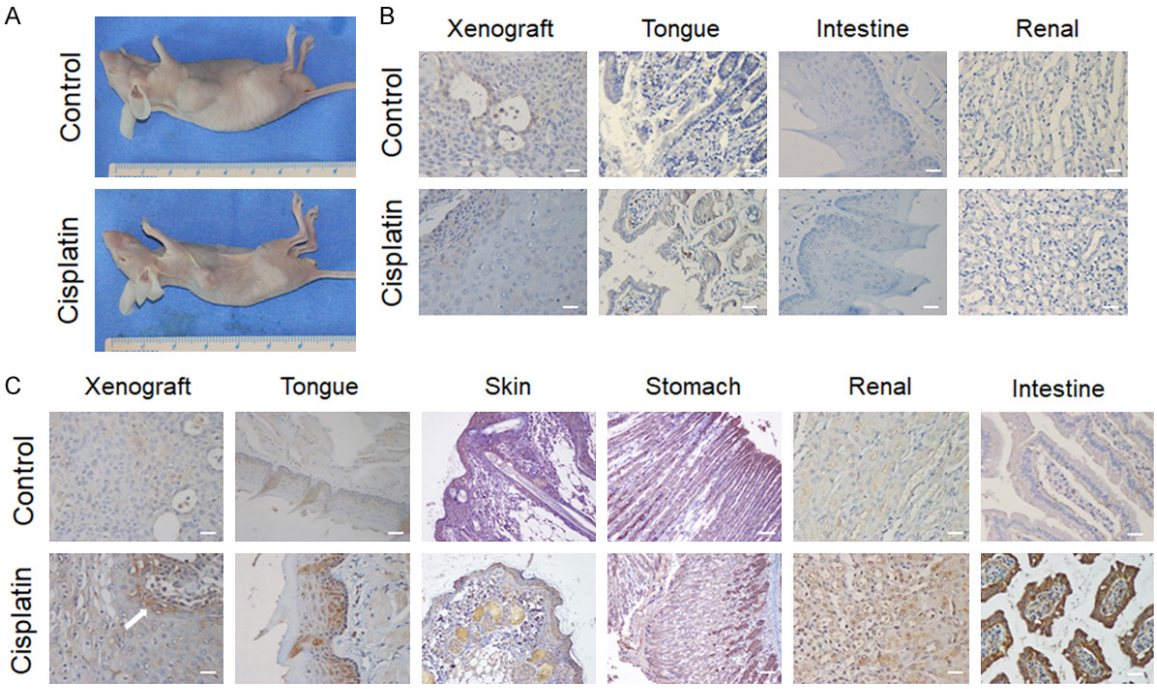


Figure S1. A. After chemotherapy, the mice appeared to have a hunched back, thin physique and other adverse reactions; B. Typical immunohistochemical analysis of GSDMD expression in OSCC xenograft mice samples, with tumour, tongue, intestine and renal tissues. GSDMD did not show an increased trend (scale bar size 20 μm); C. Immunohistochemical analysis of GSDME expression in OSCC xenograft mice samples, with xenograft, tongue, skin, stomach, renal and intestine tissues. After cisplatin treatment, GSDME was high expressed (scale bar size 20 μm).

