

## Supplementary Information

**Table S1.** The ingredients and energy of the normal chow diet and high-fat diet.

| Ingredient               | Normal chow diet (gm)<br>( #D10012G ) | High-fat diet (gm)<br>( #D12109C ) |
|--------------------------|---------------------------------------|------------------------------------|
| Casein                   | 200                                   | 200                                |
| L-Cystine                | 3                                     | 3                                  |
| Con Starch               | 397                                   | 212                                |
| Maltodextrin 10          | 132                                   | 71                                 |
| Sucrose                  | 100                                   | 113                                |
| Cellulose,BW200          | 50                                    | 50                                 |
| SoybeanOil               | 70                                    | 25                                 |
| t-Butylhydroquinone      | 0.014                                 | 0                                  |
| Mineral Mix S10022G      | 35                                    | 0                                  |
| Vitamin Mix V10037       | 10                                    | 0                                  |
| Choline Bitartrate       | 2.5                                   | 2                                  |
| Cocoa Butter             | 0                                     | 155                                |
| Mineral Mix S10021       | 0                                     | 10                                 |
| Dicalcium Phosphate      | 0                                     | 13                                 |
| Calcium Carbonate        | 0                                     | 5.5                                |
| Potassium Citrate        | 0                                     | 16.5                               |
| Vitamin Mix V10001       | 0                                     | 10                                 |
| Cholesterol              | 0                                     | 11.25                              |
| Sodium Cholate           | 0                                     | 4.5                                |
| Calorie sources (kcal %) | Normal chow diet ( kcal% )            | High-fat diet ( kcal% )            |
| Protein                  | 20.3                                  | 20                                 |
| Carbohydrate             | 63.9                                  | 40                                 |
| Fat                      | 15.8                                  | 40                                 |
| kcal/gm                  | 3.9                                   | 4.5                                |

**Table S2.** The procedures and instrument parameters of fecal metabolomics analysis based on UHPLC-Triple TOF

| Item                   | Information and parameters                                                                                                                                                                                                                         |
|------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Chromatographic column | ACQUITY UPLC HSS T3 column (100 mm × 2.1 mm i.d., 1.8 μm)                                                                                                                                                                                          |
| Mobile phase           | A: 95% water + 5% acetonitrile (containing 0.1% formic acid)<br>B: 47.5% acetonitrile + 47.5% isopropanol + 5% water (containing 0.1% formic acid)                                                                                                 |
| UPLC                   | Injection volume, 10 μL; column temperature, 45°C; flow rate, 0.4 mL/min                                                                                                                                                                           |
| MS condition           | Electrospray ionization (ESI); Positive and negative ion scanning modes                                                                                                                                                                            |
| MS parameter           | Scan type 50-1200m/z; Ion Source Gas1 50psi; Ion Source Gas2 50psi; Curtain Gas 35psi; Source Temperature 500°C; IonSpray Voltage Floating (+) 5500V; IonSpray Voltage Floating ( - ) -4500V; Declustering Potential 80V; Collision Energy 40±20eV |

**Table S3.** Detailed information of intestinal differential metabolites between HC and NC groups

| Retention time | Metabolite                                                | M/Z         | Adducts   | Formula         | VIP    | FC      | Trend | P   | HMDB number                                   | Score |
|----------------|-----------------------------------------------------------|-------------|-----------|-----------------|--------|---------|-------|-----|-----------------------------------------------|-------|
| 6.79           | Diosgenin                                                 | 437.3037406 | M+Na      | C27 H42 O3      | 2.6849 | 0.048   | ↓     | *** | HMDB0242671                                   | 44.8  |
| 8.11           | Ceanothenic Acid                                          | 455.3136384 | M+H       | C29 H42 O4      | 2.6391 | 0.1791  | ↓     | *** | HMDB0036850                                   | 44.7  |
| 4.33           | Cimifugin                                                 | 311.091276  | M+Na-H2O  | C16 H18 O6      | 2.6458 | 0.0098  | ↓     | *** | HMDB0250254                                   | 45.6  |
| 8.08           | Pi(Pgf1Alpha/18:0)                                        | 919.561419  | M-H2O-H   | C47 H87 O16 P   | 2.616  | 0.1592  | ↓     | *** | HMDB0276437                                   | 43.8  |
| 4.82           | Obtustylene                                               | 285.1138309 | M+FA-H    | C16 H16 O2      | 2.5839 | 0.0613  | ↓     | *** | HMDB0030672                                   | 46.5  |
| 6.79           | Coenzyme Q4                                               | 455.313222  | M+H       | C29 H42 O4      | 2.5471 | 0.2657  | ↓     | *** | LMPR02010003                                  | 45.1  |
| 7.62           | Ginkgolic Acid                                            | 347.2569101 | M+H       | C22 H34 O3      | 2.584  | 7.1926  | ↑     | *** | HMDB0033897                                   | 47.2  |
| 4.82           | Acetylshikonin                                            | 331.1177911 | M+H       | C18 H18O6       | 2.5509 | 0.0834  | ↓     | *** | HMDB0247936                                   | 45.9  |
| 4.82           | Pongamol                                                  | 295.095814  | M+H       | C18 H14 O4      | 2.531  | 0.284   | ↓     | *** | HMDB0253968;LMPK1<br>2120373;LMPK121206<br>14 | 48.3  |
| 4.82           | Pteric Acid                                               | 313.1069644 | M+H       | C14 H12 N6 O3   | 2.5114 | 0.3566  | ↓     | *** | HMDB0256914                                   | 46.5  |
| 4.49           | Seneciphylline                                            | 334.1636662 | M+H       | C18 H23 N O5    | 2.4739 | 0.0369  | ↓     | *** | HMDB0258231                                   | 47.5  |
| 7.96           | Limaprost                                                 | 361.2352309 | M-H2O-H   | C22 H36 O5      | 2.4637 | 0.0004  | ↓     | *** | HMDB0254093                                   | 45.1  |
| 10.16          | Dg(20:4(8Z,11Z,14Z,17Z)/15:0/0:0)                         | 603.4922824 | M+H       | C38 H66 O5      | 2.3878 | 2.6283  | ↑     | *** | HMDB0007532                                   | 44    |
| 3.75           | Dihydroconiferyl Alcohol                                  | 241.1087515 | M+Hac-H   | C10 H14 O3      | 2.3957 | 0.0685  | ↓     | *** | HMDB0303757                                   | 45.9  |
| 4.80           | Cyclokievitone                                            | 355.116506  | M+H       | C20 H18 O6      | 2.3567 | 10.5615 | ↑     | *** | HMDB0033983                                   | 46    |
| 8.66           | Pe(22:6(4Z,7Z,11E,13Z,15E,19Z)-<br>2Oh(10S,17)/22:1(13Z)) | 910.6131987 | M+CH3OH+H | C49 H84 N O10 P | 2.3135 | 3.0837  | ↑     | *** | HMDB0283903                                   | 42.2  |
| 4.37           | Coclaurine                                                | 286.1436408 | M+H       | C17 H19 N O3    | 2.2612 | 4.0769  | ↑     | *** | HMDB0303359                                   | 45.4  |
| 3.98           | 4-Ethylphenol                                             | 121.0658421 | M-H       | C8 H10 O        | 2.2817 | 10.3382 | ↑     | *** | HMDB0029306                                   | 50.6  |
| 9.06           | Pc(22:0/16:0)                                             | 856.6116884 | M+K       | C46 H92 N O8 P  | 2.2468 | 2.9736  | ↑     | *** | HMDB0008528                                   | 40.9  |
| 9.81           | 1-Eicosanoyl-Sn-Glycero-3-<br>Phosphocholine              | 552.3989407 | M+H       | C28 H58 N O7 P  | 2.2598 | 2.7717  | ↑     | *** | LMGP01050045                                  | 41.7  |
| 3.73           | Wallemine                                                 | 235.1695997 | M+H-H2O   | C15 H24 O3      | 2.1805 | 0.2376  | ↓     | *** | -                                             | 47.9  |
| 9.25           | Phosphatidylcholine Lyso 18:0                             | 1047.733119 | 2M+H      | C26 H54 N O7 P  | 2.1921 | 2.1801  | ↑     | *** | -                                             | 46.2  |
| 7.00           | 2,9,10,10A-Tetrahydrophenanthren-3-<br>One                | 303.1608825 | M+H       | C18 H22 O4      | 2.2029 | 0.3057  | ↓     | *** | -                                             | 43.1  |
| 4.47           | Zolazepam                                                 | 304.1590426 | M+NH4     | C15 H15 F N4 O  | 2.1785 | 0.231   | ↓     | *** | HMDB0260040                                   | 43.5  |
| 3.98           | 3-(3-Hydroxyphenyl)Propanoic Acid                         | 165.0560907 | M-H       | C9 H10 O3       | 2.1912 | 3.2857  | ↑     | *** | HMDB0000375                                   | 55.1  |
| 4.81           | Caffeic Acid Ester                                        | 329.1035833 | M+FA-H    | C17 H16 O4      | 2.1621 | 0.4384  | ↓     | *** | HMDB0302344                                   | 47.2  |
| 7.30           | Pe-<br>Nme(22:2(13Z,16Z)/20:5(5Z,8Z,11Z,14Z,1<br>7Z))     | 832.5860425 | M+H       | C48 H82 N O8 P  | 2.1536 | 3.1089  | ↑     | *** | HMDB0113582                                   | 47.4  |

