

Table S1 Compositions of nutrient medium for *in vitro* fermentation

experiment

| Composition                          | Content  |
|--------------------------------------|----------|
| Peptone                              | 2.0 g/L  |
| Yeast extract                        | 2.0 g/L  |
| NaHCO <sub>3</sub>                   | 2.0 g/L  |
| MgSO <sub>4</sub> ·7H <sub>2</sub> O | 0.01 g/L |
| CaCl <sub>2</sub> ·6H <sub>2</sub> O | 0.01g/L  |
| K <sub>2</sub> HPO <sub>4</sub>      | 0.04 g/L |
| KH <sub>2</sub> PO <sub>4</sub>      | 0.04 g/L |
| NaCl                                 | 0.1 g/L  |
| L-cysteine                           | 0.5 g/L  |
| Bile acid salt                       | 0.5 g/L  |
| Vitamin K                            | 10 µL/L  |
| Tween 80                             | 2 mL/L   |
| Resazurin                            | 1 g/L    |
| Chlorine heme                        | 0.05 g/L |

Table S2 Compositions of normal diet and high-fat diet (g/kg diet)

| Composition      | Normal diet (g/kg) | High-fat Diet (g/kg) |
|------------------|--------------------|----------------------|
| Casein           | 200.0              | 100.0                |
| Methionine       | 3.0                | 3.0                  |
| Corn starch      | 550.0              | 460.0                |
| Cellulose powder | 50.0               | 50.0                 |
| Corn oil         | 70.0               |                      |
| Lard             |                    | 150.0                |
| Cholesterol      |                    | 10.0                 |
| Vitamin mixture  | 10.0               | 10.0                 |
| Mineral mixture  | 35.0               | 35.0                 |
| Sodium cholate   | 2.0                | 2.0                  |
| Sucrose          | 80.0               | 80.0                 |
| Egg yolk powder  |                    | 100.0                |

Table S3 Primer sequence of the target genes for qPCR analysis

| Target gene    | Forward primer (5' to 3') | Reverse primer (5' to 3')      |
|----------------|---------------------------|--------------------------------|
| Fas            | CCACCCTGTAGGTCACCGTTT     | GTGGGTATAAGCGTTCAGCTGC         |
| Fasn           | GTGTGGTAGGCTTGGTGAAGTGTG  | GTGAGATGTGCTGCTGAGGTTGG        |
| Foxo1          | ACGAGTGGATGGTGAAGAGTG     | CCTCCCTCTGGATTGAGCATC          |
| Srebp-1c       | CAGCAGCAGTGGTGGCAGTG      | GGTTGCAGGTCAGACACAGGAAG        |
| Gck            | ATCTCTACTTCCCCAACGACC     | GTTGTGAGTACCCGCTCTG            |
| Il- $\beta$    | GGCTGCTTCCAAACCTTTGA      | GAAGACACGGATTCCATGGT           |
| Il-6           | ATGAAGTTCCTCTCTGCAAGAGAC  | CACTAGGTTTGCCGAGTAGATCTC       |
| G6pd           | ACCGCATTGACCACTACCTG      | CCCTCAGTACCAAAGGGCTC           |
| $\beta$ -Actin | CACTATCGGCAATGAGCGGTTCC   | ACTGTGTTGGCATAGAGGTCTTTAC<br>G |

Table S4 Changes of antioxidant activities of oyster mushroom in specific fermentation time interval. The results were represented as mean  $\pm$  SD (n = 3). Different superscript lowercase letters in the table indicate significant difference ( $p < 0.05$ ). OM: oyster mushroom; FOM: *Lactobacillus rhamnoses*-fermented oyster mushroom.