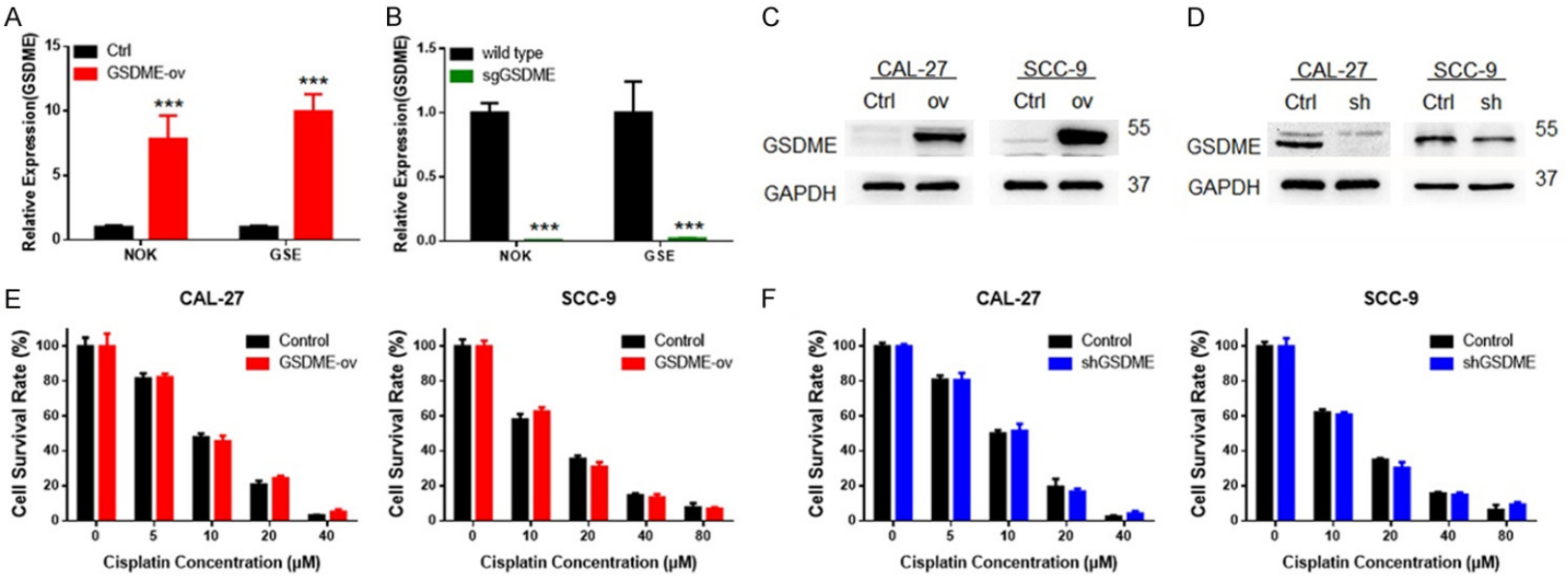
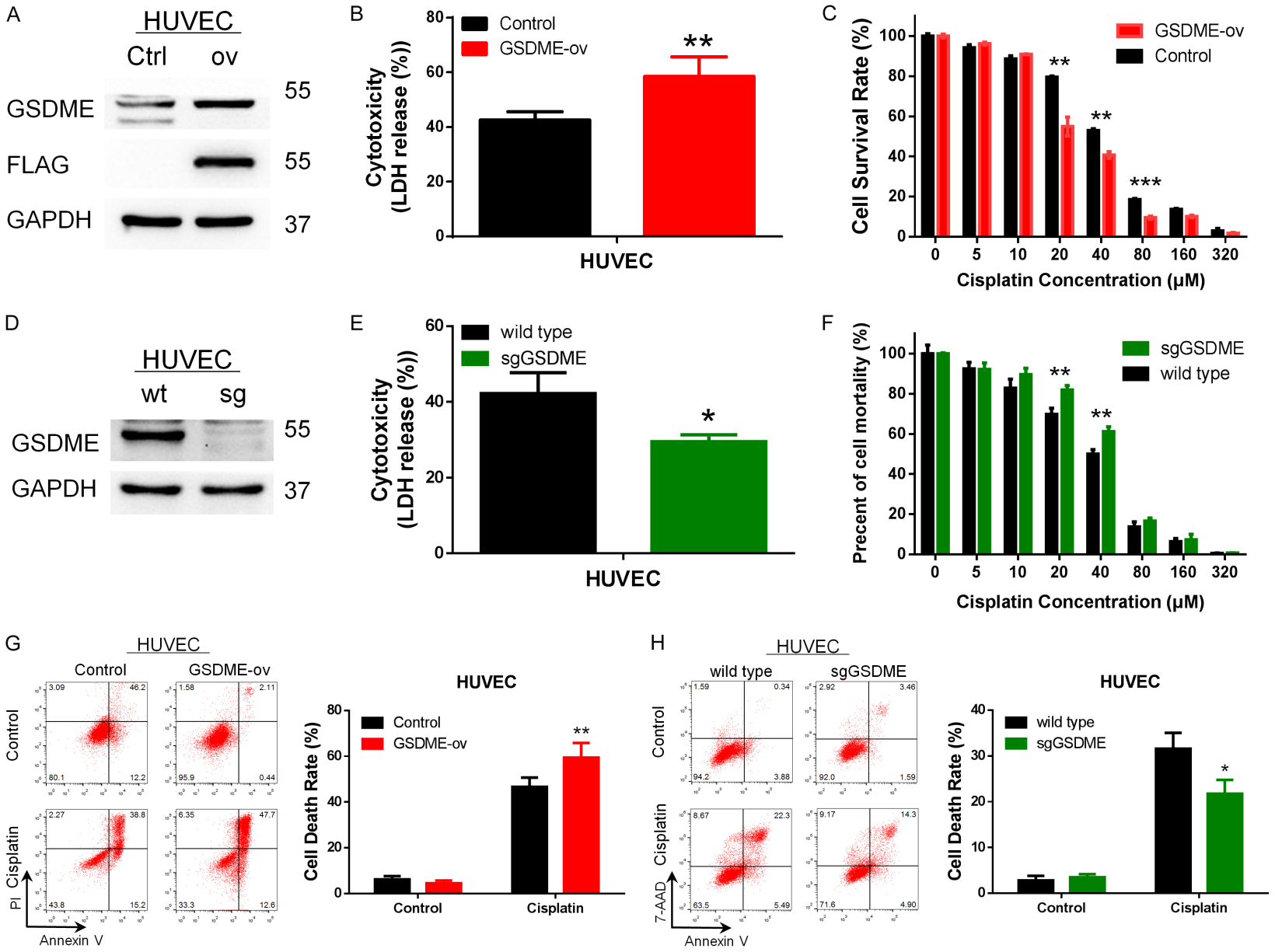


