

## *Supplementary Material*

### **Metabolite profiling of the gut microbiome in mice with dietary administration of black raspberries**

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## Supplementary Tables

Table S1. List of identified fecal metabolites that are significantly elevated in mice of BRB diet compared to mice of control diet.

| metabolites   | fold change | p-value | RT (min) | m/z      | Ontology                            |
|---|-------------|---------|----------|----------|-------------------------------------|
| Diaminopimelic acid   | 2.8         | 2.0E-04 | 1.1      | 191.1012 | Alpha amino acids                   |
| N5-(4-Methoxybenzyl)glutamine   | 2.4         | 3.5E-05 | 4.3      | 267.1347 | Alpha amino acids                   |
| 2-Aminobenzoic acid   | 42.7        | 6.3E-07 | 6.6      | 138.0559 | Aminobenzoic acids                  |
| [2-(Dimethoxymethyl)-1-heptenyl]benzene                                 | 8.9         | 7.1E-06 | 8.8      | 249.1839 | Benzene and substituted derivatives |
| 4-Methyl-1-phenyl-2-pentanol  | 4.3         | 1.7E-05 | 12.3     | 179.1407 | Benzene and substituted derivatives |
| Biliverdin  | 5.6         | 7.8E-05 | 9.7      | 583.2573 | Bilirubins                          |
| Tetrahydrobiopterin   | 995.7       | 4.0E-04 | 8.8      | 242.1274 | Biopterins and derivatives          |
| (S)-Neolyratyl acetate  | 3.9         | 5.3E-05 | 8.5      | 195.1361 | Carboxylic acid esters              |
| 3-beta-Hydroxy-4-beta-methyl-5-alpha-cholest-7-ene-4-alpha-carbaldehyde | 15.2        | 6.0E-06 | 12.0     | 429.3705 | Cholesterols and derivatives        |
| N6-Acetyl-L-lysine  | 6.6         | 2.2E-05 | 2.1      | 189.1233 | D-alpha-amino acids                 |
| Alanyl-Isoleucine   | 6.1         | 6.6E-04 | 3.8      | 203.1374 | Dipeptides                          |
| Alanyl-Phenylalanine  | 4.6         | 7.2E-06 | 5.1      | 237.1234 | Dipeptides                          |
| Asparaginyln-Leucine  | 2.7         | 3.3E-04 | 1.7      | 246.1447 | Dipeptides                          |

|                                  |      |         |      |          |  |
|----------------------------------|------|---------|------|----------|--|
| Glycyl-Methionine                | 5.0  | 7.1E-05 | 2.4  | 207.0815 | Dipeptides   |
| Glycyl-Phenylalanine             | 2.8  | 1.4E-03 | 5.1  | 223.1075 | Dipeptides   |
| Isoleucyl-Isoleucine             | 4.5  | 4.2E-03 | 6.6  | 245.1840 | Dipeptides   |
| Leucyl-Isoleucine                | 3.1  | 5.0E-06 | 5.7  | 245.1844 | Dipeptides   |
| Leucyl-phenylalanine             | 3.8  | 5.4E-04 | 5.9  | 279.1709 | Dipeptides   |
| Leucyl-Serine                    | 2.1  | 4.3E-03 | 1.8  | 219.1329 | Dipeptides   |
| Leucyl-Threonine                 | 4.0  | 8.9E-04 | 2.6  | 233.1493 | Dipeptides   |
| Methionyl-Threonine              | 4.7  | 5.3E-04 | 2.9  | 251.1057 | Dipeptides   |
| Phenylalanyl-Valine              | 5.1  | 1.8E-03 | 5.4  | 265.1554 | Dipeptides   |
| Serylisoleucine                  | 4.6  | 4.8E-04 | 4.3  | 219.1347 | Dipeptides   |
| Serylvaline                      | 7.1  | 3.9E-03 | 1.9  | 205.1173 | Dipeptides   |
| Valyl-Serine                     | 2.4  | 1.0E-03 | 1.2  | 205.1172 | Dipeptides   |
| Valyl-Valine                     | 3.1  | 1.9E-04 | 4.2  | 217.1518 | Dipeptides   |
| Cinnassiol D4 2-<br>glucoside    | 10.8 | 5.7E-07 | 8.0  | 515.2851 | Diterpene glycosides   |
| Ergosterol                       | 9.5  | 2.2E-04 | 11.7 | 397.3438 | Ergosterols and derivatives                                      |
| alpha-Rotunol                    | 17.4 | 1.7E-04 | 8.5  | 235.1681 | Eudesmane, isoeudesmane or<br>cycloeudesmane<br>sesquiterpenoids |
| Kaempferol 3-<br>sophorotrioside | 46.5 | 3.6E-05 | 3.7  | 773.2136 | Flavonoid-3-O-glycosides   |
| 4-Guanidinobutanoic acid         | 5.0  | 9.5E-04 | 1.5  | 146.0927 | Gamma amino acids and<br>derivatives                             |
| Galactosylhydroxylysine          | 3.4  | 5.9E-05 | 1.7  | 325.1617 | Glycosyl-amino acids   |

