

## **SUPPLEMENTARY MATERIAL**

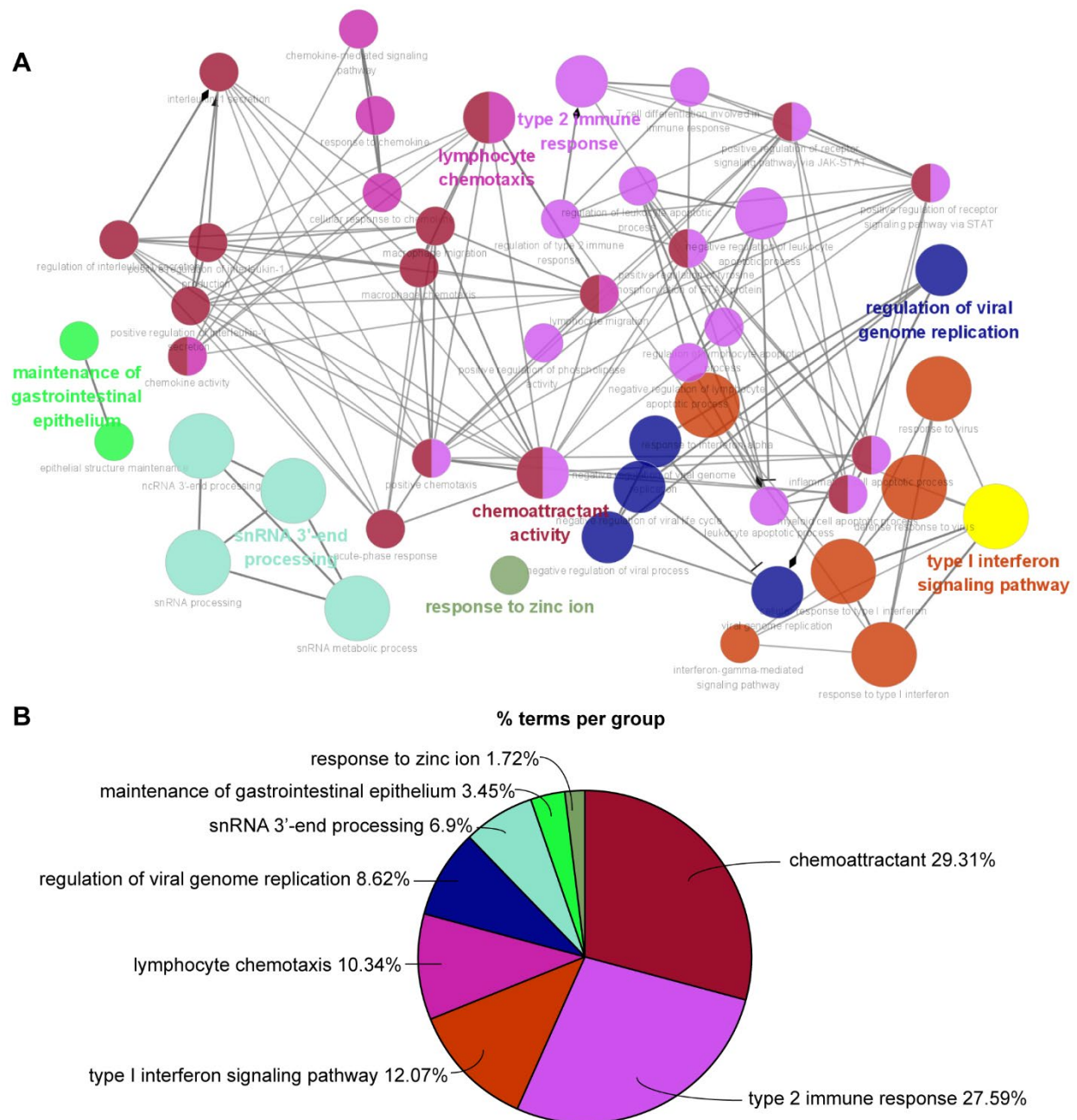
Figure S1. The GO analysis of RES pretreated samples with poly I:C transfection.

Figure S2. The GO analysis of HCT116 cells treated with OA.

