Supplementary Methods

Dosage Information

The earlier research reflected that the dosage of La in our study (1.0×10^8 CFU) was sensible[1]. Furthermore, the dosage of the mixed SCFAs including acetic acid (AA), propionic acid (PA) and butyric acid (BA) was determined according to the significantly increased SCFAs in the feces of La-treated rats. As the molar ratio among AA, PA and BA was 1：0.74：0.52, so the molar ratio among sodium acetate, sodium propionate and sodium butyrate was 1：0.74：0.52. In vitro, the minimum concentration of sodium acetate (S2889, Sigma-Aldrich) was set to 1 μM, and thus that of sodium propionate (P1880, Sigma-Aldrich) and sodium butyrate (B5887, Sigma-Aldrich) was set to 0.74 μM and 0.52 μM, respectively. Moreover, the concentrations of the mixed SCFAs solution represented by sodium acetate were prepared as 1, 10, 50, 100, 500, 1000 μM to obtained the optimal concentrations according to previous reports[2, 3]. Additionally, as documents set the concentration of SCFAs in mice between 100~200 mM[4, 5], here the concentration of sodium acetate was set to 50 mM, and thus that of sodium propionate and sodium butyrate was 37 mM and 26 mM, respectively.

Assessment of Severity of Colitis

The apparent physical signs of the animal including body weight, feces consistency and stool bleeding were defined as disease activity index (DAI) of colitis, which were monitored daily to assess the disease condition of the UC model[6]. The colon tissue fixed with 4% paraformaldehyde and embedded in paraffin were sectioned at 4 μm in thicknesses, and then hematoxylin-eosin (H&E) staining was performed according to the standard protocol. As with the previously criteria, histological pathology was used to score the severity of colonic damage, including the following indicators: degree of colonic ulcer and edema, the extent of crypt injury, and the severity and depth of inflammatory cell infiltration[7].

Serum Cytokine Quantification

The serum concentrations of inflammatory cytokines, including monocyte chemotactic protein 1 (MCP-1), tumor necrosis factor α (TNF-α) and interleukin (IL)-10 were determined by the Bio-Plex Pro^{TM} Multiplex Assay (Luminex) kit (Bio-Rad Laboratories, Inc., USA). The activities of Superoxide dismutase (SOD), CAT (Catalase), Glutathione peroxidase (GSH-Px) and Malondialdehyde (MDA) in the serum were measured by using commercial detection kits (Nanjing Jiancheng Bioengineering Institute Co., Ltd., China). All operation methods were carried out in accordance with the manufacturer's instructions.

Gene Expression Analysis by Quantitative Real Time-PCR

RNA extracted from colon or Caco-2 cells were performed using a RNAiso Plus reagent (Accurate biotechnology, China). Then, the purity and concentration of RNA were evaluated at the absorbance of 260 and 280 nm by Nanodrop 2000 (Thermo Fisher Scientific). Whereafter, RNA was reverse transcribed into cDNA using a RT Kit for qPCR with gDNA Clean (Accurate biotechnology, China). Subsequently, cDNA was amplified with a SYBR Green PCR Master Mix (TransGen Biotech, China) and specific primers (Sangon Biotech, China) in a ABI7500 Real-Time PCR detection system (Applied Biosystems, USA). The mRNA expressions of different genes were normalized to those of GAPDH which was set as a housekeeping gene. On the other hand, fecal genomic DNA was extracted using a TIANamp Stool DNA Kit, and the process of concentration determination and gene amplification were the same as those of RNA. Moreover, the data were normalized to the universal bacteria. All procedures were performed according to the manufacturer's protocol. Primer sequences were displayed in Table S1~3.

Immunoblot Analysis

Homogenized colon and cells were lysed with lysis buffer with a protease inhibitor cocktail (1：100) to obtain total protein. Then, the extracted protein was quantified by a BCA assay kit (Cwbio, China). Protein samples were loaded and separated in sodium dodecyl sulfate-polyacrylamide gel electrophoresis, and then transferred onto polyvinylidene fluoride membranes (Millipore, USA). Afterwards, the membranes were blocked with 5% bovine serum albumin in tris buffered saline with tween 20 (TBST) (w/v) for 1 h at room temperature. The primary antibodies against NLRP3 (Novus Biologicals, NBP2-12446), IL-1β (Novus Biologicals, NB600-633), Caspase-1 (Novus Biologicals, NBP1-45433), LC3A/B (Cell Signaling Technology, 4108S), p62/SQSTM1 (Proteintech, 18420-1-AP), PINK1 (Novus Biologicals, BC100-494SS), Parkin (Cell Signaling Technology, 4211T), HSP60 (Cell Signaling Technology, 12165S), Tom20 (Cell Signaling Technology, 42406S), Occludin (Abcam, ab216327) and GAPDH (Servicebio, GB11002) were incubated with at 4 ℃ overnight. After washing three times with TBST, the membranes were then incubated with secondary antibodies conjugated with horseradish peroxidase (Servicebio) at 37°C for 2 h. Finally, immunoreactive proteins were detected using an ECL kit (Millipore, USA) under a chemiluminescence signals imaging system (Tanon 5200, Shanghai, China). All the protein signals were analyzed with the Image J 1.48 software and GAPDH was set as internal control for normalization.

SCFAs Determination

The amount of SCFAs in feces was quantified as previously described[8]. Briefly, 1 mL ultra-pure water was added into 200 mg of thawed feces (5：1, v/w), and the mixture was homogenized on a vortex for 10 min. Subsequently, the tube was centrifuged at 4°C, 5000 g for 25 min and the

supernatants were filtrated with a filter membrane of 0.22 μm. Then, 50 μL of 50% H_2SO_4 was added into 500 μL of supernatant (1：10, v/v) and homogenized. Whereafter, an equal volume of ether containing internal controls (2-ethylbutyric acid) was added to extract SCFAs for 20 min, followed by centrifugation at 4°C, 10000 g for 5 min. Finally, the ether layer was separated and collected for subsequent detection.

The samples were analyzed on a gas chromatography system (GA-2010 Plus, Shimadzu, Japan) and separated with a DB-FFAP GC column (30 m × 0.32 mm × 0.25 μm) (Agilent Technologies, USA). The injection volume was set at 2 μL and the split ratio was 32：1. Nitrogen was set as the carrier gas at a flow rate of 2 mL/min. The detector and injector temperature were set at 230°C and 250°C, respectively. Oven condition was firstly kept at 100°C for 0.5 min and then increased to 170°C at a rate of 8°C/min, then ramped to 220°C at a rate of 20°C/min and maintained at for 2 min.

Assessment of Barrier Function in vitro

24-well transwell inserts (0.4 μm pore size, Corning, USA) were used for assesses of trans epithellal electric resistance (TEER). In brief, 0.2 ml Caco-2 cells at the density of 1.0 × 10^5 cells/well were seeded in the apical side, which was bathed with 0.6 mL DMEM complete medium refreshed daily in the basal side. Meanwhile, electric resistance was determined daily by an ERS-2 system (Millipore, USA). When the TEER of the monolayer cells has exceeded 1000 ohms, the cells were pretreated with LPS and/or SCFAs regulated by La (1, 10, 50 μM) for 24 h. After washed three times with Hank's balanced salt solution (HBSS), the monolayer cells were incubated with 1.0 mg/mL FITC-dextran (Aladdin, China) in HBSS on the apical side at 37°C for 2 h. Subsequently, the HBSS in the basal side was measured under a fluorescence microplate reader (Molecular Devices, USA) with the

excitation and emission wavelength at 492 nm and 520 nm, respectively. The concentration of FITC-dextran was detected by establishing a standard curve, and fluorescence transmittance (%) = the concentration of FITC-dextran in the basal side/the concentration of FITC-dextran initially added to the apical side.

