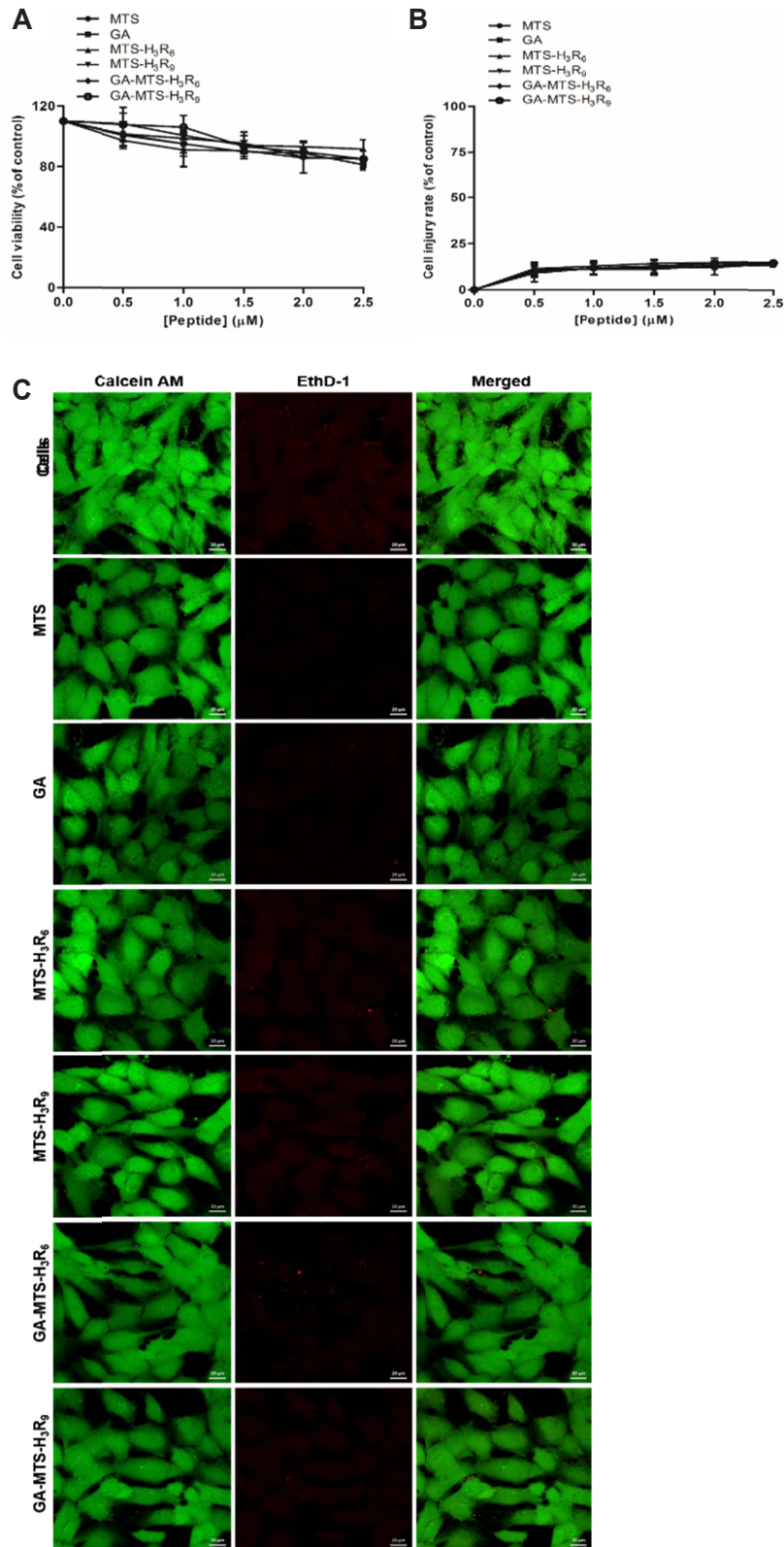


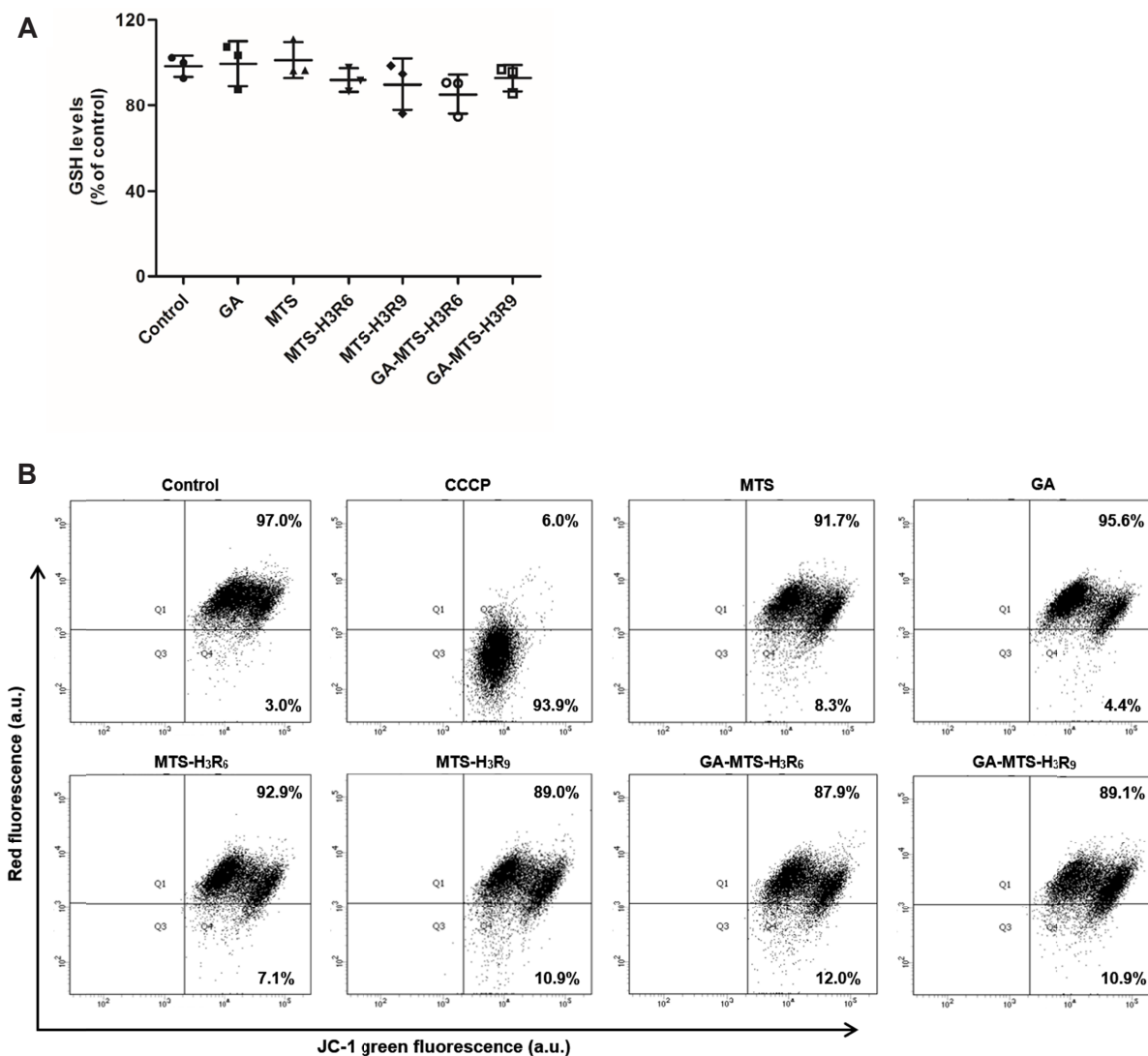
Supplementary Table 1. Molecular weight and full sequence information of synthesized MTS peptides

| Peptide name | Sequence | MS expected | MS found |
|---|---|-------------|----------|
| K (gallic acid) | K (gallic acid) | 298.3 | 297.9 |
| MTS | MLSLRQSIRFFKPATRTLCSRYLL-NH ₂ | 2,987.6 | 2,988 |
| MTS-H ₃ R ₆ | MLSLRQSIRFFKPATRTLCSRYLLHHHRRRRRRR-NH ₂ | 4,336.1 | 4,335 |
| MTS-H ₃ R ₉ | MLSLRQSIRFFKPATRTLCSRYLLHHHRRRRRRRRR-NH ₂ | 4,804.7 | 4,805 |
| GA-MTS-H ₃ R ₆ | Gallic acidKMLSLRQSIRFFKPATRTLCSRYLLHHHRRRRRRR-NH ₂ | 4,616.4 | 4,616 |