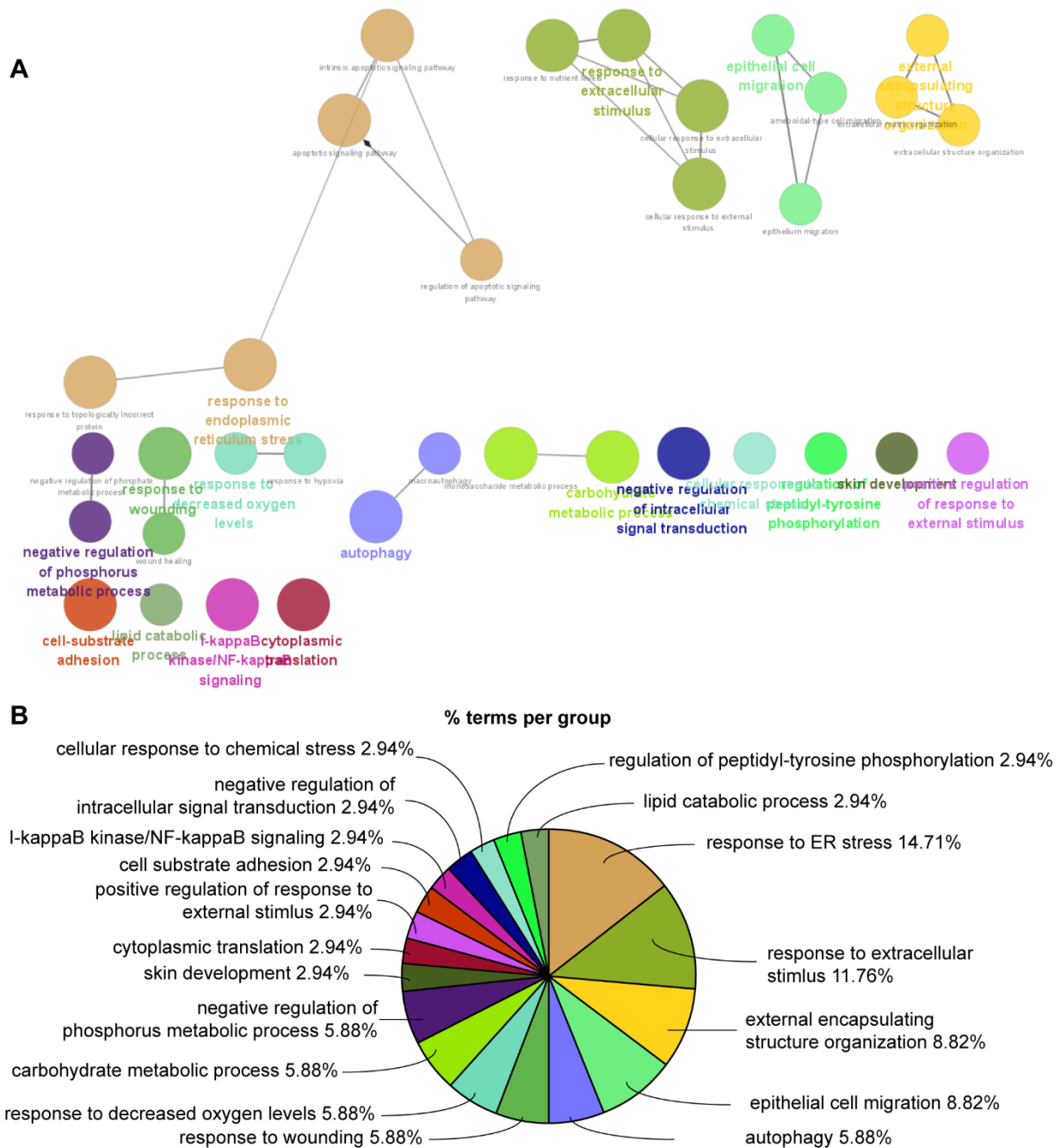
Figure S3. The TN treatment activates apoptotic and ER stress pathways.

Figure S4. The RES treatment does not rescue ER stress upon TN treatment.