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Supplementary Tables

Table S1 The sequences of qRT-PCR primers in rat experiment

Gene	Orientation	Sequence (5' → 3')	NCBI Sequence number
TNF-α	Forward	TGGGCTCCCTCTCATCAGTTCC	NM_012675.3
	Reverse	GCTCCTCCGCTTGGTGGTTTG	
IL-6	Forward	CTTCTTGGGACTGATGCTGGTGAC	NM_012589.2
	Reverse	AGGTCTGTTGGGAGTGGTATCCTC	
IFN-γ	Forward	ACCCACAGATCCAGCACAAAGC	NM_138880.3
	Reverse	CACCGACTCCTTTTCCGCTTCC	
MCP-1	Forward	GCAGGTCTCTGTCACGCTTCTG	NM_031530.1
	Reverse	GTTCTCCAGCCGACTCATTGGG	
Tff-3	Forward	TGTCAGGGTGGACTGTGGCTAC	NM_013042.2
	Reverse	GGGCACATTTGGGATGCTGGAG	
ZO-1	Forward	GCCTGCCAAGCCAGTCCATTC	NM_001106266.1
	Reverse	GGGCAACGGAGGAGGAGGAG	
Occludin	Forward	TGGAGGTGGCTTCGGAGGTTAC	NM_031329.3
	Reverse	GGAAACCCTTTGCCGCTCTGG	
IL-1β	Forward	CGACCGAACAGCCAACGAAT	NM_012675.3
	Reverse	GGGTCACAGCCAGTCCTCTT	
IL-18	Forward	CGACCGAACAGCCAACGAAT	NM_019165.2
	Reverse	GGGTCACAGCCAGTCCTCTT	
NLRP3	Forward	GCAGCGATCAACAGGCGAGAC	NM_001191642.1
	Reverse	TCCCAGCAAACCTATCCACTCCTC	
ASC	Forward	TGGTTTGCTGGATGCTCTGTATGG	NM_172322.1
	Reverse	ACAAGTTCTTGCAGGTCAGGTTCC	
Caspase 1	Forward	AAACACCCACTCGTACACGTCTTG	NM_012762.3
	Reverse	AGGTCAACATCAGCTCCGACTCTC	
GAPDH	Forward	CGACATACTCAGCACCAGCATCAC	NM_017008.4
	Reverse	ACGGCAAGTTCAACGGCACAG	
Blautia faecis	Forward	GGGGAGTACGTTCGCAAGAA	NZ_JAJCIA000000000.1
	Reverse	CTGTCCCGAAGGAAAGGGAC	
Faecalibacterium prausnitzii	Forward	TCGTGTCGTGAGATGTTGGG	NZ_CABHNC000000000.1
	Reverse	TCGCGGTCTTGCTTCTCTTT	
Ruminococcus torques	Forward	ATGGTGCGGGGGTAAAAACT	NZ_CABHNA000000000.1
	Reverse	CAGGTCGGCTACTGATCGTC	
Bacteria	Forward	ACGTCRTCCMCNCCTTCCTC	lhv_3101
	Reverse	GTGSTGCAYGGYYGTCGTCA	

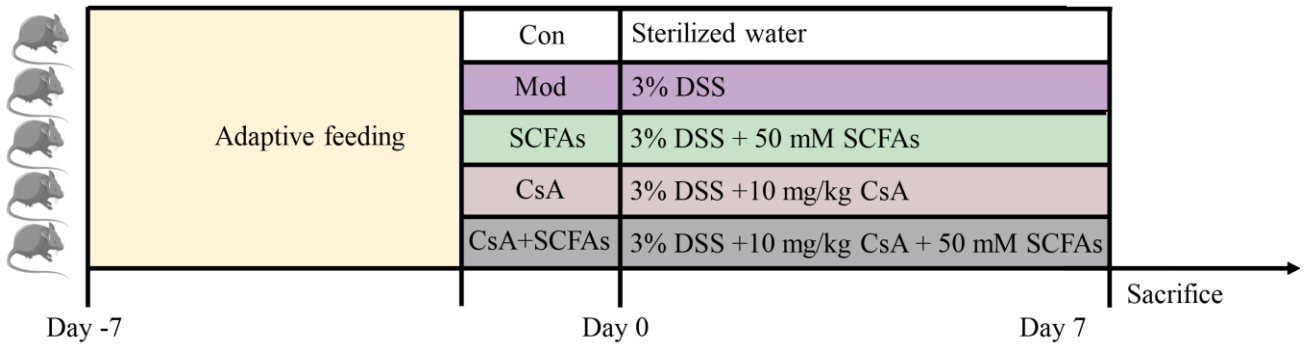
Table S2 The sequences of qRT-PCR primers in Caco-2 cell experiment

Gene	Orientation	Sequence (5' → 3')	NCBI Sequence number
GPR41	Forward	GACCTGCTCCTGCTGCTGTTC	NM_005304.5
	Reverse	GCGGTGAGATAGATGGTGGTGAAG	
GPR43	Forward	TCACGAGTTTTGGCTTCTACAG	NM_001370087.1
	Reverse	CTGCAATCACTCCATACAGAGG	
GPR109A	Forward	ACGGTGGTGGCGGTAGACAG	NM_177551.4
	Reverse	CGGCATCTTCTTCTTCAGGAGGTG	
GAPDH	Forward	GAAGGTGAAGGTCGGAGTC	NM_001256799.3
	Reverse	GAAGATGGTGATGGGATTTC	

Table S3 The sequences of qRT-PCR primers in mice experiment

Gene	Orientation	Sequence (5' → 3')	NCBI Sequence number
IL-6	Forward	CTTCTTGGGACTGATGCTGGTGAC	NM_001314054.1
	Reverse	AGGTCTGTTGGGAGTGGTATCCTC	
IL-1β	Forward	TCGCAGCAGCACATCAACAAGAG	NM_008361.4
	Reverse	AGGTCCACGGGAAAGACACAGG	
TNF-α	Forward	GCCTCTTCTCATTCCTGCTTGTGG	NM_001278601.1
	Reverse	GTGGTTTGTGAGTGTGAGGGTCTG	
IL-10	Forward	TTCTTTCAAACAAAGGACCAGC	NM_010548.2
	Reverse	GCAACCCAAGTAACCCTTAAAG	
GPR41	Forward	AGTCGCCTGGTGTGGATACTGAG	NM_001033316.2
	Reverse	GCCGAAGCAGACGAAGAAGATGAG	
GPR43	Forward	GCTGACAGGCTTCGGCTTCTAC	NM_001168509.1
	Reverse	CAGAGCAGCGATCACTCCATACAG	
GPR109A	Forward	TGGTGGTGGCTATTGTATTCAT	NM_030701.3
	Reverse	ATGTAGGTAAAGCTAAGGGTGG	
GAPDH	Forward	AGCAGTCCCGTACACTGGCAAAC	NM_001289726.1
	Reverse	TCTGTGGTGATGTAAATGTCCTCT	

Supplementary Figures

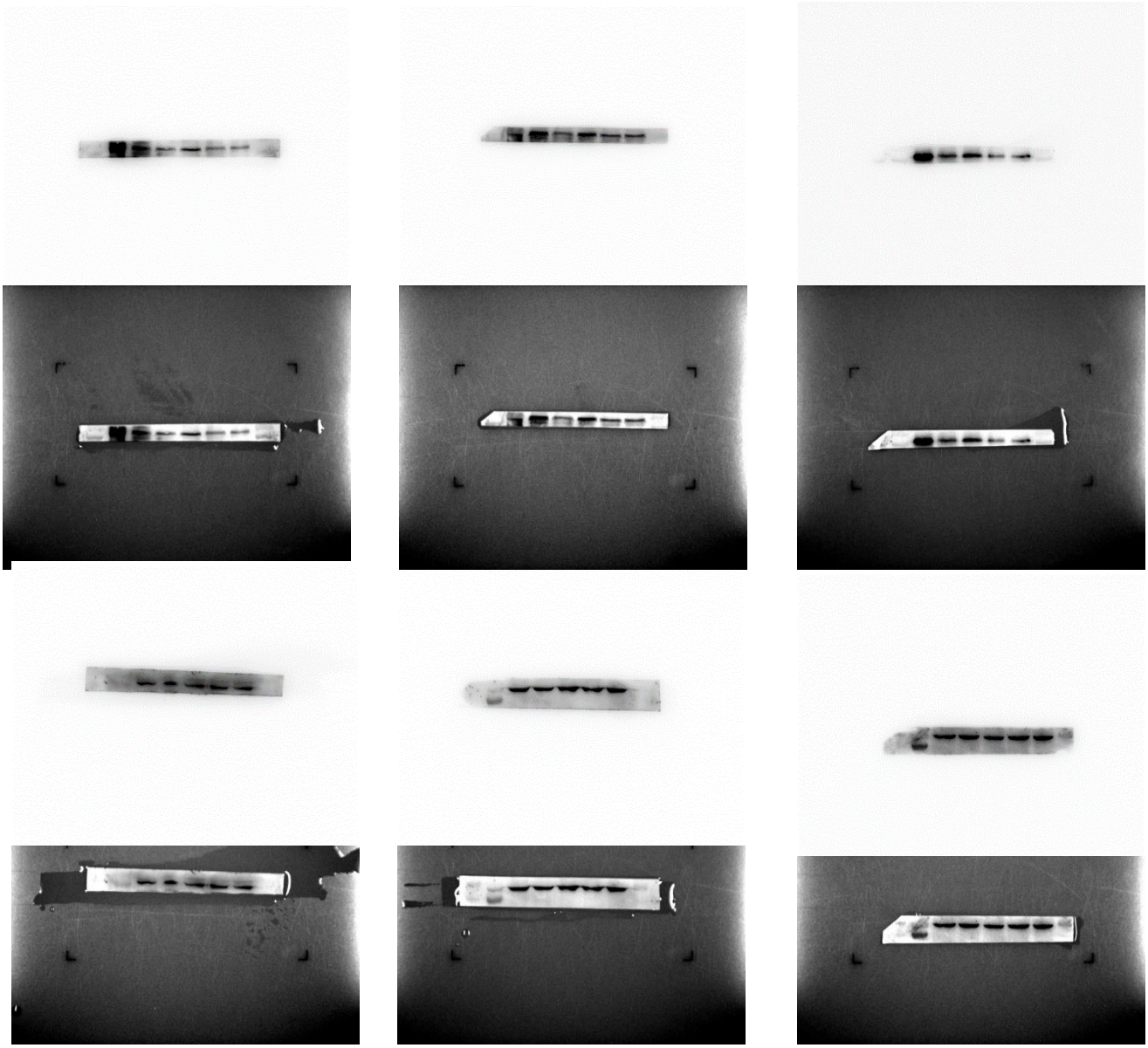


Supplementary Figure S1 Study design of the mice experiment.

