**Lactobacillus acidophilus DDS-1 Modulates Gut Microbial Co-Occurrence Networks in Aging Mice**

Ravichandra Vemuri1, 3 Christopher J. Martoni2, Kylie Kavanagh1,4 and Rajaraman Eri3

1Department of Pathology, Section on Comparative Medicine, Wake Forest School of Medicine, Medical Center Boulevard, Winston‐Salem, NC 27157, USA

2UAS Laboratories, Madison, Wisconsin, WI, 54401 USA

3College of Health and Medicine, School of Health Sciences, University of Tasmania, Launceston, 7248, TAS, Australia

4Department of Biomedicine, University of Tasmania, Hobart, 7000, TAS, Australia

**Correspondence:**

Ravichandra Vemuri and Rajaraman Eri

Department of Pathology, Section of Comparative Medicine, Wake Forest School of Medicine, Medical Center Boulevard, Winston-Salem, NC 27157, USA.

College of Health and Medicine, School of Health Sciences, University of Tasmania, Launceston, 7248, TAS, Australia

**Table S1**: Nutritional composition details of Barastoc mice standard chow

|  |
| --- |
| **Contents** |
| Minimal crude protein 20 % | Vitamin A 15 IU/g |
| Minimal crude fat 6 % | Vitamin D3 2 IU/g |
| Crude fibre 3.2 % | Vitamin E 260 mg/kg |
| Acid detergent fibre 4.4 % | Vitamin K3 55 mg/kg |
| Neutral detergent fibre 10.4 % | Vitamin B1 64 mg/kg |
| Digestible energy 12.8 MJ/kg | Vitamin B2 48 mg/kg |
| Calcium 1.14 % | Vitamin B6 30 mg/kg |
| Phosphorus 0.94 % | Vitamin B12 0.08 mg/kg |
| Sodium 0.35 % | Niacin 400 mg/kg |
| Potassium 0.82 % | Panto 220 mg/kg |
| Chloride 0.58 % | Biotin 1.48 mg/kg |
| Magnesium 0.24 % | Folic 11 mg/kg |
| Lysine 1.11 % | Iron 51 mg/kg |
| Methionine 0.37 % | Zinc 60 mg/kg |
| Linoleic 1.52 % | Manganese 120 mg/kg |
| Starch 29 % | Copper 10 mg/kg |
| Vitamin A 15 IU/g | Selenium 0.1 mg/kg |
| Vitamin D3 2 IU/g | Molybdenum 0.4 mg/kg |
| Vitamin E 260 mg/kg | Cobalt 0.6 mg/kg |
| Vitamin K3 55 mg/kg | Iodine 1 .4 mg/kg |

**Table S2:** Summary of fecal microbiome co-occurrences between young and aging mice at phylum and genus levels based on Kendall's Tau correlation analysis after which FDR (q<0.05) correction was performed.

