**Supplementary Figure 1 BCL10 is highly expressed in colorectal cancer and associated with poor patient prognosis** A: Based on HPA data, the expression profile of BCL10 across various tissues is illustrated. B: Based on HPA data, the expression profile of BCL10 across various tumors is illustrated. C: Differential BCL10 expression between the tumor/normal group (TCGA-GTEx). D: Removing the null value (NA)) Protein level BCL10 expression difference (tumor/normal group). E: Relative expression levels of BCL10 mRNA and protein in NCM-460, SW480, SW620, and HCT-116 cell lines. $^{b}P < 0.01$. $^{c}P < 0.001$. F: Association between BCL10 and survival of patients with GSE106584. G: Performing Chi-Square test on each clinical trait in the high/Low BCL10 expression group. H: ROC curves evaluate the diagnosis performance of BCL10 expression on tumor/normal groups.

**Supplementary Figure 2 Relative expression levels of BCL10 and DLAT proteins** A: Relative expression levels of BCL10 mRNA and protein following lentivirus-mediated knockdown with three distinct shRNAs in SW480 and SW620 cell lines; $^{c}P < 0.001$.B: Quantitative analysis of DLAT mRNA and protein expression after siRNA-mediated knockdown using three distinct sequences in SW480 and SW620 colorectal cancer cell lines. $^{c}P < 0.001$.

**Supplementary Figure 3 CCK-8 proliferation assay confirmed that overexpression or knockdown of BCL10 significantly affected the proliferation activity of CRC cells.**

**Supplementary Figure 4** A: Evaluation of cell viability using CCK-8 assay after 24-hour exposure to gradient concentrations of elesclomol-Cu in SW480 and SW620 cell lines, which induced cuproptosis cell death. B: The cytotoxic effects of 200 nM elesclomol-Cu were evaluated at 24, 48, and 72-hour time points using CCK-8 assay in SW480 and SW620 colorectal cancer cell lines, where cuproptosis was successfully induced.

**Supplementary Figure 5** A: The expression level of DLAT in clinical colon adenocarcinoma (COAD) tissue samples was significantly lower than that in normal tissues. B: The expression level of DLAT in COAD adjacent tissues was significantly lower than that in normal tissues. C: The low expression level of DLAT is significantly correlated with poor prognosis in patients; D、F: Cuproptosis was induced in human

colorectal carcinoma cell lines (SW480 and SW620) using a copper concentration gradient (50-800nM). Subsequent CCK-8 viability assays revealed that DLAT knockdown (siDLAT) significantly attenuated copper-induced cell death. **Supplementary Figure 6. Negative controls for immunohistochemistry (IHC) assays.**

(A) Negative control for MYC IHC (Figure 1D) using isotype-matched IgG.

(B) Negative control for Ki67 IHC (Figure 1D) with primary antibody omitted.

(C) Negative control for BCL10 IHC (Figure 6H) using adjacent normal colon tissue.

(D) Negative control for DLAT IHC (Figure 6H) with isotype-matched IgG.

(E) Negative control for p65 IHC (Figure 6H) using PBS instead of primary antibody.

(F) Negative control for p-p65 (Ser536) IHC (Figure 6H) with primary antibody omitted.

(G) Negative control for DLAT IHC (Supplementary Figure 7B) using isotype-matched IgG.

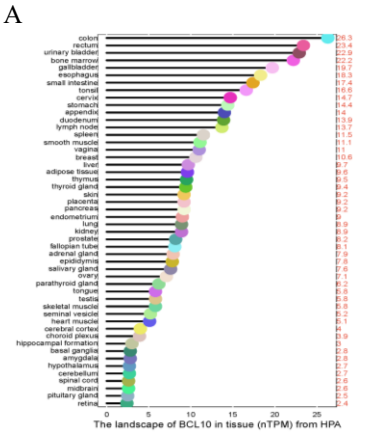
All panels: Scale bars = 50 μm. No specific staining was observed in any negative control, confirming antibody specificity.

**Supplementary Figure 7** A: The ALT and AST levels. B: Mice liver and kidney H&E sections and tumor DLAT immunohistochemistry.

