

## Methods

### Quantitative real-time RT-PCR

Quantitative real-time RT-PCR analysis of the expression of the inflammatory factors was performed using total RNA and the SYBR Green reagent (Bio-Rad) in CFX96 Real-Time System (Bio-Rad, Hercules, CA, USA). Gene expression levels were normalized to that of GAPDH. The results were analyzed using 2- $\Delta\Delta C_t$  method. Primer sequence information used for qPCR analysis is listed below. The experiments were performed in triplicate and repeated twice.

### In Vitro Sequestration of LPS by Cationic Resins

LPS was dissolved in pure water and specific adsorption was recorded at 258 nm.

Cholestyramine, polystyrene powder, and Pierce High-Capacity Endotoxin Removal Resin (catalog no. 88270; Thermo Fisher Scientific) were mixed with LPS solution. The mixtures were incubated for 1 h. After centrifuging at 500g for 1 min, the supernatant was filtered through a 0.45-micron filter, and adsorption was measured at 258 nm for the unbound LPS. The experiment was repeated three times.

### Reagents and antibodies

**Reagents:** Chloroquine diphosphate salt (Sigma, C6628); Lipopolysaccharides from *Escherichia coli* O111:B4 (Sigma, L2630); Chenodeoxycholic acid (Aladdin, C1049021); Rapamycin (MCE, HY-10219); MG132 (MCE, HY-13259); ECL for Western Blot (Bio-Rad, #170-5061); H.E staining (Biosharp, BL700A); Masson's staining (Baso, BA4079A); Transwell (Falcon, 353097); DAB for IHC (Origene, ZLI-9018); Paraformaldehyde (Sigma, 441244).

**Primary Antibodies:** YAP1 (CST, 14074); Type 1 Collagen-UNLB (Southern Biotech, 1310-61); P62 (Zenbio, 380612); CK19 (Abcam, ab52625); Ki67 (CST, 12202); Phospho-AKT (Ser473) (CST, 23430); AKT (CST, 9272); mTOR (CST, 2983); Phospho-mTOR (Ser2448) (CST, 5536); Phospho-Drosophila p70 S6 Kinase (Thr398) (CST, 9209); p70 S6 Kinase (CST, 9092); Phospho-TFEB (Ser211) (Affinity, AF3708); TLR-4 (Santa Cruz Biotechnology, sc-293072); FXR (Proteintech, 25055-1-AP); LC3B (Abclonal, A19665); LC3 (Proteintech, 14600-1-AP); P21 for human (Zenbio, 382492); p21 (Zenbio, 385235); Vimentin (Proteintech, 60330-1-Ig); ZO-1 (Santa Cruz Biotechnology, sc-8146); CDH1 (Abways, CY1155); Cyclin D1 (Abclonal, A19038); ATG7 (Abways, CY5658); ATG5 (Abways, CY5766); Occludin (Santa Cruz biotechnology, sc-8144); Cystatin A (Abmart, TD7458); Cathepsin L (Abcam, ab58991); HA-Tag (CST, 3724); Beta-ACTIN (Abclonal, AC026); GAPDH (Zenbio, 200306-7E4).

**Secondary Antibodies:** Anti HRP-linked-rabbit IgG (Santa Cruz Biotechnology, sc2313); Anti HRP-linked-mouse IgG (Santa Cruz Biotechnology, sc2314); Anti HRP-linked-goat IgG (Santa Cruz Biotechnology, sc2033);

### Plasmids

Plasmid pLVX-Puro-CTSL-WT or pLVX-Puro-CTSL-C138S were stored in our laboratory. HA-CSTA and HA-CSTA-T96M were constructed into pLVX-Puro by double enzyme digestion and confirmed by sequencing analysis. CTSL-HA and CTSL-HA-C138S were previously constructed by Dr. Zhang Chunyan and stored at our lab. Tandem monomeric mRFP-GFP-tagged LC3 was a kind gift from Dr. Ying Tong. The shRNAs were cloned into pLKO.1. The sequence information of the primers used for variants and shRNA were as following.

Human-shCTSL-1: 5-AAGGCGATGCACAACAGATTA-3;  
Human-shCTSL-2: 5-GAATTGCCTCAGCTACTCTAA -3;  
Human-shATG5-1: 5-GATTCATGGAATTGAGCCAAT-3  
Human-shATG5-2: 5-GCAGAACCATACTATTTGCTT-3  
Human-shATG7-1: 5-GCCTGCTGAGGAGCTCTCCAT-3  
Human-shATG7-2: 5-CCAGAGAGTTTACCTCTCATT-3  
Human-shTLR-4-1: 5-CCAAGTAGTCTAGCTTTCTTA-3  
Human-shTLR-4-2: 5-CGTTTGGTTCTGGGAGAATTT-3  
Human-shFXR-1: 5-CCACTTCTTGATGTGCTACAA-3  
Human-shFXR-2: 5-GCCTGACTGAATTACGGACAT-3  
HA-HOMO-CSTA: Forward: CGCGGAATTCGCCACCATGTACCC ATACGACGTCCCAGAC  
TACGCTATACCTGGAGGCT  
Reverse: GGCG GGATCC CTAAAAGCCCGTCA  
HA-HOMO-CSTA-T96M: Forward: CGCGGAATTCGCCACCATGTACCC ATACGACGTCCC  
AGAC TACGCTATACCTGGAGGCT  
Reverse: GGCG GGATCC CTAAAAGCCCATCAGC

### **Primers**

Mouse-IL1-beta:

Forward: 5-GAAATGCCACCTTTTGACAGTG-3

Reverse: 5-TGGATGCTCTCATCAGGACAG-3

Mouse-IL4:

Forward: 5-GGTCTCAACCCCCAGCTAGT-3

Reverse: 5-GCCGATGATCTCTCTCAAGTGAT-3

Mouse-IL6:

Forward: 5-TAGTCCTTCCTACCCCAATTTCC-3

Reverse: 5-TTGGTCCTTAGCCACTCCTTC-3

Mouse-Arg1:

Forward: 5-CTCCAAGCCAAAGTCCTTAGAG-3

Reverse: 5-AGGAGCTGTCATTAGGGACATC-3

Mouse-TNF-alpha:

Forward: 5-CCCTCACACTCAGATCATCTTCT-3

Reverse: 5-GCTACGACGTGGGCTACAG-3