The following were supplementary figures for western blot:

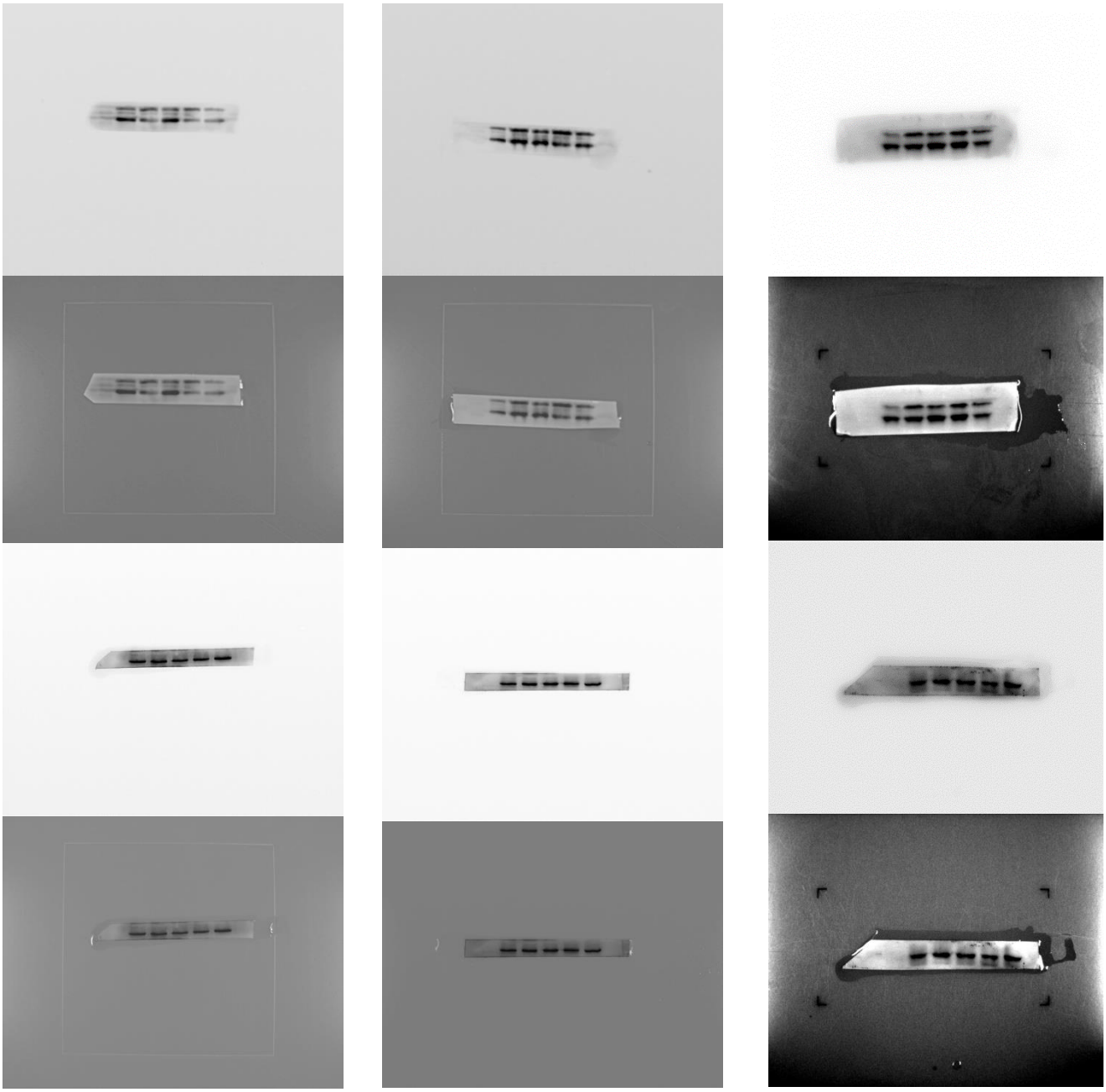
C57BL/6 mice Occludin： *left* **Con DSS DSS+50mM SCFAs DSS+CsA DSS+CsA+50mM SCFAs** *right*

C57BL/6 mice GAPDH： *left* **Con DSS DSS+50mM SCFAs DSS+CsA DSS+CsA+50mM SCFAs** *right*



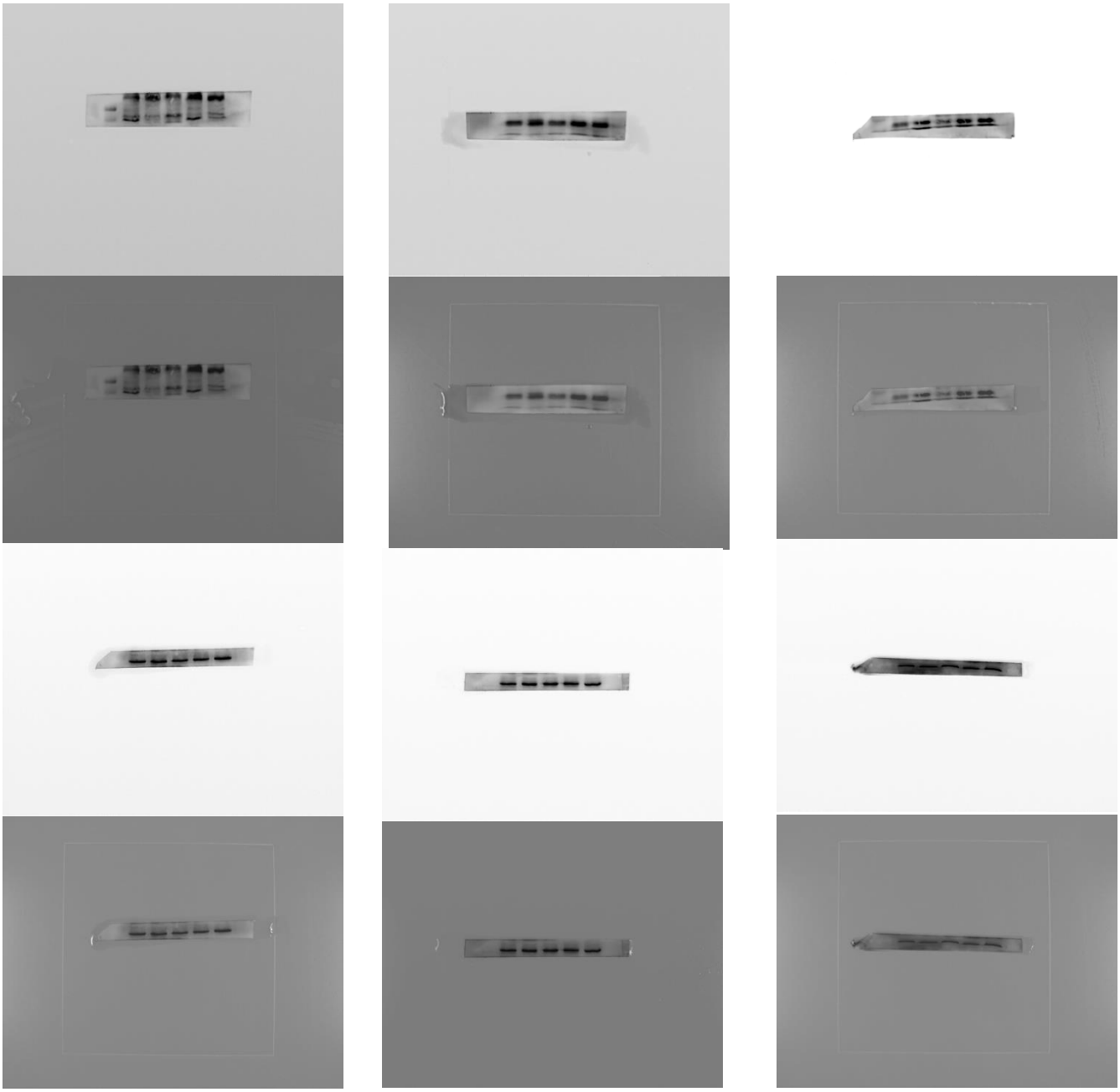
C57BL/6 mice LC3 II/I： *left* ***Con DSS DSS+50mM SCFAs DSS+CsA DSS+CsA+50mM SCFAs*** *right*

C57BL/6 mice GAPDH： *left* ***Con DSS DSS+50mM SCFAs DSS+CsA DSS+CsA+50mM SCFAs*** *right*



