**Supplementary Table S4**. The list of statistically significant genes and reactions that show differential abundance between the young and older individuals.

|  |  |  |
| --- | --- | --- |
| Gene\_Family | p-value | p-adj\* |
| 6.3.2.8 | 1.66E-09 | 7.93E-07 |
| 6.3.2.9 | 4.19E-08 | 1.00E-05 |
| 5.1.1.3 | 9.00E-08 | 1.43E-05 |
| 6.3.2.10 | 1.98E-07 | 2.37E-05 |
| 6.3.2.9|unclassified | 9.93E-05 | 0.0095 |
| 6.3.2.8|g\_\_Eubacterium.s\_\_Eubacterium\_hallii | 0.0003 | 0.0205 |
| 5.1.1.3|unclassified | 0.0005 | 0.0272 |
| 1.3.1.98|unclassified | 0.0005 | 0.0272 |
| 6.3.2.10|unclassified | 0.0004 | 0.0272 |
| 6.3.2.4|g\_\_Faecalibacterium.s\_\_Faecalibacterium\_prausnitzii | 0.0007 | 0.0333 |
| 6.3.2.8|g\_\_Faecalibacterium.s\_\_Faecalibacterium\_prausnitzii | 0.0009 | 0.0386 |
| 2.5.1.7|g\_\_Faecalibacterium.s\_\_Faecalibacterium\_prausnitzii | 0.0011 | 0.0395 |
| 6.3.2.8|unclassified | 0.001 | 0.0395 |
| 6.3.2.8|g\_\_Blautia.s\_\_Ruminococcus\_obeum | 0.0012 | 0.0403 |
| 6.3.2.10|g\_\_Faecalibacterium.s\_\_Faecalibacterium\_prausnitzii | 0.0013 | 0.0403 |
| 2.5.1.7|g\_\_Eubacterium.s\_\_Eubacterium\_hallii | 0.0017 | 0.0456 |
| 6.3.2.8|g\_\_Collinsella.s\_\_Collinsella\_aerofaciens | 0.0017 | 0.0456 |
| 6.3.2.9|g\_\_Faecalibacterium.s\_\_Faecalibacterium\_prausnitzii | 0.0015 | 0.0456 |
| 6.3.2.4|g\_\_Eubacterium.s\_\_Eubacterium\_hallii | 0.0019 | 0.0487 |
| 5.1.1.3|g\_\_Faecalibacterium.s\_\_Faecalibacterium\_prausnitzii | 0.0025 | 0.0593 |
| 6.3.2.10|g\_\_Eubacterium.s\_\_Eubacterium\_hallii | 0.0029 | 0.0666 |
| 6.3.2.4|unclassified | 0.004 | 0.087 |
| 6.3.2.9|g\_\_Eubacterium.s\_\_Eubacterium\_hallii | 0.0044 | 0.0923 |
| 2.5.1.7|unclassified | 0.0049 | 0.0934 |
| 6.3.2.8|g\_\_Bifidobacterium.s\_\_Bifidobacterium\_longum | 0.0047 | 0.0934 |
| 6.3.2.4|g\_\_Bifidobacterium.s\_\_Bifidobacterium\_longum | 0.0056 | 0.1021 |
| 6.3.2.4|g\_\_Collinsella.s\_\_Collinsella\_aerofaciens | 0.0062 | 0.109 |
| 6.3.2.10|g\_\_Dorea.s\_\_Dorea\_longicatena | 0.0066 | 0.1123 |
| 2.5.1.7|g\_\_Collinsella.s\_\_Collinsella\_aerofaciens | 0.0078 | 0.1285 |
| 6.3.2.10|g\_\_Bifidobacterium.s\_\_Bifidobacterium\_longum | 0.0082 | 0.1311 |