Figure S2. GSDME expression does not affect the sensitivity of OSCC cells to cisplatin chemotherapy. A. PCR confirmed that GSDME was overexpressed in NOKs and GSEs; B. PCR confirmed that GSDME was inhibited in NOKs and GSEs; C. Immunoblot confirmed that GSDME was overexpressed in the OSCC cell line (CAL-27 and SCC-9); D. Immunoblot confirmed that GSDME was inhibited in the OSCC cell line (CAL-27 and SCC-9); E. Gradient concentration of cisplatin-treated GSDME overexpressing OSCC cell lines; increased GSDME expression does not affect the cellular cisplatin sensitivity; F. Gradient concentration of the cisplatin-treated OSCC cell line with inhibited GSDME expression; decreased GSDME expression does not affect the cellular cisplatin tolerance.


A
HUVEC
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ov
GSDME
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GAPDH
55
55
37
B
Control
GSDME-ov
Cytotoxicity (LDH release (%))
HUVEC
C
GSDME-ov
Control
Cell Survival Rate (%)
Cisplatin Concentration (μM)
D
HUVEC
wt
sg
GSDME
GAPDH
55
37
E
wild type
sgGSDME
Cytotoxicity (LDH release (%))
HUVEC
F
sgGSDME
wild type
Precent of cell mortality (%)
Cisplatin Concentration (μM)
G
HUVEC
Control
GSDME-ov
Control
Cisplatin
PI
Annexin V
Cell Death Rate (%)
H
HUVEC
wild type
sgGSDME
Control
Cisplatin
7-AAD
Annexin V
Cell Death Rate (%)

Figure S3. GSDME expression in HUVECs regulates the chemotherapy sensitivity of these cells. A. Immunoblot confirmed that GSDME was overexpressed in HUVECs; the Flag-tag was successfully fused to GSDME; B. The cytotoxicity assay revealed elevated LDH release in GSDME overexpressing HUVECs compared with control cells after cisplatin treatment; C. Gradient concentration of cisplatin-treated GSDME-ov HUVECs and decreased cisplatin tolerance was confirmed; D. Immunoblot analysis confirmed that GSDME was knockout in HUVECs; E. Cytotoxicity assay revealed decreases in LDH release in GSDME-knockout HUVECs compared with control cells after cisplatin treatment; F. Gradient concentration of cisplatin-treated HUVECs with GSDME knockout, and increased cisplatin tolerance; G. FCM detected the cisplatin-sensitive effect on GSDME-ov cell lines using HUVECs; H. FCM detected the cisplatin-tolerant effect on the GSDME-knockout HUVECs; (cisplatin treatment: 40 μM, 24 hours for B, E, G, and H).