|                                |        |         |      |          |                                       |
|--------------------------------|--------|---------|------|----------|---------------------------------------|
| Protocatechuic acid            | 889.5  | 1.3E-06 | 4.9  | 155.0341 | Hydroxybenzoic acid derivatives       |
| Dehydrozingerone               | 35.9   | 3.6E-03 | 6.1  | 193.0874 | Hydroxycinnamic acids and derivatives |
| 5,6-Dihydro-11-methoxyyangonin | 5.1    | 2.5E-05 | 1.1  | 291.1228 | Kavalactones                          |
| Pyrraline                      | 3.1    | 1.0E-03 | 2.5  | 255.1317 | L-alpha-amino acids                   |
| Kinocoumarin                   | 44.7   | 7.5E-04 | 10.0 | 381.2081 | Linear pyranocoumarins                |
| 15,16-DiHODE                   | 1.9    | 2.1E-03 | 9.5  | 313.2351 | Lineolic acids and derivatives        |
| Alpha-Linolenic acid           | 3.0    | 1.6E-05 | 12.0 | 279.2306 | Lineolic acids and derivatives        |
| Corchorifatty acid A           | 8.6    | 1.9E-04 | 9.3  | 309.2028 | Lineolic acids and derivatives        |
| Stearidonic acid               | 10.9   | 8.7E-06 | 12.3 | 277.2149 | Lineolic acids and derivatives        |
| 12,13-DHOME                    | 2.0    | 9.5E-03 | 10.4 | 315.2509 | Long-chain fatty acids                |
| 15(16)-EpODE                   | 2.9    | 1.5E-04 | 8.5  | 295.2254 | Long-chain fatty acids                |
| N-Oleoylethanolamine           | 3.5    | 5.8E-03 | 13.5 | 326.3049 | N-acylethanolamines                   |
| menaquinone-1                  | 3.6    | 3.0E-03 | 4.7  | 243.1351 | Naphthalenes                          |
| Alanyl-Leucine                 | 3.2    | 4.7E-05 | 4.7  | 203.1397 | Peptides                              |
| Protoporphyrin IX              | 18.0   | 3.2E-05 | 13.7 | 563.2662 | Porphyrins                            |
| 15-Deoxy-d-12,14-PGJ2          | 9.1    | 4.6E-06 | 12.3 | 317.2080 | Prostaglandins and related compounds  |
| Prostaglandin E2               | 2.6    | 1.5E-03 | 8.8  | 353.2348 | Prostaglandins and related compounds  |
| 1-Pyrroline                    | 3937.9 | 9.5E-06 | 2.5  | 70.0665  | Pyrrolines                            |
| Bisacurone epoxide             | 13.0   | 9.9E-07 | 5.9  | 269.1749 | Sesquiterpenoids                      |

