**** **Supplementary Figure 1 |** (a) Western blot analysis of BiP, cleaved/total caspase 3, RIP and GSDMD using β-actin as the loading control in SgNC and SgDDRGK1 ATDC5 chondrocytes treated with Tg for 24 h. (b) Quantification of the IOD/Area ratio of Alcian blue staining in cells shown in Figure 2F using the Image Pro Plus 6.0 software. (c) Quantification of the IOD/Area ratio of Alcian blue staining in the pellets shown in Figure 2G using the Image Pro Plus 6.0 software. (d) Quantification of the IOD of Safranin O-Fast green staining in the pellets shown in Figure 2H using the Image Pro Plus 6.0 software. All data are presented as the mean ± SD. \*P < 0.05, \*\*P < 0.01, \*\*\*P < 0.001 and \*\*\*\*P < 0.0001.

**** **Supplementary Figure 2 |** (a) Quantification of the IOD/Area ratio of Alcian blue staining in cells shown in Figure 2A using the Image Pro Plus 6.0 software. (b) Cell viability of O/E-C and O/E ATDC5 chondrocytes 24, 48, 72 and 96 h after incubation. (c) Western blot analysis of IRE1α, BiP, CHOP, cleaved/total caspase 3 ratio, cleaved/total PARP ratio and DDRGK1 expression using β-actin as the loading control in SgNC and SgDDRGK1 ATDC5 chondrocytes after treatment with thapsigargin for 24 h. (d) Flow cytometry analysis of O/E-C and O/E ATDC5 chondrocytes 24 h after treatment with or without thapsigargin (6.25 nM).

**** **Supplementary Figure 3 |** (a) Co-immunoprecipitation analysis of the possible interaction between Flag-IRE1α and UFM1 using Flag-tagged beads in 293T cells. (b) Co-immunoprecipitation analysis of the potential interaction between HA-UFM1 and IRE1α using HA-tagged beads in 293T cells. (c) Co-immunoprecipitation analysis of the possible interaction between Flag-IRE1α and UFM1 using Flag-tagged beads in SgNC and SgDDRGK1 ATDC5 chondrocytes. (d) Co-Immunoprecipitation analysis of the possible interaction between HA-UFM1 and IRE1α using HA-tagged beads in SgNC and SgDDRGK1 ATDC5 chondrocytes.

**** **Supplementary Figure 4 |** (a-h) Reverse transcription-quantitative PCR analysis of the relative mRNA expression levels of DDRGK1, IRE1α, BiP, CHOP, Bax, Bcl-2, Col2a1 and SOX9 using β-actin as the internal reference in SgNC and SgDDRGK1 ATDC5 chondrocytes treated with thapsigargin for 24 h. (g) Immunofluorescence analysis of IRE1α and CHOP expression in the pellet culture of SgNC and SgDDRGK1 ATDC5 chondrocytes 21 days after culture in chondrogenesis medium.