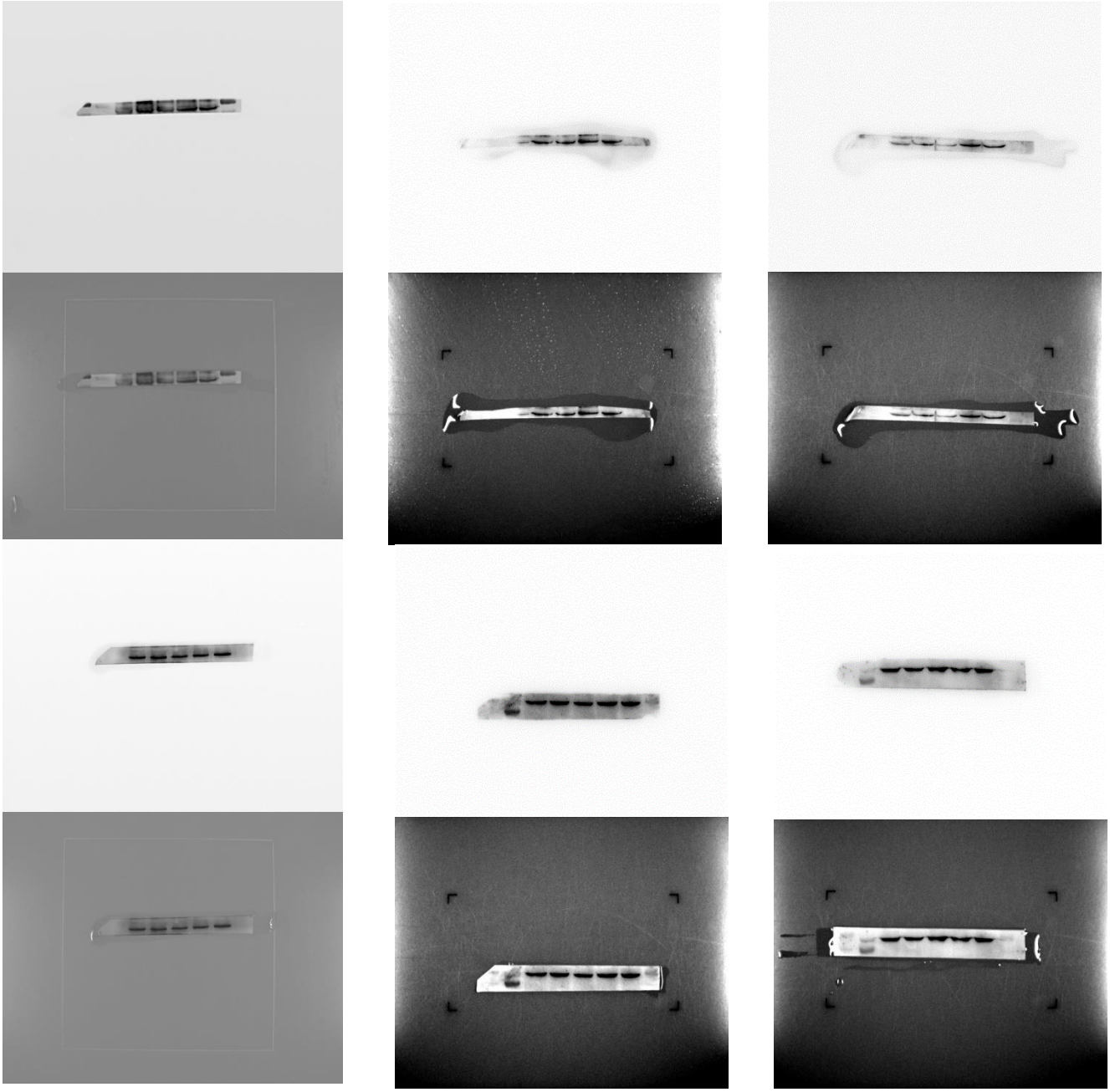
C57BL/6 mice Tomm20： *left* **Con DSS DSS+50mM SCFAs DSS+CsA DSS+CsA+50mM SCFAs** *right*

C57BL/6 mice GAPDH： *left* **Con DSS DSS+50mM SCFAs DSS+CsA DSS+CsA+50mM SCFAs** *right*

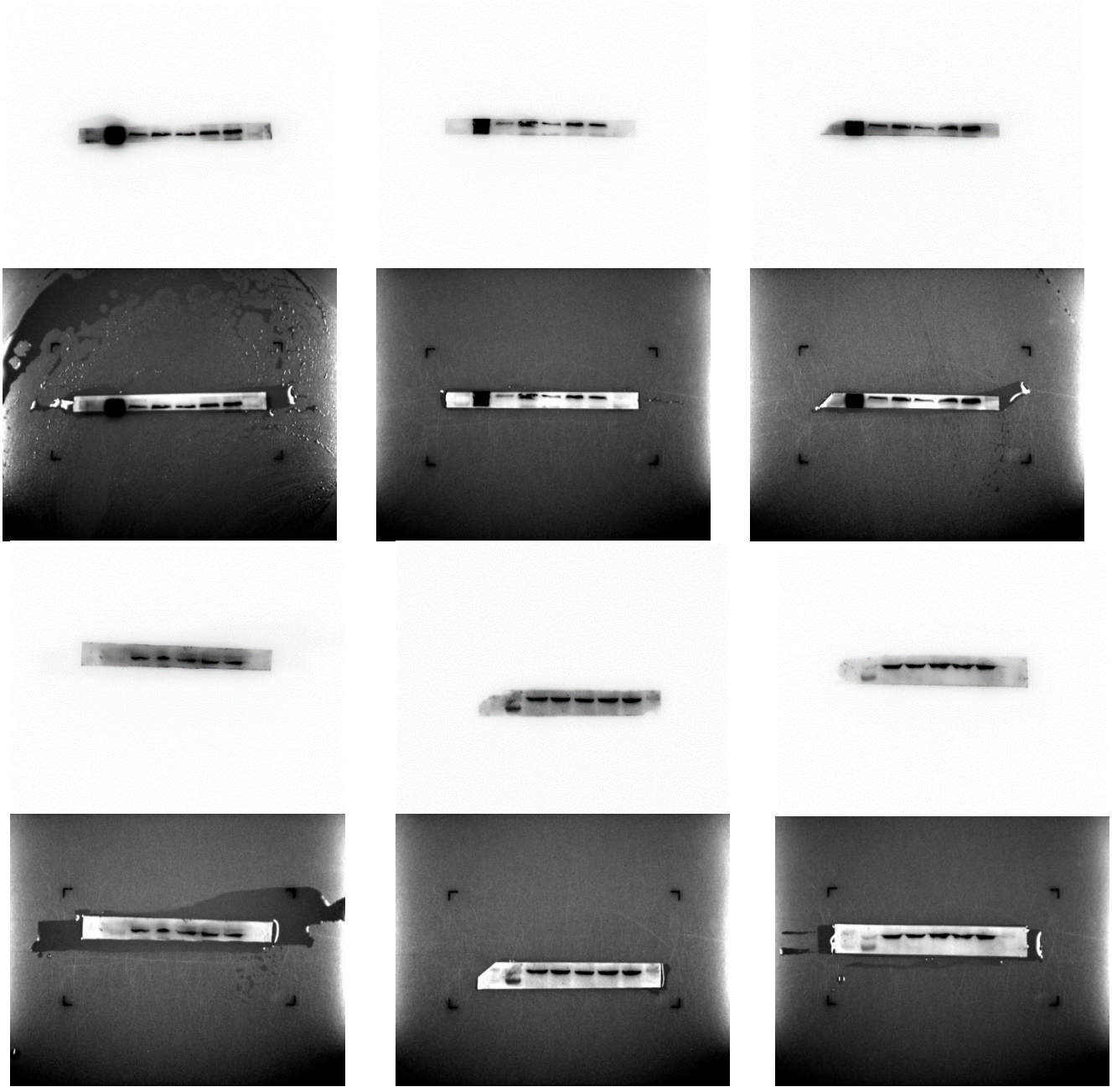


C57BL/6 mice HSP60： *left* **Con DSS DSS+50mM SCFAs DSS+CsA DSS+CsA+50mM SCFAs** *right*

C57BL/6 mice GAPDH： *left* **Con DSS DSS+50mM SCFAs DSS+CsA DSS+CsA+50mM SCFAs** *right*