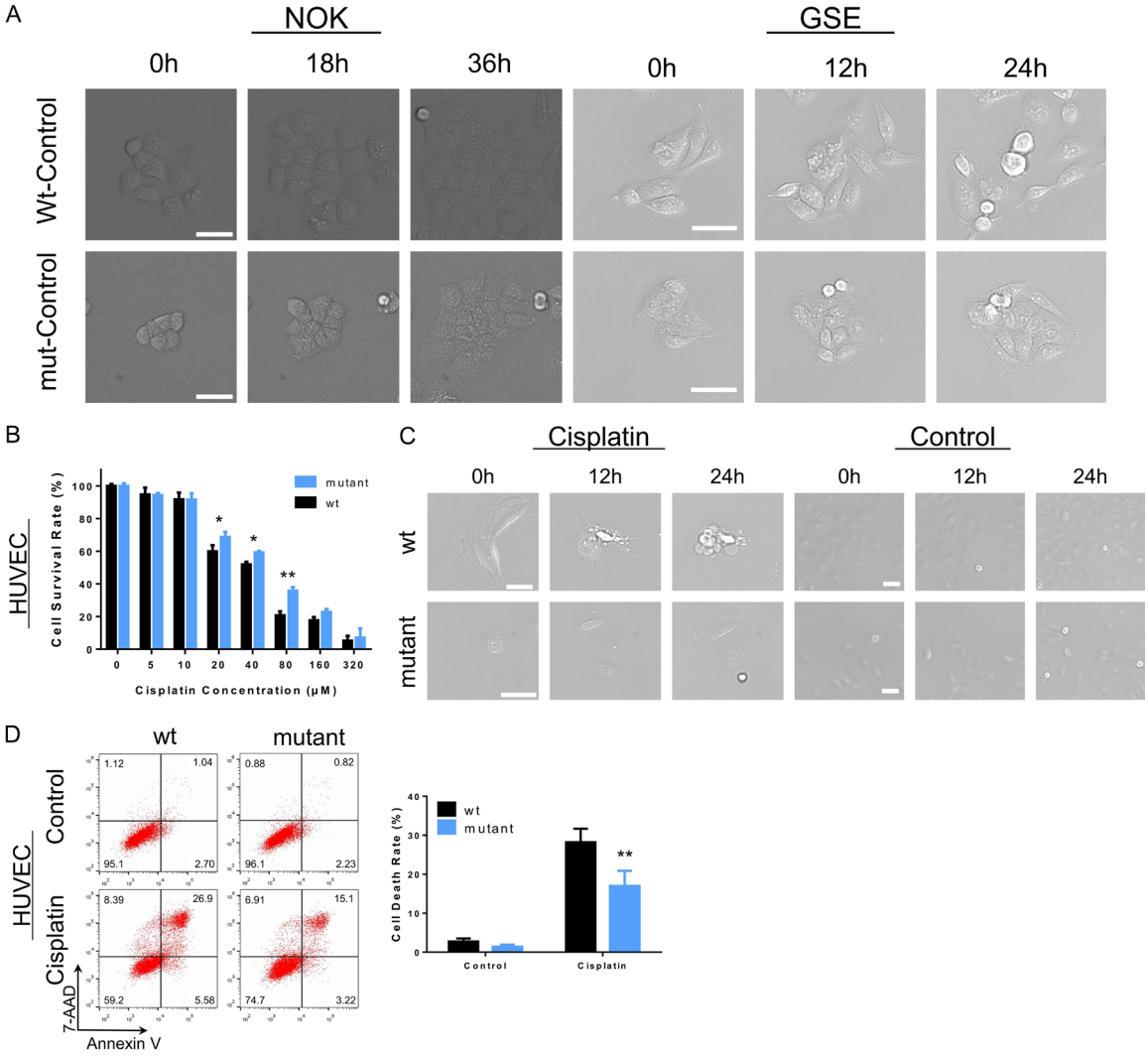

Figure S4. A. Microscope image of GSDME-wt and GSDME-mut cell lines of NOKs and GSEs during cisplatin treatments (control group, scale bar: 50 μm); B. Gradient concentration of cisplatin-treated GSDME-wt/mut HUVECs; the GSDME-mut cell line was more tolerant than the GSDME-wt ones; C. Microscope capture during the cell death process induced by cisplatin of HUVECs GSDME-wt/mutant cell lines (scale bar: 50 μm); D. FCM detected the cisplatin-tolerant effect on the GSDME-wt/mut HUVECs; under same concentration, cisplatin induced more cell death in the GSDME-wt group; (cisplatin treatment: 40 μM, 24 hours for B, C, and D).

