (R11).



Supplemental Figure 2. Characterization of c-Myc knockout in endothelium. (A) Representative fluorescent images of heart, liver and brain sections from CT and EC-Myc KO Cre reporter mice. GFP expression indicates Cre-mediated recombination in endothelium. **(B)** Representative images of liver sections stained with a FITC-conjugated anti-GFP antibody to amplify the signal. **(C)** PCR findings confirming Cre-mediated *Myc* deletion in aorta tissues from EC-Myc KO mice. Short fragment was amplified (indicating excision). **(D)** qPCR analysis of *Myc* and *Cdkn1a* expression in isolated endothelial cells from liver of CT and EC-Myc KO mice. Results are normalized to the control group (n = 3). CT, control; EC-Myc KO, endothelial c-Myc knockout; cMyc Flx Mut, floxed *Myc* allele. cMyc Flox WT, wild-type *Myc* allele. cMyc Flx EX, excised *Myc* allele. *p<0.05.





Supplemental Figure 3. Endothelial c-Myc loss promotes liver cancer-related gene expression changes after short-exposure to HFD. (A) Top five hepatotoxicity functions identified by Ingenuity Pathway Analysis in CT and EC-Myc KO livers in response to HFD exposure. **(B)** Venn diagrams indicating the number of HCC-related genes significantly altered in CT and EC-Myc KO liver. The left panels represent results in males (n = 4) and the right panels represent results in females (n = 3). CT, control; EC-Myc KO, endothelial c-Myc knockout; CTD, low-fat control diet; HFD, high-fat diet; HCC, hepatocellular carcinoma.