

## Supplementary material

**Table S1** Details of antibodies.

Antibody	Molecular weight	Catalog number	Dilution	Company	Area
FFAR2	50 kDa	19952-1-AP	1:1000	Proteintech	Wuhan, China
$\beta$ -Arrestin 2	50 kDa	10171-1-AP	1:1000	Proteintech	Wuhan, China
I $\kappa$ B $\alpha$	35 kDa	ab32518	1:4000	Abcam	Cambridge, MA, USA
p-I $\kappa$ B $\alpha$ (Ser32/Ser36)	39 kDa	AF2002	1:1000	Affinity	Cincinnati, OH, USA
TAB1	55 kDa	67020-1-IG	1:5000	Proteintech	Wuhan, China
TAK1	67 kDa	12330-2-AP	1:1000	Proteintech	Wuhan, China
p-TAK1 (Thr184/Thr187)	70 kDa	AF4379	1:1000	Affinity	Cincinnati, OH, USA
IKK $\alpha/\beta$	85 kDa	ab178870	1:1000	Abcam	Cambridge, MA, USA
p-IKK $\alpha/\beta$ (Ser180/Ser181)	87 kDa	AF3013	1:1000	Affinity	Cincinnati, OH, USA
NF- $\kappa$ B p65/RelA	60 kDa	A18210	1:1000	ABclonal	Wuhan, China
p-NF- $\kappa$ B p65 (Ser536)	65 kDa	AF2006	1:1000	Affinity	Cincinnati, OH, USA
IL-1 $\beta$	30 kDa	A16288	1:1000	ABclonal	Wuhan, China
IL-6	24 kDa	12912S	1:1000	Cell Signaling Technology	Beverly, MA, USA
IL-1 $\alpha$	20 kDa	A2170	1:1000		Wuhan, China
TNF- $\alpha$	25 kDa	A0277	1:1000	ABclonal	Wuhan, China
MCP1	26 kDa	66272-1-Ig	1:1000	Proteintech	Wuhan, China
GAPDH	37 kDa	E-AB-20032	1;2000	Elabscience	Wuhan, China
Goat Anti-Rabbit (H+L)	/	E-AB-1003	1;4000	Elabscience	Wuhan, China
Goat Anti-Mouse (H+L)	/	E-AB-1001	1;4000	Elabscience	Wuhan, China

**Table S2** Relative abundance of top 20 genera.

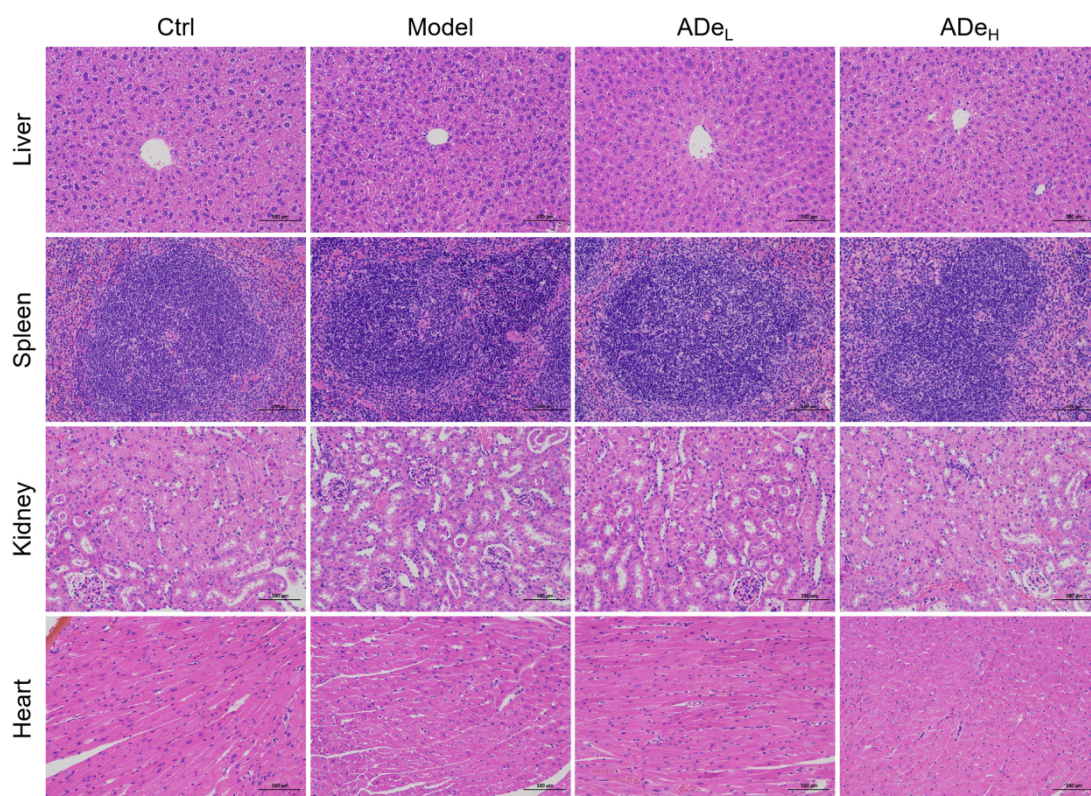
<b>Sample</b>	<b>Mean of Ctrl</b>	<b>Mean of Model</b>	<b>Mean of ADL</b>	<b>Mean of ADH</b>
<i>Clostridium</i>	0.004202	0.01461	0.002916	0.001994
<i>Turicibacter</i>	0.000745	0.006197	0.002047	0.003385
<i>Phascolarctobacterium</i>	0.013097	0.014018	0.006649	0.006049
<i>Oscillospira</i>	0.018361	0.040055	0.041611	0.025535
<i>Adlercreutzia</i>	0.002303	0.002173	0.001303	0.001486
<i>Desulfovibrio</i>	0.008533	0.011349	0.012245	0.009161
<i>Mucispirillum</i>	0.000834	0.001717	0.001831	0.001791
<i>Bifidobacterium</i>	0.001513	0.001591	0.000462	0.001888
<i>Roseburia</i>	0.004639	0.001511	0.000454	0.000057
<i>[Ruminococcus]</i>	0.007662	0.007036	0.008931	0.005189
<i>Lactobacillus</i>	0.099375	0.057621	0.031702	0.057311
<i>Ruminococcus</i>	0.004628	0.011089	0.015433	0.016147
<i>Coprococcus</i>	0.023208	0.016967	0.019242	0.012326
<i>Paraprevotella</i>	0.001101	0.002141	0.008284	0.003426
<i>Sutterella</i>	0.003923	0.004417	0.006274	0.006652
<i>Bacteroides</i>	0.004252	0.004971	0.008614	0.010838
<i>Allobaculum</i>	0.041358	0.007517	0.010727	0.015557
<i>Flexispira</i>	0.001899	0.001738	0.00299	0.004929
<i>Parabacteroides</i>	0.000769	0.000841	0.002604	0.002768
<i>Akkermansia</i>	0.002036	0.001084	0.001581	0.002793

