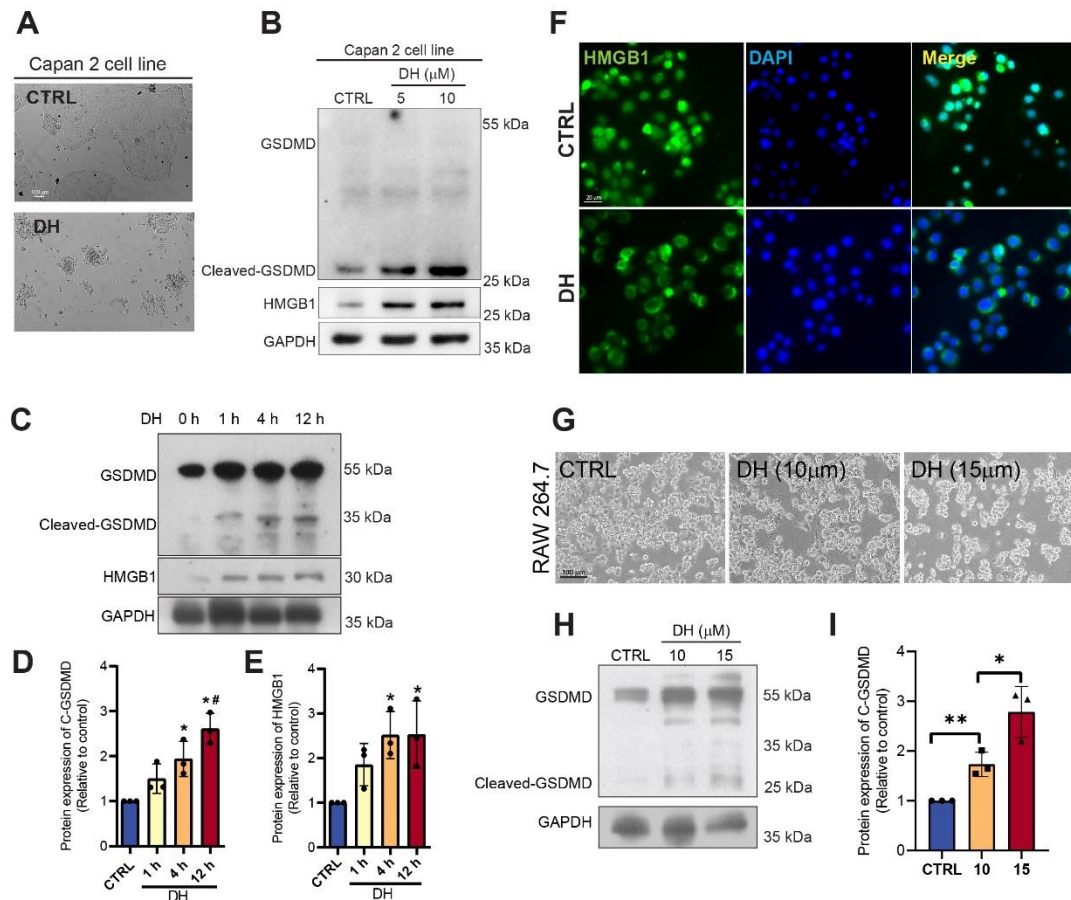
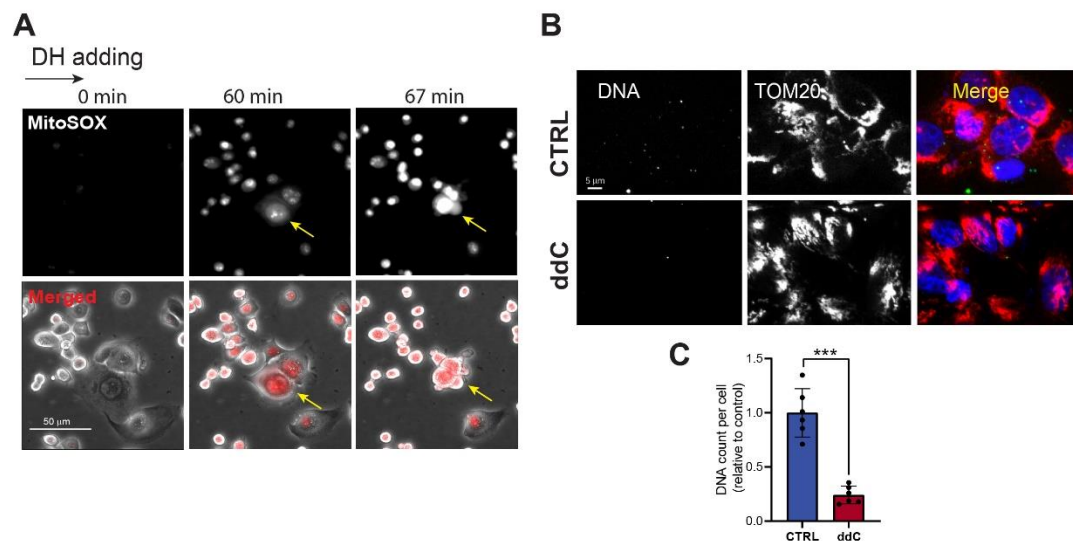


