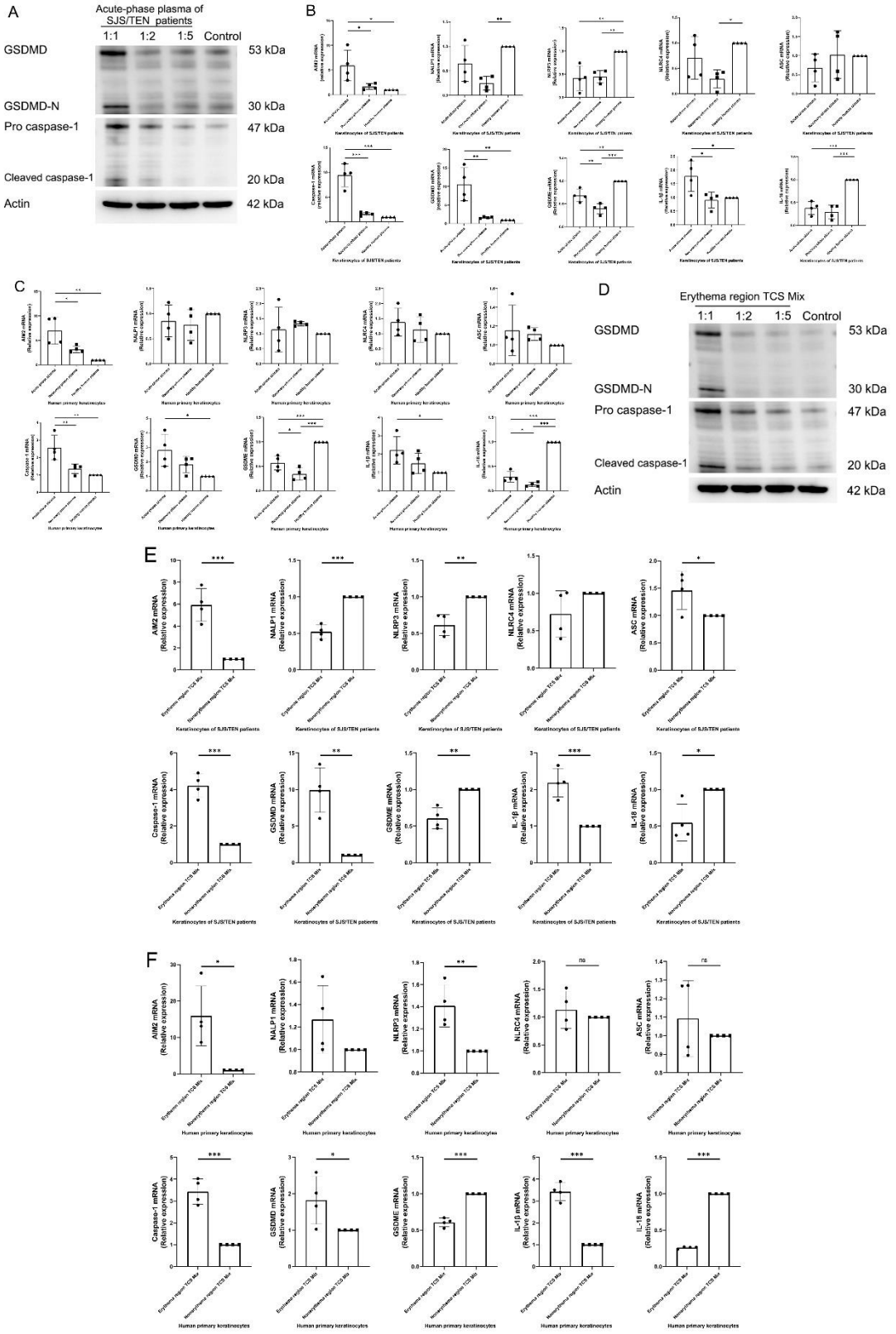


Fig. S1 Acute-phase plasma or TCS mix from erythematous lesions induce the expression of pyroptosis related genes in SJS/TEN keratinocytes but not in healthy human primary keratinocytes in vitro. A The acute-plasma was diluted with culture medium to achieve different concentrations and then was used as cell death stimulus. Protein levels of caspase-1 and GSDMD in SJS/TEN keratinocytes and healthy human primary keratinocytes stimulated by plasma (n=3 per group) were