| Sample  | Antioxidant activities         |                               |                                  |                                 |
|---------|--------------------------------|-------------------------------|----------------------------------|---------------------------------|
|         | DPPH<br>(mmol TE/100g)         | ABTS<br>(mmol TE/100g)        | Reducing power<br>(mmol TE/100g) | FRAP<br>(mmol TE/100g)          |
| OM-0h   | 39.83 $\pm$ 0.90 <sup>c</sup>  | 65.78 $\pm$ 0.12 <sup>e</sup> | 9.60 $\pm$ 0.53 <sup>d</sup>     | 136.97 $\pm$ 3.18 <sup>de</sup> |
| OM-12h  | 40.24 $\pm$ 0.51 <sup>bc</sup> | 67.21 $\pm$ 0.17 <sup>d</sup> | 8.08 $\pm$ 0.25 <sup>e</sup>     | 139.49 $\pm$ 5.69 <sup>d</sup>  |
| OM-24h  | 40.92 $\pm$ 0.30 <sup>b</sup>  | 63.83 $\pm$ 0.58 <sup>g</sup> | 10.90 $\pm$ 0.66 <sup>c</sup>    | 133.39 $\pm$ 0.31 <sup>e</sup>  |
| OM-36h  | 40.96 $\pm$ 0.07 <sup>b</sup>  | 67.70 $\pm$ 0.09 <sup>c</sup> | 9.21 $\pm$ 0.08 <sup>d</sup>     | 127.62 $\pm$ 0.21 <sup>f</sup>  |
| FOM-0h  | 40.52 $\pm$ 0.44 <sup>bc</sup> | 65.17 $\pm$ 0.33 <sup>f</sup> | 14.04 $\pm$ 0.41 <sup>b</sup>    | 174.37 $\pm$ 0.90 <sup>c</sup>  |
| FOM-12h | 44.18 $\pm$ 0.77 <sup>a</sup>  | 75.03 $\pm$ 0.05 <sup>a</sup> | 19.42 $\pm$ 0.04 <sup>a</sup>    | 214.25 $\pm$ 0.99 <sup>b</sup>  |
| FOM-24h | 44.54 $\pm$ 0.25 <sup>a</sup>  | 74.70 $\pm$ 0.09 <sup>a</sup> | 19.41 $\pm$ 0.02 <sup>a</sup>    | 220.14 $\pm$ 0.67 <sup>a</sup>  |
| FOM-36h | 44.18 $\pm$ 0.25 <sup>a</sup>  | 73.13 $\pm$ 0.08 <sup>b</sup> | 18.89 $\pm$ 0.16 <sup>a</sup>    | 215.63 $\pm$ 0.37 <sup>b</sup>  |

Table S5 Significantly different metabolites and their related metabolic pathways

| <b>Metabolite</b>      |                  |                   |                  |                   | <b>Pathways</b>                                                                                    |
|------------------------|------------------|-------------------|------------------|-------------------|----------------------------------------------------------------------------------------------------|
|                        | <b>NC-vs-HFD</b> | <b>HFD-vs-LGG</b> | <b>HFD-vs-OM</b> | <b>HFD-vs-FOM</b> |                                                                                                    |
| <b>Glucose</b>         |                  |                   |                  |                   |                                                                                                    |
| D-mannose              | ↓                |                   |                  |                   | Fructose and mannose metabolism<br>Amino sugar nucleotide sugar metabolism<br>Galactose metabolism |
| D-mannitol 1-phosphate | ↓                |                   |                  |                   | Fructose and mannose metabolism                                                                    |
| Galactitol             |                  |                   |                  | ↓                 | Fructose and mannose metabolism                                                                    |
|                        | ↑                |                   |                  | ↓                 | Galactose metabolism                                                                               |
| L-rhamnofuranose       |                  |                   | ↓                |                   | Fructose and mannose metabolism                                                                    |
| Mannitol               |                  |                   |                  | ↓                 | Fructose and mannose metabolism                                                                    |