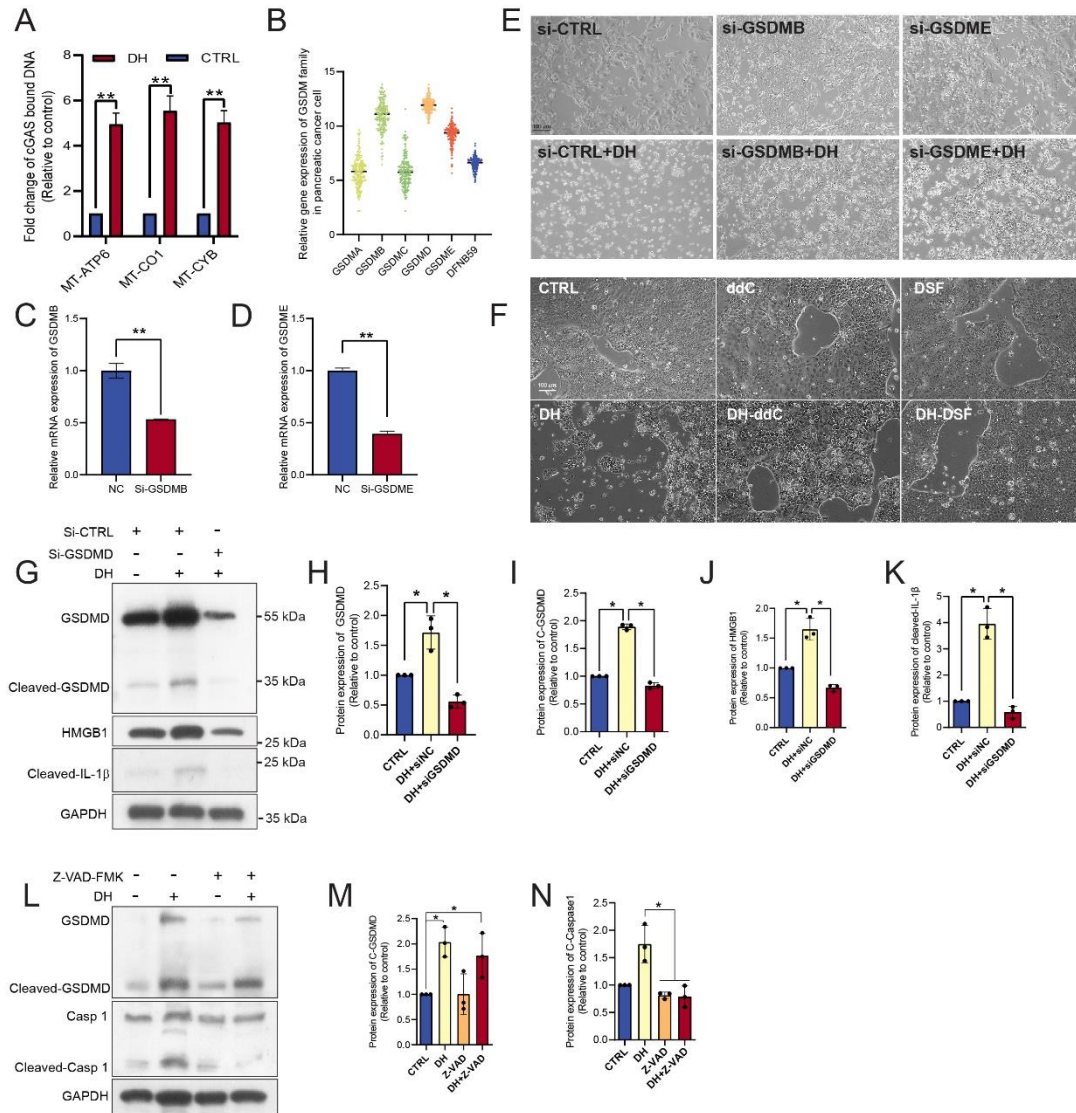
## Supplementary data



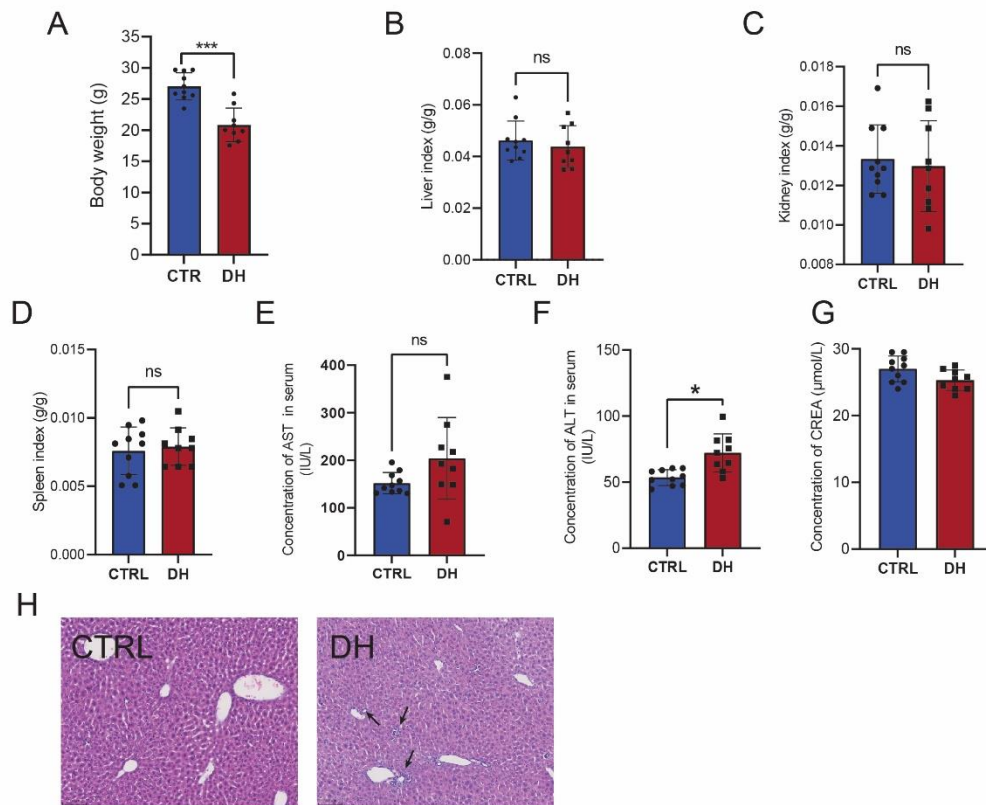
**Supplementary Figure 1.** **A.** Morphology observation of Capan 2 cell lines after treatment of vehicle or DH (10  $\mu$ M). **B.** Representative Western Blot images of pyroptosis-related proteins expression in Capan 2 cells after DH treatment. **C.** Representative Western Blot images of pyroptosis-related proteins expression in PANC 1 cells after DH treatment for different time points. **D-E.** Quantification of cleaved-GSDMD, HMGB1 protein expressions in **C**.  $n = 3$ . **F.** Representative fluorescent images of PANC1 cells with or without DH treatment (1 h). Scale bar, 20  $\mu$ m. Green, HMGB1; Blue, DAPI. **G.** Representative images of RAW 264.7 cells with or without DH treatment. Scale bar, 100  $\mu$ m. **H.** Representative Western Blot images of pyroptosis-related proteins in PANC1 cells after DH treatment or not. **I.** Quantification of cleaved-GSDMD protein expression in **G**. Data was shown as mean  $\pm$  SD. Unpaired t-test was used. \* $p < 0.05$ ; \*\* $p < 0.01$ .