|                               |        |         |      |          |              |
|-------------------------------|--------|---------|------|----------|--------------|
| 13'-Hydroxy-alpha-tocopherol  | 4869.8 | 1.1E-06 | 11.9 | 447.3793 | Tocopherols  |
| 13'-Carboxy-alpha-tocotrienol | 2.9    | 4.4E-08 | 8.9  | 455.3189 | Tocotrienols |
| Alpha-Tocotrienol             | 4.9    | 1.1E-06 | 11.2 | 425.3386 | Tocotrienols |

Table S2. MS/MS spectral match of the identified metabolites.

| Metabolite                              | Score* | m/z      | Precursor          | Database    | Fragments**   |
|---|--------|----------|--------------------|-------------|---|
| (S)-Neolarytyl acetate                  | 7.5    | 195.1361 | [M+H] <sup>+</sup> | HMDB0041497 | 41.0362, 55.0540,<br>79.0524, 91.0535,<br>93.0688, 135.1166 |
| [2-(Dimethoxymethyl)-1-heptenyl]benzene | 7.4    | 249.1839 | [M+H] <sup>+</sup> | HMDB0036221 | 67.0523, 91.0529,<br>93.0687, 95.0852                       |
| 12,13-DHOME                             | 7.2    | 315.2509 | [M+H] <sup>+</sup> | HMDB0004705 | 67.0562, 197.1469   |
| 13'-Carboxy-alpha-tocotrienol           | 6.0    | 455.3189 | [M+H] <sup>+</sup> | HMDB0012556 | 165.0894, 437.3058  |
| 13'-Hydroxy-alpha-tocopherol            | 6.1    | 447.3793 | [M+H] <sup>+</sup> | HMDB0012559 | 55.0572, 69.0670,<br>111.1157, 165.0886                     |
| 15(16)-EpODE                            | 7.0    | 295.2254 | [M+H] <sup>+</sup> | HMDB0010206 | 43.0546, 139.1119,<br>205.1663, 277.2138                    |
| 15,16-DiHODE                            | 7.1    | 313.2351 | [M+H] <sup>+</sup> | HMDB0010208 | 43.0547, 249.2150,<br>277.2152, 295.2203                    |
| 15-Deoxy-d-12,14-PGJ2                   | 8.1    | 317.208  | [M+H] <sup>+</sup> | HMDB0005079 | 151.1491, 161.1313  |
| 1-Pyrroline                             | 8.7    | 70.0665  | [M+H] <sup>+</sup> | HMDB0012497 | 41.0404, 42.0405,<br>43.0531, 44.0540                       |

|   |     |          |                    |             |  |
|---|-----|----------|--------------------|-------------|--|
| 2-Aminobenzoic acid   | 7.0 | 138.0559 | [M+H] <sup>+</sup> | HMDB0001123 | 65.0396, 120.0449                                    |
| 3-beta-Hydroxy-4-beta-methyl-5-alpha-cholest-7-ene-4-alpha-carbaldehyde | 7.1 | 429.3705 | [M+H] <sup>+</sup> | HMDB0059643 | 57.0697, 69.0701                                     |
| 4-Guanidinobutanoic acid  | 8.2 | 146.0927 | [M+H] <sup>+</sup> | HMDB0003464 | 41.0405, 56.0503, 60.0577, 87.0454, 128.0831         |
| 4-Methyl-1-phenyl-2-pentanol  | 8.3 | 179.1407 | [M+H] <sup>+</sup> | HMDB0031568 | 67.0566, 69.0712, 79.0541, 81.0690, 91.0523, 93.0719 |
| 5,6-Dihydro-11-methoxyyangonin  | 7.1 | 291.1228 | [M+H] <sup>+</sup> | HMDB0038722 | 43.0180, 83.0594, 99.0446, 129.0630, 187.0663        |
| Alanyl-Isoleucine   | 7.6 | 203.1374 | [M+H] <sup>+</sup> | HMDB0028690 | 44.0469, 84.0752, 86.0926                            |
| Alanyl-Leucine  | 8.2 | 203.1397 | [M+H] <sup>+</sup> | HMDB0028691 | 44.0512, 86.0974, 132.1021                           |
| Alanyl-Phenylalanine  | 7.8 | 237.1234 | [M+H] <sup>+</sup> | HMDB0028694 | 44.0508, 120.0806, 166.0858                          |
| Alpha-Linolenic acid  | 7.6 | 279.2306 | [M+H] <sup>+</sup> | HMDB0001388 | 69.0701, 81.0707, 95.0846, 109.1022, 123.1168        |
| alpha-Rotunol   | 7.7 | 235.1681 | [M+H] <sup>+</sup> | HMDB0035869 | 41.0365, 69.0701, 95.0865, 199.1434                  |

