

**Supplementary Figure 1.** The correlation between ten cuproptosis-related gene expression levels and various clinicopathological features in hepatocellular carcinoma (HCC) patients using Wilcoxon signed-rank test or Kruskal-Wallis test from the TCGA database.

The correlation between various clinicopathological features and cuproptosis-related genes expression levels in HCCs, including *SLC25A3* (**A**), *SCO2* (**B**), *AOC1* (**C**), *PDHA1* (**D**), *MTF1* (**E**), MT-*CO1* (**F**), *ACO1* (**G**), *FDX2* (**H**), *NUBP2* (**I**), and *CIAPIN1* (**J**). (Note: ACO1, aconitase 1; AOC1, amine oxidase copper containing 1; CIAPIN1, cytokine induced apoptosis inhibitor 1; FDX2, ferredoxin 2; G, histologic grade; HCC, hepatocellular carcinoma; M, distant metastasis ; MT-CO1, mitochondrially encoded cytochrome c oxidase I; MTF1, metal regulatory transcription factor 1; N, lymph node metastasis; NUBP2, nucleotide binding protein 2; PDHA1, pyruvate dehydrogenase E1 subunit alpha 1; SCO2, synthesis of cytochrome c oxidase 2; SLC25A3, solute carrier family 25 member 3; Stage, clinical stage; T, tumor stage; TCGA, The Cancer Genome Atlas; "\*", P < 0.05; "\*\*", P < 0.01; "\*\*\*", P < 0.001.)



**Supplementary Figure 2.** The test about mRNA expressions of ten cuproptosis-related genes in the boxplot, clinical stage, and overall survival in hepatocellular carcinoma (HCC) by GEPIA2 database.

The cuproptosis-related gene including *ATP7A* (**A**), *SLC25A3* (**B**), *SCO2* (**C**), *COA6* (**D**), *ATP6AP1* (**E**), *DLAT* (**F**), *ACP1* (**G**), *FDX2* (**H**), *ISCA2* (**I**), and *NDOR1* (**J**). (Note: ACP1, acid phosphatase 1; ATP6AP1, ATPase H+ transporting accessory protein 1; ATP7A, copper-transporting p-type adenosine triphosphatase 1; COA6, cytochrome c oxidase assembly factor 6; DLAT, dihydrolipoamide S-acetyltransferase; FDX2, ferredoxin 2; HCC, hepatocellular carcinoma; ISCA2, iron-sulfur cluster assembly 2; NDOR1, NADPH dependent diflavin oxidoreductase 1; SCO2, synthesis of cytochrome c oxidase 2; SLC25A3, solute carrier family 25 member 3; GEPIA2, Gene Expression Profiling Interactive Analysis 2.)



**Supplementary Figure 3.** The test about mRNA expressions of other ten cuproptosis-related genes in the boxplot, clinical sage, and overall survival in hepatocellular carcinoma (HCC) by GEPIA2 database.

The cuproptosis-related gene including *AOC1* (**A**), *TMEM199* (**B**), *FDX1* (**C**), *LIPT1* (**D**), *PDHA1* (**E**), *MTF1* (**F**), MT-*CO1* (**G**), *ACO1* (**H**), *NUBP2* (**I**), and *CIAPIN1* (**J**). (Note: ACO1, aconitase 1; AOC1, amine oxidase copper containing 1; CIAPIN1, cytokine induced apoptosis inhibitor 1; FDX1, ferredoxin 1; HCC, hepatocellular carcinoma; LIPT1, lipoyltransferase 1; MT-CO1, mitochondrially encoded cytochrome c oxidase I; MTF1, metal regulatory transcription factor 1; NUBP2, nucleotide binding protein 2; PDHA1, pyruvate dehydrogenase E1 subunit alpha 1; GEPIA2, Gene Expression Profiling Interactive Analysis 2; TMEM199, transmembrane protein 199.)



**Supplementary Figure 4.** The protein expression of cuproptosis-related genes between HCC and normal liver tissues in the Human Protein Atlas (HPA) database.

The protein expression of cuproptosis-related genes using the same antibody in each HCC patient and normal liver sample from HPA database, including SCO2 (**A**), COA6 (**B**), AOC1 (**C**), TMEM199 (**D**), FDX1 (**E**), LIPT1 (**F**), DLAT (**G**), PDHA1 (**H**), MTF1 (**I**), MT-CO1 (**J**), ACO1 (**K**), ACP1 (**L**), FDX2 (**M**), NUBP2 (**N**), CIAPIN1 (**O**), ISCA2 (**P**), and NDOR1 (**Q**). (Note: ACO1, aconitase 1; ACP1, acid phosphatase 1; AOC1, amine oxidase copper containing 1; CIAPIN1, cytokine induced apoptosis inhibitor 1; COA6, cytochrome c oxidase assembly factor 6; DLAT, dihydrolipoamide S-acetyltransferase; FDX1, ferredoxin 1; FDX2, ferredoxin 2; HCC, hepatocellular carcinoma; HPA, Human Protein Atlas; ISCA2, iron-sulfur cluster assembly 2; LIPT1, lipoyltransferase 1; MT-CO1, mitochondrially encoded cytochrome c oxidase I; MTF1, metal regulatory transcription factor 1; NDOR1, NADPH dependent diflavin oxidoreductase 1; NUBP2, nucleotide binding protein 2; PDHA1, pyruvate dehydrogenase E1 subunit alpha 1; SCO2, synthesis of cytochrome c oxidase 2; TMEM199, transmembrane protein 199.)