**Supplementary Figure 2. A.** Representative time-lapse images of PANC1 cells after treating with DH. Cells were pretreated with MitoSox. Scale bar, 50  $\mu$ m. Red, MitoSox. **B.** Representative immunofluorescent images of PANC1 cells with or without ddC treatment. Scale bar, 5  $\mu$ m. **C.** Quantification of DNA positive staining area in images in B.  $n=6$ . Data was shown as mean  $\pm$  SD. Unpaired t-test was used. \*\*\*  $p < 0.001$ .



**Supplementary Figure 3.** **A.** Comparison of cGAS-bound mtDNA after DH treatment. *MT-ATP6*, *MT-CO1*, and *MT-CYB* are all mitochondrial genes. **B.** Comparison of gene expressions of GSDM family in pancreatic cancer in TCGA database. **C.** Comparison of gene expressions of GSDMB after transfecting GSDMB siRNA. *n*=3. **D.** Comparison of gene expressions of GSDME after transfecting GSDME siRNA. *n*=3. **E.** Representative images of cell morphology after silencing different GSDM genes and treatment of DH or not. **F.** Representative images of cell morphology after different treatment. **G.** Representative Western Blot images of pyroptosis-related proteins in PANC1 cells after silence GSDMD (oligo 2). **H-K.** Quantification of GSDMD, cleaved-GSDMD, HMGB1, and cleaved-IL-1 $\beta$  protein expressions in **G**. *n* = 3. **L.** Representative Western Blot images of pyroptosis-related proteins in PANC1 cells after different treatment. **M** and **N.** Quantification of cleaved-GSDMD and Caspase 1 protein expressions in **L**. Data was shown as mean  $\pm$  SD. Unpaired t-test was used. \*\* *p* < 0.01.

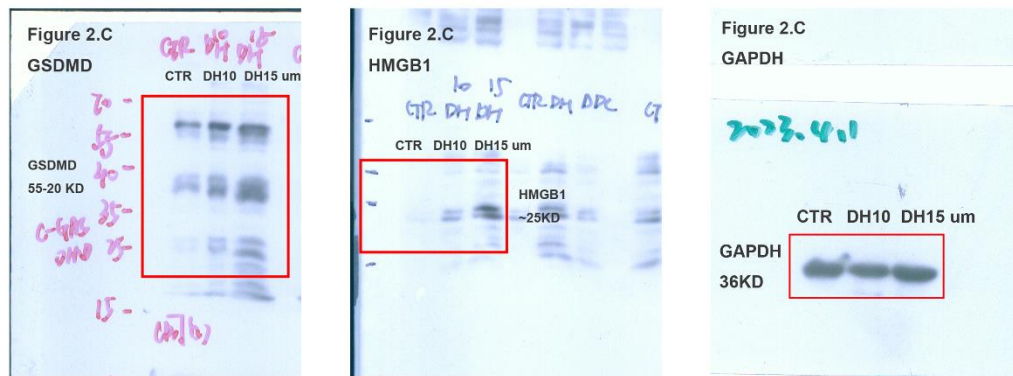


**Supplementary Figure 4. Organ weights and determination of liver or kidney function after DH treatment.** **A.** Body weight of nude mice after xenograft PANC-1 cells. Mice were administrated with DH or not.  $n=9$ . **B-D.** Organ indexes in nude mice with xenograft of PANC-1 cells after administration of DH or not. **B.** liver index ( $n=9$ ); **C.** kidney index ( $n=9,10$ ); **D.** spleen index ( $n=9,10$ ). **E-F.** Determination of AST or ALT concentrations in serum of nude mice with xenograft of PANC-1 cells after administration of DH or not. **E.** AST ( $n=9$ ); **F.** ALT ( $n=9,10$ ) **G.** Determination of CREA concentrations in serum of nude mice with xenograft of PANC-1 cells after administration of DH or not. ( $n=9,10$ ). **H.** HE staining of liver section from mice with or without DH treatment. Infiltration sites of Inflammatory cells (black arrow). Data was shown as mean  $\pm$  SD. Unpaired  $t$ -test was used. \*\*  $p < 0.01$ ; \*\*\*  $p < 0.001$ .