quantified by western blotting. Actin was used as the loading control. B, C mRNA expression levels of NLRP1, AIM2, NLRP3, NLRC4, ASC, caspase-1, GSDMD, GSDME, IL-1β and IL-18 in SJS/TEN keratinocytes and healthy human primary keratinocytes stimulated by plasma (n=4 per group) were analyzed by qRT-PCR. Data were normalized to actin mRNA expression. D The TCS mix from SJS/TEN erythematous lesions was diluted with culture medium to achieve different concentrations and then was used as cell death stimulus. Protein levels of caspase-1 and GSDMD in SJS/TEN keratinocytes and healthy human primary keratinocytes stimulated by TCS mix (n=3 per group) were quantified by western blotting. Actin was used as the loading control. E, F mRNA expression levels of NALP1, AIM2, NLRP3, NLRC4, ASC, caspase-1, GSDMD, GSDME, IL-1β and IL-18 in SJS/TEN keratinocytes and healthy human primary keratinocytes stimulated by TCS mix (n=4 per group) were analyzed by qRT-PCR. Data were normalized to actin mRNA expression.

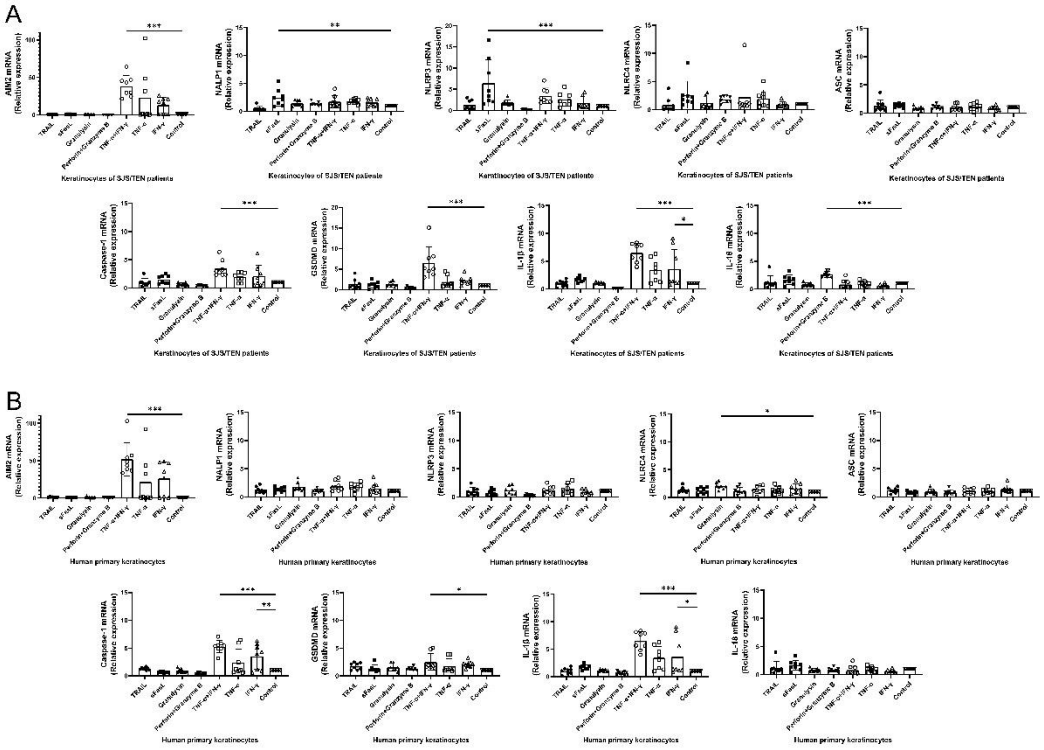


Fig. S2 The mRNA expression levels of AIM2, caspase-1, GSDMD and IL-1β were increased in keratinocytes stimulated by TNF-α combined with IFN-γ. A, B mRNA expression levels of NALP1, AIM2, NLRP3, NLRC4, ASC, caspase-1, GSDMD, IL-1β and IL-18 in SJS/TEN keratinocytes and healthy human primary keratinocytes stimulated by several soluble factors (n=8 per group) were analyzed by qRT-PCR. Data were normalized to actin mRNA expression.

