ESM methods

Materials. Tunicamycin (TM) and thapsigargin (TG) were purchased from Sigma-aldrich (St. Louis, MO). Tauroursodeoxycholic acid (TUDCA), 4-Phenylbutyrate (PBA) and Cucurbitacin I were obtained from EMD Chemicals (Gibbstown, NJ, USA). Antibodies against ICAM-1, TNF-α, VEGF, ATF4 and C/EBP homologous protein (CHOP) were purchased from Santa Cruz Biotechnology (Santa Cruz, CA, USA). Antibodies against phosphorylated and total RNA-dependent protein kinase-like ER kinase (PERK), eukaryotic translation initiation factor-2α (eIF-2α) and STAT3 were obtained from Cell signaling Technology (Boston, MA, USA). Anti-GRP78 and anti-β-actin antibodies were obtained from Abcam Inc. (Cambridge, MA, USA). FITC-conjugated or HRP-conjugated secondary antibodies, and DAPI were purchased from Jackson Immunoresearch Laboratories (West Grove, PA, USA) and Vector laboratories (Bulingame, CA, USA), respectively.

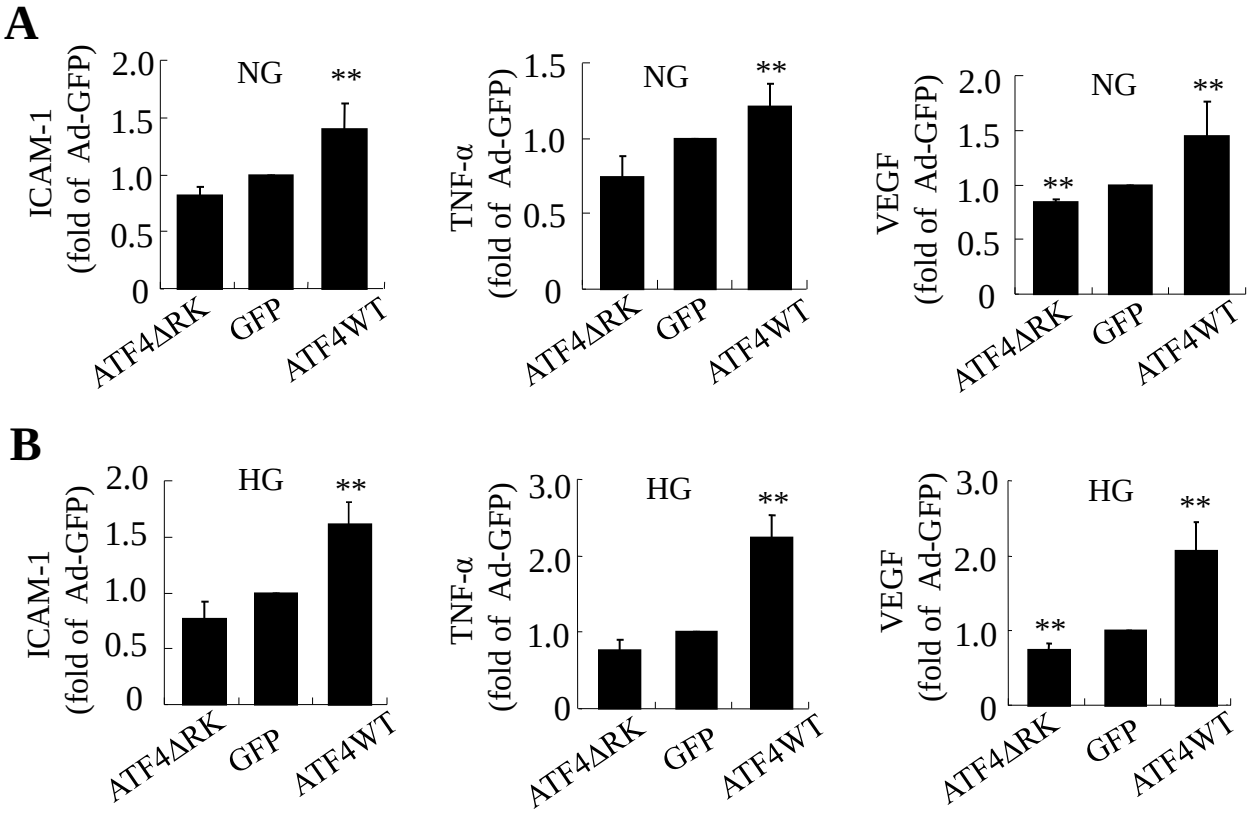
Quantification of BRB breakdown. Mice were deeply anesthetized and injected intraventricularly FITC-conjugated dextran (4.4 kDa, Sigma) at 50 mg/kg BW. After 15 minutes, the chest cavity was opened and a 31-gauge cannula was introduced into the aorta. A blood sample was collected, and the vessels were perfused with PBS (500 ml/kg BW). Immediately after perfusion, retinas were carefully dissected, weighed, and homogenized in 150µl of diH_2O. FITC-dextran in the retinal homogenate was extracted by centrifugation at 7,000 rpm for 90mins at 4°C through a 30,000 molecular weight filter (Millipore, Bedford, MA, USA). Blood samples were centrifuged at 7,000 rpm for 20 minutes at 4°C, and the supernatant was diluted at 1:100 with diH_2O. Fluorescence in retina and plasma samples was measured using spectrofluorometer with excitation of 485 nm and emission of 538 nm and calculated according to a standard curve. BRB breakdown was quantified using the following equation:

$$\frac{\text{Retinal FITC-dextran (µg)/retinal weight (g)}}{\text{Plasma FITC-dextran concentration (µg/µL)} \times \text{circulation time (h)}}$$

ESM Table 1. Sequences of primers used in real-time RT-PCR.

Gene	forward	reverse
ICAM-1	TGCGTTTTGGAGCTAGCGGACCA	CGAGGACCATACAGCACGTGCCAG
TNF-α	CGGTGCCTATGTCTCAGCCT	TTGGGCAGATTGACCTCAGC
CHOP	GTCCCTAGCTTGGCTGACAGA	TGGAGAGCGAGGGCTTTG
ATF4	CCCCCTTCGACCAGTCGGGT	CCGCCTTGTCGCTGGAGAACC

ESM Figure 1



Densitometric quantification of Western blots in Figure 7B. Results were expressed as mean ± SD, n=3. **p<0.01 vs. GFP. NG: normal glucose (5 mmol/l); HG: high glucse (25 mmol/l).