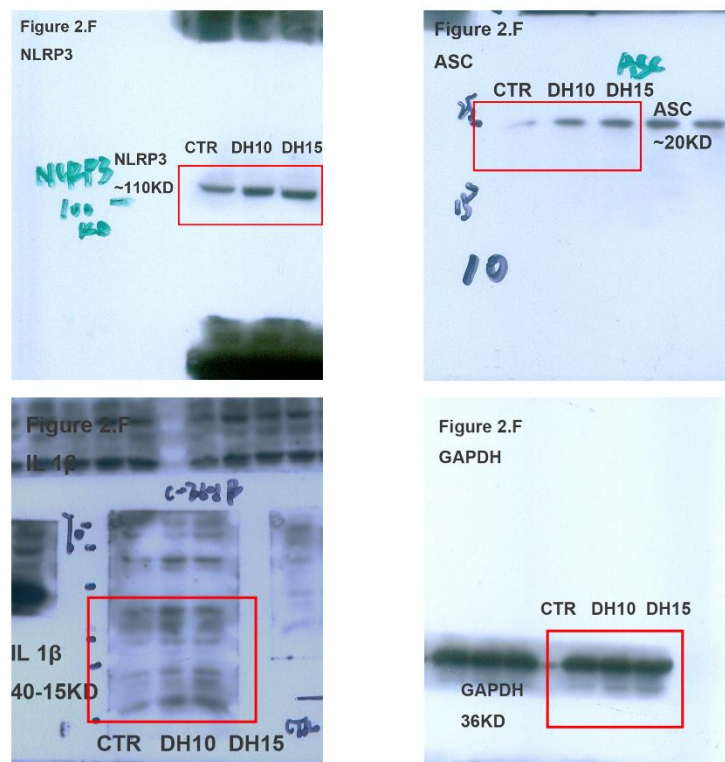
Supplementary Table 1. The sequences of primers (SYBR) for RT-qPCR

Gene	Sequences(5'-3')	
<i>18S</i>	F: 5'-TCTTCATTGACCAAGGAAATCGG-3'	R: 5'- TCCGGGGTGCATTATCTCTAC-3'
<i>MT-ATP6</i>	F: 5'- ACCACAAGGCACACCTACAC-3'	R: 5'- TATTGCTAGGGTGGCGCTTC-3'
<i>MT-CO1</i>	F: 5'- ATACCAAACGCCCTCTTCG-3'	R: 5'- TGTTGAGGTTGCGGTCTGTT-3'
<i>MT-CYB</i>	F: 5'- AGCCAACCCCTTAAACACCC-3'	R: 5'- TGTTAGGGACGGATCGGAGA-3'
<i>GSDMB</i>	F: 5'- GAAACTCTGGAGACGGTAAAGG-3'	R: 5'- GATAGCTCAGGACCCGATTTG-3'
<i>GSDME</i>	F: 5'- AACTCCAGATCATTCCCACAC-3'	R: 5'- CTGCACAATCCCAAACCTTTC-3'

**Fig2.C**

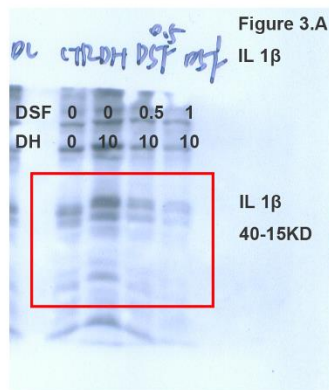
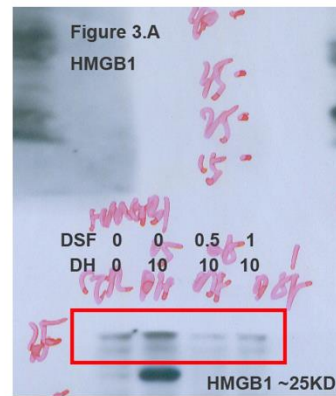