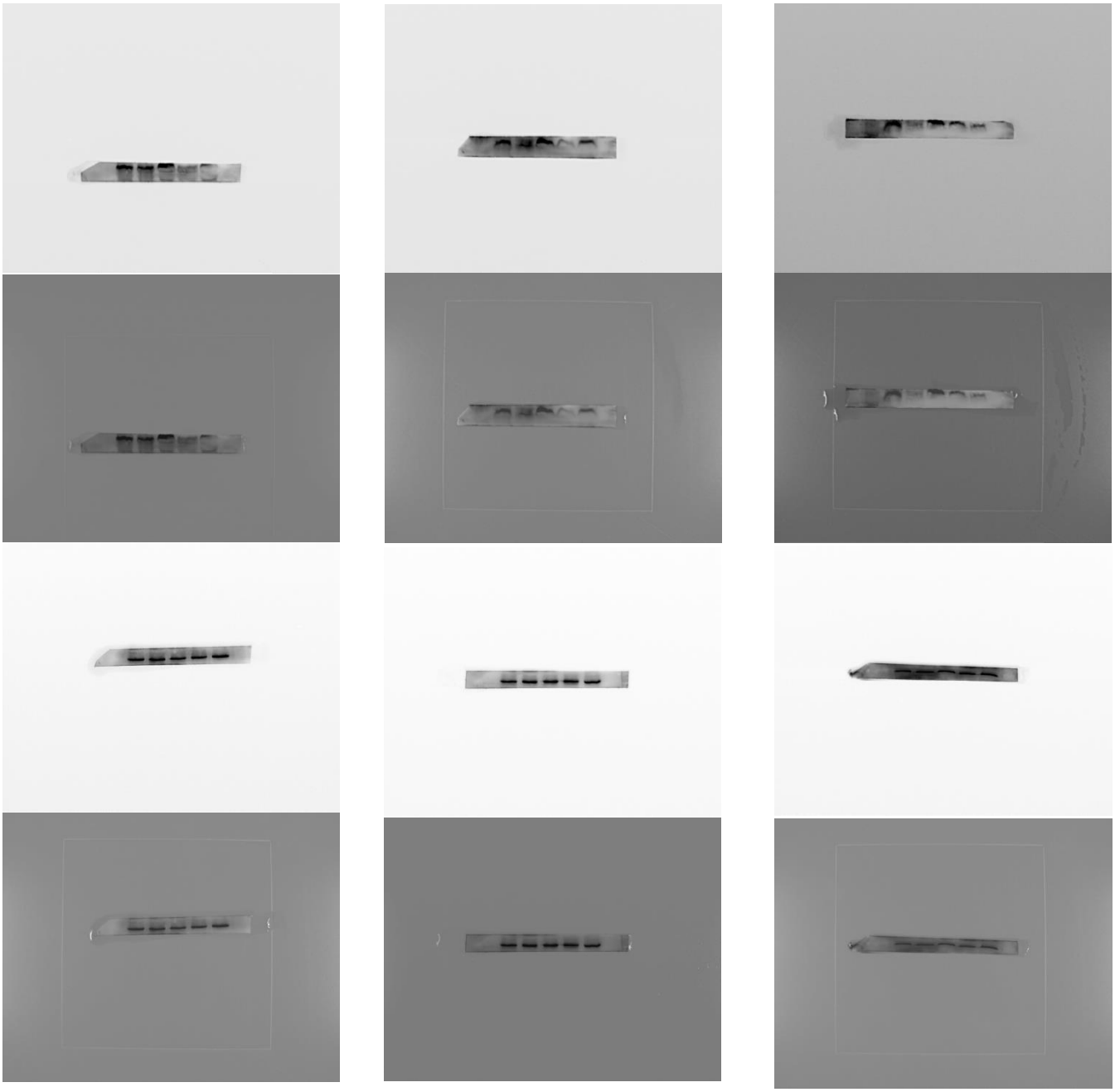


C57BL/6 mice P62： *left* **Con DSS DSS+50mM SCFAs DSS+CsA DSS+CsA+50mM SCFAs** *right*
C57BL/6 mice GAPDH： *left* **Con DSS DSS+50mM SCFAs DSS+CsA DSS+CsA+50mM SCFAs** *right*

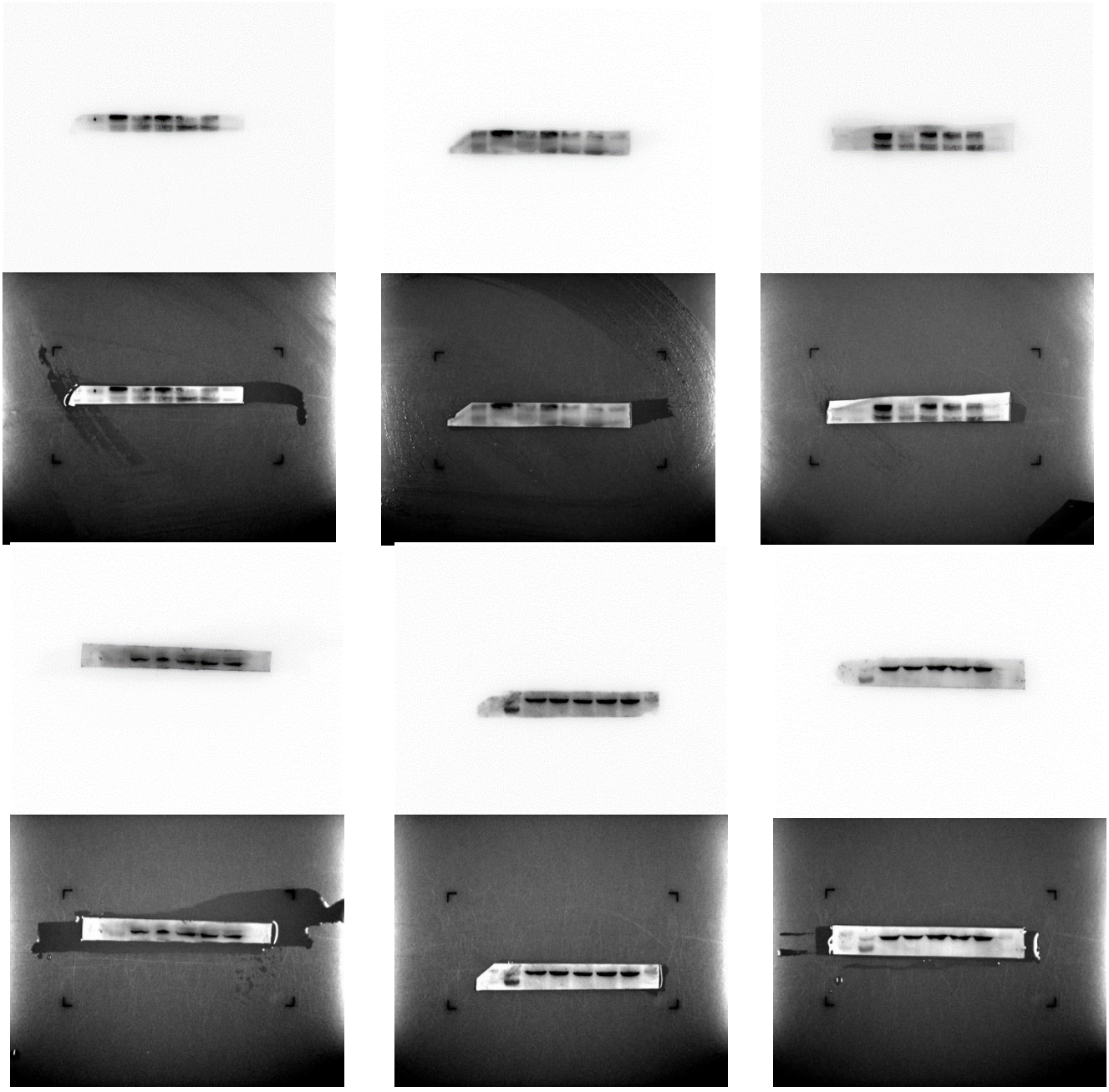


C57BL/6 mice Parkin： *left* **Con DSS DSS+50mM SCFAs DSS+CsA DSS+CsA+50mM SCFAs** *right*

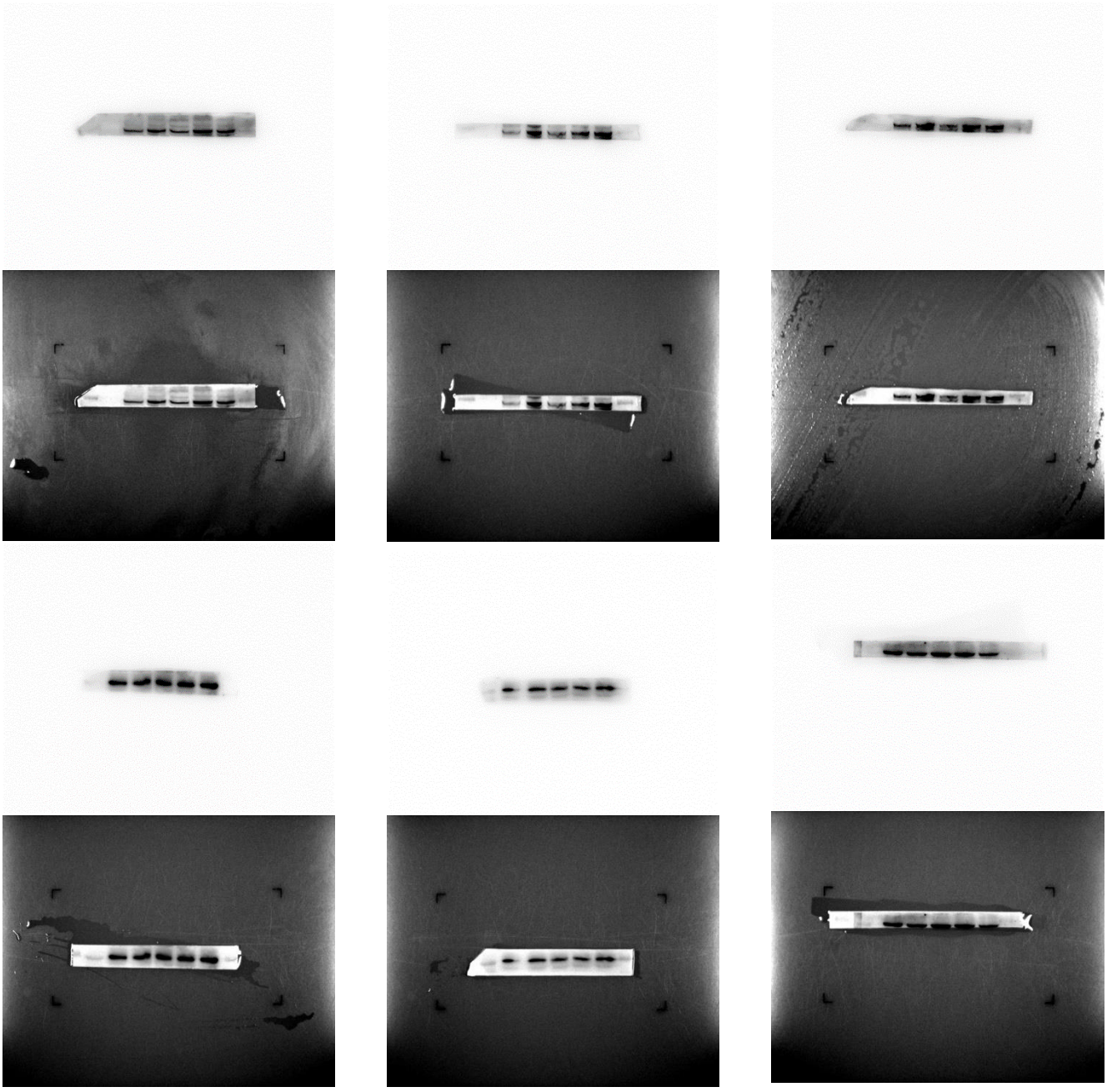
C57BL/6 mice GAPDH： *left* **Con DSS DSS+50mM SCFAs DSS+CsA DSS+CsA+50mM SCFAs** *right*