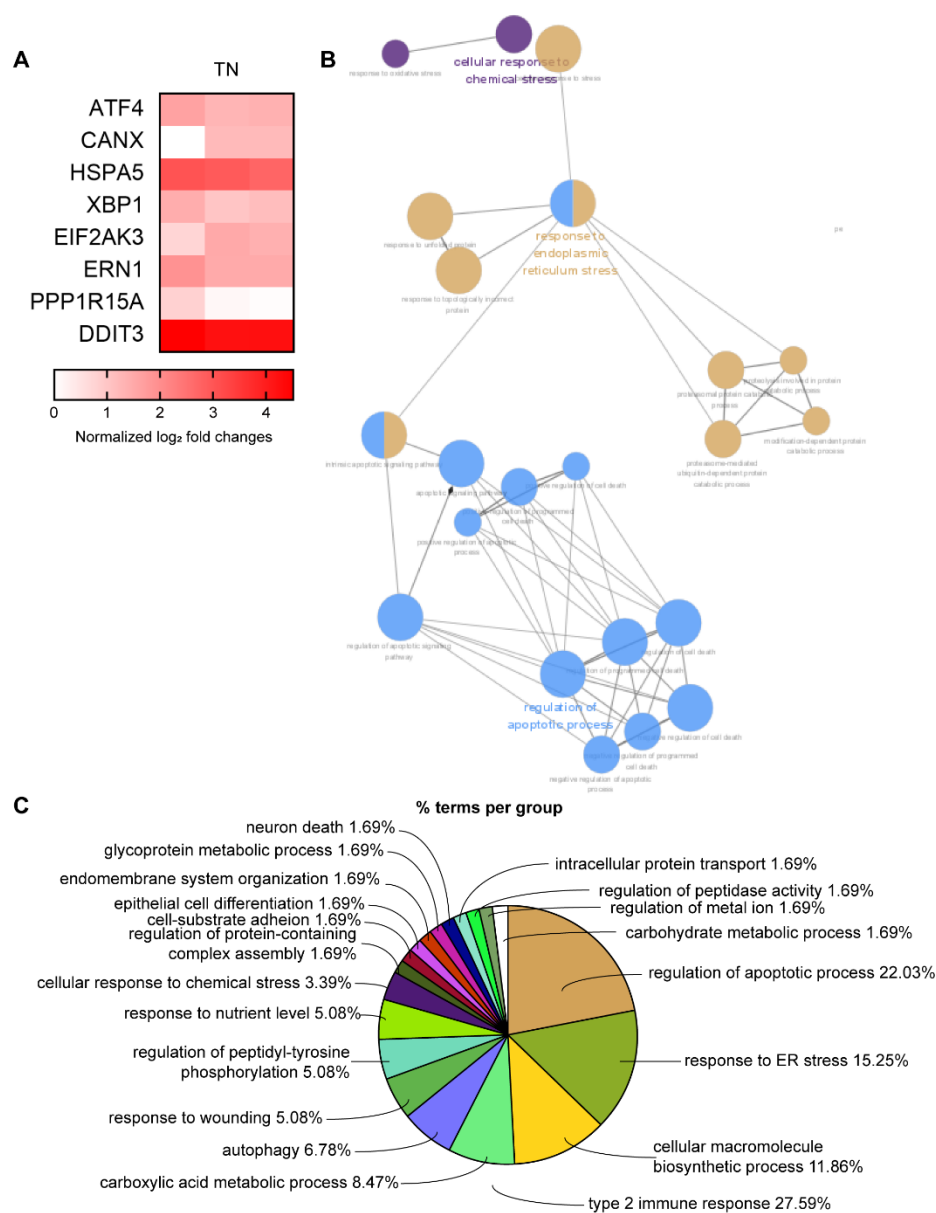
Table S1. Primer sequences for RT-qPCR.