**Fig2.F**





**Fig3.A**



**Fig3.F**

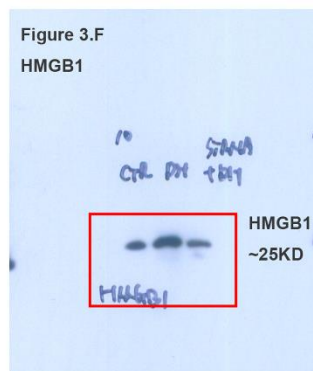


Fig5.C

Figure 5.C  
GSDMD

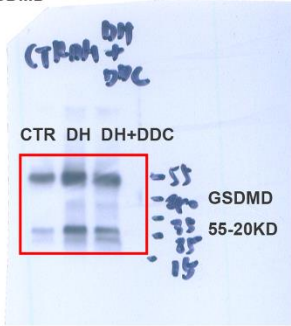


Figure 5.C  
GAPDH

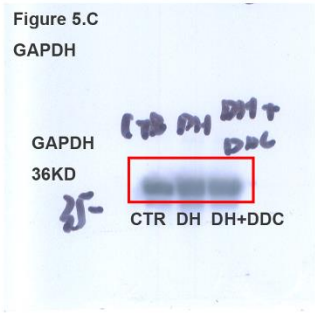


Figure 5.C  
IL 1 $\beta$



Figure 5.C  
HMGB1

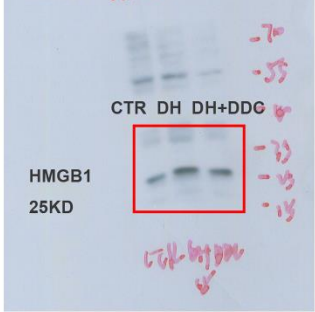


Figure 5.C  
GAPDH

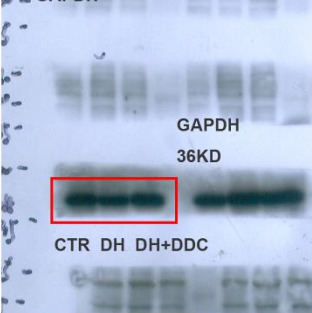




Fig6.C

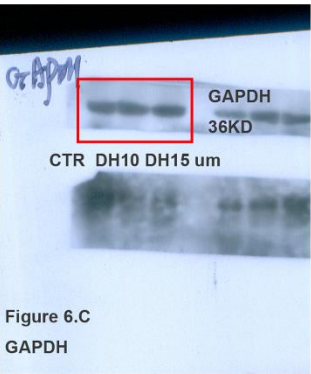
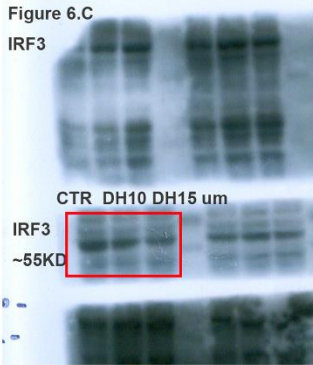