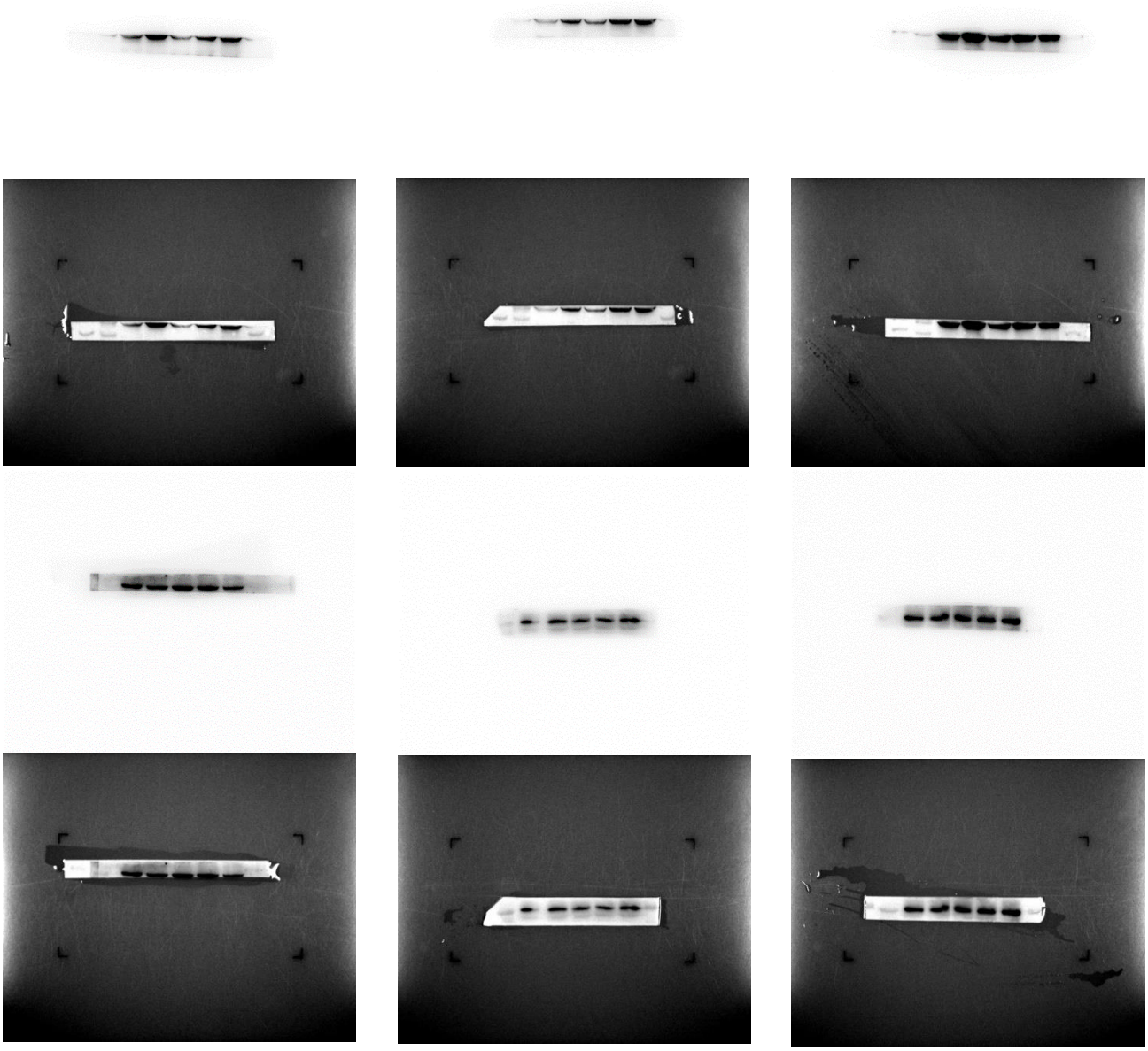
C57BL/6 mice Pink1： *left* **Con DSS DSS+50mM SCFAs DSS+CsA DSS+CsA+50mM SCFAs** *right*
C57BL/6 mice GAPDH： *left* **Con DSS DSS+50mM SCFAs DSS+CsA DSS+CsA+50mM SCFAs** *right*



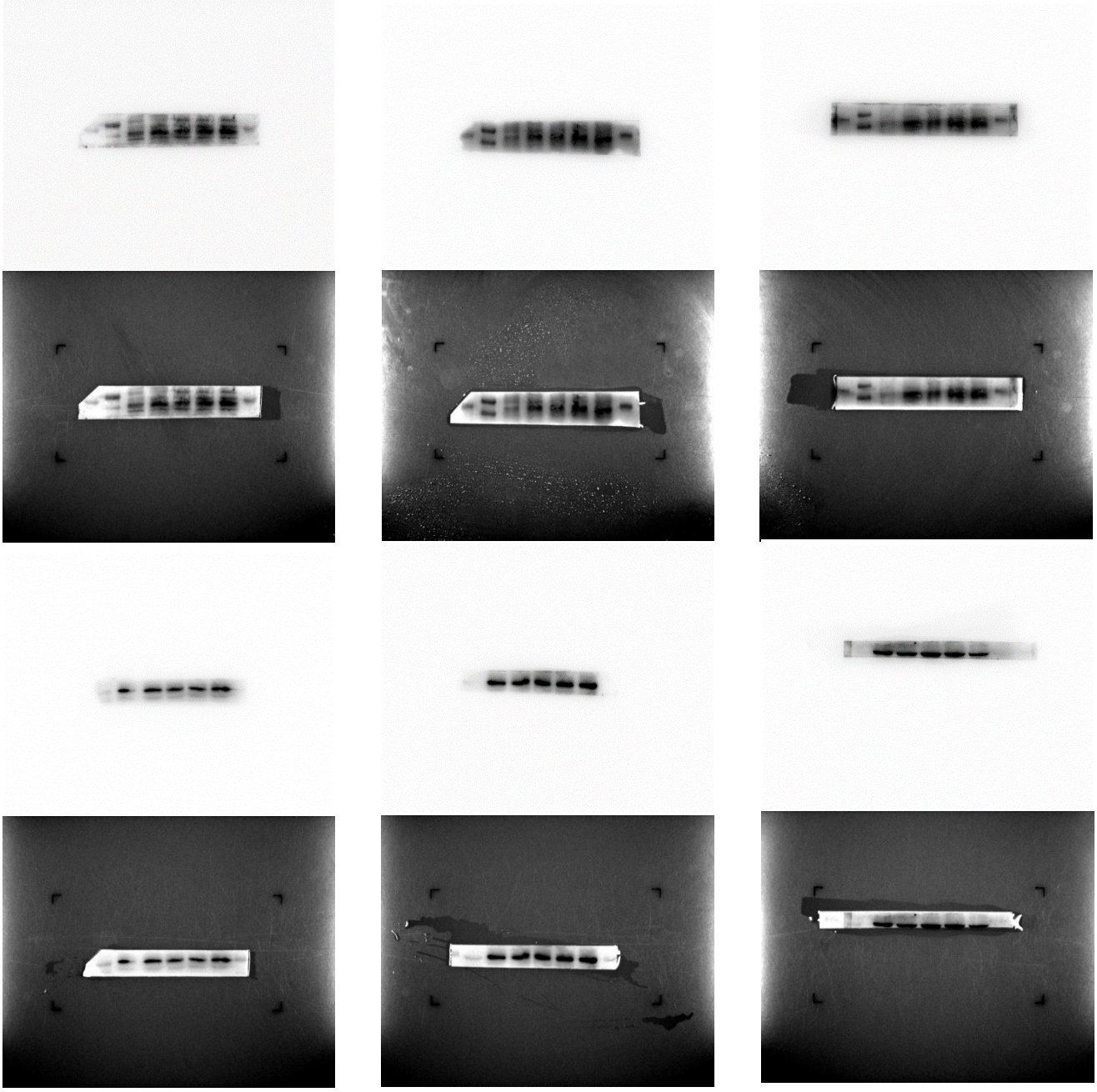
C57BL/6 mice NLRP3： *left* **Con DSS DSS+50mM SCFAs DSS+CsA DSS+CsA+50mM SCFAs** *right*
C57BL/6 mice GAPDH： *left* **Con DSS DSS+50mM SCFAs DSS+CsA DSS+CsA+50mM SCFAs** *right*