|       |                                                   |             |          |                 |        |         |   |     |              |      |
|-------|---------------------------------------------------|-------------|----------|-----------------|--------|---------|---|-----|--------------|------|
| 6.88  | Porrigenin A                                      | 471.3080604 | M+Na     | C27 H44 O5      | 2.1195 | 0.3527  | ↓ | *** | HMDB0032783  | 46.4 |
| 4.51  | (6S,8Z)-6-Hydroxy-3-Oxotetradecenoic Acid         | 301.1657485 | M+FA-H   | C14 H24 O4      | 2.1469 | 0.2235  | ↓ | *** | HMDB0062364  | 48   |
| 7.23  | Fa(18:1+2O)                                       | 315.251994  | M+H      | C18 H34 O4      | 2.1088 | 0.274   | ↓ | *** | -            | 50.3 |
| 6.05  | Frequentin                                        | 253.1433197 | M+H      | C14 H20 O4      | 2.1211 | 0.1737  | ↓ | *** | -            | 46.8 |
| 9.30  | Pc(20:1/0:0)                                      | 550.3832921 | M+H      | C28 H56 N O7 P  | 2.1152 | 2.2849  | ↑ | *** | LMGP01050047 | 46.8 |
| 6.60  | 17-Aag                                            | 568.3010983 | M+H-H2O  | C31 H43 N3 O8   | 2.1072 | 0.2198  | ↓ | *** | HMDB0244762  | 45   |
| 7.45  | Asperagenin                                       | 471.3095933 | M+Na     | C27 H44 O5      | 2.1054 | 0.4715  | ↓ | *** | HMDB0034293  | 47.9 |
| 3.72  | 2-Methylbenzoic Acid                              | 195.0667325 | M+Hac-H  | C8 H8 O2        | 2.104  | 5.2268  | ↑ | *** | HMDB0002340  | 48.7 |
| 7.16  | Curcumenol                                        | 235.1689615 | M+H      | C15 H22 O2      | 2.1019 | 0.2518  | ↓ | *** | HMDB0033960  | 51   |
| 8.59  | Lysopc(20:3(5Z,8Z,11Z)/0:0)                       | 590.3427957 | M+FA-H   | C28 H52 N O7 P  | 2.0824 | 6.0307  | ↑ | *** | HMDB0010393  | 46.6 |
| 1.33  | 6-Benzoyl-2-Methylbenzo[De]Isoquinoline-1,3-Dione | 316.0995543 | M+H      | C20 H13 N O3    | 2.0786 | 0.2851  | ↓ | *** | -            | 43.7 |
| 10.12 | 6-Isobutyl-4-Hydroxy-2-Pyrone                     | 333.1333737 | 2M-H     | C9 H11 O3-      | 2.0721 | 10.728  | ↑ | *** | HMDB0304229  | 47   |
| 7.34  | Pi(34:0)                                          | 837.5501788 | M-H      | C43 H83 O13 P   | 2.0603 | 3.0459  | ↑ | *** | HMDB0009781  | 42.2 |
| 8.72  | 5-Hexyltetrahydro-2-Furanoctanoic Acid            | 299.2570493 | M+H      | C18 H34 O3      | 2.0651 | 0.3074  | ↓ | *** | HMDB0031127  | 47.4 |
| 8.67  | Pc(20:0/Txb2)                                     | 902.6101633 | M-H      | C48 H90 N O12 P | 2.0464 | 10.2953 | ↑ | *** | HMDB0286972  | 41.8 |
| 8.73  | Palmitoleic Acid Ethyl Ester                      | 247.2413411 | M+H-2H2O | C18 H34 O2      | 2.0463 | 0.2807  | ↓ | *** | -            | 45.1 |
| 8.56  | 3Beta,7Alpha-Dihydroxy-5-Cholestenoate            | 433.328006  | M+H      | C27 H44 O4      | 2.038  | 0.464   | ↓ | *** | HMDB0012454  | 47.6 |
| 6.61  | Eremopetasinorol                                  | 209.1528152 | M+H      | C13 H20 O2      | 2.039  | 0.1273  | ↓ | *** | HMDB0029668  | 48.3 |
| 9.84  | Cis-4,10,13,16-Docosatetraenoic Acid              | 663.5324733 | 2M-H     | C22 H36 O2      | 2.0124 | 0.175   | ↓ | *** | -            | 52   |
| 7.60  | N-Eicosapentaenoyl Arginine                       | 459.3359458 | M+H      | C26 H42 N4 O3   | 2.0168 | 0.4611  | ↓ | *** | HMDB0242065  | 45.4 |
| 7.44  | 25-Hydroxyvitamin D3 3-Sulfate Ester              | 498.3216884 | M+NH4    | C27 H44 O5 S    | 2.0016 | 2.6924  | ↑ | *** | HMDB0245688  | 47.2 |