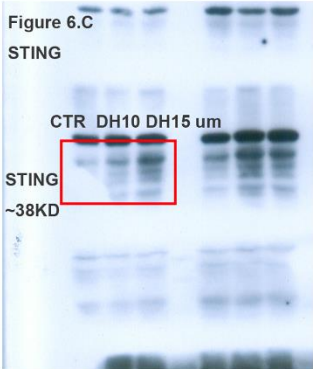
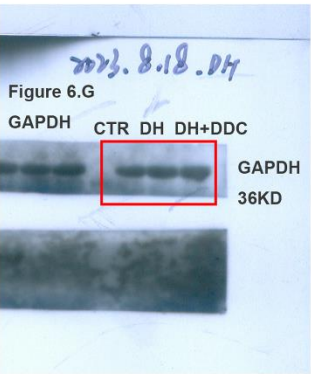
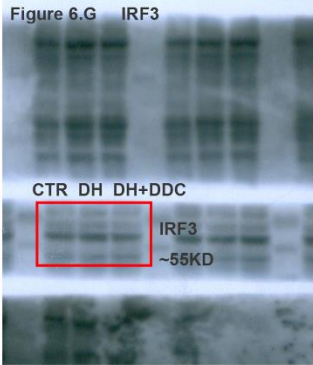
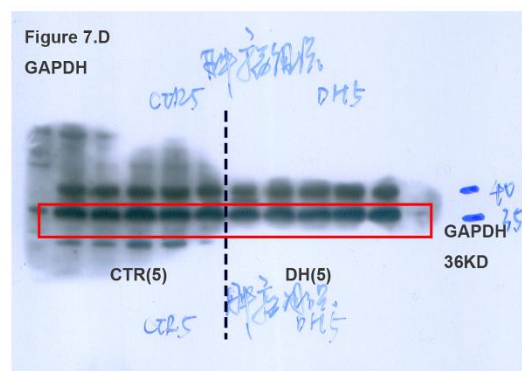
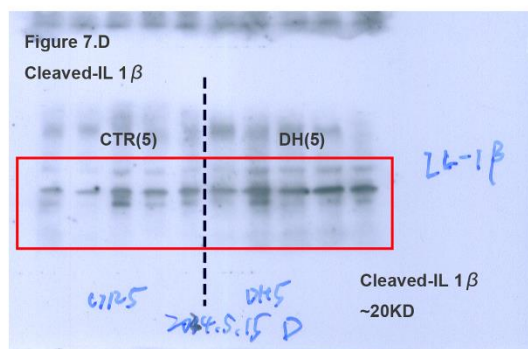
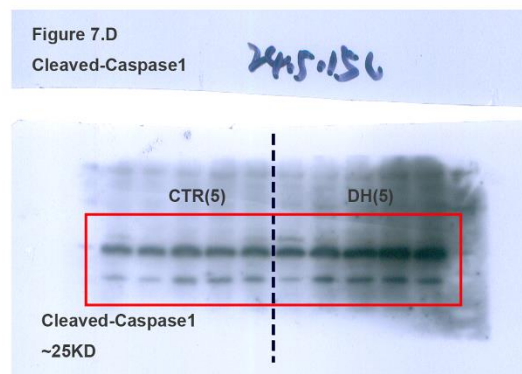
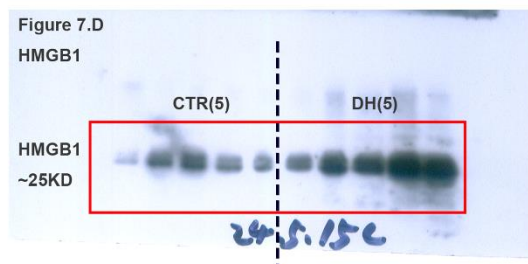
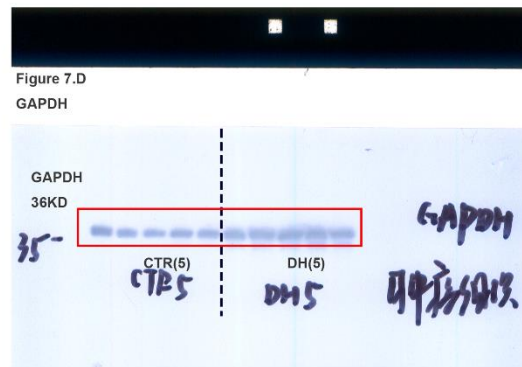
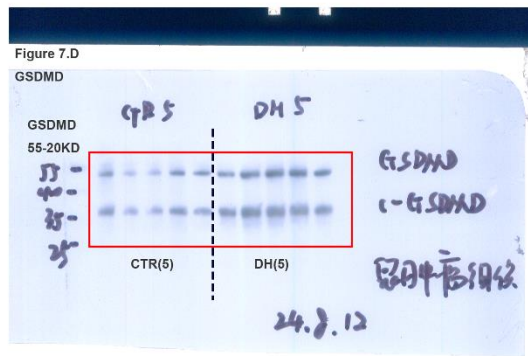


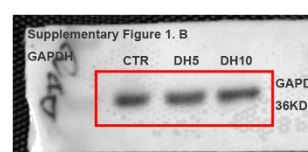
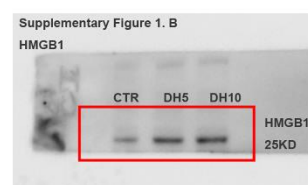
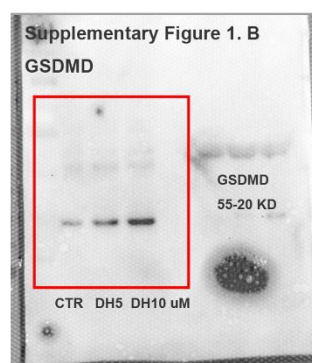
Fig6.G