| GA-MTS-H ₃ R ₉ | Gallic acidKMLSLRQSIRFFKPATRTLCSRYLLHHHRRRRRRRRR-NH ₂ | 5,085.0 | 5,085 |
| FITC-K (gallic acid) | FITC-aca-K (gallic acid) | 800.9 | 800.3 |
| FITC-MTS | FITC-aca-MLSLRQSIRFFKPATRTLCSRYLL-NH ₂ | 3,490.2 | 3,490 |
| FITC-MTS-H ₃ R ₆ | FITC-aca-MLSLRQSIRFFKPATRTLCSRYLLHHHRRRRRRR-NH ₂ | 4,838.0 | 4,838 |
| FITC-MTS-H ₃ R ₉ | FITC-aca-MLSLRQSIRFFKPATRTLCSRYLLHHHRRRRRRRRR-NH ₂ | 5,307.2 | 5,307 |
| FITC-GA-MTS-H ₃ R ₆ | FITC-aca-K(gallic acid)MLSLRQSIRFFKPATRTLCSRYLLHHHRRRRRRR-NH ₂ | 5,119.0 | 5,119 |
| FITC-GA-MTS-H ₃ R ₉ | FITC-aca-K(gallic acid)MLSLRQSIRFFKPATRTLCSRYLLHHHRRRRRRRRR-NH ₂ | 5,587.5 | 5,586 |