|                                  |     |          |                    |             |  |
|----------------------------------|-----|----------|--------------------|-------------|--|
| Alpha-Tocotrienol                | 6.7 | 425.3386 | [M+H] <sup>+</sup> | HMDB0006327 | 69.0683, 109.1019,<br>165.0837, 243.1411               |
| Asparaginy-Leucine               | 7.6 | 246.1447 | [M+H] <sup>+</sup> | HMDB0028735 | 86.0978  |
| Biliverdin                       | 6.7 | 583.2573 | [M+H] <sup>+</sup> | HMDB0001008 | 297.1207, 583.2532                                     |
| Bisacurone epoxide               | 7.1 | 269.1749 | [M+H] <sup>+</sup> | HMDB0038503 | 43.0541, 171.1141,<br>187.1458                         |
| Cinnassiol D4 2-<br>glucoside    | 7.5 | 515.2851 | [M+H] <sup>+</sup> | HMDB0035065 | 337.2336, 497.2750                                     |
| Corchorifatty acid A             | 7.1 | 309.2028 | [M+H] <sup>+</sup> | HMDB0032664 | 135.0765, 273.1796,<br>291.1888                        |
| Dehydrozingerone                 | 8.0 | 193.0874 | [M+H] <sup>+</sup> | HMDB0032591 | 51.0258, 57.0337,<br>147.0804, 175.0675                |
| Diaminopimelic acid              | 7.9 | 191.1012 | [M+H] <sup>+</sup> | HMDB0001370 | 56.0455, 70.0592,<br>145.0952                          |
| Ergosterol                       | 7.4 | 397.3438 | [M+H] <sup>+</sup> | HMDB0000878 | 83.0832, 123.1146                                      |
| Galactosylhydroxylysine          | 7.3 | 325.1617 | [M+H] <sup>+</sup> | HMDB0000600 | 55.0599, 72.0861                                       |
| Glycyl-Methionine                | 7.8 | 207.0815 | [M+H] <sup>+</sup> | HMDB0028847 | 87.0263, 105.0542                                      |
| Glycyl-Phenylalanine             | 7.9 | 223.1075 | [M+H] <sup>+</sup> | HMDB0028848 | 91.0538, 103.0537,<br>120.0803                         |
| Isoleucyl-Isoleucine             | 7.6 | 245.184  | [M+H] <sup>+</sup> | HMDB0028910 | 69.0674, 86.0959,<br>132.0931                          |
| Kaempferol 3-<br>sophorotrioside | 7.1 | 773.2136 | [M+H] <sup>+</sup> | HMDB0032008 | 287.0541, 447.0873,<br>575.1480, 593.1464,<br>611.1648 |
| Kinocoumarin                     | 7.0 | 381.2081 | [M+H] <sup>+</sup> | HMDB0039033 | 69.0674, 363.1992                                      |