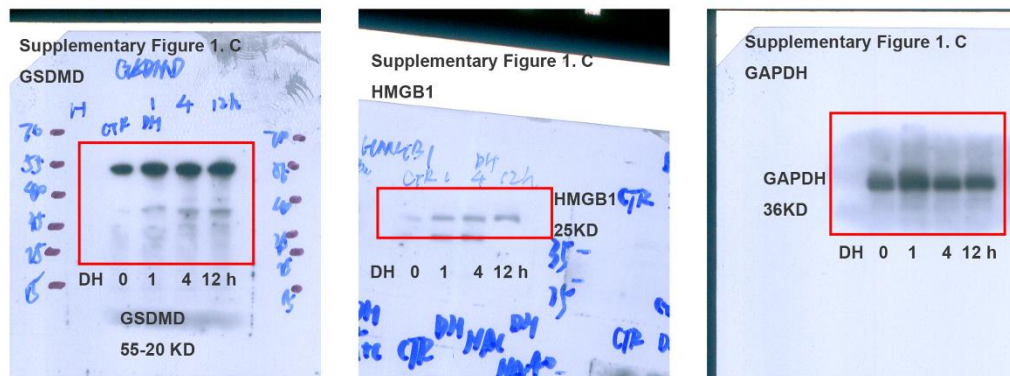
**Fig7.D**



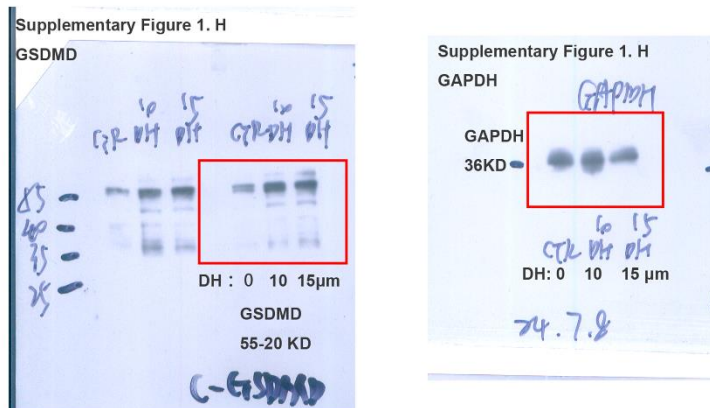
**SFig1.B**



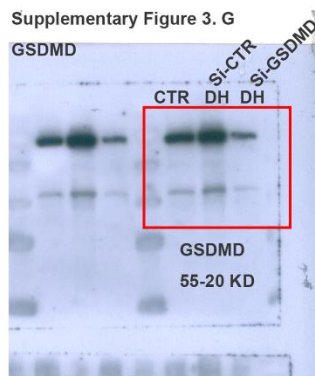
## SFig1.C



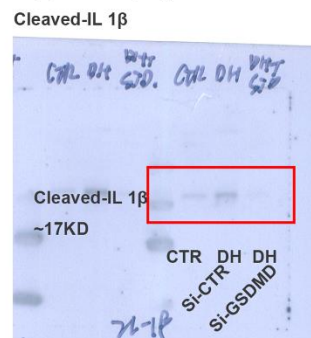
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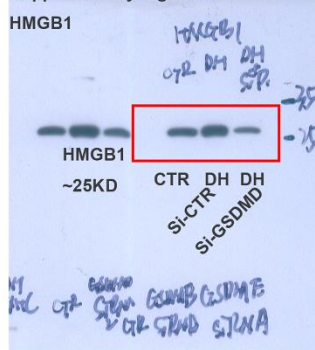
### SFig3.G



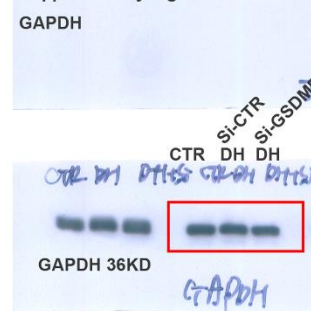
Supplementary Figure 3. G



Supplementary Figure 3. G



Supplementary Figure 3. G



### SFig3.L