|  |  |
| --- | --- |
| **Young Control (Phylum)** | **Young Probiotic (Phylum)** |
| **Taxon1** | **Taxon2** | **Correlation (p<0.05)** | **Association** | **Taxon1** | **Taxon2** | **Correlation (p<0.05)** | **Association** |
| Firmicutes | Cyanobacteria | 1 | Positive | Firmicutes | Bacteroidetes | 1 | Positive |
| Firmicutes | Verrucomicrobia | 0.6 | Positive | Firmicutes | Proteobacteria | 0.6 | Positive |
| Firmicutes | Proteobacteria | 1 | Positive | Firmicutes | Cyanobacteria | -0.6 | Negative |
| Firmicutes | Bacteroidetes | -1 | Negative | Firmicutes | Actinobacteria | -0.5 | Negative |
| Bacteroidetes | Cyanobacteria | -1 | Negative | Bacteroidetes | Proteobacteria | 0.6 | Positive |
| Bacteroidetes | Firmicutes | -1 | Negative | Bacteroidetes | Cyanobacteria | 0.5 | Negative |
| Bacteroidetes | Verrucomicrobia | -0.6 | Negative | Bacteroidetes | Actinobacteria | 0.3 | Negative |
| Bacteroidetes | Proteobacteria | -1 | Negative | Bacteroidetes | Firmicutes | 1 | Positive |
| Verrucomicrobia | Cyanobacteria | 0.5 | Positive | Verrucomicrobia | Cyanobacteria | -0.3 | Negative |
| Verrucomicrobia | Firmicutes | 0.6 | Positive | Verrucomicrobia | Actinobacteria | -1 | Negative |
| Verrucomicrobia | Proteobacteria | 0.6 | Positive | Proteobacteria | Firmicutes | 1 | Positive |
| Verrucomicrobia | Bacteroidetes | -1 | Negative | Proteobacteria | Bacteroidetes | 1 | Positive |
| Proteobacteria | Cyanobacteria | 0.6 | Positive | Proteobacteria | Cyanobacteria | -1 | Negative |
| Proteobacteria | Firmicutes | 1 | Positive | Proteobacteria | Actinobacteria | -0.5 | Negative |
| Proteobacteria | Verrucomicrobia | 0.5 | Positive | Cyanobacteria | Firmicutes | -0.6 | Negative |
| Proteobacteria | Bacteroidetes | -1 | Negative | Cyanobacteria | Proteobacteria | -0.5 | Negative |
| Cyanobacteria | Firmicutes | 1 | Positive | Cyanobacteria | Bacteroidetes | -1 | Negative |
| Cyanobacteria | Proteobacteria | 0.5 | Positive | Cyanobacteria | Actinobacteria | -0.7 | Negative |
| Cyanobacteria | Bacteroidetes | -1 | Negative | Actinobacteria | Firmicutes | -0.5 | Negative |
| Cyanobacteria | Verrucomicrobia | 0.5 | Positive | Actinobacteria | Proteobacteria | -0.5 | Negative |
|  |  |  |  | Actinobacteria | Bacteroidetes | -1 | Negative |
|  |  |  |  | Actinobacteria | Cyanobacteria | -0.5 | Negative |
| **Young Control (Genus)** | **Young Probiotic (Genus)** |
| **Taxon1** | **Taxon2** | **Correlation (p<0.05)** | **Association** | **Taxon1** | **Taxon2** | **Correlation (p<0.05)** | **Association** |
| Prevotella | Cyanobacteria | 1 | Positive | Prevotella | Sutterella | 1 | Positive |
| Prevotella | Lachnospira | 0.6 | Positive | Prevotella | Ruminococcus | 0.6 | Positive |
| Lachnospira | Prevotella | 0.6 | Positive | Lachnospira | Lactobacillus | 1 | Positive |
| Lachnospira | Cyanobacteria | 0.3 | Positive | Lachnospira | Ruminococcus | 0.6 | Positive |
| Lachnospira | Ruminococcus | -0.5 | Negative | Lachnospira | Sutterella | -1 | Negative |
| Lachnospira | Rikenella | 1 | Positive | Lachnospira | Oscillospira | 0.5 | Positive |
| Lachnospira | Oscillospira | 0.5 | Positive | Lactobacillus | Lachnospira | 1 | Positive |