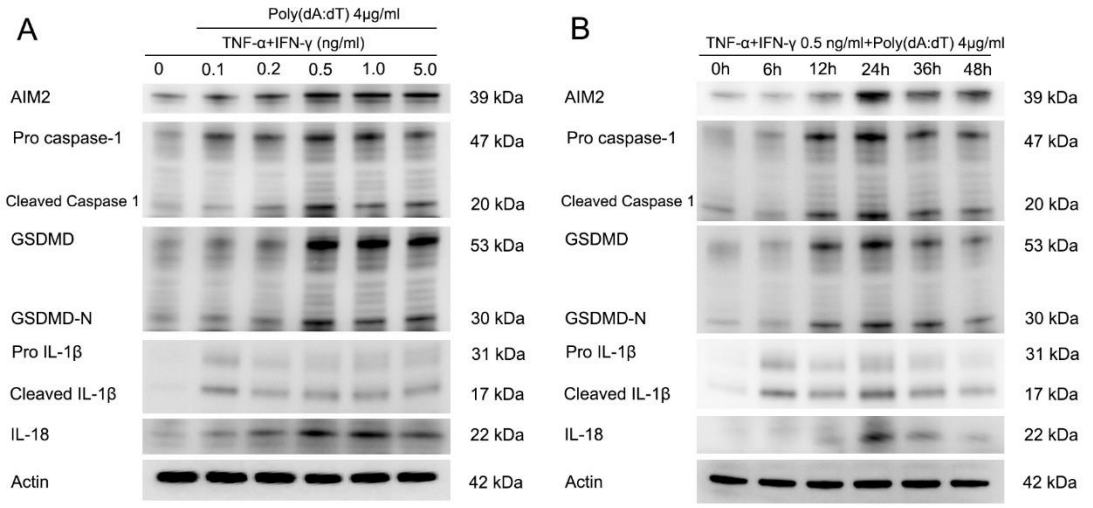


Fig. S3 Comparison of stimulation with different periods of time or various concentrations of TNF-α and IFN-γ in human primary keratinocytes. A Human primary keratinocytes treated with varying concentrations of TNF-α and IFN-γ for 24h, protein levels of caspase-1 and GSDMD were quantified by western blotting. Actin was used as the loading control. B Human primary keratinocytes treated with TNF-α combined with IFN-γ (0.5ng/mL) for various durations, protein levels of caspase-1 and GSDMD were quantified by western blotting. Actin was used as the loading control.