**Table S4.** Detailed information of intestinal differential metabolites between CA and HC groups

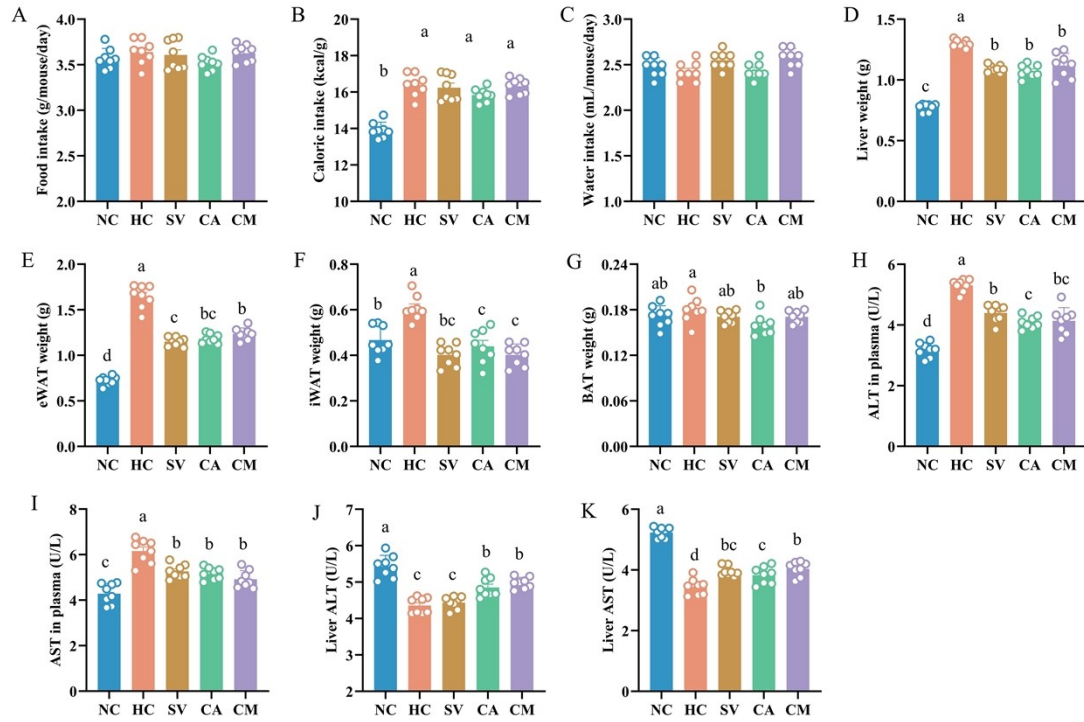
| Retention time | Metabolite                                                                  | M/Z         | Adducts        | Formula        | VIP    | FC      | Trend | P   | HMDB number                             | Score |
|----------------|-----------------------------------------------------------------------------|-------------|----------------|----------------|--------|---------|-------|-----|-----------------------------------------|-------|
| 8.73           | 3-Hydroxyoctadecanoic Acid                                                  | 301.2723023 | M+H            | C18 H36 O3     | 3.4053 | 23.5446 | ↑     | *** | -                                       | 44.6  |
| 8.72           | 5-Hexyltetrahydro-2-Furanoctanoic Acid                                      | 299.2570493 | M+H            | C18 H34 O3     | 3.1689 | 4.5833  | ↑     | *** | HMDB0031127                             | 47.4  |
| 8.74           | (R)-2-Hydroxystearic Acid                                                   | 599.5234668 | 2M-H           | C18 H36 O3     | 3.1862 | 6.1632  | ↑     | *** | -                                       | 54.8  |
| 8.73           | Palmitoleic Acid Ethyl Ester                                                | 247.2413411 | M+H-2H2O       | C18 H34 O2     | 3.0722 | 5.0879  | ↑     | *** | -                                       | 45.1  |
| 8.72           | Dg(15:0/Pgf1Alpha/0:0)                                                      | 619.4867905 | M+H-2H2O       | C38 H70 O8     | 3.0081 | 11.0369 | ↑     | *** | HMDB0295383                             | 42.1  |
| 9.21           | Methyl Oleate                                                               | 297.2771285 | M+H            | C19 H36 O2     | 3.0223 | 4.3516  | ↑     | *** | HMDB0034451;LMFAO 7010965               | 49.8  |
| 4.82           | Obtustylene                                                                 | 285.1138309 | M+FA-H         | C16 H16 O2     | 2.7669 | 12.1561 | ↑     | *** | HMDB0030672                             | 46.5  |
| 8.31           | Pgp(20:1(11Z)/18:2(9Z,12Z))                                                 | 898.5648326 | M+NH4          | C44 H82 O13 P2 | 2.5943 | 3.3062  | ↑     | *** | HMDB0116451                             | 45.1  |
| 8.75           | (+/-)-Menthyl Acetate                                                       | 199.1673921 | M+H            | C12 H22 O2     | 2.5893 | 5.3855  | ↑     | *** | HMDB0041264                             | 46.4  |
| 3.49           | Cyclamate                                                                   | 178.0543737 | M-H            | C6 H13 N O3 S  | 2.6595 | 0.1786  | ↓     | *** | -;HMDB0031340                           | 47.5  |
| 4.49           | Seneciophylline                                                             | 334.1636662 | M+H            | C18 H23 N O5   | 2.4656 | 22.9155 | ↑     | *** | HMDB0258231                             | 47.5  |
| 3.47           | 2-Phenoxypropanoic Acid                                                     | 165.0557228 | M-H            | C9 H10 O3      | 2.4357 | 0.1619  | ↓     | *** | -                                       | 48.8  |
| 5.12           | Calendasaponin B                                                            | 977.4680191 | M+Na-H2O       | C48 H76 O20    | 2.382  | 2.5526  | ↑     | *** | HMDB0039009                             | 41.2  |
| 8.73           | Pa(18:0/18:1(12Z)-2Oh(9,10))                                                | 752.5372455 | M+NH4          | C39 H75 O10 P  | 2.29   | 4.0464  | ↑     | *** | HMDB0263631                             | 42.7  |
| 4.82           | Pongamol                                                                    | 295.095814  | M+H            | C18 H14 O4     | 2.2605 | 2.6316  | ↑     | *** | HMDB0253968;LMPK1 2120373; LMPK12120614 | 48.3  |
| 4.80           | Cyclokieveitone                                                             | 355.116506  | M+H            | C20 H18 O6     | 2.2519 | 0.3084  | ↓     | *** | HMDB0033983                             | 46    |
| 3.75           | Dihydroconiferyl Alcohol                                                    | 241.1087515 | M+Hac-H        | C10 H14 O3     | 2.3178 | 9.0703  | ↑     | *** | HMDB0303757                             | 45.9  |