|                |   |  |  |                                                                                                                                                                                                                                                                                                                                                                                             |
|----------------|---|--|--|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 2-oxoglutarate | ↓ |  |  | <p>Glucagon signaling pathway</p> <p>Citrate cycle (TCA cycle)</p> <p>Butanoate metabolism</p> <p>Glyoxylate and dicarboxylate metabolism</p> <p>D-glutamine and D-glutamate metabolism</p> <p>Arginine biosynthesis</p> <p>Alanine, aspartate and glutamate metabolism</p> <p>Biosynthesis of amino acids</p> <p>Lysine biosynthesis</p> <p>Bile secretion</p> <p>Histidine metabolism</p> |
| Succinate      | ↓ |  |  | <p>Glucagon signaling pathway</p> <p>Pyruvate metabolism</p> <p>Citrate cycle (TCA cycle)</p> <p>Carbon metabolism</p> <p>Butanoate metabolism</p>                                                                                                                                                                                                                                          |

|                           |   |  |  |   |                                                                                                                                                                                                                                                                                                                                          |
|---------------------------|---|--|--|---|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                           |   |  |  |   | <p>Glyoxylate and dicarboxylate metabolism</p> <p>Propanoate metabolism</p> <p>Succinate</p> <p>Phenylalanine metabolism</p> <p>Tyrosine metabolism</p> <p>Alanine, aspartate and glutamate metabolism</p>                                                                                                                               |
| L-glutamate               | ↓ |  |  |   | <p>Glutathione metabolism</p> <p>Carbon metabolism</p> <p>Butanoate metabolism</p> <p>Glyoxylate and dicarboxylate metabolism</p> <p>D-glutamine and D-glutamate metabolism</p> <p>Alanine, aspartate and glutamate metabolism</p> <p>Biosynthesis of amino acids</p> <p>Histidine metabolism</p> <p>Arginine and proline metabolism</p> |
| Bis-gamma-glutamylcystine |   |  |  | ↓ | <p>Glutathione metabolism</p>                                                                                                                                                                                                                                                                                                            |

|                        |   |  |   |   |                                                                                                                                                                                                             |
|------------------------|---|--|---|---|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Glutathione            |   |  | ↓ |   | Glutathione metabolism                                                                                                                                                                                      |
| B-D-fructose           | ↓ |  |   |   | Amino sugar nucleotide sugar metabolism                                                                                                                                                                     |
| D-glucono-1,5-lactone  | ↓ |  |   |   | Carbon metabolism                                                                                                                                                                                           |
| 3-phosphonooxypyruvate |   |  |   | ↓ | Carbon metabolism<br>Biosynthesis of amino acids<br>Glycine, serine and threonine metabolism                                                                                                                |
| L-serine               |   |  |   | ↑ | Carbon metabolism<br>Glyoxylate and dicarboxylate metabolism<br>Biosynthesis of amino acids<br>Cysteine and methionine metabolism<br>Glycine, serine and threonine metabolism<br>Cyanoamino acid metabolism |



|                              |   |  |   |  |                                                                                                                                                |
|------------------------------|---|--|---|--|------------------------------------------------------------------------------------------------------------------------------------------------|
| 2-phosphoglycolate           |   |  | ↑ |  | Carbon metabolism<br>Glyoxylate and dicarboxylate metabolism<br>Biosynthesis of secondary metabolism                                           |
| O-phospho-L-serine           |   |  | ↓ |  | Carbon metabolism<br>Biosynthesis of amino acids<br>Cysteine and methionine metabolism<br>Glycine, serine and threonine metabolism             |
| 2-hydroxyglutarate           | ↑ |  |   |  | Butanoate metabolism                                                                                                                           |
| L-glutamine                  | ↑ |  |   |  | Glyoxylate and dicarboxylate metabolism<br>Arginine biosynthesis<br>Alanine, aspartate and glutamate metabolism<br>Biosynthesis of amino acids |
| S-methylalanine semialdehyde |   |  | ↓ |  | Propanoate metabolism                                                                                                                          |