| Ruminococcus | Lachnospira | -1 | Negative | Lactobacillus | Ruminococcus | 0.6 | Positive |
| Ruminococcus | Oscillospira | -0.5 | Negative | Lactobacillus | Sutterella | -1 | Negative |
| Ruminococcus | Cyanobacteria | -0.3 | Negative | Lactobacillus | Oscillospira | 0.3 | Positive |
| Cyanobacteria | Oscillospira | 0.6 | Positive | Ruminococcus | Prevotella | 0.6 | Positive |
| Cyanobacteria | Rikenella | 0.5 | Positive | Ruminococcus | Lachnospira | 0.6 | Positive |
| Cyanobacteria | Ruminococcus | -0.3 | Negative | Ruminococcus | Lactobacillus | 0.6 | Positive |
| Cyanobacteria | Lachnospira | 0.3 | Positive | Ruminococcus | Sutterella | -0.6 | Negative |
| Cyanobacteria | Oscillospira | 1 | Positive | Ruminococcus | Bacteroides | 0.3 | Positive |
| Cyanobacteria | Prevotella | 1 | Positive | Sutterella | Ruminococcus | -0.6 | Negative |
| Rikenella | Cyanobacteria | 0.5 | Positive | Sutterella | Lactobacillus | -1 | Negative |
| Rikenella | Lachnospira | 1 | Positive | Sutterella | Prevotella | 1 | Positive |
| Oscillospira | Lachnospira | 0.5 | Positive | Sutterella | Lachnospira | 0.5 | Positive |
| Oscillospira | Cyanobacteria | 0.6 | Positive | Sutterella | Bacteroides | -1 | Negative |
| Oscillospira | Ruminococcus | -0.5 | Negative | Sutterella | Oscillospira | -0.5 | Negative |
|  |  |  |  | Bacteroides | 0.3 | Ruminococcus | Positive |
|  |  |  |  | Bacteroides | -1 | Sutterella | Negative |
|  |  |  |  | Oscillospira | Sutterella | -0.5 | Negative |
|  |  |  |  | Oscillospira | Lactobacillus | 0.3 | Positive |
|  |  |  |  | Oscillospira | Lachnospira | 0.5 | Positive |
|  |  |  |  | Oscillospira | Ruminococcus | 0.3 | Positive |
| **Aging Control (Phylum)** | **Aging Probiotic (Phylum)** |
| **Taxon1** | **Taxon2** | **Correlation (p<0.05)** | **Association** | **Taxon1** | **Taxon2** | **Correlation (p<0.05)** | **Association** |
| Firmicutes | Proteobacteria | -0.5 | Negative | Firmicutes | Actinobacteria | 0.3 | Positive |
| Firmicutes | Bacteroidetes | -1 | Negative | Firmicutes | Proteobacteria | -0.3 | Negative |
| Firmicutes | Verrucomicrobia | -0.3 | Negative | Firmicutes | Bacteroidetes | -1 | Negative |
| Bacteroidetes | Firmicutes | -1 | Negative | Firmicutes | Verrucomicrobia | -0.5 | Negative |
| Bacteroidetes | Verrucomicrobia | 0.5 | Positive | Bacteroidetes | Firmicutes | -1 | Negative |
| Bacteroidetes | Proteobacteria | 0.3 | Positive | Bacteroidetes | Verrucomicrobia | 0.3 | Positive |
| Verrucomicrobia | Firmicutes | -0.3 | Negative | Bacteroidetes | Proteobacteria | 0.5 | Positive |
| Verrucomicrobia | Bacteroidetes | 0.5 | Positive | Bacteroidetes | Actinobacteria | -0.3 | Negative |
| Proteobacteria | Bacteroidetes | 0.3 | Positive | Proteobacteria | Firmicutes | -0.3 | Negative |
| Proteobacteria | Firmicutes | -0.5 | Negative | Proteobacteria | Bacteroidetes | 0.5 | Positive |
|  |  |  |  | Proteobacteria | Actinobacteria | -0.3 | Negative |
|  |  |  |  | Verrucomicrobia | Bacteroidetes | 0.3 | Positive |
|  |  |  |  | Verrucomicrobia | Firmicutes | -0.5 | Negative |
|  |  |  |  | Verrucomicrobia | Actinobacteria | -0.3 | Negative |
|  |  |  |  | Actinobacteria | Verrucomicrobia | -0.3 | Negative |