| 3.72           | 2-Methylbenzoic Acid                                                        | 195.0667325 | M+Hac-H        | C8 H8 O2       | 2.3681 | 0.358   | ↓     | *** | HMDB0002340                             | 48.7  |
| 4.49           | N-Dihydroferuloyltyramine                                                   | 316.1539339 | M+H            | C18 H21 N O4   | 2.2828 | 0.4255  | ↓     | *** | HMDB0033028                             | 46.2  |
| 9.20           | Tg(15:0/14:1(9Z)/22:4(7Z,10Z,13Z,16Z))                                      | 859.6832457 | M+Na-2H        | C54 H94 O6     | 2.2354 | 2.9229  | ↑     | *** | HMDB0043183                             | 40    |
| 5.99           | Nb-P-Coumaroyltryptamine                                                    | 307.1444093 | M+H            | C19 H18 N2 O2  | 2.228  | 0.3343  | ↓     | *** | HMDB0041518                             | 45.9  |
| 8.98           | Pe(P-18:1(11Z)/16:1(9Z))                                                    | 717.5587431 | M+NH4          | C39 H74 N O7 P | 2.1428 | 0.3966  | ↓     | *** | HMDB0011405                             | 43.3  |
| 7.00           | 2-Hydroxy-6,7-Dimethoxy-1,1-Dimethyl-2,9,10,10A-Tetrahydrophenanthren-3-One | 303.1608825 | M+H            | C18 H22 O4     | 2.1301 | 2.7158  | ↑     | *** | -                                       | 43.1  |
| 7.24           | Pi(18:2(9Z,12Z)/Pgf1Alpha)                                                  | 989.5587363 | M+CH3OH+N<br>a | C47 H83 O16 P  | 2.1892 | 3.7918  | ↑     | *** | HMDB0276747                             | 44.1  |
| 5.01           | 1-(1-(Tert-Butoxycarbonyl)Piperidin-4-Yl)Azetidine-3-Carboxylic Acid        | 339.1895733 | M+CH3OH+N<br>a | C14 H24 N2 O4  | 2.1662 | 3.6687  | ↑     | *** | HMDB0247560                             | 46.3  |
| 6.09           | Pa(18:1(12Z)-2Oh(9,10)/8:0)                                                 | 617.3420624 | M+Na           | C29 H55 O10 P  | 2.1816 | 3.2093  | ↑     | *** | HMDB0266642                             | 47.2  |
| 5.76           | 4-(8-Amino-1,2,3,4-Tetrahydro-2-Methyl-4-Isoquinoliny)-2-Methoxyphenol      | 339.169951  | M+CH3OH+N<br>a | C17 H20 N2 O2  | 2.1654 | 0.4431  | ↓     | *** | HMDB0246296                             | 47.1  |
| 5.03           | N-Trans-Feruloyltyramine                                                    | 312.1231953 | M-H            | C18 H19 N O4   | 2.1717 | 0.1643  | ↓     | *** | HMDB0029365                             | 49    |

|      |                                                  |             |         |                |        |        |   |     |             |      |
|------|--------------------------------------------------|-------------|---------|----------------|--------|--------|---|-----|-------------|------|
| 8.08 | Pi(Pgf1Alpha/18:0)                               | 919.561419  | M-H2O-H | C47 H87 O16 P  | 2.0416 | 3.4358 | ↑ | **  | HMDB0276437 | 43.8 |
| 5.99 | 2-Phenyl-3-(3,4,5-Trimethoxyphenyl)Acrylonitrile | 337.1543992 | M+ACN+H | C18 H17 N O3   | 2.0647 | 0.4318 | ↓ | *** | -           | 45.5 |
| 6.05 | Frequentin                                       | 253.1433197 | M+H     | C14 H20 O4     | 2.0249 | 4.4889 | ↑ | *** | -           | 46.8 |
| 4.82 | Pteric Acid                                      | 313.1069644 | M+H     | C14 H12 N6 O3  | 2.0661 | 2.0442 | ↑ | *** | HMDB0256914 | 46.5 |
| 4.51 | (6S,8Z)-6-Hydroxy-3-Oxotetradecenoic Acid        | 301.1657485 | M+FA-H  | C14 H24 O4     | 2.2079 | 3.3916 | ↑ | *** | HMDB0062364 | 48   |
| 5.24 | 4-Tert-Butylphenyl Salicylate                    | 315.1243731 | M+FA-H  | C17 H18 O3     | 2.0183 | 2.5305 | ↑ | *** | HMDB0041314 | 46.1 |
| 9.01 | Lysopc(P-18:1(9Z)/0:0)                           | 550.346638  | M+FA-H  | C26 H52 N O6 P | 2.0255 | 0.2255 | ↓ | *** | HMDB0010408 | 45   |
| 3.39 | 3-(3-Sulfooxyphenyl)Propanoic Acid               | 245.0124429 | M-H     | C9 H10 O6 S    | 2.041  | 0.2031 | ↓ | *** | -           | 51.5 |
| 6.90 | Pregnanediol 3-O-Glucuronide                     | 495.2947114 | M-H     | C27 H44 O8     | 2.0036 | 0.3416 | ↓ | *** | HMDB0010318 | 45.7 |
| 3.98 | 4-Ethylphenol                                    | 121.0658421 | M-H     | C8 H10 O       | 1.9212 | 0.4627 | ↓ | **  | HMDB0029306 | 50.6 |