|                                    |   |   |   |   |                                                                                                                                                                                          |
|------------------------------------|---|---|---|---|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Adenylic acid                      |   | ↓ | ↓ |   | PI3K-Akt signaling pathway<br>mTOR signaling pathway<br>FOXO signaling pathway<br>AMPK signaling pathway<br>Regulation of lipolysis in adipocyte<br>Biosynthesis of secondary metabolism |
| UDP-N-acetyl-alpha-D-glucosamine   |   |   | ↑ |   | Insulin resistance<br>Amino sugar and nucleotide sugar metabolism                                                                                                                        |
| <b>Amino acid</b>                  |   |   |   |   |                                                                                                                                                                                          |
| D-glutamine                        | ↑ |   |   |   | D-glutamine and D-glutamate metabolism                                                                                                                                                   |
| ®-2,3-Dihydroxy-3-methylpentanoate | ↑ |   |   |   | Valine, leucine and isoleucine biosynthesis<br>Biosynthesis of amino acids                                                                                                               |
| 2-methyl-3-oxopropanoate           |   |   |   | ↑ | Valine, leucine and isoleucine biosynthesis                                                                                                                                              |
| (S)-Methylmalonate semialdehyde    |   |   | ↓ |   | Valine, leucine and isoleucine degradation                                                                                                                                               |

|                                               |   |  |   |   |                                                                                    |
|-----------------------------------------------|---|--|---|---|------------------------------------------------------------------------------------|
| L-citrulline                                  | ↓ |  |   |   | Arginine biosynthesis                                                              |
| Prephenate                                    | ↑ |  |   |   | Biosynthesis of amino acids                                                        |
| O-succinyl-L-homoserine                       | ↓ |  |   |   | Biosynthesis of amino acids<br>Cysteine and methionine metabolism                  |
| 3-dehydroshikimate                            |   |  |   | ↓ | Biosynthesis of amino acids<br>Phenylalanine, tyrosine and tryptophan biosynthesis |
| Linatine                                      | ↑ |  |   |   | Arginine and proline metabolism                                                    |
| N-succinyl-L-glutamate 5-semialdehyde         | ↓ |  |   |   | Arginine and proline metabolism                                                    |
| 4-(L-gamma-Glutamylamino) butanoate           | ↓ |  |   |   | Arginine and proline metabolism                                                    |
| N <sub>2</sub> -(D-1-carboxyethyl)-L-arginine |   |  | ↓ |   | Arginine and proline metabolism                                                    |
| 1-aminocyclopropane-1-carboxylate             | ↓ |  |   |   | Cysteine and methionine metabolism                                                 |

|                                           |   |  |   |   |                                                                                                                          |
|-------------------------------------------|---|--|---|---|--------------------------------------------------------------------------------------------------------------------------|
| 2,3-diketo-5-methylthiopentyl-1-phosphate | ↓ |  |   |   | Cysteine and methionine metabolism                                                                                       |
| Ophthalmate                               | ↑ |  |   | ↑ | Cysteine and methionine metabolism                                                                                       |
| L-cysteate                                |   |  |   | ↑ | Cysteine and methionine metabolism                                                                                       |
| Hydantoin-5-propionate                    |   |  | ↑ |   | Histidine metabolism                                                                                                     |
| Gentisic acid                             | ↓ |  |   |   | Tyrosine metabolism                                                                                                      |
| L-adrenaline                              |   |  |   | ↑ | Tyrosine metabolism<br>Regulation of lipolysis in adipocyte                                                              |
| 4-hydroxyphenylacetaldehyde               |   |  | ↓ |   | Tyrosine metabolism<br>Biosynthesis of secondary metabolism                                                              |
| N, N-dimethylglycine                      | ↓ |  |   | ↑ | Glycine, serine and threonine metabolism                                                                                 |
| L-tryptophan                              |   |  |   | ↓ | Glycine, serine and threonine metabolism<br>Tryptophan metabolism<br>Phenylalanine, tyrosine and tryptophan biosynthesis |