|                               |     |          |                    |             |  |
|-------------------------------|-----|----------|--------------------|-------------|--|
| Leucyl-Isoleucine             | 7.7 | 245.1844 | [M+H] <sup>+</sup> | HMDB0028932 | 69.0649, 86.0908                                     |
| Leucyl-phenylalanine          | 8.2 | 279.1709 | [M+H] <sup>+</sup> | HMDB0013243 | 69.0704, 86.0967,<br>120.0800, 166.0857              |
| Leucyl-Serine                 | 7.8 | 219.1329 | [M+H] <sup>+</sup> | HMDB0028938 | 60.0436, 69.0685,<br>86.0950                         |
| Leucyl-Threonine              | 7.6 | 233.1493 | [M+H] <sup>+</sup> | HMDB0028939 | 74.0600, 86.0974,<br>102.0555, 120.0640              |
| menaquinone-1                 | 6.5 | 243.1351 | [M+H] <sup>+</sup> | ECMDB20441  | 41.0403, 225.1245                                    |
| Methionyl-Threonine           | 7.0 | 251.1057 | [M+H] <sup>+</sup> | HMDB0028983 | 56.0498, 74.0594,<br>102.0552, 104.0511              |
| N5-(4-Methoxybenzyl)glutamine | 7.2 | 267.1347 | [M+H] <sup>+</sup> | HMDB0033598 | 82.0364, 136.0748                                    |
| N6-Acetyl-L-lysine            | 7.8 | 189.1233 | [M+H] <sup>+</sup> | HMDB0000206 | 72.0817  |
| N-Oleoylethanolamine          | 6.0 | 326.3049 | [M+H] <sup>+</sup> | HMDB02088   | 41.0372, 62.0603,<br>247.2483                        |
| Phenylalanyl-Valine           | 7.8 | 265.1554 | [M+H] <sup>+</sup> | HMDB0029008 | 72.0820, 103.0546,<br>120.0815                       |
| Prostaglandin E2              | 7.9 | 353.2348 | [M+H] <sup>+</sup> | HMDB0001220 | 55.0561, 93.0710,<br>259.1657, 293.2043,<br>335.2321 |
| Protocatechuic acid           | 6.6 | 155.0341 | [M+H] <sup>+</sup> | HMDB01856   | 109.0297, 137.0244                                   |
| Protoporphyrin IX             | 7.1 | 563.2662 | [M+H] <sup>+</sup> | HMDB0000241 | 563.2623   |
| Pyrraline                     | 7.2 | 255.1317 | [M+H] <sup>+</sup> | HMDB0033143 | 124.0360, 126.0504,<br>138.0498                      |



|                     |     |          |                    |             |   |
|---------------------|-----|----------|--------------------|-------------|---|
| Serylisoleucine     | 8.1 | 219.1347 | [M+H] <sup>+</sup> | HMDB0029042 | 44.0511, 60.0454,<br>86.0967, 132.1017,<br>173.1280 |
| Serylvaline         | 7.9 | 205.1173 | [M+H] <sup>+</sup> | HMDB0029052 | 42.0343, 60.0445,<br>118.0846, 159.1094             |
| Stearidonic acid    | 7.5 | 277.2149 | [M+H] <sup>+</sup> | HMDB0006547 | 43.0562, 55.0545,<br>79.0545, 121.1018,<br>135.1160 |
| Tetrahydrobiopterin | 7.9 | 242.1274 | [M+H] <sup>+</sup> | HMDB0000027 | 214.1153, 225.0936                                  |
| Valyl-Serine        | 7.7 | 205.1172 | [M+H] <sup>+</sup> | HMDB0029136 | 55.0547, 72.0792                                    |
| Valyl-Valine        | 7.4 | 217.1518 | [M+H] <sup>+</sup> | HMDB0029140 | 55.0555, 72.0810                                    |

\* The match scores were generated by MS-FINDER (cut-off: 6.0).

\*\* The experimental spectra were matched against HMDB and ECMDB to confirm the identification from MS-FINDER.