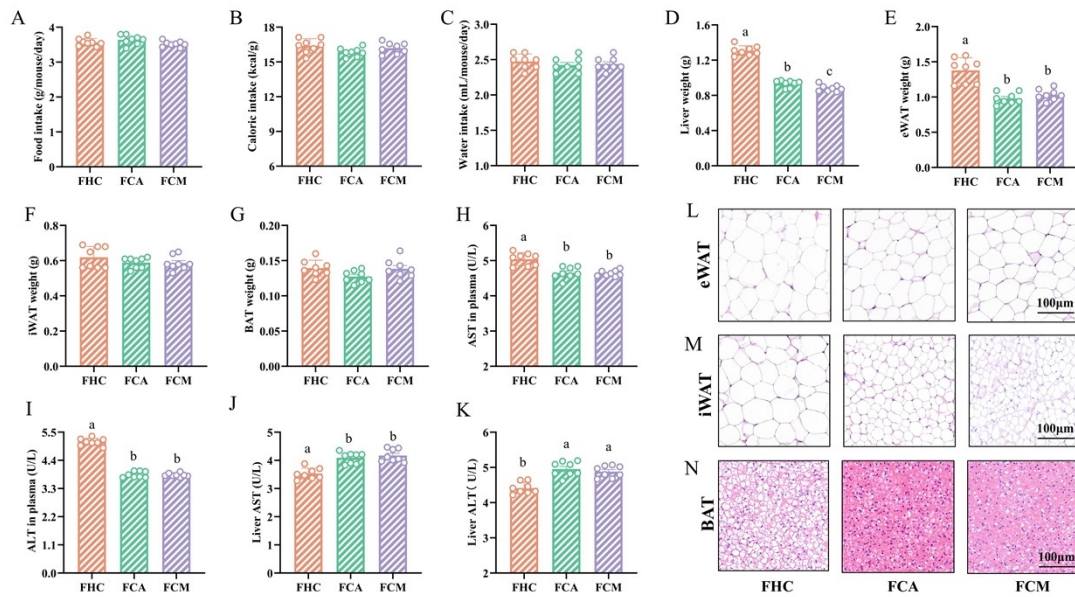
**Table S5.** Detailed information of intestinal differential metabolites between CM and HC groups

