Supplementary figure legends

Supplemental Fig. 1 PCA method was used to observe the overall distribution trend between the control and cisplatin groups.

Supplemental Fig. 2 Cluster analysis chart based on lipid metabolomics results of the control group and cisplatin-induced AKI group (n = 8).

Supplemental Fig. 3 Lipid maps annotation based on lipid metabolomics sequencing (n = 8).

Supplemental Fig. 4 Enrichment analysis of KEGG-related pathways based on lipid metabolomics results (n = 8).

Supplemental Fig. 5 The degree of renal injury increased gradually with the prolongation of cisplatin stimulation time. (A, B) BUN and SCr levels from animal models treated with cisplatin for 1, 2, 4 days (n = 5). (C) Western blot images and corresponding quantifications of NGAL in HK2 cells exposed to cisplatin for 3, 6, 12,24h. **** p < 0.0001, *** p < 0.001, ** p < 0.01, * p < 0.05.

Supplemental Fig. 6 UCP1 and lipid droplets were mainly located in renal tubules. (A) Representative confocal microscopic images of lectin and UCP1 in the kidneys of control mice. (B) Representative confocal microscopic images of AQP1 and UCP1 in the kidneys of control mice. (C) Representative confocal microscopic images of AQP1 and BODIPY dye in the
kidneys of mice treated with cisplatin. Nuclei are counterstained with DAPI.

**Supplemental Fig. 7 The content of triglyceride (TG) in renal tissues.** (A, B) Specific administration methods of animal models. (C) Relative TG content (gprot/L) in AKI models induced by cisplatin with control or UCP1 adenovirus injection tested by TG assay kit. (D) Relative TG content (gprot/L) in AKI models induced by cisplatin with CL316243 treatment.

**** p < 0.0001, *** p < 0.001, ** p < 0.01, * p < 0.05.

**Supplemental Fig. 8 The relative protein level of LC3 in HK2 cells.** (A, B) Western blot images and corresponding quantifications of LC3 in HK2 cells exposed to cisplatin with or without UCP1 overexpression. **** p < 0.0001, *** p < 0.001, ** p < 0.01, * p < 0.05.
Supplemental Fig. 1
Supplemental Fig. 2

Cluster analysis chart

<table>
<thead>
<tr>
<th>Ctrl</th>
<th>Cisplatin</th>
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The figure shows a cluster analysis chart comparing Ctrl and Cisplatin conditions. The horizontal axis represents different samples, and the vertical axis represents the expression levels of genes. The color gradient indicates the expression levels, with blue representing low expression and red representing high expression.
Supplemental Fig. 3

Lipidmaps annotation

Fatty Acyls [FA]
- Other Fatty Acyls [FA00]
- Octadecanoid FA02
- Hydrocarbons [FA11]
- Fatty esters [FA07]
- Fatty amides [FA08]
- Fatty aldehydes [FA06]
- Fatty alcohols [FA05]
- Fatty acyl glycosides [FA13]
- Fatty Acids and Conjugates [FA01]
- Sphingoside FA03
- Docosanoids [FA04]

Glycerolipids [GL]
- Triacylglycerols [GL03]
- Other Glycerolipids [GL00]
- Monoradylglycerols [GL01]
- Diradylglycerols [GL02]

Glycerophospholipids [GP]
- Phosphatidylethanolamine [GP20]
- Other Glycerophospholipids [GP00]
- Glycerophosphoethanolamines [GP31]
- Glycerophosphoinositol [GP16]
- Glycerophosphorylcholine [GP12]
- Glycerophosphorylcholines [GP12]
- Glycerophosphocholines [GP02]
- Glycerophosphates [GP01]

Polyketides [PK]
- Macrolides and lactone polyketides [PK04]
- Flavonoids [PK07]
- Cytochalasines [PK11]

Prenol Lipids [PR]
- Stigmasterol and hoprostanones [PR02]
- Polyprenols [PR03]
- Prenol [PR04]
- Hopanoids [PR04]

Saccharolipids [SL]
- Acylquinones [SL03]

Sphingolipids [SP]
- Sphingoid bases [SP01]
- Phosphosphingolipids [SP03]
- Neutral glycosphingolipids [SP05]
- Ceramides [SP02]
- Acidic glycosphingolipids [SP06]

Sterol Lipids [ST]
- Steroids [ST03]
- Bile acids and derivatives [ST04]
Supplemental Fig. 4

KEGG pathway annotation

Cellular Processes
- Cell growth and death: 2

Environmental Information Processing
- Signal transduction: 1

Metabolism
- Metabolism of cofactors and vitamins: 3
- Lipid metabolism: 12
- Global and overview maps: 16
- Amino acid metabolism: 1

Organismal Systems
- Nervous system: 1
- Immune system: 1
- Endocrine system: 4
- Digestive system: 4
- Circulatory system: 2

Number of Metabolites
Supplemental Fig. 5

A

B

C

kDa

NGAL

GAPDH

Ctrl 3 h 6 h 12 h 24 h
Supplemental Fig. 7

A

Euthanasia

Adenovirus intrarenal injection

Euthanasia

Cisplatin ip. (25mg kg⁻¹)

B

Euthanasia

Cisplatin ip. (25mg kg⁻¹)

CL316243 iv. (2 mg kg⁻¹) and ip. (2 mg kg⁻¹)

C

D

TG

Ad-CtrlAd-UCP1

Ad-CtrlAd-UCP1

Sham

Cisplatin

TG

Cisplatin

CL316243

- + +

****

##

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Supplemental Fig. 8