| 6.3.2.10|g\_\_Collinsella.s\_\_Collinsella\_aerofaciens | 0.009 | 0.1395 |
| 6.3.2.4|g\_\_Blautia.s\_\_Ruminococcus\_obeum | 0.0097 | 0.1433 |
| 6.3.2.10|g\_\_Bacteroides.s\_\_Bacteroides\_vulgatus | 0.0099 | 0.1433 |
| 2.5.1.7|g\_\_Blautia.s\_\_Ruminococcus\_obeum | 0.0108 | 0.1512 |
| 2.5.1.7|g\_\_Dorea.s\_\_Dorea\_longicatena | 0.0117 | 0.1578 |
| 2.5.1.7|g\_\_Bifidobacterium.s\_\_Bifidobacterium\_longum | 0.0122 | 0.1578 |
| 6.3.2.9|g\_\_Bacteroides.s\_\_Bacteroides\_uniformis | 0.012 | 0.1578 |
| 6.3.2.8|g\_\_Parabacteroides.s\_\_Parabacteroides\_merdae | 0.0129 | 0.1621 |
| 6.3.2.9|g\_\_Bifidobacterium.s\_\_Bifidobacterium\_longum | 0.0133 | 0.1628 |
| 5.1.1.3|g\_\_Collinsella.s\_\_Collinsella\_aerofaciens | 0.0142 | 0.1693 |
| 5.1.1.3|g\_\_Bacteroides.s\_\_Bacteroides\_uniformis | 0.0148 | 0.1726 |
| 6.3.2.8|g\_\_Bacteroides.s\_\_Bacteroides\_vulgatus | 0.0154 | 0.1755 |
| 6.3.2.9|g\_\_Parabacteroides.s\_\_Parabacteroides\_merdae | 0.016 | 0.1783 |
| 6.3.2.4|g\_\_Dorea.s\_\_Dorea\_longicatena | 0.0178 | 0.1936 |
| 5.1.1.3|g\_\_Blautia.s\_\_Ruminococcus\_obeum | 0.0199 | 0.1937 |
| 5.1.1.3|g\_\_Bifidobacterium.s\_\_Bifidobacterium\_adolescentis | 0.0207 | 0.1937 |
| 5.1.1.3|g\_\_Alistipes.s\_\_Alistipes\_indistinctus | 0.0195 | 0.1937 |
| 6.3.2.4|g\_\_Parabacteroides.s\_\_Parabacteroides\_merdae | 0.0227 | 0.1937 |
| 6.3.2.4|g\_\_Coprococcus.s\_\_Coprococcus\_comes | 0.0215 | 0.1937 |
| 6.3.2.4|g\_\_Bacteroides.s\_\_Bacteroides\_caccae | 0.0209 | 0.1937 |
| 6.3.2.8|g\_\_Eubacterium.s\_\_Eubacterium\_siraeum | 0.0219 | 0.1937 |
| 6.3.2.8|g\_\_Dorea.s\_\_Dorea\_longicatena | 0.0225 | 0.1937 |
| 6.3.2.8|g\_\_Bacteroides.s\_\_Bacteroides\_uniformis | 0.022 | 0.1937 |
| 6.3.2.8|g\_\_Bacteroides.s\_\_Bacteroides\_ovatus | 0.0216 | 0.1937 |
| 6.3.2.9|g\_\_Eubacterium.s\_\_Eubacterium\_rectale | 0.0224 | 0.1937 |
| 6.3.2.9|g\_\_Bifidobacterium.s\_\_Bifidobacterium\_adolescentis | 0.0184 | 0.1937 |
| 2.5.1.7|g\_\_Bacteroides.s\_\_Bacteroides\_vulgatus | 0.0234 | 0.196 |
| 5.1.1.3|g\_\_Escherichia.s\_\_Escherichia\_coli | 0.0247 | 0.1963 |
| 6.3.2.4|g\_\_Bifidobacterium.s\_\_Bifidobacterium\_adolescentis | 0.0245 | 0.1963 |
| 6.3.2.4|g\_\_Bacteroides.s\_\_Bacteroides\_vulgatus | 0.026 | 0.1963 |