| Retention time | Metabolite                                                             | M/Z        | Adducts        | Formula         | VIP    | FC      | Trend | P   | Library ID               | Score |
|----------------|------------------------------------------------------------------------|------------|----------------|-----------------|--------|---------|-------|-----|--------------------------|-------|
| 8.73           | 3-Hydroxyoctadecanoic Acid                                             | 301.27230  | M+H            | C18 H36 O3      | 3.1379 | 23.8378 | ↑     | *** | -                        | 44.6  |
| 8.72           | 5-Hexyltetrahydro-2-Furanoctanoic Acid                                 | 299.25705  | M+H            | C18 H34 O3      | 3.0459 | 4.9608  | ↑     | *** | HMDB0031127              | 47.4  |
| 8.72           | Dg(15:0/Pgf1Alpha/0:0)                                                 | 619.48679  | M+H-2H2O       | C38 H70 O8      | 3.0258 | 13.0524 | ↑     | *** | HMDB0295383              | 42.1  |
| 8.74           | (R)-2-Hydroxystearic Acid                                              | 599.52347  | 2M-H           | C18 H36 O3      | 2.8352 | 6.1839  | ↑     | *** | -                        | 54.8  |
| 8.73           | Palmitoleic Acid Ethyl Ester                                           | 247.24134  | M+H-2H2O       | C18 H34 O2      | 2.8103 | 5.094   | ↑     | *** | -                        | 45.1  |
| 9.21           | Methyl Oleate                                                          | 297.27713  | M+H            | C19 H36 O2      | 2.7644 | 4.3039  | ↑     | *** | HMDB0034451;LMFA07010965 | 49.8  |
| 7.34           | Pi(34:0)                                                               | 837.55018  | M-H            | C43 H83 O13 P   | 2.5819 | 0.2405  | ↓     | *** | HMDB0009781              | 42.2  |
| 3.72           | 2-Methylbenzoic Acid                                                   | 195.06673  | M+Hac-H        | C8 H8 O2        | 2.5794 | 0.1023  | ↓     | *** | HMDB0002340              | 48.7  |
| 5.76           | 4-(8-Amino-1,2,3,4-Tetrahydro-2-Methyl-4-Isoquinoliny)-2-Methoxyphenol | 339.16995  | M+CH3OH+N<br>a | C17 H20 N2 O2   | 2.4335 | 0.2295  | ↓     | *** | HMDB0246296              | 47.1  |
| 8.59           | Lysopc(20:3(5Z,8Z,11Z)/0:0)                                            | 590.34280  | M+FA-H         | C28 H52 N O7 P  | 2.4024 | 0.1339  | ↓     | *** | HMDB0010393              | 46.6  |
| 8.31           | Pgp(20:1(11Z)/18:2(9Z,12Z))                                            | 898.56483  | M+NH4          | C44 H82 O13 P2  | 2.3687 | 3.3127  | ↑     | *** | HMDB0116451              | 45.1  |
| 8.73           | Pa(18:0/18:1(12Z)-2Oh(9,10))                                           | 752.53725  | M+NH4          | C39 H75 O10 P   | 2.3222 | 4.6348  | ↑     | *** | HMDB0263631              | 42.7  |
| 4.49           | N-Dihydroferuloyltyramine                                              | 316.15393  | M+H            | C18 H21 N O4    | 2.3548 | 0.3276  | ↓     | *** | HMDB0033028              | 46.2  |
| 3.49           | Cyclamate                                                              | 178.05437  | M-H            | C6 H13 N O3 S   | 2.3532 | 0.1722  | ↓     | *** | -;HMDB0031340            | 47.5  |
| 8.75           | (+/-)-Menthyl Acetate                                                  | 199.16739  | M+H            | C12 H22 O2      | 2.3214 | 5.1825  | ↑     | *** | HMDB0041264              | 46.4  |
| 9.25           | Phosphatidylcholine Lyso 18:0                                          | 1047.73312 | 2M+H           | C26 H54 N O7 P  | 2.3034 | 0.4676  | ↓     | *** | -                        | 46.2  |
| 6.09           | Pa(18:1(12Z)-2Oh(9,10)/8:0)                                            | 617.34206  | M+Na           | C29 H55 O10 P   | 2.2795 | 3.8534  | ↑     | *** | HMDB0266642              | 47.2  |
| 3.47           | 2-Phenoxypropanoic Acid                                                | 165.05572  | M-H            | C9 H10 O3       | 2.2757 | 0.0946  | ↓     | *** | -                        | 48.8  |
| 8.67           | Pc(20:0/Txb2)                                                          | 902.61016  | M-H            | C48 H90 N O12 P | 2.2692 | 0.1355  | ↓     | *** | HMDB0286972              | 41.8  |
| 8.08           | Pi(Pgf1Alpha/18:0)                                                     | 919.56142  | M-H2O-H        | C47 H87 O16 P   | 2.2567 | 4.3375  | ↑     | *** | HMDB0276437              | 43.8  |
| 3.98           | 4-Ethylphenol                                                          | 121.06584  | M-H            | C8 H10 O        | 2.238  | 0.2539  | ↓     | *** | HMDB0029306              | 50.6  |
| 8.28           | Lysopc(22:6(4Z,7Z,10Z,13Z,16Z,19Z)/0:0)                                | 612.32852  | M+FA-H         | C30 H50 N O7 P  | 2.2318 | 0.1644  | ↓     | *** | HMDB0010404              | 48.6  |
| 5.12           | Calendasaponin B                                                       | 977.46802  | M+Na-H2O       | C48 H76 O20     | 2.2155 | 2.6074  | ↑     | *** | HMDB0039009              | 41.2  |
| 4.80           | Cyclokievitone                                                         | 355.11651  | M+H            | C20 H18 O6      | 2.1803 | 0.2123  | ↓     | *** | HMDB0033983              | 46    |
| 5.99           | Nb-P-Coumaroyltryptamine                                               | 307.14441  | M+H            | C19 H18 N2 O2   | 2.2124 | 0.242   | ↓     | *** | HMDB0041518              | 45.9  |
| 9.30           | Lysopc(20:1(11Z)/0:0)                                                  | 594.37389  | M+FA-H         | C28H56NO7P      | 2.1992 | 0.2882  | ↓     | *** | HMDB0010391              | 47.6  |
| 5.01           | 1-(1-(Tert-Butoxycarbonyl)Piperidin-4-Yl)Azetidine-3-Carboxylic Acid   | 339.18957  | M+CH3OH+N<br>a | C14 H24 N2 O4   | 2.1857 | 4.2421  | ↑     | *** | HMDB0247560              | 46.3  |
| 3.98           | 3-(3-Hydroxyphenyl)Propanoic Acid                                      | 165.05609  | M-H            | C9 H10 O3       | 2.1623 | 0.4148  | ↓     | *** | HMDB0000375              | 55.1  |
| 9.81           | 1-Eicosanoyl-Sn-Glycero-3-Phosphocholine                               | 552.39894  | M+H            | C28 H58 NO 7P   | 2.1644 | 0.4428  | ↓     | *** | LMGP01050045             | 41.7  |
| 8.90           | Cholylcitrulline                                                       | 548.36679  | M+H-H2O        | C30 H51 N3 O7   | 2.1626 | 0.3117  | ↓     | *** | HMDB0242383              | 44    |
| 5.94           | Pa(8:0/18:1(12Z)-2Oh(9,10))                                            | 617.34200  | M+Na           | C29H55O10P      | 2.1752 | 3.5113  | ↑     | *** | HMDB0266641              | 46.6  |