|                          |   |   |   |  |                                                                                             |
|--------------------------|---|---|---|--|---------------------------------------------------------------------------------------------|
|                          |   |   |   |  | Biosynthesis of amino acids                                                                 |
| Xanthurenic acid         | ↓ |   |   |  | Tryptophan metabolism                                                                       |
| 5-hydroxyindoleacetate   |   |   | ↑ |  | Tryptophan metabolism                                                                       |
| Picolinic acid           |   |   | ↓ |  | Tryptophan metabolism                                                                       |
| Phenethylamine           |   | ↓ |   |  | Phenylalanine metabolism                                                                    |
| N-acetyl-L-phenylalanine |   |   | ↓ |  | Phenylalanine metabolism                                                                    |
| <b>Fatty acid</b>        |   |   |   |  |                                                                                             |
| Hexadecanoic acid        | ↑ |   | ↓ |  | Fatty acid elongation<br>Biosynthesis of unsaturated fatty acids<br>Fatty acid biosynthesis |
| $\alpha$ -linolenic acid | ↑ |   |   |  | Biosynthesis of unsaturated fatty acids<br>$\alpha$ -linolenic acid metabolism              |
| linolenic acid           |   |   | ↑ |  | Biosynthesis of unsaturated fatty acids                                                     |

|                                         |   |   |   |   |                                                                             |
|-----------------------------------------|---|---|---|---|-----------------------------------------------------------------------------|
| Prostaglandin H2                        | ↑ |   |   |   | Arachidonic acid metabolism                                                 |
| Taurocholate                            |   | ↑ |   | ↑ | Bile secretion<br>Primary bile acid biosynthesis                            |
| Linoleic acid                           |   |   | ↑ |   | Linoleic acid metabolism                                                    |
| Rumenic acid                            |   |   | ↑ |   | Linoleic acid metabolism                                                    |
| 9-oxoode                                |   |   | ↑ |   | Linoleic acid metabolism                                                    |
| (9Z)-12,13-dihydroxyotadec-9-enoic acid |   |   |   | ↑ | Linoleic acid metabolism                                                    |
| Adenosine                               |   |   | ↓ |   | Regulation of lipolysis in adipocyte<br>Aldosterone synthesis and secretion |
| 7-methylxanthine                        |   | ↓ |   |   | Biosynthesis of secondary metabolism                                        |
| Dehypoxanthine futalosine               |   | ↑ |   |   | Biosynthesis of secondary metabolism                                        |
| 7-dehydrodesmosterol                    |   |   | ↑ |   | Steroid biosynthesis                                                        |