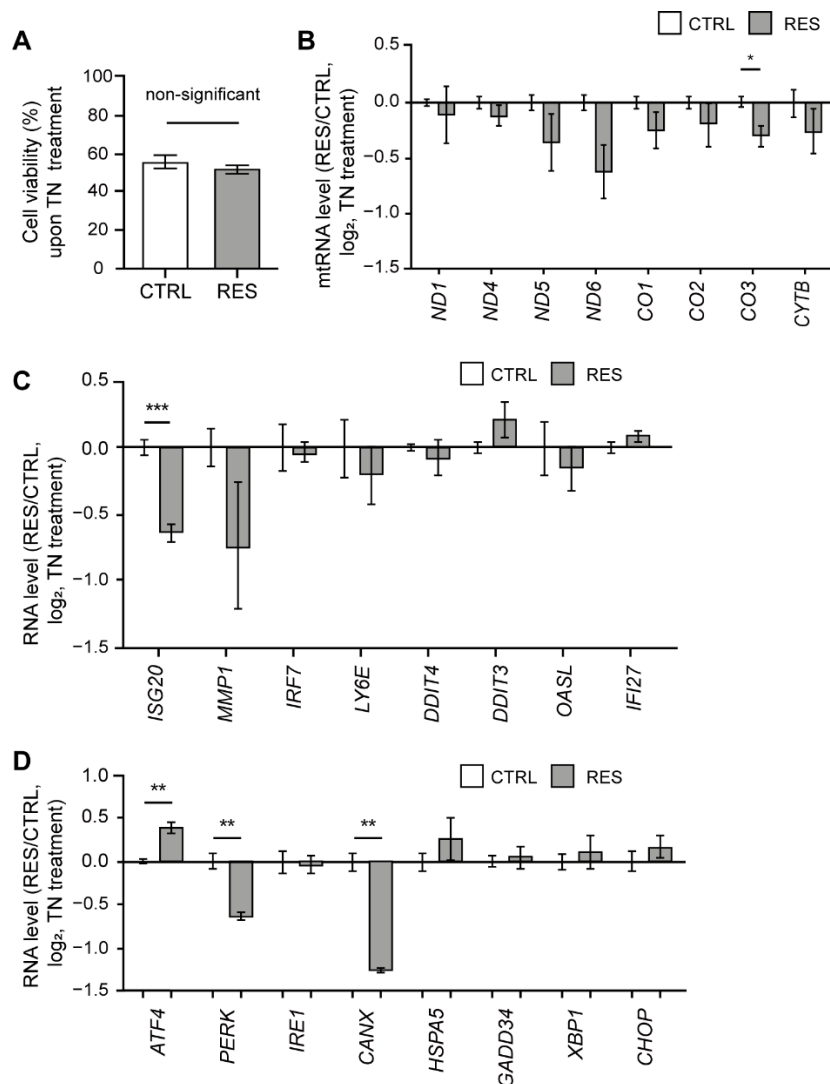
**Figure S1.** The GO analysis of RES pretreated samples with poly I:C transfection. (A) The GO of the top 200 genes whose log<sub>2</sub> fold change upon poly I:C transfection was rescued by RES-pretreatment in NS-SV-AC cells. (B) A pie chart showing the class of genes rescued by RES-pretreatment upon poly I:C transfection in RES-pretreated NS-SV-AC cells.



**Figure S2.** The GO analysis of HCT116 cells treated with OA. (A) The GO analysis of OA-treated samples. Genes whose log<sub>2</sub> fold change was upregulated over 0.585 and p-value less than 0.05 upon OA treatment were analyzed. (B) A pie chart showing the class of genes whose expression was upregulated by OA treatment.



**Figure S3.** The TN treatment activates apoptotic and ER stress pathways. (A) Heatmap of DEGs related to ER stress upon TN treatment. The color represents the log<sub>2</sub> fold change of genes normalized to DMSO-treated control. Each column represents a log<sub>2</sub> fold change of three biological replicates with TN treatment normalized by the average of control. (B) GO analysis of TN-treated samples. Genes whose log<sub>2</sub> fold change was upregulated over 0.585 and p-value less than 0.05 upon TN treatment were analyzed. (C) A pie chart showing the class of genes whose expression was upregulated by TN treatment.



**Figure S4.** The RES treatment does not rescue ER stress by TN treatment. (A) Cell viability upon TN treatment with or without RES treatment measured by SRB assay. (B-D) The ratios of mtRNAs (B), ISGs (C), and ER stress-related genes (D) in RES and TN co-treated cells compared to those in TN-only treated cells (control). For ratios, Cq values were first normalized to that of *ACTB* mRNA. For untreated samples, the values were normalized to those of control cells without TN treatment. Similarly, RNAs from cells co-treated with RES and TN were normalized separately using RNAs from cells treated with TN only. Unless mentioned otherwise, three independent experiments were carried out, and error bars denote s.e.m. All statistical significances were calculated using one-tailed Student's t-tests, \* $p \leq 0.05$ , \*\* $p \leq 0.01$ , and \*\*\* $p \leq 0.001$ .