|  |  |  |  | Actinobacteria | Bacteroidetes | -0.3 | Negative |
|  |  |  |  | Actinobacteria | Firmicutes | 0.3 | Positive |
|  |  |  |  | Actinobacteria | Proteobacteria | -0.3 | Negative |
| **Aging Control (Genus)** | **Aging Probiotic (Genus)** |
| **Taxon1** | **Taxon2** | **Correlation (p<0.05)** | **Association** | **Taxon1** | **Taxon2** | **Correlation (p<0.05)** | **Association** |
| Prevotella | Cyanobacteria | 0.5 | Positive | Prevotella | Akkermansia | 0.6 | Positive |
| Prevotella | Ruminococcus | -0.3 | Negative | Prevotella | Bacteroides | -0.3 | Negative |
| Prevotella | Oscillospira | -1 | Negative | Prevotella | Lactobacillus | -1 | Negative |
| Cyanobacteria | Prevotella | 0.5 | Positive | Prevotella | Oscillospira | -0.5 | Negative |
| Cyanobacteria | Ruminococcus | -0.5 | Negative | Akkermansia | Prevotella | 0.6 | Positive |
| Cyanobacteria | Oscillospira | -1 | Negative | Akkermansia | Bacteroides | -0.5 | Negative |
| Cyanobacteria | Sutterella | -0.5 | Negative | Akkermansia | Lactobacillus | -1 | Negative |
| Ruminococcus | Prevotella | -0.3 | Negative | Akkermansia | Oscillospira | -0.6 | Negative |
| Ruminococcus | Cyanobacteria | -0.5 | Negative | Akkermansia | Sutterella | 1 | Positive |
| Ruminococcus | Sutterella | 1 | Positive | Lactobacillus | Prevotella | -1 | Negative |
| Oscillospira | Prevotella | -1 | Negative | Lactobacillus | Akkermansia | -1 | Negative |
| Oscillospira | Cyanobacteria | -1 | Negative | Lactobacillus | Sutterella | 1 | Positive |
| Oscillospira | Lachnospira | 1 | Positive | Lactobacillus | Oscillospira | 0.6 | Positive |
| Lachnospira | Oscillospira | 1 | Positive | Lactobacillus | Lachnospira | 1 | Positive |
|  |  |  |  | Sutterella | Lactobacillus | 1 | Positive |
|  |  |  |  | Sutterella | Akkermansia | 1 | Positive |
|  |  |  |  | Sutterella | Bacteroides | 0.6 | Positive |
|  |  |  |  | Sutterella | Oscillospira | -1 | Negative |
|  |  |  |  | Sutterella | Ruminococcus | 0.5 | Positive |
|  |  |  |  | Sutterella | Lactobacillus | 1 | Positive |
|  |  |  |  | Lachnospira | Lactobacillus | 1 | Positive |
|  |  |  |  | Lachnospira | Bacteroides | 0.6 | Positive |
|  |  |  |  | Lachnospira | Sutterella | 1 | Positive |
|  |  |  |  | Lachnospira | Ruminococcus | -0.5 | Negative |
|  |  |  |  | Lachnospira | Oscillospira | 1 | Positive |
|  |  |  |  | Oscillospira | Lachnospira | 1 | Positive |
|  |  |  |  | Oscillospira | Sutterella | -1 | Negative |
|  |  |  |  | Oscillospira | Lactobacillus | 0.6 | Positive |
|  |  |  |  | Oscillospira | Bacteroides | -0.4 | Negative |
|  |  |  |  | Bacteroides | Oscillospira | -0.4 | Negative |
|  |  |  |  | Bacteroides | Lachnospira | 0.6 | Positive |
|  |  |  |  | Bacteroides | Sutterella | 0.6 | Positive |
|  |  |  |  | Bacteroides | Ruminococcus | 0.5 | Positive |
|  |  |  |  | Bacteroides | Akkermansia | -0.5 | Negative |
|  |  |  |  | Bacteroides | Prevotella | -0.3 | Negative |
|  |  |  |  | Rikenella | Akkermansia | -0.6 | Negative |
|  |  |  |  | Rikenella | Sutterella | -1 | Negative |
|  |  |  |  | Ruminococcus | Lachnospira | -0.5 | Negative |
|  |  |  |  | Ruminococcus | Sutterella | 0.5 | Positive |
|  |  |  |  | Ruminococcus | Bacteroides | 0.5 | Positive |