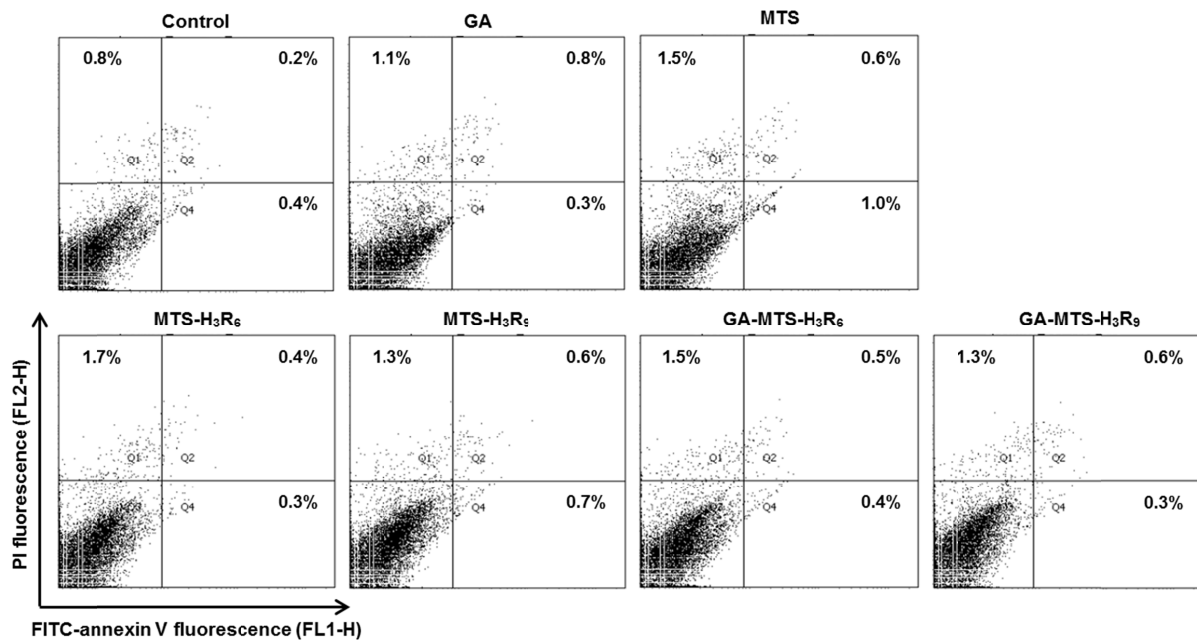
MTS, mitochondria targeting sequence; GA, gallic acid; MTS, mitochondria targeting sequence.



Supplementary Fig. 1. Cell viability was evaluated using WST-1 and LDH assay. (A) and (B) AC16 cells were exposed to various concentrations of GA, MTS, MTS-H₃R₆, MTS-H₃R₉, GA-MTS-H₃R₆, and GA-MTS-H₃R₉ up to 2.5 μM for 24 h. Panel (A) presents the results of the WST-1 assay and Panel (B) presents the results of LDH assay. (C) AC16 cells were the same conditions as those panel (A). The Cell viability was analyzed Live/dead assay with calcein AM (green) and EthD-1 (red). The cell fluorescence images were analyzed by confocal microscopy. Scale bar is 20 μm . Data are indicated as the mean \pm SD (n = 3) of three independent experiments. LDH, lactate dehydrogenase; GA, gallic acid; MTS, mitochondria targeting sequence; calcein AM, calcein acetoxyethyl ester; EthD-1, ethidium homodimer-1.



Supplementary Fig. 2. ROS levels and mitochondrial membrane potential (MMP) with GA-MTS-H₃R₉. (A) AC16 cells were exposed to 1 μ M GA, MTS, MTS-H₃R₆, MTS-H₃R₉, GA-MTS-H₃R₆, and GA-MTS-H₃R₉ for 16 h. Intracellular ROS levels were assessed by GSH assay. (B) AC16 cells were treated using the same conditions as those in panel (A). The cells were added to 2 μ M JC-1 and then incubated for 20 min. MMP was determined by flow cytometry analysis. Data are indicated as the mean \pm SD ($n = 3$) of three independent experiments. ROS, reactive oxygen species; GA, gallic acid; GSH, glutathione; MTS, mitochondria targeting sequence; CCCP, carbonyl cyanide 3-chlorophenylhydrazone.



Supplementary Fig. 3. Apoptosis by GA-MTS-H₃R₉. AC16 cells were exposed to 1 μ M GA, MTS, MTS-H₃R₆, MTS-H₃R₉, GA-MTS-H₃R₆, and GA-MTS-H₃R₉ for 24 h. Apoptosis levels for each group were measured by flow cytometry analysis after annexin V staining. Q1 shows necrotic cells. Q2 shows late apoptotic cells, Q3 shows intact cells, and Q4 shows early apoptotic cells. GA, gallic acid; MTS, mitochondria targeting sequence.