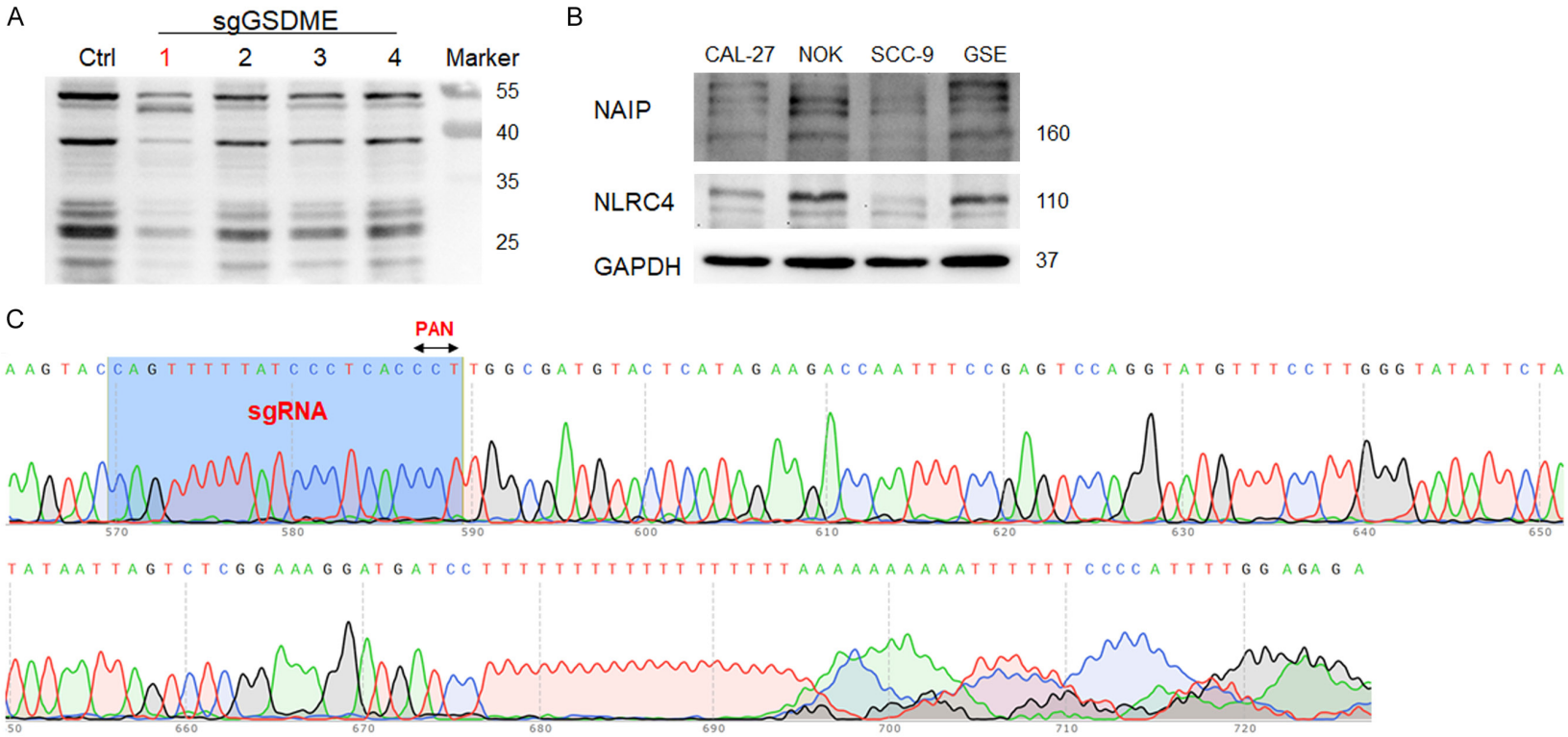

Figure S5. Construction and verification of GSDME knockout cell line. A. After transfecting px458-sgGSDME in NOKs, monoclonal immunoblot was used to detect the expression of GSDME, and clone 1 was selected for sequencing verification; B. Immunoblot detection of NAIP-NLRC4 expression in OSCC tumour cells and normal tissue cells and found that the expression of NAIP-NLRC4 in tumour cells was lower than that in normal tissue cells; C. DNA sequencing of sgGSDME cells; it was found that the sgRNA sequence was truncated, confirming the function of sgRNA.