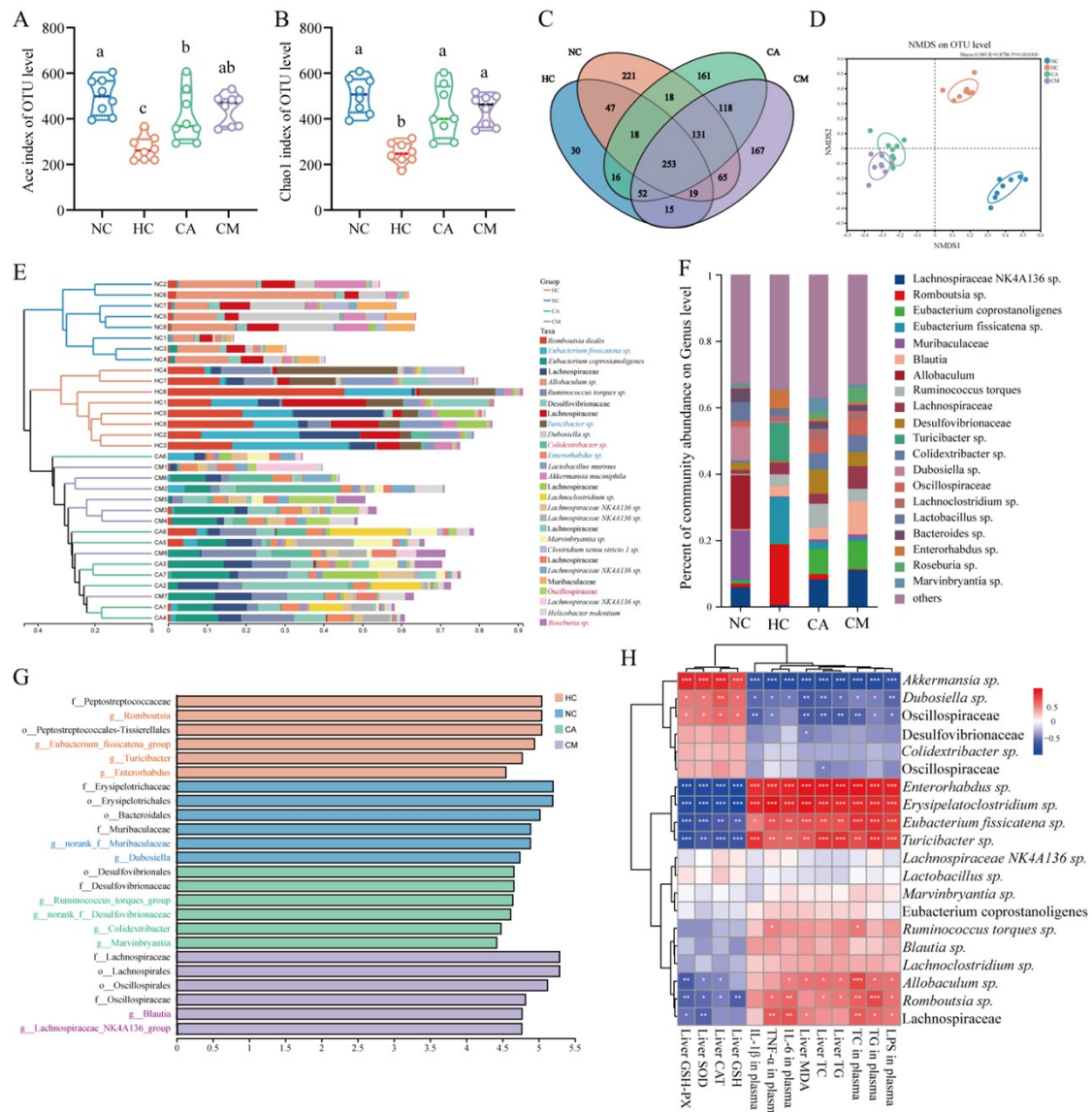
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|------|-----------------------------------------------------------------------------|-----------|---------|----------------|--------|---------|---|-----|------------------------|------|
| 8.98 | Pe(P-18:1(11Z)/16:1(9Z))                                                    | 717.55874 | M+NH4   | C39 H74 NO 7P  | 2.1202 | 0.3003  | ↓ | *** | HMDB0011405            | 43.3 |
| 5.72 | 2-(1-{2-[3-(Methylthio)Anilino]-2-Oxoethyl}Cyclopentyl)Acetic Acid          | 308.13387 | M+H     | C16 H21 N O 3S | 2.1202 | 4.5719  | ↑ | *** | -                      | 43   |
| 9.47 | 20-Hydroxy-6Z,15Z-Eicosadienoic Acid                                        | 323.25756 | M-H     | C20 H36 O3     | 2.1266 | 5.2415  | ↑ | *** | HMDB0245564            | 46.9 |
| 5.99 | 2-Phenyl-3-(3,4,5-Trimethoxyphenyl)Acrylonitrile                            | 337.15440 | M+ACN+H | C18 H17 N O3   | 2.1259 | 0.3389  | ↓ | *** | -                      | 45.5 |
| 9.06 | Pc(22:0/16:0)                                                               | 856.61169 | M+K     | C46 H92 N O8 P | 2.078  | 0.4521  | ↓ | *** | HMDB0008528            | 40.9 |
| 9.01 | Lysopc(P-18:1(9Z)/0:0)                                                      | 550.34664 | M+FA-H  | C26 H52 N O6 P | 2.0807 | 0.0588  | ↓ | *** | HMDB0010408            | 45   |
| 7.94 | Myristoyllysophosphatidylcholine                                            | 468.30891 | M+H     | C22 H46 N O7 P | 2.0688 | 0.0935  | ↓ | *** | -                      | 42.3 |
| 6.05 | Frequentin                                                                  | 253.14332 | M+H     | C14 H20 O4     | 2.0356 | 4.9415  | ↑ | *** | -                      | 46.8 |
| 9.46 | 8Alpha-13(16),14-Labdadien-8-Ol                                             | 349.27225 | M+Hac-H | C20 H34 O      | 2.0562 | 4.6801  | ↑ | *** | HMDB0035276            | 48.9 |
| 6.79 | Diterpene Alkaloid                                                          | 464.30013 | M+Hac-H | C24 H39 N O4   | 2.0504 | 0.2429  | ↓ | *** | HMDB0251489            | 43   |
| 7.00 | 2-Hydroxy-6,7-Dimethoxy-1,1-Dimethyl-2,9,10,10A-Tetrahydrophenanthren-3-One | 303.16088 | M+H     | C18 H22 O4     | 2.0319 | 2.821   | ↑ | *** | -                      | 43.1 |
| 4.49 | Seneciophylline                                                             | 334.16367 | M+H     | C18 H23 N O5   | 1.984  | 19.0034 | ↑ | *** | HMDB0258231            | 47.5 |
| 9.20 | Tg(15:0/14:1(9Z)/22:4(7Z,10Z,13Z,16Z))                                      | 859.68325 | M+Na-2H | C54 H94 O6     | 2.0402 | 3.0401  | ↑ | *** | HMDB0043183            | 40   |
| 9.27 | Docosahexaenoic Acid                                                        | 655.46991 | 2M-H    | C22 H32 O2     | 2.0115 | 0.3423  | ↓ | *** | HMDB0002183;PW_C001472 | 53.7 |
| 5.03 | N-Trans-Feruloyltyramine                                                    | 312.12320 | M-H     | C18 H19 N O4   | 1.9852 | 0.1218  | ↓ | *** | HMDB0029365            | 49   |