**Table S3:** Summary of mucosal microbiome co-occurrences between young and aging mice at phylum and genus levels based on Kendall's Tau correlation analysis after which FDR (q<0.05) correction was performed.

|  |  |
| --- | --- |
| **Young Control (Phylum)** | **Young Probiotic (Phylum)** |
| **Taxon1** | **Taxon2** | **Correlation (p<0.05)** | **Association** | **Taxon1** | **Taxon2** | **Correlation (p<0.05)** | **Association** |
| Firmicutes | Bacteroidetes | 1 | Positive | Firmicutes | Bacteroidetes | 1 | Positive |
| Firmicutes | Proteobacteria | -0.2 | Negative | Firmicutes | Cyanobacteria | -0.5 | Negative |
| Firmicutes | Cyanobacteria | -0.2 | Negative | Firmicutes | Actinobacteria | -0.3 | Negative |
| Firmicutes | Actinobacteria | -0.3 | Negative | Bacteroidetes | Firmicutes | 1 | Positive |
| Bacteroidetes | Firmicutes | 1 | Positive | Bacteroidetes | Cyanobacteria | -0.5 | Negative |
| Bacteroidetes | Proteobacteria | -0.3 | Negative | Bacteroidetes | Actinobacteria | -0.5 | Negative |
| Bacteroidetes | Cyanobacteria | -0.2 | Negative | Actinobacteria | Bacteroidetes | -0.5 | Negative |
| Bacteroidetes | Actinobacteria | -0.2 | Negative | Actinobacteria | Firmicutes | -0.3 | Negative |
| Proteobacteria | Firmicutes | -1 | Negative | Actinobacteria | Proteobacteria | -0.5 | Negative |
| Proteobacteria | Bacteroidetes | -1 | Negative | Actinobacteria | Verrucomicrobia | -0.3 | Negative |
| Proteobacteria | Verrucomicrobia | -0.5 | Negative | Cyanobacteria | Firmicutes | -0.5 | Negative |
| Verrucomicrobia | Proteobacteria | -0.5 | Negative | Cyanobacteria | Bacteroidetes | -0.5 | Negative |
| Verrucomicrobia | Cyanobacteria | -0.3 | Negative | Cyanobacteria | Verrucomicrobia | -0.3 | Negative |
| Verrucomicrobia | Actinobacteria | -0.3 | Negative | Cyanobacteria | Proteobacteria | -0.3 | Negative |
| Cyanobacteria | Firmicutes | -0.2 | Negative | Proteobacteria | Cyanobacteria | -0.3 | Negative |
| Cyanobacteria | Verrucomicrobia | -0.3 | Negative | Proteobacteria | Actinobacteria | -0.5 | Negative |
| Cyanobacteria | Bacteroidetes | -0.2 | Negative | Proteobacteria | Verrucomicrobia | -0.5 | Negative |
| Actinobacteria | Verrucomicrobia | -0.3 | Negative | Verrucomicrobia | Proteobacteria | -0.5 | Negative |
| Actinobacteria | Bacteroidetes | -0.2 | Negative | Verrucomicrobia | Cyanobacteria | -0.3 | Negative |
| Actinobacteria | Firmicutes | -0.3 | Negative | Verrucomicrobia | Actinobacteria | -0.3 | Negative |
| **Young Control (Genus)** | **Young Probiotic (Genus)** |
| **Taxon1** | **Taxon2** | **Correlation (p<0.05)** | **Association** | **Taxon1** | **Taxon2** | **Correlation (p<0.05)** | **Association** |
| Prevotella | Rikenella | 0.6 | Positive | Prevotella | Rikenella | -1 | Negative |
| Prevotella | Odoribacter | -0.3 | Negative | Prevotella | Oscillospira | 0.6 | Positive |
| Prevotella | Ruminococcus | -0.5 | Negative | Prevotella | Ruminococcus | -0.5 | Negative |
| Prevotella | Akkermansia | -0.3 | Negative | Prevotella | Akkermansia | -1 | Negative |
| Prevotella | Lachnospira | -1 | Negative | Prevotella | Lachnospira | 1 | Positive |
| Prevotella | Bacteroides | -1 | Negative | Prevotella | Sutterella | 1 | Positive |
| Ruminococcus | Prevotella | -0.5 | Negative | Sutterella | Prevotella | 1 | Positive |
| Ruminococcus | Akkermansia | 0.5 | Positive | Sutterella | Akkermansia | -1 | Negative |
| Ruminococcus | Odoribacter | -0.5 | Negative | Sutterella | Lachnospira | -0.6 | Negative |
| Ruminococcus | Bacteroides | -1 | Negative | Sutterella | Rikenella | -1 | Negative |
| Ruminococcus | Oscillospira | -1 | Negative | Sutterella | Oscillospira | 1 | Positive |
| Ruminococcus | Rikenella | -1 | Negative | Akkermansia | Prevotella | -1 | Negative |
| Bacteroides | Prevotella | -1 | Negative | Akkermansia | Sutterella | -1 | Negative |
| Bacteroides | Ruminococcus | -1 | Negative | Akkermansia | Rikenella | 1 | Positive |