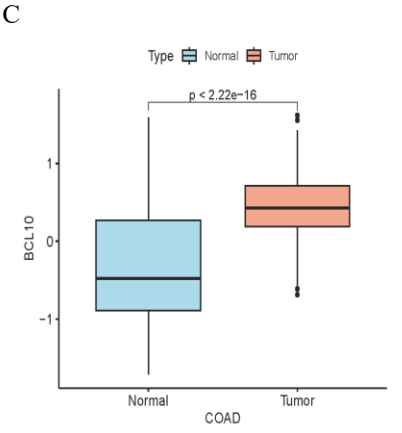
**Supplementary Table 1 Primers list**

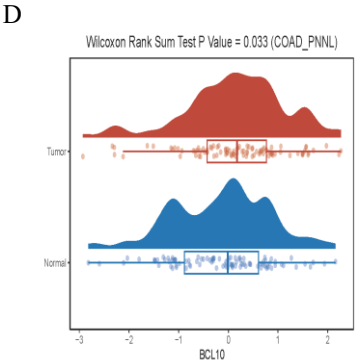
| Gene | Primers |
|---|---|
| L13-F | CGGACCGTGCGAGGTAT |
| L13-R | CACCATCCGCTTTTTCTTGTC |
| DLAT-F | CGGAACTCCACGAGTGACC |
| DLAT-R | CCCCGCCATACCCTGTAGT |
| BCL10-F | GTGAAGAAGGACGCCTTAGAAA |
| BCL10-R | TCAACAAGGGTGTCCAGACCT |
| FDX1-F | TGCCAGATCGAGCATGTCATT |
| FDX1-R | TGCCAGATCGAGCATGTCATT |
| LIAS-F | GTATGTGAGGAAGCTCGATGTC |
| LIAS-R | CACCCATCAACATGATCGTGG |
| GLS-F | AGGGTCTGTTACCTAGCTTGG |
| GLS-R | ACGTTCGCAATCCTGTAGATTT |
| DLD-F | CACTGCTACGAAAGCTGATGG |
| DLD-R | TAACTTCTGAACCCGTGGCTA |
| PDHB-F | AAGAGGCGCTTTCACTGGAC |
| PDHB-R | ACTAACCTTGTATGCCCCATCA |
| PDHA-F | TGGTAGCATCCCGTAATTTTGC |
| PDHA-R | ATTCGGCGTACAGTCTGCATC |
| CDKN2A-F | GGGTTTTCGTGGTTCACATCC |
| CDKN2A-R | CTAGACGCTGGCTCCTCAGTA |
| SLC31A1-F | GGGGATGAGCTATATGGACTCC |
| SLC31A1-R | TCACCAAACCGGAAAACAGTAG |
| DLST-F | GAACTGCCCTCTAGGGAGAC |
| DLST-R | AACCTTCCTGCTGTTAGGGTA |
| ATP7A-F | TGACCCTAAACTACAGACTCCAA |
| ATP7A-R | CGCCGTAACAGTCAGAAACAA |

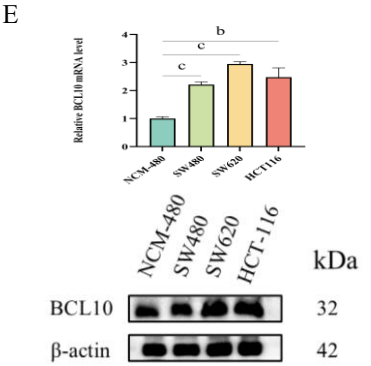
| | |
|---|---|
| LIPT1-F | CCTCTGTTGTAATTGGTAGGCAT |
| LIPT1-R | CTGGGGTTGGACAGCATTCAG |
| ATP7B-F | GCCAGCATTGCAGAAGGAAAG |
| ATP7B-R | TGATAAGTGATGACGGCCTCT |

