**Table S1 Sequencing results of the 18 fecal samples.**

| Sample ID | PE Reads | Raw Tags | Clean Tags | Effective Tags | Effective (%) | OTUs |
|---|---|---|---|---|---|---|
| Ctrl-1 | 80073 | 75621 | 73259 | 70676 | 88.26 | 306 |
| Ctrl-2 | 80002 | 75757 | 72883 | 66132 | 82.66 | 296 |
| Ctrl-3 | 80411 | 77169 | 75044 | 64911 | 80.72 | 289 |
| Ctrl-4 | 80055 | 76485 | 74213 | 65525 | 81.85 | 291 |
| Ctrl-5 | 80203 | 77184 | 75193 | 73262 | 91.35 | 290 |
| Ctrl-6 | 79854 | 77037 | 75004 | 71301 | 89.29 | 302 |
| HFS-1 | 80191 | 77471 | 75953 | 70816 | 88.31 | 290 |
| HFS-2 | 80218 | 77233 | 75867 | 71888 | 89.62 | 287 |
| HFS-3 | 79661 | 77119 | 75967 | 72137 | 90.55 | 220 |
| HFS-4 | 80072 | 76956 | 75214 | 71969 | 89.88 | 249 |
| HFS-5 | 79666 | 77078 | 75634 | 72322 | 90.78 | 236 |
| HFS-6 | 79920 | 77082 | 75564 | 72401 | 90.59 | 250 |
| HFS+M-CGA-1 | 79798 | 77142 | 75426 | 69183 | 86.7 | 244 |
| HFS+M-CGA-2 | 80028 | 77887 | 76199 | 64100 | 80.1 | 243 |
| HFS+M-CGA-3 | 80163 | 77885 | 76497 | 69552 | 86.76 | 230 |
| HFS+M-CGA-4 | 79957 | 77616 | 76362 | 69565 | 87 | 211 |
| HFS+M-CGA-5 | 79806 | 77638 | 77068 | 72074 | 90.31 | 212 |
| HFS+M-CGA-6 | 79820 | 77447 | 76768 | 70287 | 88.06 | 207 |
| Total | 1360078 | 1310360 | 1281347 | 1187814 | 87.33 | 4653 |

**Supplemental methods:**

**Quantitative reverse transcriptase polymerase chain reaction**

For quantitative reverse transcription polymerase chain reaction (qRT-PCR), total RNA was extracted from tissues as previously described. Reverse transcription and SYBG qPCR were performed as the manufacturer's instruction (TsingKe Biological Technology, Beijing, China). qPCR was performed using a BioRad CFX96 qPCR System. The fold-changes to GAPDH were determined using the comparative threshold cycle (Ct) method. Primers used in this work are shown in Table S2.

**Western blotting**

Tissue or cell samples were homogenized in RIPA lysis buffer (GBC BIO Technologies

Inc., Guangzhou, China, G3424). After centrifugation, the total protein concentration in the supernatant was determined by a BCA protein assay reagent kit (GBC, G3422). 30 μg of protein for each sample was denatured in a metal heater for 5 minutes then separated by SDS-PAGE and transferred onto polyvinylidene difluoride (PVDF) membrane. The membrane was blocked within 5% nonfat dry milk in Tris-buffered saline for 2h, followed by incubation with rabbit anti-FXR antibody (1:2000 dilution, Abcam, Waltham, MA, USA, ab235094) or anti-TGR5 (TGR5) antibody (1:1000 dilution, Abcam, ab72608) at room temperature for 1h and then overnight at 4℃. For GAPDH, the membranes were stripped and reprobed with rabbit anti-GAPDH antibody (GAPDH) (1:4000 dilution, Affinity Biosciences LTD, Changzhou, China, AF7021). After washing with Tris-buffered saline, membranes were incubated with goat anti-rabbit horseradish peroxidase-conjugated secondary antibody (1:1500 dilution, Affinity, S0001) and visualized using enhanced chemiluminescence. The intensities of blotted bands were quantified with the software ImageJ (free download from http://rsbweb.nih.gov/ij/).