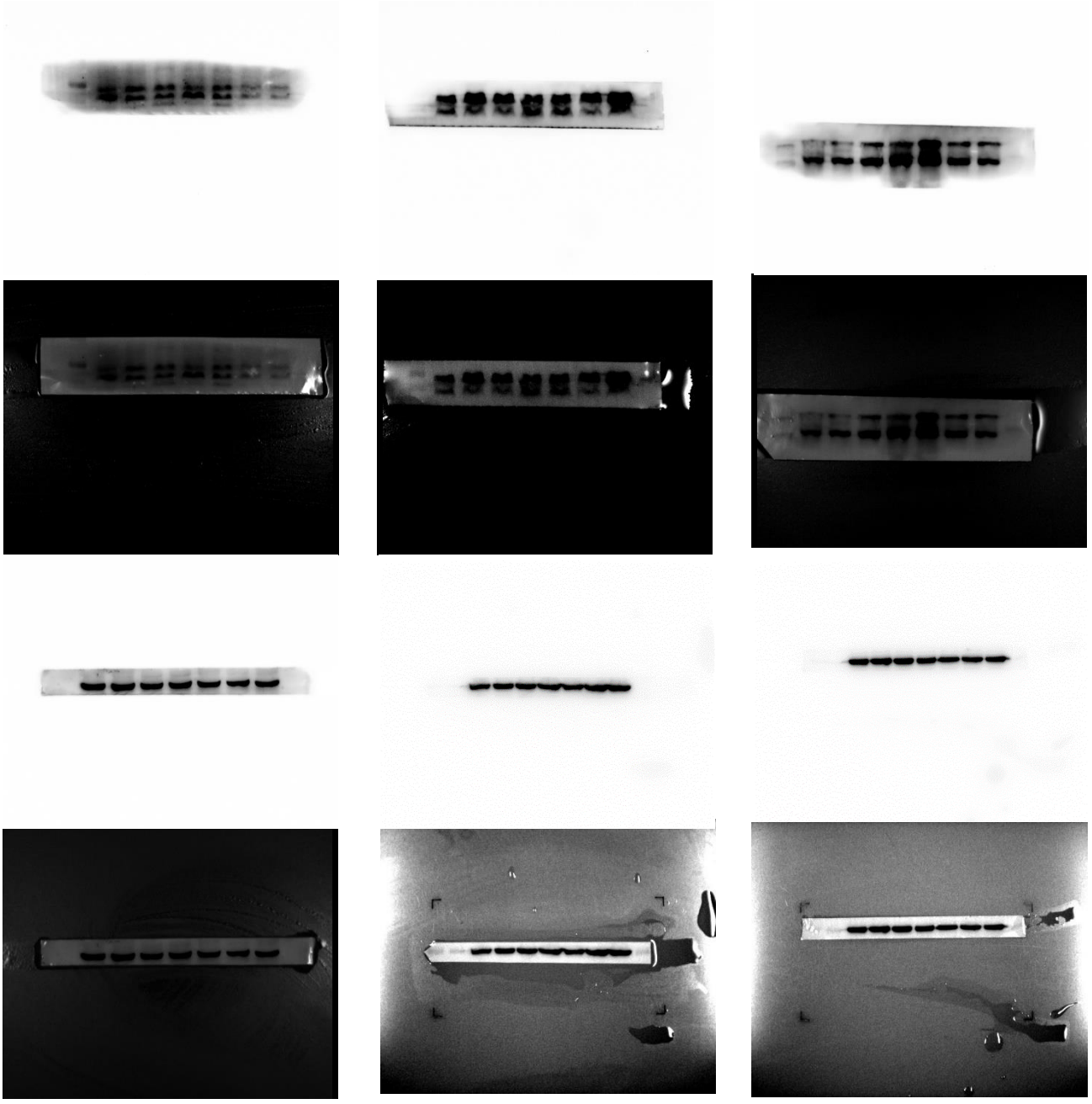
C57BL/6 mice Caspase 1： *left* **Con DSS DSS+50mM SCFAs DSS+CsA DSS+CsA+50mM SCFAs** *right*
C57BL/6 mice GAPDH： *left* **Con DSS DSS+50mM SCFAs DSS+CsA DSS+CsA+50mM SCFAs** *right*



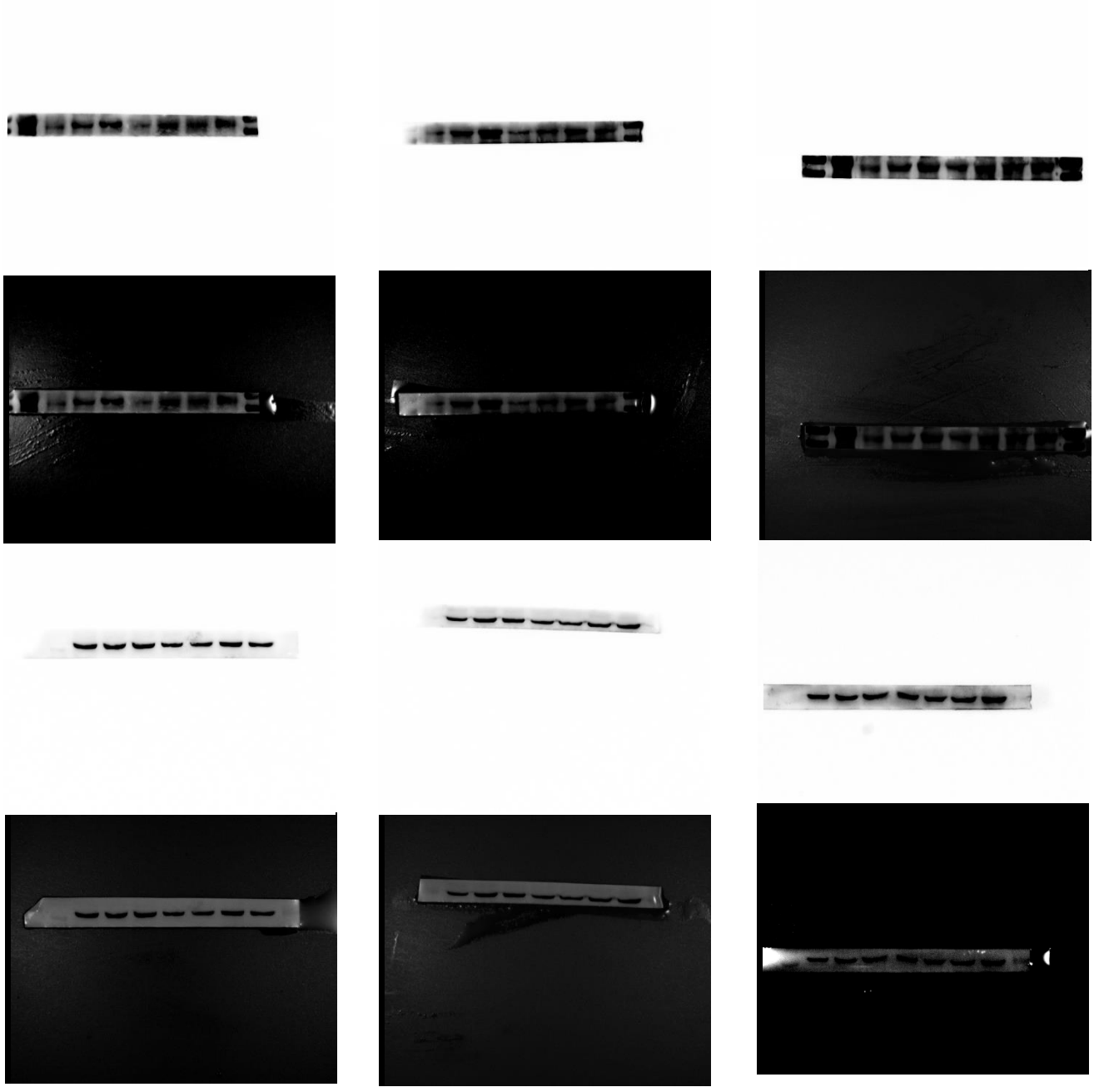
C57BL/6 mice IL-1β： *left* **Con DSS DSS+50mM SCFAs DSS+CsA DSS+CsA+50mM SCFAs** *right*
C57BL/6 mice GAPDH： *left* **Con DSS DSS+50mM SCFAs DSS+CsA DSS+CsA+50mM SCFAs** *right*



SD rats LC3 II/I： *left* **Con PBS Blank La Hk-La La-Sup Mes** *right*
SD rats GAPDH： *left* **Con PBS Blank La Hk-La La-Sup Mes** *right*