**Table S3** Significantly different metabolites.

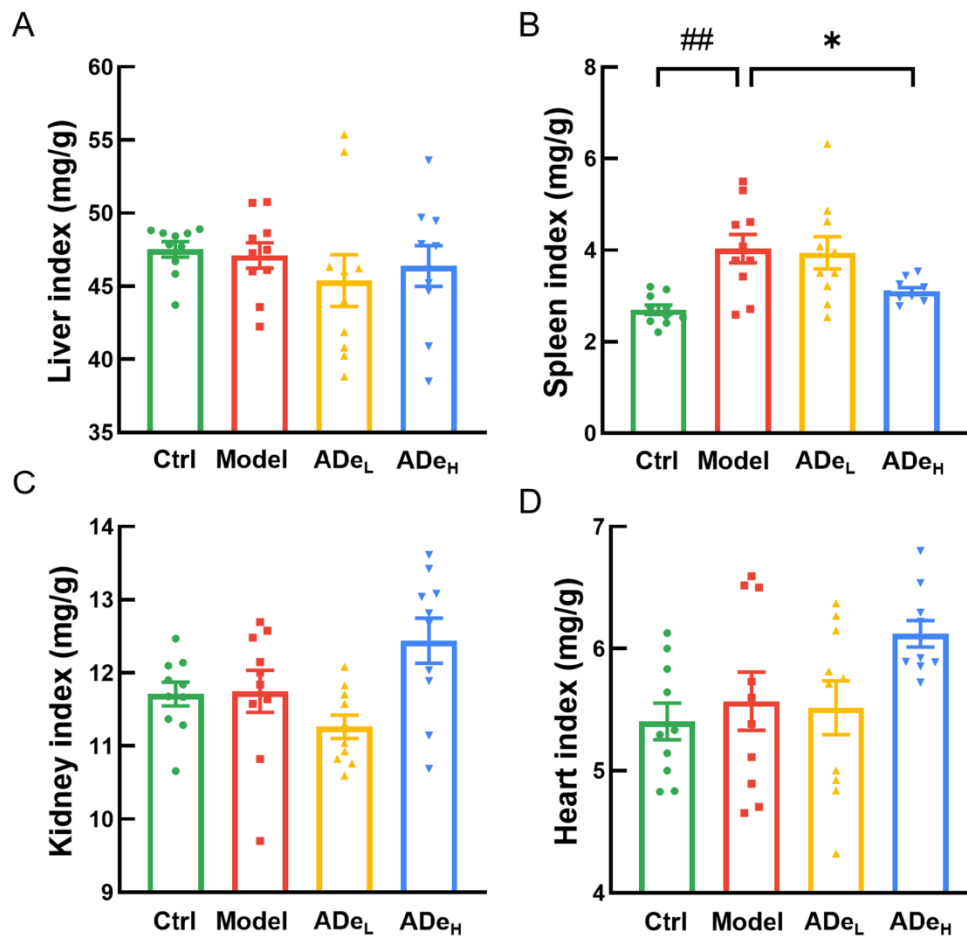
Adduct	Name	Mean of Ctrl	Mean of Model	Mean of 0.45g/kg	Mean of 1.35g/kg
(M-H)-	Orotate	19282.34	39213.20	19932.81	27283.77
(M+H)+	Allantoin	19046.22	26409.58	23434.82	17906.86
M+	Choline	35549.59	41856.17	29123.37	23283.80
(M-H)-	(+)-12-HETE	800438.63	964611.34	899755.80	888147.88
(M-H)-	cis-9-Palmitoleic acid	549657.15	616645.32	545667.01	441609.74
(M-H)-	Nervonic acid	22326.85	24278.77	15080.39	16818.34
(M+H)+	Creatinine	50917.70	58337.68	51521.48	38833.17
(M-H)-	Thymidine	7895.45	19949.32	16114.46	15049.20
(M-H)-	2'-Deoxyuridine	21523.55	42700.72	37930.36	31855.35
(M-H)-	2-Ethyl-2-Hydroxybutyric acid	30571.13	39644.76	38311.58	23152.79
(M-H)-	7Z, 10Z, 13Z, 16Z, 19Z-Docosapentaenoic acid	261366.53	268411.64	204910.19	247925.21
(M+H-H <sub>2</sub> O)+	DL-Indole-3-lactic acid	47974.53	47582.66	37473.85	27348.72
(M-H)-	Behenic acid	10484.59	9857.15	5039.71	6100.14
(M-H)-	Dihomo-gamma-Linolenic Acid	184990.83	175296.86	133159.36	136644.00
(M-H)-	Ethyl glucuronide	3116.66	7241.27	8389.99	4229.35
(M+H)+	L-Carnitine	1645264.84	1503513.57	1227646.83	793151.79
(M+H)+	Pantothenate	42146.06	42576.09	42524.08	35201.10
(M+CH <sub>3</sub> CN+H)+	1-Palmitoyllysophosphatidylcholine	62345.50	56843.03	31813.78	47735.45
(M+Na-2H)-	1-Oleoyl-L-alpha-lysophosphatidic acid	49069.27	45624.58	29159.38	41434.13
(M-H <sub>2</sub> O-H)-	Glycerol 3-phosphate	87002.12	75628.16	61269.38	59063.14
(M+H)+	Taurine	186273.48	188442.61	211033.62	86242.75