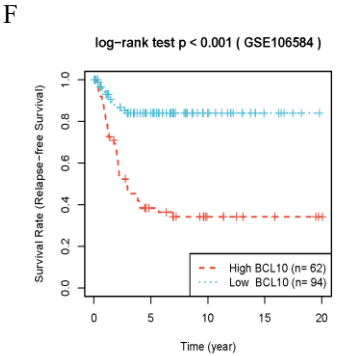

A
The landscape of BCL10 in tissue (nTPM) from HPA

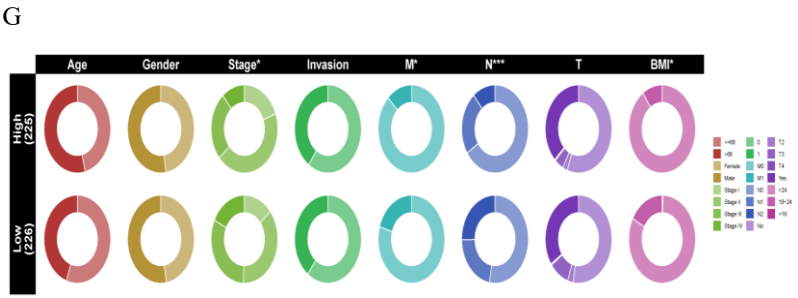

B
The landscape of BCL10 in Cancer Cell (nTPM) from HPA

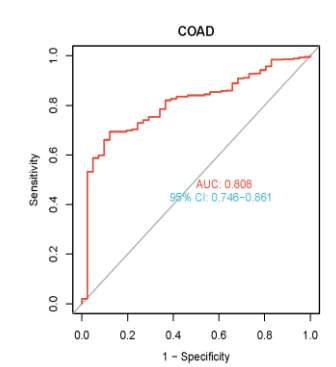

C
Type
Normal
Tumor
p < 2.22e−16
BCL10
Normal
Tumor
COAD


D
Wilcoxon Rank Sum Test P Value = 0.033 (COAD_PNNL)
Tumor
Normal
BCL10

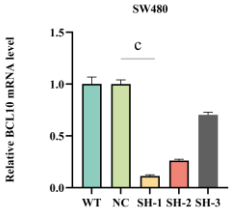

E
Relative BCL10 mRNA level
NCM-480
SW480
SW620
HCT116
kDa
BCL10
32
β-actin
42

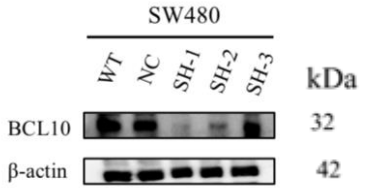

F
log−rank test p < 0.001 ( GSE106584 )
Survival Rate (Relapse−free Survival)
High BCL10 (n= 62)
Low BCL10 (n= 94)
Time (year)

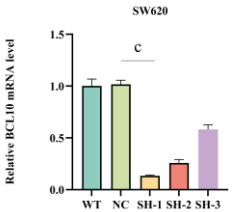

G
Age
Gender
Stage*
Invasion
M*
N***
T
BMI*
High (225)
Low (226)