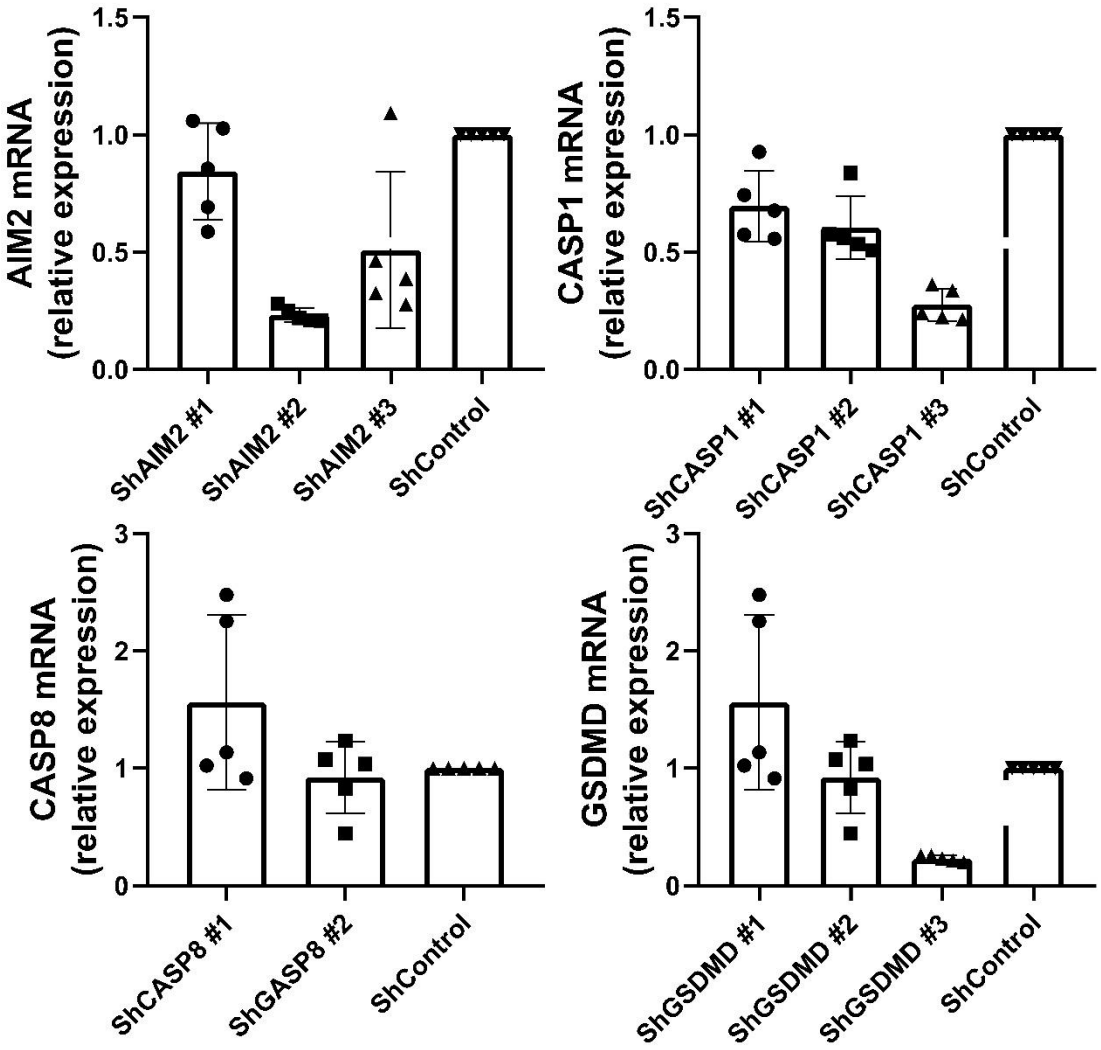


Fig. S4 Transfection efficiency for knock-down was determined via qRT-PCR. ShRNA knockdown efficiency was identified by detecting the levels of AIM2, caspase-1, caspase-8 and GSDMD mRNA through qRT-PCR (n=5 per group). Data were normalized to actin mRNA expression. For each gene, 2-3 shRNA sequences were designed, and the one had the highest knockdown efficiency (shAIM2#2/shCasp1#3/shGSDMD#3/shCasp8#2) was chosen for shRNA plasmid transfection.