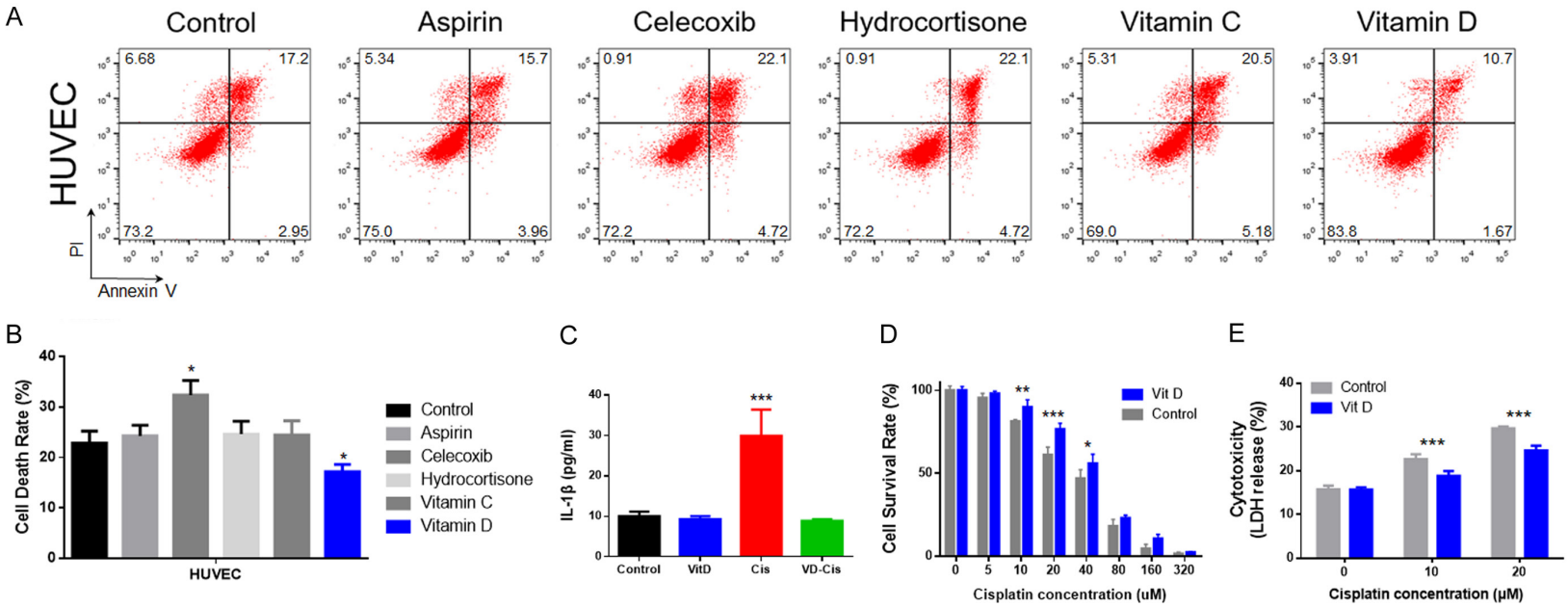

Figure S6. (A) FCM revealed cisplatin-induced cell death in HUVECs after pre-treatment with aspirin, celecoxib, hydrocortisone, vitamin C and vitamin D; (B) Statistical analysis of the cell death rates shown in (A); (C) ELISA revealed reduced IL-1β secretion in HUVECs pre-treated with vitamin D; (D) Gradient concentration of cisplatin-treated HUVECs pre-treated with vitamin D, which increased cisplatin tolerance; (E) Cytotoxicity assay revealed that LDH release was reduced in HUVECs pre-treated with vitamin D compared with control cells after cisplatin treatment. (cisplatin treatment: 40 μM, 24 hours for B-D).