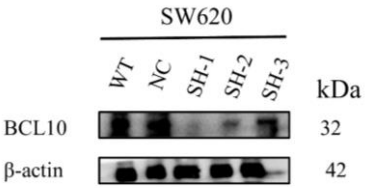

H
COAD
Sensitivity
1 − Specificity
AUC: 0.808
95% CI: 0.746−0.861

A

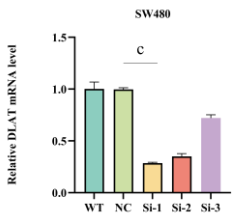

SW480
Relative BCL10 mRNA level
1.5
1.0
0.5
0.0
c
WT NC SH-1 SH-2 SH-3

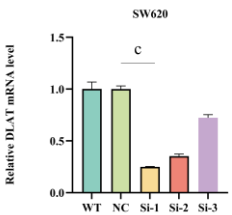

SW480
WT NC SH-1 SH-2 SH-3
kDa
BCL10
32
β-actin
42

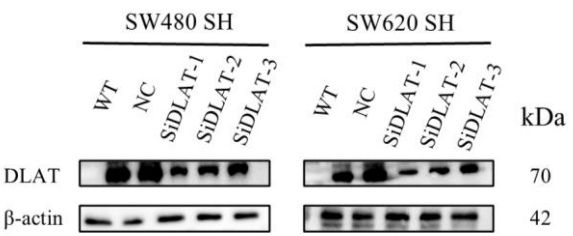

SW620
Relative BCL10 mRNA level
1.5
1.0
0.5
0.0
c
WT NC SH-1 SH-2 SH-3

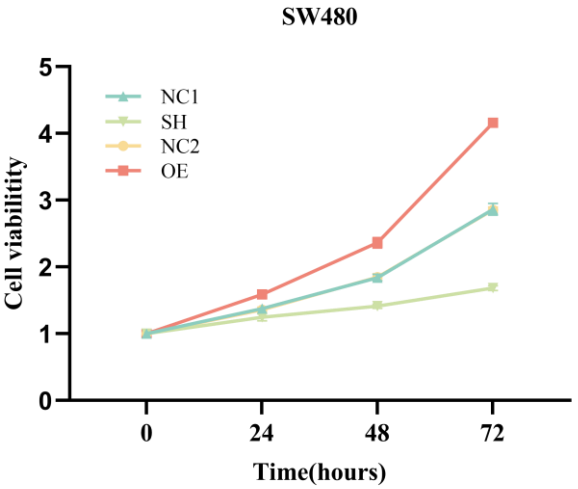

SW620
WT NC SH-1 SH-2 SH-3
kDa
BCL10
32
β-actin
42

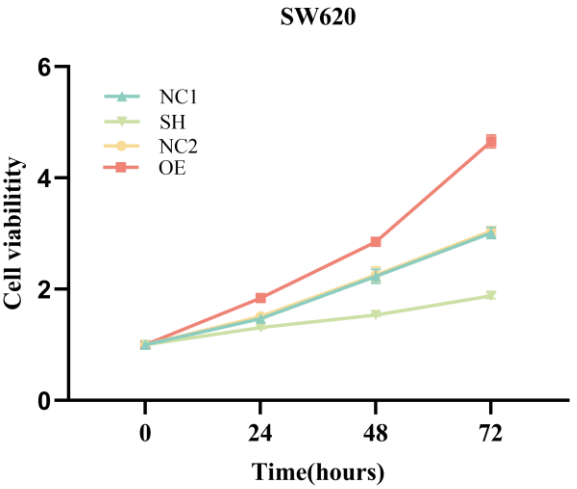
B


SW480
Relative DLAT mRNA level
1.5
1.0
0.5
0.0
c
WT NC Si-1 Si-2 Si-3

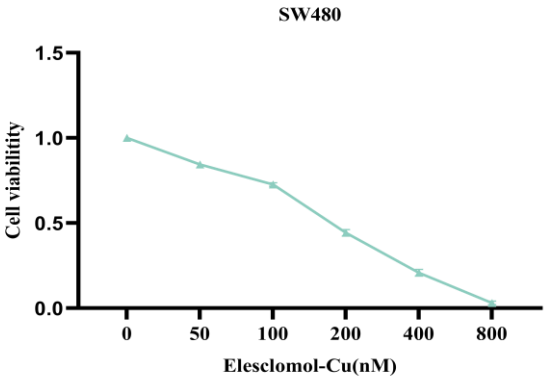

SW620
Relative DLAT mRNA level
1.5
1.0
0.5
0.0
c
WT NC Si-1 Si-2 Si-3

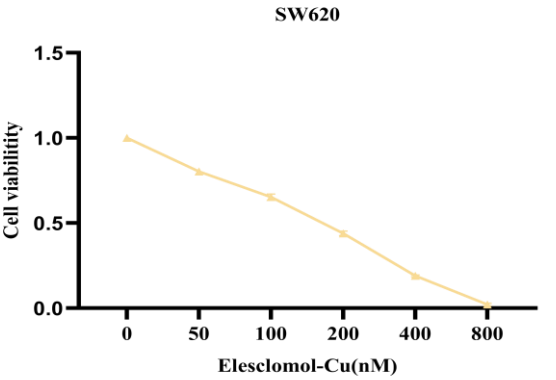

SW480 SH
SW620 SH
WT NC SiDLAT-1 SiDLAT-2 SiDLAT-3
WT NC SiDLAT-1 SiDLAT-2 SiDLAT-3
kDa
DLAT
70
β-actin
42


