

## Supporting Information

### **Differential effects of ellagic acid on non-alcoholic fatty liver disease in mice: grouped by urolithin A -producing capacity**

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**Table S3. The detailed results from the pathway analysis.**

Table S1. The initial content of urolithin A in feces of EA administration mice

| Mouse ID | Urolithin A (UroA)<br>Concentration (ng/g feces) |
|----------|--------------------------------------------------|
| 25       | 145.34                                           |
| 36       | 136.99                                           |
| 27       | 131.31                                           |
| 24       | 130.84                                           |
| 21       | 128.26                                           |
| 35       | 125.82                                           |
| 31       | 125.33                                           |
| 29       | 118.48                                           |
| 39       | 111.55                                           |
| 23       | 109.16                                           |
| 34       | 68.05                                            |
| 40       | 64.36                                            |
| 30       | 54.79                                            |
| 32       | 52.72                                            |
| 22       | 51.53                                            |
| 38       | 42.35                                            |
| 26       | 30.31                                            |
| 37       | 26.25                                            |
| 28       | 22.55                                            |
| 33       | 15.14                                            |

Table S2. Content of urolithins in feces of HFFD-induced NAFLD mice (n = 5).

| Group | Uro A (ng/g)    |
|-------|-----------------|
| C     | NF              |
| M     | NF              |
| H     | 128.59 ± 7.00 a |
| L     | 27.32 ± 10.09 b |

NF: not found. C, control group; M, model group; H, high UroA production group; L, low UroA production group; UroA, urolithin A. Values are expressed as mean ± SEM, and different letters represent significant differences ( $p < 0.05$ ) among groups.

Table S3. The detailed results from the pathway analysis.