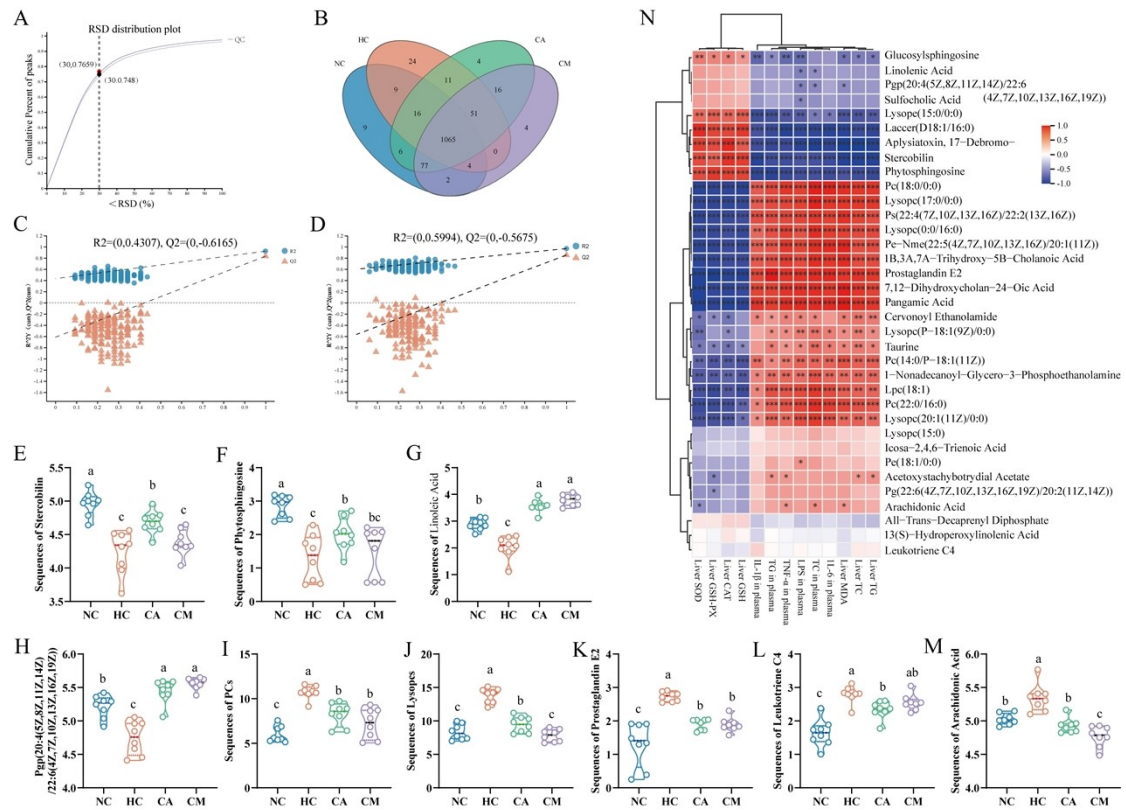
**Fig. S1** Effect of CA and CM supplementation on HFD-induced hyperlipidemia in mice. (A) Food intake, (B) Caloric intake, (C) Water intake, (D) Liver, (E) Epididymal white adipose tissue (eWAT), (F) Inguinal white adipose tissue (iWAT), and (G) Brown adipose tissue (BAT) mass. (H) ALT and (I) AST levels in plasma; (J) ALT and (K) AST levels in Liver. Differences between groups were analysed using one-way ANOVA followed by Tukey's post hoc test. Statistical significance was set at  $P < 0.05$ . Different letters indicate significant differences between groups. HFD, high-fat diet; NC, normal control group; HC, hyperlipidaemic group; SV, simvastatin control group (HFD and 30 mg/kg SV); CA, cinnamic acid group (HFD and 20 mg/kg CA); CM, cinnamaldehyde group (HFD and 20 mg/kg CM); ANOVA, analysis of variance.



**Fig. S2** FMT confirms the role of gut microbiota in CA and CM against hyperlipidemia. (A) Food intake, (B) Caloric intake, (C) Water intake, (D) Liver, (E) eWAT, (F) iWAT, and (G) BAT mass, (H) AST and (I) ALT levels in plasma; (J) AST and (K) ALT levels in Liver. Representative H&E staining of (L) eWAT, (M) iWAT, and (N) BAT from mice. Scale bar, 100 μm. Data are presented as the mean of biological replicates ± SEM (n = 8). Differences between groups were analyzed using one-way ANOVA followed by Tukey's post-hoc test. Statistical significance was set at  $P < 0.05$ . Different letters indicate significant differences between groups. HFD, high-fat diet; FHC, fecal microbiota transplantation of the HC group; FCA, fecal microbiota transplantation of the CA group; FCM, fecal microbiota transplantation of the CM group. ANOVA, analysis of variance.



**Fig. S3** Effect of CA and CM on the gut microbiota of HFD-induced mice. (A) The Ace index at the OTU level. (B) The Chao1 index at the OTU level. (C) The Venn diagram showed the number of differential OTUs. (D) The NMDS of gut microbiota. (E) Hierarchical clustering tree on OTU level of gut microbiota. (F) The composition profile of gut microbiota assessed at phylum level. (G) The histogram of LDA score based on LEfSe analysis (LDA score >4 was used as a threshold value of characteristic taxon, n = 8). (H) Spearman correlation between gut microbial genus and biochemical index. Data are presented as the mean of biological replicates  $\pm$  SEM (n = 8). Data are presented as the mean of biological replicates  $\pm$  SEM (n = 8). Differences between groups were analyzed using one-way ANOVA followed by Tukey's post-hoc test. Statistical significance was set at  $P < 0.05$ . Different letters indicate significant differences between groups. NC, normal control group; HC, hyperlipidemia group; CA, cinnamic acid group (HFD and 20 mg/kg CA); CM, cinnamaldehyde group (HFD and 20 mg/kg CM). ANOVA, analysis of variance.



**Fig. S4** Effect of CA and CM on the gut metabolite profiles of HFD-induced mice. (A) RSD distribution plot. (B) Venn diagram showed the number of differential metabolites. The permutation test (200 times) based on the OPLS-DA model between (C) CA and HC groups, (D) CM and HC groups. Sequences of (E) Stercobilin, (F) Phytosphingosine, (G) Linoleic Acid, (H) Pgp(20:4(5Z,8Z,11Z,14Z)/22:6(4Z,7Z,10Z,13Z,16Z,19Z)), (I) PCs, (J) Lysopcs, (K) Prostaglandin E2, (L) Leukotriene C4, (M) Arachidonic Acid. (N) Spearman correlation between metabolites and biochemical index.