**Table S1.** Primer sequences for RT-qPCR.

| <b>Gene</b>           | <b>Forward Primer (5'-3')</b> | <b>Reverse Primer (5'-3')</b>                  |
|-----------------------|-------------------------------|--|
| ND1                   | TCAAACCTCAAACCTACGCCCTG       | GTTGTGATAAGGGTGGAGAGG                          |
| ND4                   | CTCACACTCATTCTCAACCCC         | TGTTTGTCGTAGGCAGATGG                           |
| ND5                   | CTAGGCCTTCTTACGAGCC           | CGCAAATGGGCGGTAGGCGTGT<br>TTGGGTTGAGGTGATGATG  |
| ND6                   | TGCTGTGGGTGAAAGAGTATG         | CGCAAATGGGCGGTAGGCGTGC<br>CCATAATCATACAAAGCCCC |
| CO1                   | GCCATAACCCAATACCAAACG         | TTGAGGTTGCGGTCTGTTAG                           |
| CO2                   | CTAGTCCTGTATGCCCTTTTCC        | GTAAAGGATGCGTAGGGATGG                          |
| CO3                   | CCTTTTACCACTCCAGCCTAG         | CTCCTGATGCGAGTAATACGG                          |
| CYTB                  | CAATTATACCCTAGCCAACCCC        | GGATAGTAATAGGGCAAGGACG                         |
| IRF7                  | CTGTGGACACCTGTGACACC          | TGCCCTCTCAGGAGCCAA                             |
| IFI27                 | ATCAGCAGTGACCAGTGTGG          | ATCAGCAGTGACCAGTGTGG                           |
| STAT1                 | AACCTCGACAGTCTTGGCAC          | CACTGAGACATCCTGCCACC                           |
| IFIT3                 | GAAGGAACTGGGCCGCTGCTAAG       | GCCCTGGCCCATTTCCTCACTACC                       |
| I $\kappa$ B $\alpha$ | CTCCGAGACTTTCGAGGAAATAC       | GCCATTGTAGTTGGTAGCCTTCA                        |
| MX1                   | TTCTGGGTTCGGAGGCTACAG         | TGGATGGCGGCGTTCT                               |
| IRF3                  | ACACATACTGGGCAGTGAGC          | CTACAATGAAGGGCCCCAGG                           |
| IFI44                 | CTGATTACAAAAGAAGACATGACAGAC   | AGGCAAAACCAAAGACTCCA                           |
| ISG20                 | GGTGCTGTGCTGTACGACAA          | GAGCTGCAGGATCTCTAGCC                           |
| MMP1                  | AGAAAGAAGACAAAGGCAAGTTGA      | TTCCCAGTCACTTTCAGCCC                           |
| LY6E                  | CTCCAGGCAGGACGGCCATC          | CGAGATTCCCAATGCCGGCACT                         |
| OASL                  | GCGGAGCCCATCACGGTCAC          | AGGACCACCGCAGGCCTTGA                           |
| DDIT3<br>(CHOP)       | GTTCCAGCCACTCCCCATTA          | GTCCCGAAGGAGAAAGGCAA                           |
| DDIT4                 | AACTTGTGTGCCAACCTGA           | CAGGCGCAGTAGTTCTTTGC                           |
| ATF4                  | AGTTCGACTTGGATGCCCTG          | CCAACGTGGTCAGAAGGTCA                           |
| PERK                  | TGATGTTGTTTTGGTTGGAGGA        | TCGTCACTATCCCATTGGCG                           |
| IRE1                  | CAGCAGACTTTGTCATCGGC          | CTCTCGGGTTTTGGTGTCGT                           |
| CANX                  | AGCCAAGAAAGACGATACCGA         | GAGATGGCATGATGCTTGGC                           |
| HSPA5                 | CACTCCTGAAGGGGAACGTC          | TCAAAGACCGTGTTCTCGGG                           |

|        |                       |                      |
|--------|-----------------------|----------------------|
| GADD34 | CTGGCTGGTGGGAAGCAGTAA | TATGGGGGATTGCCAGAGGA |
| XBP1   | AAGTTCTGCTTCTGTCGGGG  | CTGGGCTGGCACCATGAG   |
| ACTB   | CCTGTACGCCAACACAGTGC  | ATACTCCTGCTTGCTGATCC |