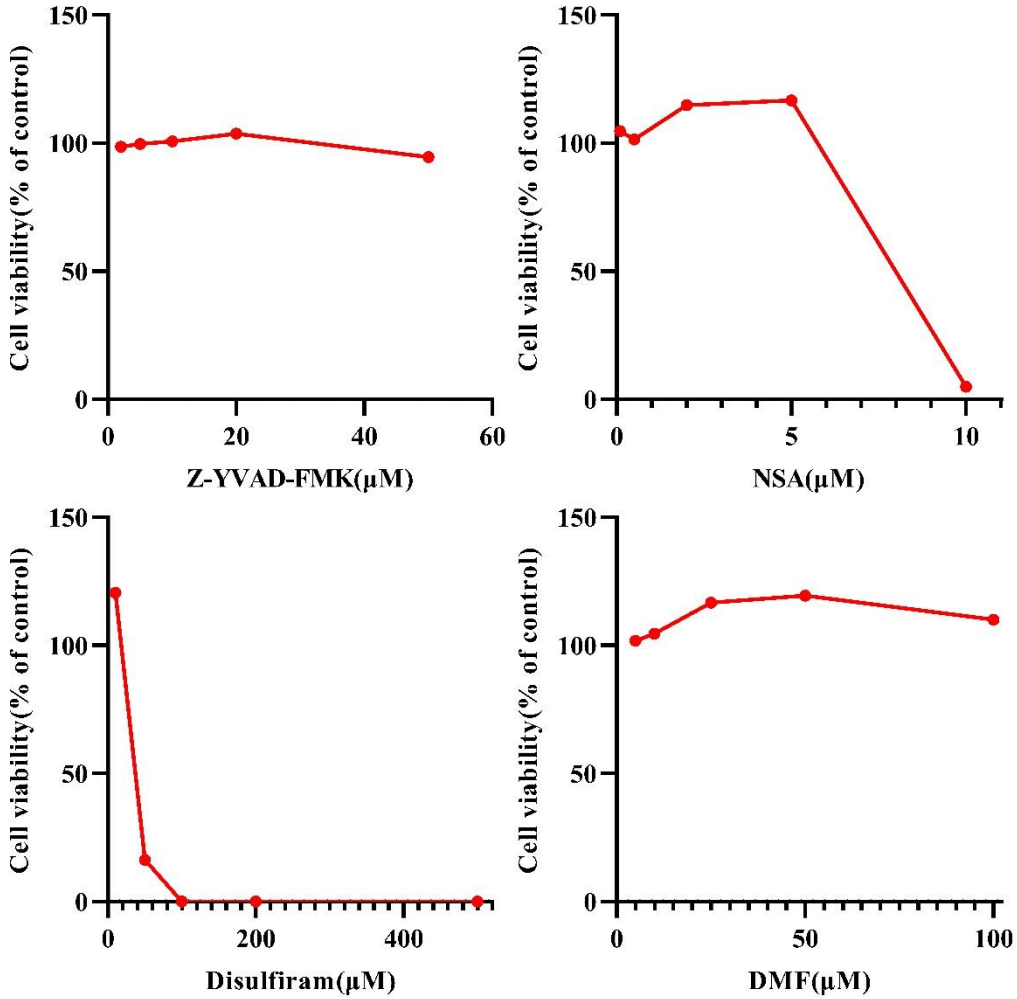


Fig. S5 Cell viability was evaluated in human primary keratinocytes treated with diverse concentrations of inhibitors Z-YVAD-FMK, NSA, disulfiram and DMF via Cell Counting Kit-8. The concentration range without any effect on cell viability was used for the inhibition of pyroptosis in human primary keratinocytes.

**Supplementary table 1. Primer sequences for real-time quantitative PCR.**

| | Forward 5'-3' | Reverse 5'-3' |
|---|---|---|
| Homo AIM2 | TCAAGCTGAAATGAGTCCTGC | CTTGGGTCTCAAACGTGAAGG |
| Homo NALP1 | CCACAACCCTCTGTCTACATTAC | GCCCCATCTAACCCATGCTTC |
| Homo NLRP3 | CGTGAGTCCCATTAAGATGGAGT | CCCGACAGTGGATATAGAACAGA |
| Homo NLRC4 | TGCCCAGAAATCGAAGCCC | GGCACCAAACTGCCGTATG |
| Homo ASC | TGGATGCTCTGTACGGGAAG | CCAGGCTGGTGTGAAACTGAA |
| Homo caspase 1 | TTTCCGCAAGGTTCGATTTTCA | GGCATCTGCGCTCTACCATC |
| Homo caspase 8 | AAAAGCAAACCTCGGGATAC | CCAAGTGTGTTCCATTCCTGTC |
| Homo GSDMD | GGACAGGCAAAGATCGCAG | CACTCAGCGAGTACACATTCATT |
| Homo GSDME | CCCAGGATGGACCATTAAGTGT | GGTTCCAGGACCATGAGTAGTT |
| Homo IL-1β | ATGATGGCTTATTACAGTGGCAA | GTCGGAGATTCGTAGCTGGA |
| Homo IL-18 | ACAGCTTCGGGAAGAGGAAAGGAA | TGTCTTCTACTGGTTCAGCAGCCA |
| Homo Actin | TCATGAAGTGTGACGTGGACATC | CAGGAGGAGCAATGATCTTGATCT |

**Supplementary table 2. The ShRNA sequences used for transfection.**

| Name | 5'-3' |
|---|---|
| AIM2 #1 | CCCGAAGATCAACACGCTTCA |
| AIM2 #2 | GGAACAATTGTGAATGGTTTG* |
| AIM2 #3 | GCAAACTACATACTGCAAA |
| CASP1 #1 | GAAGACTCATTGAACATAT |
| CASP1 #2 | AAGAGATCCTTCTGTAAAGGT |
| CASP1 #3 | CCAGATATACTACAACTCAAT* |
| GSDMD #1 | GTGTGTCAACCTGTCTATCAA |
| GSDMD #2 | CCTTCTCTTCCCGGATAAGAA |
| GSDMD #3 | GGAGACCATCTCCAAGGAACT* |
| CASP8 #1 | GGAACAACTGGACAGTGAAGA |
| CASP8 #2 | GGGTCATGCTCTATCAGATTT* |

*Used for subsequent experiments.