**Quantification of Klebsiella in total DNA from fecal samples**

Then genomic DNA was extracted according to the manufacture's protocol of Stool Genomic DNA Kit (Transgen Biotech, Beijing, China, EE301-01) as we described before[1]. The concentration of fecal DNA was measured by NanoDrop 2000 UV-Vis spectrophotometers (Thermo Fisher, Waltham, MA, USA). The semi-quantified PCR was performed to determine the relative abundance of Klebsiella by the ratio of specific

Klebsiella amplification (Khe in Table S1) to universal 16srDNA amplification (16srDNA in Table S1). Analysis and fold-change were assessed using the comparative threshold cycle (Ct) method.

**Isolation of *Klebsiella* strains from the colonic feces of HFS+M-CGA mice**

500 mg of fecal samples from HFS+M-CGA mice were collected in sterile tubes and used for the isolation of *Klebsiella* strains according to a protocol we previously described[1]. The bacterial suspension was spread on the BHI agar (Qingdao Hope Bio-Tcehnology Co., Ltd, Qingdao, China) and incubated at 37℃ for two days. *Klebsiella oxytoca* isolates were examined by PCR with primers Khe/infB/pgi/mdh (housekeeping genes, seen in Table S2) and confirmed by DNA sequencing (TsingKe Biological Technology, Beijing, China). After growing in the media BHI at 37℃ overnight, $OD_{600}$ was checked to quantify the *K. oxytoca* cells. Then the bacterial cells were collected by centrifugation, washed by PBS for 5 times and then suspended in McCoy's 5A medium or PBS for subsequent treatment.

**Treatment of *Klebsiella* strains on human intestinal cells HT29**

The human intestinal cancer cell line HT29 was purchased from Procell Life Science & Technology Co., Ltd. (Procell, Wuhan, China, CL-0118). The HT29 cells were routinely propagated in McCoy's 5A medium, supplemented with 10% fetal bovine serum (HyClone, Logan, Utah, USA, SV30160.03) and 1% Pen-Strep Solution (Procell, PB180120). To avoid the overgrowth of bacteria, HT29 cells were treated with

$10^8$ cfu/ml *K. oxytoca* in serum-free medium for 4 h. At the end of the experiments, cells were harvested for the following tests of Western blotting.

**Treatment of *Klebsiella* strains on HFS-induced hypertensive mice**

Mice were randomly divided into four groups: $10^8$ cfu/mouse of *K. oxytoca* was used to treat HFS-induced hypertensive mice daily by gavage administration (HFS+Ko); 100 mg/kg/d of CGA was received in HFS-fed mice (HFS+M-CGA); HFS-induced hypertensive group (HFS); control group (Ctrl). The experiment lasted 8 weeks. BP was monitored via the tail cuff method. The measurements were performed between 1:00 pm and 4:00 pm. The approval number of animal ethical committee for this experiment is ZYD-2020-086.

**BA composition analysis**

100 μl of each serum sample was collected in sterile tubes and sent to the BioNovoGene Technologies Inc (Suzhou, China). LC-MS/MS analysis was used to determine the profiles of BAs in the serum samples. Briefly, each serum sample was mixed with 300 μl of methanol: water (4:1, v/v) solution, vortexed for 60s and placed at -20℃ for 30 min to precipitate proteins. After centrifugation at 12000g at 4℃ for 10 min, the supernatant was transferred to a fresh tube, dried by vacuum concentrator at 25℃ and then further extracted by 100 μl of methanol: water (4:1, v/v) solution. After centrifugation at 12000g at 4℃ for 10 min, the supernatant was carefully transferred to sample vials for LC-MS/MS analysis. Chromatographic separation of the metabolites

was performed on an ExionLCTMAD system (AB Sciex, USA) equipped with an ACQUITY UPLC BEH C18 column (100 mm × 2.1 mm i.d., 1.7 μm; Waters, Milford, USA). The elution solvents were 0.01% formic acid/water (A) and acetonitrile (B). The elution gradient over 38 min at a flow rate of 0.25 ml/min was as follows: 0~4 min (25% B), 4~9 min (25~30% B), 9~14 min (30~36% B), 14~18 min (36~38% B), 18~24 min (38~50% B), 24~32 min (50~75% B), 32~35 min (75~100% B), and 35~38 min (100~25% B). The UPLC system was coupled to a quadrupole-time-of-flight mass spectrometer (Triple TOFTM5600+, AB Sciex, USA) equipped with an electrospray ionization (ESI) source operating in positive and negative modes. 40 bile acid standards were accurately prepared and diluted to obtain a series of calibration concentrations for quantitative analysis of BAs.