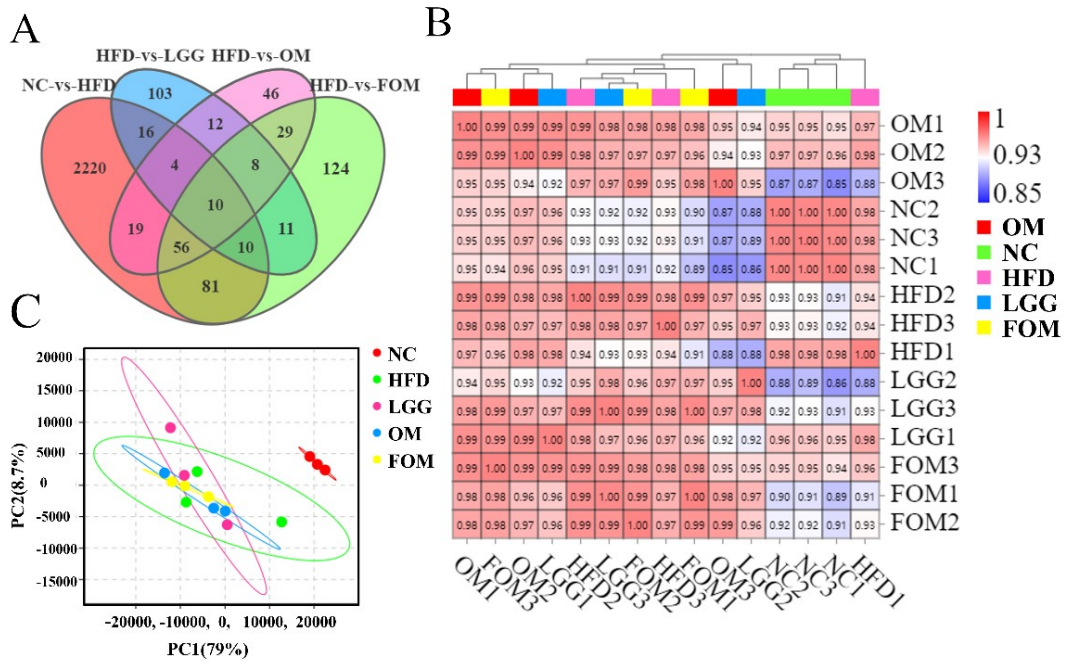


Fig. S1 Functional annotation and identification of DEGs by Venn analysis

(A), correlation analysis (B) and PCA analysis (C).

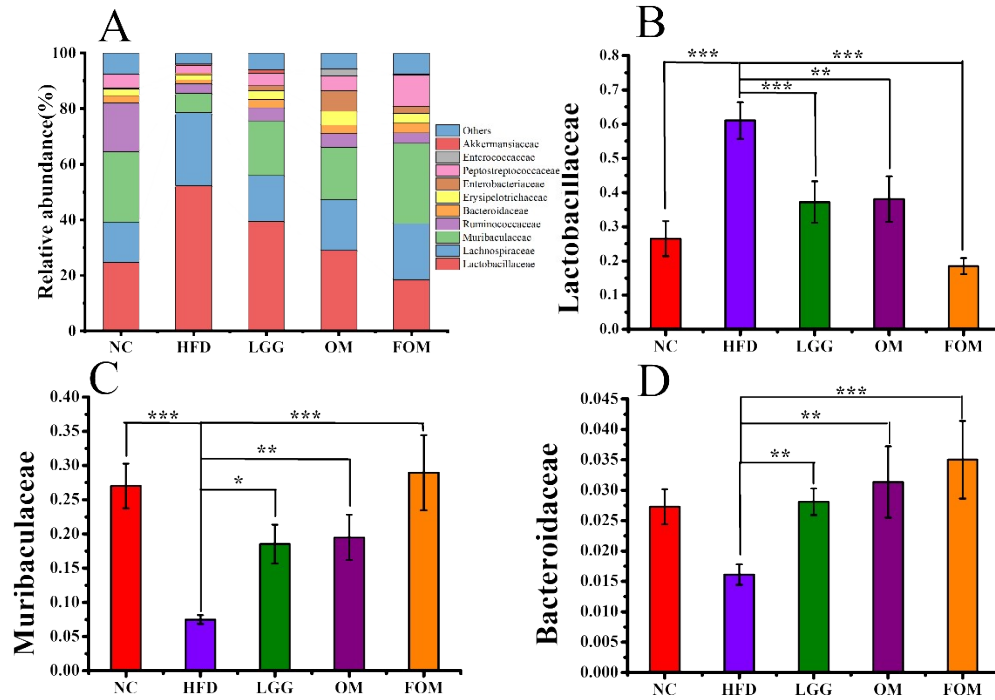


Fig. S2 Gut microbiota composition at the family level in HFD-induced obesity rats. (A) Relative abundance of top 10 gut microbiota. Relative abundance of *Lactobacillaceae* (B), *Muribaculaceae* (C) and (D) *Bacteroidaceae*.