| Bacteroides | Rikenella | 0.6 | Positive | Akkermansia | Lachnospira | -0.6 | Negative |
| Bacteroides | Odoribacter | -0.5 | Negative | Akkermansia | Oscillospira | -0.6 | Negative |
| Bacteroides | Lachnospira | 1 | Positive | Lachnospira | Akkermansia | -0.6 | Negative |
| Bacteroides | Akkermansia | -0.3 | Negative | Lachnospira | Prevotella | 1 | Positive |
| Akkermansia | Bacteroides | -0.3 | Negative | Lachnospira | Sutterella | -0.6 | Negative |
| Akkermansia | Ruminococcus | 0.5 | Positive | Lachnospira | Oscillospira | -1 | Negative |
| Akkermansia | Prevotella | -0.3 | Negative | Oscillospira | Lachnospira | -1 | Negative |
| Akkermansia | Odoribacter | -0.3 | Negative | Oscillospira | Prevotella | 1 | Positive |
| Akkermansia | Rikenella | -0.5 | Negative | Oscillospira | Sutterella | -0.6 | Negative |
| Akkermansia | Lachnospira | 1 | Positive | Oscillospira | Akkermansia | -0.6 | Negative |
| Lachnospira | Akkermansia | 1 | Positive | Oscillospira | Rikenella | -1 | Negative |
| Lachnospira | Rikenella | -1 | Negative | Rikenella | Oscillospira | -1 | Negative |
| Lachnospira | Prevotella | -1 | Negative | Rikenella | Prevotella | -1 | Negative |
| Lachnospira | Bacteroides | 1 | Positive | Rikenella | Sutterella | -1 | Negative |
| Lachnospira | Odoribacter | 0.6 | Positive | Rikenella | Lachnospira | -1 | Negative |
| Odoribacter | Lachnospira | 0.6 | Positive | Rikenella | Akkermansia | 1 | Positive |
| Odoribacter | Akkermansia | -0.3 | Negative |  |  |  |  |
| Odoribacter | Bacteroides | -0.5 | Negative |  |  |  |  |
| Odoribacter | Ruminococcus | -0.5 | Negative |  |  |  |  |
| Odoribacter | Rikenella | 1 | Positive |  |  |  |  |
| Odoribacter | Prevotella | -0.3 | Negative |  |  |  |  |
| Rikenella | Odoribacter | 1 | Positive |  |  |  |  |
| Rikenella | Lachnospira | -1 | Negative |  |  |  |  |
| Rikenella | Bacteroides | 0.6 | Positive |  |  |  |  |
| Rikenella | Ruminococcus | -0.5 | Negative |  |  |  |  |
| Rikenella | Prevotella | 0.6 | Positive |  |  |  |  |
| Rikenella | Akkermansia | -0.3 | Negative |  |  |  |  |
| Oscillospira | Ruminococcus | -1 | Negative |  |  |  |  |
| **Aging Control (Phylum)** | **Aging Probiotic (Phylum)** |
| Firmicutes | Bacteroidetes | 1 | Positive | Firmicutes | Actinobacteria | 1 | Positive |
| Firmicutes | Cyanobacteria | -0.3 | Negative | Firmicutes | Proteobacteria | -0.5 | Negative |
| Bacteroidetes | Cyanobacteria | -0.3 | Negative | Firmicutes | Verrucomicrobia | -0.2 | Negative |
| Bacteroidetes | Firmicutes | 1 | Positive | Firmicutes | Bacteroidetes | -1 | Negative |
| Cyanobacteria | Firmicutes | -0.3 | Negative | Bacteroidetes | Firmicutes | -1 | Negative |
| Cyanobacteria | Bacteroidetes | -0.3 | Negative | Bacteroidetes | Proteobacteria | 0.5 | Positive |
| Cyanobacteria | Proteobacteria | -0.5 | Negative | Bacteroidetes | Verrucomicrobia | 0.6 | Positive |
| Cyanobacteria | Verrucomicrobia | -0.1 | Negative | Bacteroidetes | Actinobacteria | -0.2 | Negative |
| Verrucomicrobia | Cyanobacteria | -0.1 | Negative | Proteobacteria | Actinobacteria | -0.2 | Negative |
| Verrucomicrobia | Proteobacteria | -0.1 | Negative | Proteobacteria | Firmicutes | -0.5 | Negative |
| Proteobacteria | Verrucomicrobia | -0.1 | Negative | Proteobacteria | Bacteroidetes | 0.5 | Positive |
| Proteobacteria | Cyanobacteria | -0.5 | Negative | Proteobacteria | Verrucomicrobia | 0.6 | Positive |
|  |  |  |  | Verrucomicrobia | Proteobacteria | 0.6 | Positive |
|  |  |  |  | Verrucomicrobia | Firmicutes | -0.2 | Negative |
|  |  |  |  | Verrucomicrobia | Bacteroidetes | 0.6 | Positive |
|  |  |  |  | Verrucomicrobia | Cyanobacteria | 0.5 | Positive |
|  |  |  |  | Actinobacteria | Bacteroidetes | -0.2 | Negative |
|  |  |  |  | Actinobacteria | Proteobacteria | -0.2 | Negative |
|  |  |  |  | Actinobacteria | Firmicutes | 1 | Positive |
|  |  |  |  | Cyanobacteria | Verrucomicrobia | 0.5 | Positive |