SW480
NC1
SH
NC2
OE
Cell viability
0
1
2
3
4
5
0
24
48
72
Time(hours)

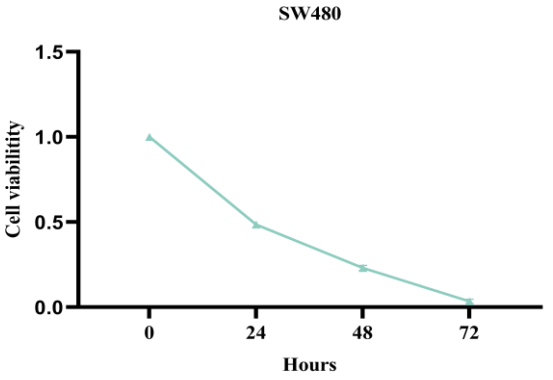

SW620
NC1
SH
NC2
OE
Cell viability
0
2
4
6
0
24
48
72
Time(hours)

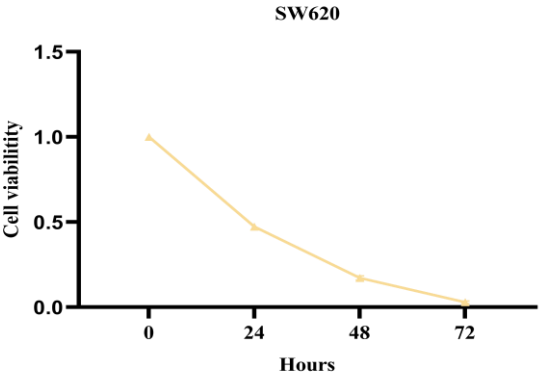
A


SW480
Cell viability
1.5
1.0
0.5
0.0
0
50
100
200
400
800
Elesclomol-Cu(nM)

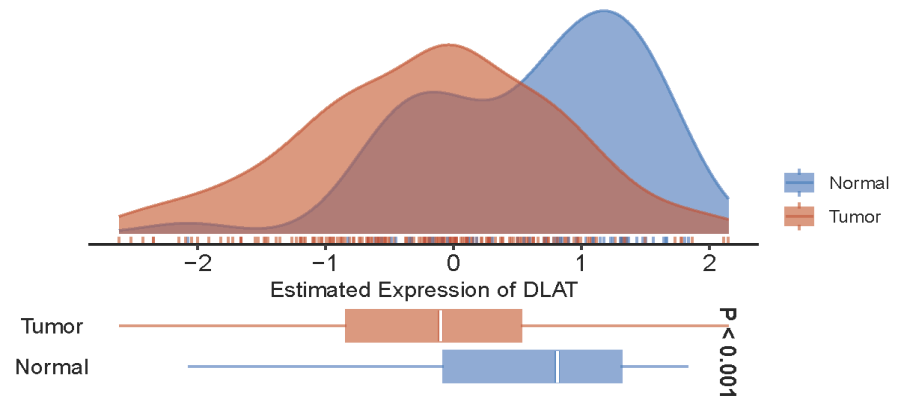

SW620
Cell viability
1.5
1.0
0.5
0.0
0
50
100
200
400
800
Elesclomol-Cu(nM)