| 6.3.2.4|g\_\_Bacteroides.s\_\_Bacteroides\_dorei | 0.0262 | 0.1963 |
| 6.3.2.8|g\_\_Bifidobacterium.s\_\_Bifidobacterium\_adolescentis | 0.0267 | 0.1963 |
| 6.3.2.9|g\_\_Collinsella.s\_\_Collinsella\_aerofaciens | 0.0266 | 0.1963 |
| 6.3.2.10|g\_\_Dorea.s\_\_Dorea\_formicigenerans | 0.026 | 0.1963 |
| 6.3.2.10|g\_\_Bifidobacterium.s\_\_Bifidobacterium\_adolescentis | 0.0257 | 0.1963 |
| 5.1.1.3|g\_\_Bifidobacterium.s\_\_Bifidobacterium\_longum | 0.0271 | 0.1965 |
| 2.5.1.7|g\_\_Bacteroides.s\_\_Bacteroides\_uniformis | 0.0287 | 0.2044 |
| 6.3.2.10|g\_\_Blautia.s\_\_Ruminococcus\_obeum | 0.0306 | 0.2151 |
| 2.5.1.7|g\_\_Alistipes.s\_\_Alistipes\_shahii | 0.0318 | 0.2158 |
| 6.3.2.9|g\_\_Bacteroides.s\_\_Bacteroides\_ovatus | 0.0315 | 0.2158 |
| 6.3.2.10|g\_\_Bacteroides.s\_\_Bacteroides\_uniformis | 0.032 | 0.2158 |
| 2.5.1.7|g\_\_Bifidobacterium.s\_\_Bifidobacterium\_adolescentis | 0.0334 | 0.2219 |
| 2.5.1.7|g\_\_Eubacterium.s\_\_Eubacterium\_siraeum | 0.0356 | 0.2289 |
| 2.5.1.7|g\_\_Akkermansia.s\_\_Akkermansia\_muciniphila | 0.0356 | 0.2289 |
| 5.1.1.3|g\_\_Eubacterium.s\_\_Eubacterium\_rectale | 0.0366 | 0.2289 |
| 6.3.2.8|g\_\_Bacteroides.s\_\_Bacteroides\_dorei | 0.036 | 0.2289 |
| 6.3.2.9|g\_\_Alistipes.s\_\_Alistipes\_shahii | 0.0369 | 0.2289 |
| 2.5.1.7|g\_\_Eubacterium.s\_\_Eubacterium\_rectale | 0.0392 | 0.2345 |
| 6.3.2.10|g\_\_Alistipes.s\_\_Alistipes\_shahii | 0.0386 | 0.2345 |
| 6.3.2.10|g\_\_Akkermansia.s\_\_Akkermansia\_muciniphila | 0.0392 | 0.2345 |
| 6.3.2.4|g\_\_Alistipes.s\_\_Alistipes\_indistinctus | 0.0404 | 0.2356 |
| 6.3.2.10|g\_\_Coprococcus.s\_\_Coprococcus\_comes | 0.0401 | 0.2356 |
| 6.3.2.8|g\_\_Coprococcus.s\_\_Coprococcus\_comes | 0.0432 | 0.2488 |
| 6.3.2.4|g\_\_Escherichia.s\_\_Escherichia\_coli | 0.0444 | 0.2525 |
| 6.3.2.8|g\_\_Akkermansia.s\_\_Akkermansia\_muciniphila | 0.0456 | 0.2566 |
| 6.3.2.9|g\_\_Akkermansia.s\_\_Akkermansia\_muciniphila | 0.0466 | 0.2588 |
| 6.3.2.9|g\_\_Dorea.s\_\_Dorea\_formicigenerans | 0.0473 | 0.26 |
| 6.3.2.9|g\_\_Coprococcus.s\_\_Coprococcus\_comes | 0.0482 | 0.2619 |
| 5.1.1.3|g\_\_Bacteroides.s\_\_Bacteroides\_vulgatus | 0.0496 | 0.2662 |