After UPLC-TOF/MS analyses, the data were imported into the Progenesis QI 2.3 (Nonlinear Dynamics, Waters, USA) for peak detection and alignment. Following normalization procedures and imputation, statistical analysis was performed on log transformed data to identify significant differences in BA levels between comparable groups. All the concentrations of BAs were scaled to Pareto Scaling prior to conducting the Orthogonal partial least squares discriminate analysis (OPLS-DA). The model parameters R2 and Q2 were used to evaluate the model validity and the P values were estimated with paired Student's t-test on Single dimensional statistical analysis.

**Effects of Deoxycholic acid on vasoconstriction in arterioles of mice**

The aortas of mice were isolated and placed in cold PSS buffer (NaCl 130mM, KCl

4.7 mM, $KH_2PO_4$ 1.18mM, $MgSO_4$ 1.17mM, $NaHCO_3$ 14.9mM, glucose 5.5mM, EDTA 0.026mM) pre-equilibrated with 95% $O_2$ and 5% $CO_2$. Then the aortas were carefully cleaned off adhering fat tissues, and cut into segments of 2 to 3 mm in length. Every aortic ring was suspended by 2 parallel stainless wires and attached to force transducer in a warmed bath chamber containing PSS (pH7.4, 37°C). During the initial equilibration period of 1h, the rings were set to a base tension of 5mN. After stably exposed to 60 mM KCl, vessels were sub-maximally pre-contracted with phenylephrine (PE, 1μM, Sigma, Milwaukee, Wisconsin, USA) and the endothelial function was evaluated by vascular relaxation in response to cumulative doses (0-200 μmol/L) of DCA, CA or control solution. Aortic ring tension changes were recorded by Chart software (DMT620M, Denmark).

**Effects of Deoxycholic acid on HFS-hypertension**

Based on previous studies[2], 0.2% DCA was mixed in 4% NaCl-contained diet. Mice were randomly divided into two groups: one group was fed with HFS diet plus extra 0.2% DCA (HFS+DCA); the other group was only administered with HFS (HFS). The animal experiment lasted for 6 weeks. BP was recorded by the tail cuff method. The approval number of animal ethical committee for this experiment is ZYD-2021-138.

Table S2 Sequences of the primers used in this work

| Gene | Species | Sense Primer sequences | Antisense primer sequences |
|---|---|---|---|
| GAPDH | Mouse | ATGGTGAAGGTCGGTGTGAA | GGTCGTTGATGGCAACAATCTC |

| | | | |
|---|---|---|---|
| FXR | Mouse | CATCCGTGTGGCATTTGACC | CAACTGAGAAGGAGCCGAGG |
| TGR5 | Mouse | TCATCGTCATCGCCAACCTG | CAGTAGCCCTGATGGTTCCG |
| ASBT | Mouse | GGCTACAGCCTGGGTTTCTT | CACCAGGTTGAGATCCTCGG |
| GPR43 | Mouse | CGACTAGAGATGGCTGTGGT | AGAAGATGAGCAGTGTGGCT |
| GPR41 | Mouse | TCCAGCCTGGCTTTCCAATA | GCCTGCAGGAGACATTTCAG |
| Olrf78 | Mouse | AAGCGACTGGCTTTCTGTCA | GCCTTAGCTCGCTCAGACTT |
| FXR | Human | CTGCGTGATGGACATGTACATG | CCTGCAAAACTTGGTTGTGGAGG |
| GAPDH | Human | GATGACATCAAGAAGGTGGTG | GCTGTAGCCAAATTCGTTGTC |
| Khe | | TGATTGCATTCGCCACTGG | GGTCAACCCAACGATCCTG |
| 16srDNA | | TGCCAGCAGCCGCGGTAATAC | CTTGTGCGGGCCCCCGTC |
| infB | | CTCTCTGCTGGACTACATTCG | CGCTTTCAGCTCCAGAACTTC |
| mdh | | CCCAACTGCCTTCAGGTTCAG | CCTTCCACGTAGGCGCATTC |
| pgi | | GAGAAAAACCTGCCGGTGC | CGGTTAATCAGGCCGTTAGTG |

## Reference:


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2. Y. Zhang, I. L. Csanaky, L. D. Lehman-McKeeman and C. D. Klaassen, Loss of organic anion transporting polypeptide 1a1 increases deoxycholic acid absorption in mice by increasing intestinal permeability, *Toxicol Sci*, 2011, **124**, 251-260.