B

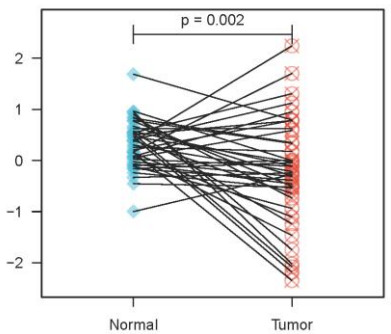

SW480
Cell viability
1.5
1.0
0.5
0.0
0
24
48
72
Hours


SW620
Cell viability
1.5
1.0
0.5
0.0
0
24
48
72
Hours

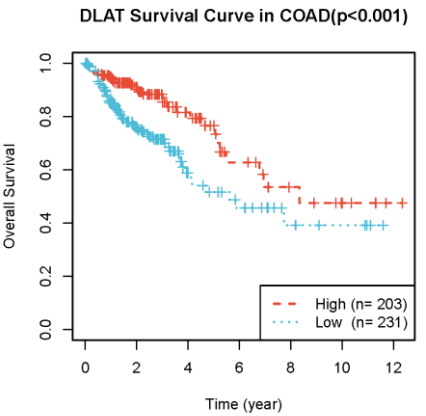
A


Normal
Tumor
−2
−1
0
1
2
Estimated Expression of DLAT
Tumor
Normal
P < 0.001

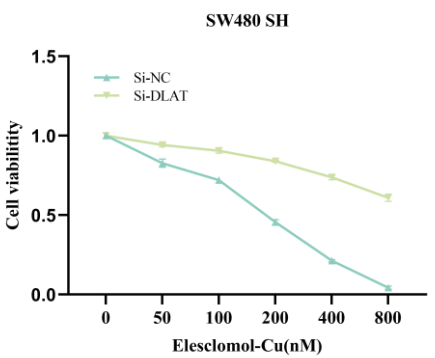
B


p = 0.002
2
1
0
−1
−2
Normal
Tumor

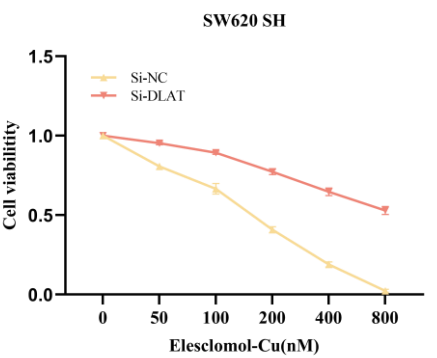
C


DLAT Survival Curve in COAD(p<0.001)
Overall Survival
0.0
0.2
0.4
0.6
0.8
1.0
0
2
4
6
8
10
12
Time (year)
High (n= 203)
Low (n= 231)

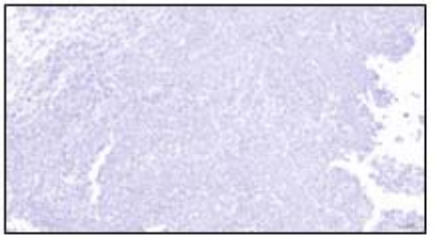
D


SW480 SH
Si-NC
Si-DLAT
Cell viability
1.5
1.0
0.5
0.0
0
50
100
200
400
800
Elesclomol-Cu(nM)

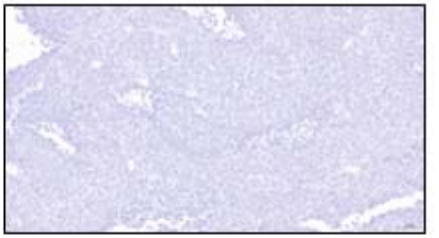
E


SW620 SH
Si-NC
Si-DLAT
Cell viability
1.5
1.0
0.5
0.0
0
50
100
200
400
800
Elesclomol-Cu(nM)