| Pathway Name                                           | Total | Expected | Hits | Raw p    | -log10(p) | Holm<br>adjust | FDR      | Impact  |
|--------------------------------------------------------|-------|----------|------|----------|-----------|----------------|----------|---------|
| Biosynthesis of unsaturated fatty acids                | 36    | 0.73143  | 6    | 5.46E-05 | 4.2625    | 0.004371       | 0.004371 | 0       |
| Phenylalanine, tyrosine and tryptophan<br>biosynthesis | 4     | 0.08127  | 2    | 0.00234  | 2.6307    | 0.18488        | 0.093612 | 1       |
| Histidine metabolism                                   | 16    | 0.32508  | 3    | 0.003568 | 2.4476    | 0.27826        | 0.095132 | 0.34426 |
| Pantothenate and CoA biosynthesis                      | 20    | 0.40635  | 3    | 0.006871 | 2.163     | 0.52909        | 0.11861  | 0.04762 |
| beta-Alanine metabolism                                | 21    | 0.42667  | 3    | 0.007906 | 2.102     | 0.60089        | 0.11861  | 0.39925 |
| Valine, leucine and isoleucine biosynthesis            | 8     | 0.16254  | 2    | 0.010379 | 1.9839    | 0.77839        | 0.11861  | 0       |
| Phenylalanine metabolism                               | 8     | 0.16254  | 2    | 0.010379 | 1.9839    | 0.77839        | 0.11861  | 0.35714 |
| Primary bile acid biosynthesis                         | 46    | 0.9346   | 3    | 0.064037 | 1.1936    | 1              | 0.64037  | 0.00758 |
| Linoleic acid metabolism                               | 5     | 0.10159  | 1    | 0.097661 | 1.0103    | 1              | 0.86716  | 1       |
| Nitrogen metabolism                                    | 6     | 0.1219   | 1    | 0.11605  | 0.93534   | 1              | 0.86716  | 0       |
| Lysine degradation                                     | 30    | 0.60952  | 2    | 0.12236  | 0.91235   | 1              | 0.86716  | 0       |
| Thiamine metabolism                                    | 7     | 0.14222  | 1    | 0.13408  | 0.87263   | 1              | 0.86716  | 0       |
| Glycine, serine and threonine metabolism               | 33    | 0.67048  | 2    | 0.14313  | 0.84428   | 1              | 0.86716  | 0       |
| Taurine and hypotaurine metabolism                     | 8     | 0.16254  | 1    | 0.15175  | 0.81886   | 1              | 0.86716  | 0.42857 |
| Arginine and proline metabolism                        | 36    | 0.73143  | 2    | 0.1646   | 0.78357   | 1              | 0.87786  | 0.02442 |
| Pyrimidine metabolism                                  | 39    | 0.79238  | 2    | 0.18663  | 0.72903   | 1              | 0.91326  | 0.05261 |
| Valine, leucine and isoleucine degradation             | 40    | 0.8127   | 2    | 0.19407  | 0.71205   | 1              | 0.91326  | 0       |
| Arachidonic acid metabolism                            | 44    | 0.89397  | 2    | 0.22421  | 0.64935   | 1              | 0.99647  | 0.29133 |
| Arginine biosynthesis                                  | 14    | 0.28444  | 1    | 0.25067  | 0.60089   | 1              | 1        | 0.11675 |
| Butanoate metabolism                                   | 15    | 0.30476  | 1    | 0.26603  | 0.57506   | 1              | 1        | 0       |
| Nicotinate and nicotinamide metabolism                 | 15    | 0.30476  | 1    | 0.26603  | 0.57506   | 1              | 1        | 0.1943  |
| Ubiquinone and other terpenoid-quinone<br>biosynthesis | 18    | 0.36571  | 1    | 0.31031  | 0.50821   | 1              | 1        | 0       |
| Propanoate metabolism                                  | 22    | 0.44698  | 1    | 0.36533  | 0.43731   | 1              | 1        | 0       |
| Pyruvate metabolism                                    | 23    | 0.4673   | 1    | 0.37841  | 0.42204   | 1              | 1        | 0       |
| Glycolysis / Gluconeogenesis                           | 26    | 0.52825  | 1    | 0.4161   | 0.38081   | 1              | 1        | 0       |
| Purine metabolism                                      | 70    | 1.4222   | 2    | 0.42046  | 0.37628   | 1              | 1        | 0.02769 |
| Glutathione metabolism                                 | 28    | 0.56889  | 1    | 0.43998  | 0.35657   | 1              | 1        | 0.01966 |
| Alanine, aspartate and glutamate metabolism            | 28    | 0.56889  | 1    | 0.43998  | 0.35657   | 1              | 1        | 0.19712 |
| Porphyrin metabolism                                   | 31    | 0.62984  | 1    | 0.47404  | 0.32418   | 1              | 1        | 0       |
| Glyoxylate and dicarboxylate metabolism                | 32    | 0.65016  | 1    | 0.48494  | 0.31431   | 1              | 1        | 0       |
| Sphingolipid metabolism                                | 32    | 0.65016  | 1    | 0.48494  | 0.31431   | 1              | 1        | 0.06191 |
| Cysteine and methionine metabolism                     | 33    | 0.67048  | 1    | 0.49562  | 0.30485   | 1              | 1        | 0.10446 |
| Glycerophospholipid metabolism                         | 36    | 0.73143  | 1    | 0.5264   | 0.27869   | 1              | 1        | 0.02582 |
| Steroid hormone biosynthesis                           | 87    | 1.7676   | 2    | 0.53632  | 0.27057   | 1              | 1        | 0.03729 |
| Fatty acid elongation                                  | 39    | 0.79238  | 1    | 0.55535  | 0.25544   | 1              | 1        | 0       |
| Fatty acid degradation                                 | 39    | 0.79238  | 1    | 0.55535  | 0.25544   | 1              | 1        | 0       |
| Tyrosine metabolism                                    | 42    | 0.85333  | 1    | 0.58258  | 0.23464   | 1              | 1        | 0.13972 |
| Fatty acid biosynthesis                                | 47    | 0.95492  | 1    | 0.62442  | 0.20452   | 1              | 1        | 0.01473 |