(M-H)-	3,4-Dihydroxybenzoate (Protocatechuic acid)	25965.26	16725.51	10280.99	5804.65
(M+H-H <sub>2</sub> O)+	L-Glutamate	40602.05	33500.89	33988.40	22134.09
M+	alpha-Tocopherol (Vitamin E)	173847.09	161320.69	144436.26	173276.27
(M+K)+	Ile-Asn	21848.69	14682.02	12172.01	14646.87
(M+H)+	Anthranilic acid (Vitamin L1)	109909.56	91434.55	133647.14	72262.15
(M+H)+	1-Palmitoyl-sn-glycero-3-phosphocholine	52426.69	35313.38	69672.19	19681.84
(M+H-H <sub>2</sub> O)+	1-Aminocyclopropanecarboxylic acid	16108.77	18325.88	27232.87	24930.57
(M-H)-	3-Indolepropionic acid	19264.12	6850.39	7837.07	8644.35

(M+H-H <sub>2</sub> O)+	Dopamine	11857.67	5984.61	7642.94	5839.46
(M-H)-	Phenol	26535.33	17734.05	22560.08	16790.92
(M+CH <sub>3</sub> COO+2H)+	Cyclohexylamine	16149.28	7295.55	9055.07	10006.53
(M+H)+	L-Palmitoylcarnitine	23467.00	20233.18	27983.09	22442.88
(M+H)+	Nicotinamide N-oxide	11999.32	7114.54	11521.63	15643.40
M+	1-Methylnicotinamide	27252.88	17201.35	24155.77	23874.91
(M-H)-	Cyclopiazonic Acid	8828.82	4707.96	9773.92	10128.77

## Figure List



**Figure S1** Histopathological analysis of the liver, spleen, kidney, and heart via H&E staining (200×; scale bar: 100 μm).



**Figure S2** The effect of ADe on organ indices in CAC mice. the (A) liver, (B) spleen, (C) kidney, and (D) heart. Data are presented as the means ± S.E.M. Different groups performed with one-way ANOVA followed by a post hoc multiple comparisons (Dunnett) test.  $^{##}p < 0.01$  vs. Ctrl group;  $^{*}p < 0.05$  vs. model group.