A

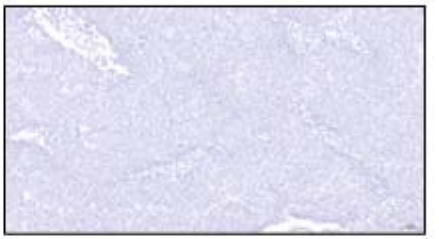


B



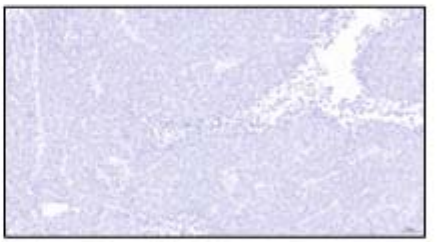
C

D

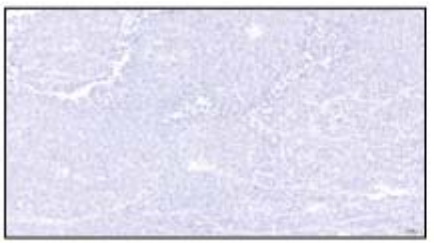


E

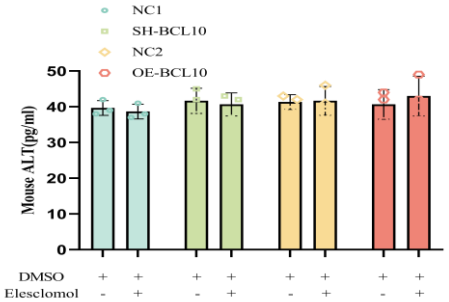
F

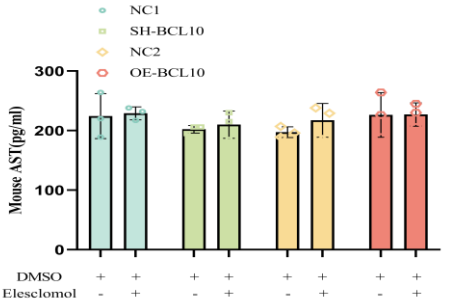


G

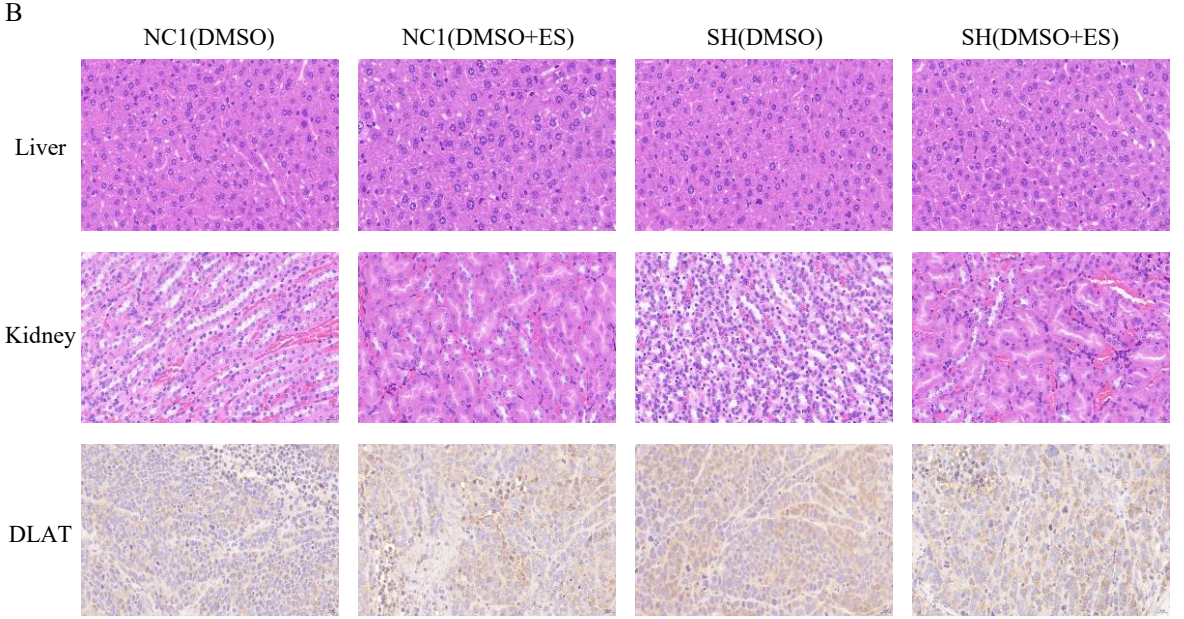


A


NC1
SH-BCL10
NC2
OE-BCL10
Mouse ALT(pg/ml)
50
40
30
20
10
0
DMSO
Elesclomol


NC1
SH-BCL10
NC2
OE-BCL10
Mouse AST(pg/ml)
300
200
100
0
DMSO
Elesclomol

B


NC1(DMSO)
NC1(DMSO+ES)
SH(DMSO)
SH(DMSO+ES)
Liver
Kidney
DLAT