| **Aging Control (Genus)** | **Aging Probiotic (Genus)** |
| **Taxon1** | **Taxon2** | **Correlation (p<0.05)** | **Association** | **Taxon1** | **Taxon2** | **Correlation (p<0.05)** | **Association** |
| Prevotella | Sutterella | 1 | Positive | Prevotella | Akkermansia | 0.6 | Positive |
| Prevotella | Bacteroides | -1 | Negative | Prevotella | Oscillospira | -1 | Negative |
| Prevotella | Ruminococcus | 0.6 | Positive | Prevotella | Ruminococcus | -0.6 | Negative |
| Prevotella | Lactobacillus | -1 | Negative | Prevotella | Lactobacillus | -1 | Negative |
| Prevotella | Lachnospira | -0.4 | Positive | Prevotella | Lachnospira | -0.5 | Negative |
| Prevotella | Rikenella | 1 | Positive | Prevotella | Rikenella | -0.6 | Negative |
| Bacteroides | Prevotella | -1 | Negative | Akkermansia | Prevotella | 0.6 | Positive |
| Bacteroides | Ruminococcus | -0.5 | Negative | Akkermansia | Oscillospira | -1 | Negative |
| Bacteroides | Lactobacillus | 1 | Positive | Akkermansia | Ruminococcus | -0.3 | Negative |
| Bacteroides | Lachnospira | 0.6 | Positive | Akkermansia | Lactobacillus | -1 | Negative |
| Bacteroides | Sutterella | 0.5 | Positive | Akkermansia | Lachnospira | -1 | Negative |
| Bacteroides | Rikenella | -1 | Negative | Akkermansia | Rikenella | -1 | Negative |
| Lactobacillus | Bacteroides | 1 | Positive | Ruminococcus | Lactobacillus | 1 | Positive |
| Lactobacillus | Prevotella | -1 | Negative | Ruminococcus | Lachnospira | 1 | Positive |
| Lactobacillus | Lachnospira | -0.5 | Negative | Ruminococcus | Rikenella | 0.6 | Positive |
| Lactobacillus | Sutterella | -0.3 | Negative | Ruminococcus | Prevotella | -0.6 | Negative |
| Lactobacillus | Ruminococcus | 0.6 | Positive | Ruminococcus | Oscillospira | 1 | Positive |
| Sutterella | Lactobacillus | -0.3 | Negative | Ruminococcus | Prevotella | -0.6 | Negative |
| Sutterella | Bacteroides | 0.5 | Positive | Ruminococcus | Akkermansia | -0.6 | Negative |
| Sutterella | Prevotella | 1 | Positive | Oscillospira | Ruminococcus | 1 | Positive |
| Sutterella | Lachnospira | -0.5 | Negative | Oscillospira | Prevotella | -1 | Negative |
| Sutterella | Rikenella | -1 | Negative | Oscillospira | Akkermansia | -1 | Negative |
| Sutterella | Ruminococcus | 0.5 | Positive | Oscillospira | Lactobacillus | 1 | Positive |
| Lachnospira | Sutterella | -0.5 | Negative | Oscillospira | Lachnospira | 1 | Positive |
| Lachnospira | Lactobacillus | -0.5 | Negative | Oscillospira | Rikenella | 0.6 | Positive |
| Lachnospira | Bacteroides | 0.6 | Positive | Rikenella | Oscillospira | 0.6 | Positive |
| Lachnospira | Prevotella | -0.4 | Positive | Rikenella | Ruminococcus | 0.6 | Positive |
| Lachnospira | Ruminococcus | -0.6 | Negative | Rikenella | Prevotella | -0.6 | Negative |
| Ruminococcus | Lachnospira | -0.6 | Negative | Rikenella | Akkermansia | -1 | Negative |
| Ruminococcus | Lactobacillus | 0.6 | Positive | Rikenella | Lactobacillus | 1 | Positive |
| Ruminococcus | Bacteroides | -0.5 | Negative | Rikenella | Lachnospira | 1 | Positive |
| Ruminococcus | Prevotella | 0.6 | Positive | Lactobacillus | Rikenella | 1 | Positive |
| Ruminococcus | Sutterella | 0.5 | Positive | Lactobacillus | Oscillospira | 1 | Positive |
| Rikenella | Sutterella | -1 | Negative | Lactobacillus | Ruminococcus | 1 | Positive |
| Rikenella | Bacteroides | -1 | Negative | Lactobacillus | Akkermansia | -1 | Negative |
| Rikenella | Prevotella | 1 | Positive | Lactobacillus | Prevotella | -0.5 | Positive |
|  |  |  |  | Lactobacillus | Lachnospira | 1 | Positive |
|  |  |  |  | Lachnospira | Lactobacillus | 1 | Positive |
|  |  |  |  | Lachnospira | Rikenella | 1 | Positive |
|  |  |  |  | Lachnospira | Oscillospira | 1 | Positive |
|  |  |  |  | Lachnospira | Ruminococcus | 1 | Positive |
|  |  |  |  | Lachnospira | Akkermansia | -1 | Negative |
|  |  |  |  | Lachnospira | Prevotella | -0.5 | Positive |