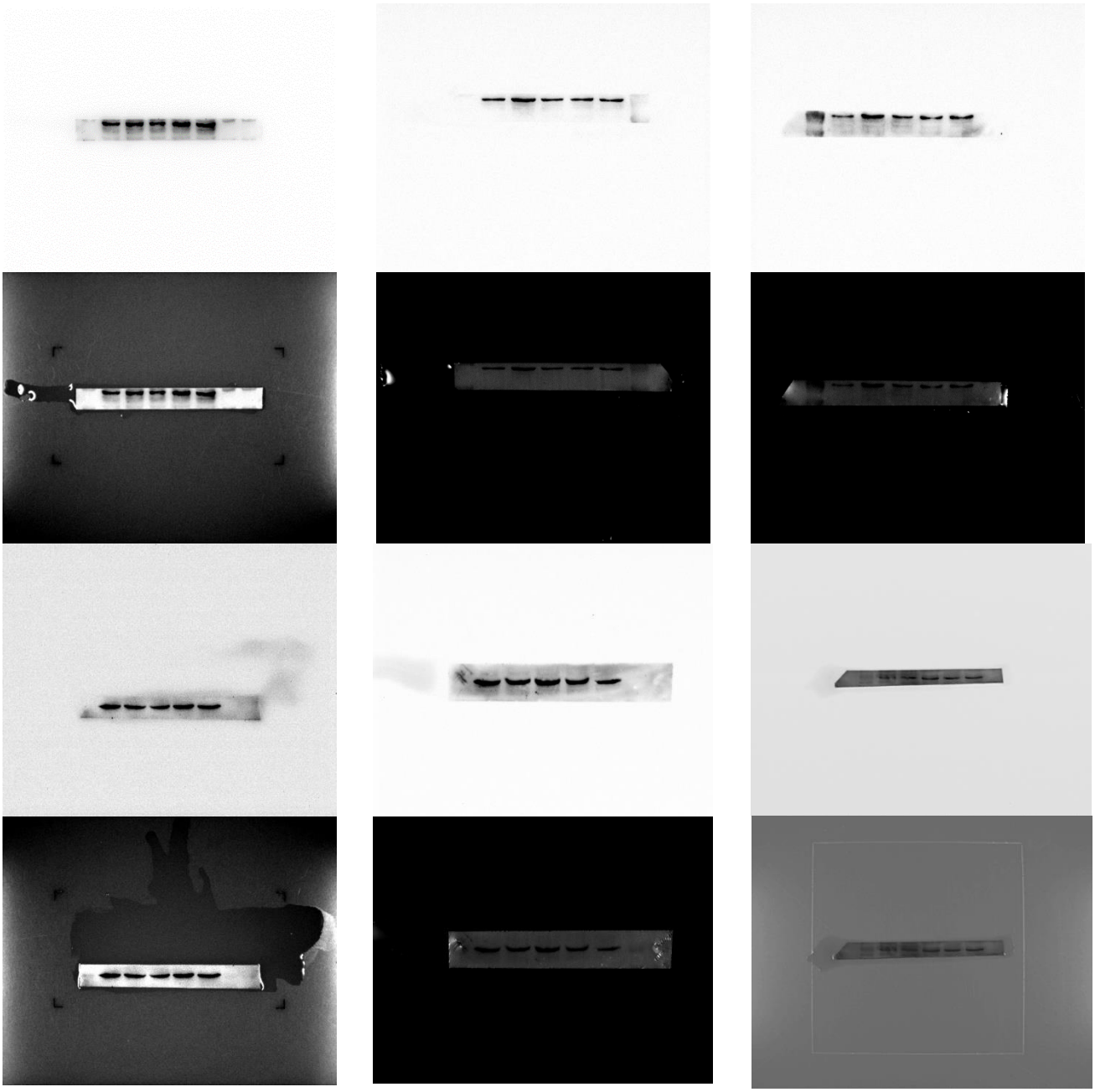


SD rats P62： *left* **Con PBS Blank La Hk-La La-Sup Mes** *right*
SD rats GAPDH： *left* **Con PBS Blank La Hk-La La-Sup Mes** *right*

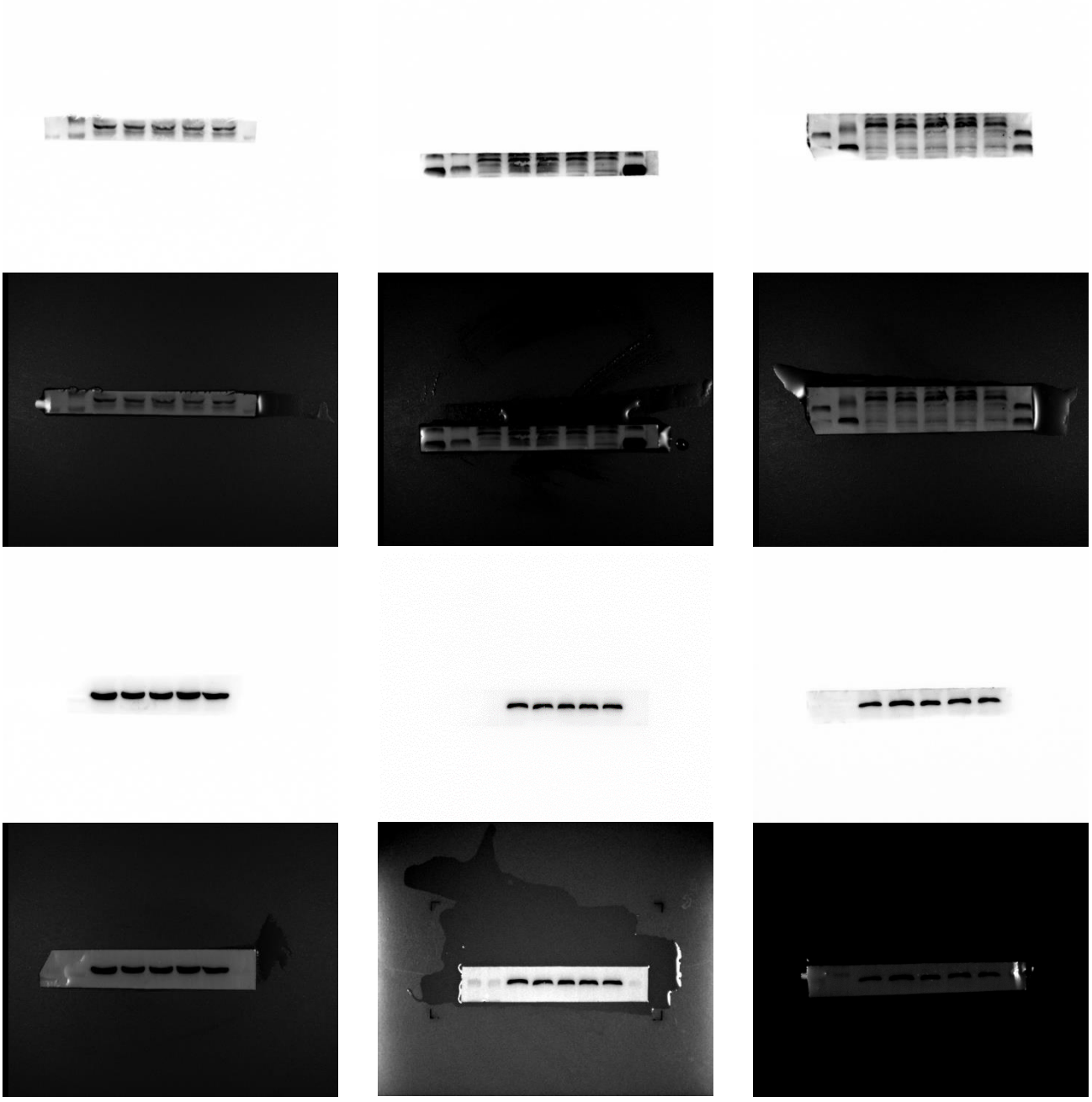


Caco-2 cell Occludin： *left* **Con LPS LPS+50μM SCFAs LPS+10μM SCFAs LPS+1μM SCFAs** *right*
Caco-2 cell GAPDH： *left* **Con LPS LPS+50μM SCFAs LPS+10μM SCFAs LPS+1μM SCFAs** *right*

Caco-2 cell IL-1β： *left* **Con LPS LPS+50μM SCFAs LPS+10μM SCFAs LPS+1μM SCFAs** *right*
Caco-2 cell GAPDH： *left* **Con LPS LPS+50μM SCFAs LPS+10μM SCFAs LPS+1μM SCFAs** *right*



Caco-2 cell HDAC 1： *left* **Con LPS LPS+50μM SCFAs LPS+10μM SCFAs LPS+1μM SCFAs** *right*
Caco-2 cell GAPDH： *left* **Con LPS LPS+50μM SCFAs LPS+10μM SCFAs LPS+1μM SCFAs** *right*



Caco-2 cell HDAC2： *left* **Con LPS LPS+50μM SCFAs LPS+10μM SCFAs LPS+1μM SCFAs** *right*
Caco-2 cell GAPDH： *left* **Con LPS LPS+50μM SCFAs LPS+10μM SCFAs LPS+1μM SCFAs** *right*