**Table S4:** Summary of cecal microbiome co-occurrences between young and aging mice at phylum and genus levels based on Kendall's Tau correlation analysis after which FDR (q<0.05) correction was performed.

|  |  |
| --- | --- |
| **Young Control (Phylum)** | **Young Probiotic (Phylum)** |
| **Taxon1** | **Taxon2** | **Correlation (p<0.05)** | **Association** | **Taxon1** | **Taxon2** | **Correlation (p<0.05)** | **Association** |
| Firmicutes | Bacteroidetes | -1 | Negative | Firmicutes | Bacteroidetes | 1 | Positive |
| Firmicutes | Cyanobacteria | -0.5 | Negative | Firmicutes | Cyanobacteria | -0.5 | Negative |
| Firmicutes | Verrucomicrobia | -0.6 | Negative | Firmicutes | Verrucomicrobia | 0.6 | Positive |
| Firmicutes | Proteobacteria | -0.3 | Negative | Firmicutes | Actinobacteria | -0.3 | Negative |
| Proteobacteria | Firmicutes | -0.3 | Negative | Actinobacteria | Firmicutes | -0.3 | Negative |
| Proteobacteria | Bacteroidetes | 1 | Positive | Actinobacteria | Bacteroidetes | -0.2 | Negative |
| Proteobacteria | Cyanobacteria | 0.6 | Positive | Actinobacteria |  Proteobacteria |  -0.5 | Negative |
| Cyanobacteria | Verrucomicrobia | 0.5 | Positive | Actinobacteria | Verrucomicrobia | -0.4 | Negative |
| Cyanobacteria | Proteobacteria | 0.4 | Positive | Verrucomicrobia | Actinobacteria | -0.4 | Negative |
| Cyanobacteria | Firmicutes | -0.5 | Negative | Verrucomicrobia | Firmicutes | 0.3 | Positive |
| Cyanobacteria | Bacteroidetes | 1 | Positive | Verrucomicrobia | Bacteroidetes | 1 | Positive |
| Bacteroidetes | Cyanobacteria | 1 | Positive | Verrucomicrobia | Cyanobacteria | -1 | Negative |
| Bacteroidetes | Proteobacteria | 1 | Positive | Verrucomicrobia | Proteobacteria | -0.4 | Negative |
| Bacteroidetes | Firmicutes | -1 | Negative | Proteobacteria | Verrucomicrobia | -0.6 | Negative |
| Bacteroidetes | Verrucomicrobia | -0.5 | Negative | Proteobacteria | Actinobacteria | -0.5 | Negative |
| Verrucomicrobia | Bacteroidetes | -0.5 | Negative | Proteobacteria | Cyanobacteria | -0.3 | Negative |
| Verrucomicrobia | Firmicutes | -0.6 | Negative | Cyanobacteria | Proteobacteria | -0.3 | Negative |
| Verrucomicrobia | Cyanobacteria | 0.5 | Positive | Cyanobacteria | Firmicutes | -0.3 | Negative |
|  |  |  |  | Cyanobacteria | Verrucomicrobia | -1 | Negative |
|  |  |  |  | Cyanobacteria | Bacteroidetes | 1 | Positive |
|  |  |  |  | Bacteroidetes | Cyanobacteria | -1 | Negative |
|  |  |  |  | Bacteroidetes | Verrucomicrobia | -1 | Negative |
|  |  |  |  | Bacteroidetes | Actinobacteria | -0.2 | Negative |
|  |  |  |  | Bacteroidetes | Firmicutes | 0.3 | Positive |
| **Young Control (Genus)** | **Young Probiotic (Genus)** |
| **Taxon1** | **Taxon2** | **Correlation (p<0.05)** | **Association** | **Taxon1** | **Taxon2** | **Correlation (p<0.05)** | **Association** |
| Prevotella | Oscillospira | 0.6 | Positive | Prevotella | Oscillospira | 0.6 | Positive |
| Prevotella | Akkermansia | -0.5 | Negative | Prevotella | Akkermansia | -0.5 | Negative |
| Prevotella | Lachnospira | -1 | Negative | Prevotella | Lachnospira | 1 | Positive |
| Prevotella | Sutterella | -0.4 | Negative | Prevotella | Sutterella | 0.4 | Positive |
| Prevotella | Bacteroides | -1 | Negative | Prevotella | Lactobacillus | 0.4 | Positive |
| Bacteroides | Prevotella | -1 | Negative | Prevotella | odoribacteria | 0.6 | Positive |
| Bacteroides | Oscillospira | -0.6 | Negative | Prevotella | Rikenella | -1 | Negative |
| Bacteroides | Rikenella | 0.6 | Positive | Prevotella | Ruminococcus | 1 | Positive |
| Bacteroides | Lachnospira | 1 | Positive | Prevotella | Bacteroides | 1 | Positive |
| Bacteroides | Sutterella | -0.3 | Negative | Bacteroides | Prevotella | 1 | Positive |
| Bacteroides | Ruminococcus | -0.6 | Negative | Bacteroides | Oscillospira | -0.5 | Negative |
| Ruminococcus | Bacteroides | -0.6 | Negative | Bacteroides | Akkermansia | -0.5 | Negative |
| Ruminococcus | Akkermansia | 0.5 | Positive | Bacteroides | Lachnospira | 1 | Positive |
| Ruminococcus | Sutterella | 0.6 | Positive | Bacteroides | Sutterella | 0.6 | Positive |
| Ruminococcus | Lachnospira | -1 | Negative | Bacteroides | Lactobacillus | 0.4 | Positive |
| Lachnospira | Ruminococcus | -1 | Negative | Bacteroides | odoribacteria | -0.4 | Negative |
| Lachnospira | Bacteroides | 1 | Positive | Bacteroides | Rikenella | -1 | Negative |
| Lachnospira | Prevotella | -1 | Negative | Rikenella | Bacteroides | -1 | Negative |
| Lachnospira | Oscillospira | -0.6 | Negative | Rikenella | Prevotella | -1 | Negative |
| Oscillospira | Lachnospira | -0.6 | Negative | Rikenella | Oscillospira | -0.4 | Negative |
| Oscillospira | Prevotella | 0.6 | Positive | Rikenella | Odoribacteria | -0.5 | Negative |
| Oscillospira | Bacteroides | -0.6 | Negative | Rikenella | Lachnospira | 1 | Positive |
| Oscillospira | Sutterella | -0.3 | Negative | Rikenella | Sutterella | 0.5 | Positive |
| Oscillospira | Akkermansia | -0.6 | Negative | Rikenella | Ruminococcus | -0.6 | Negative |
| Akkermansia | Oscillospira | -0.6 | Negative | Rikenella | Lactobacillus | -0.4 | Negative |
| Akkermansia | Ruminococcus | 0.5 | Positive | Lactobacillus | Rikenella | -0.4 | Negative |
| Akkermansia | Prevotella | -0.5 | Negative | Lactobacillus | Prevotella | 0.4 | Positive |
| Akkermansia | Sutterella | 0.6 | Positive | Lactobacillus | Bacteroides | 0.4 | Positive |
| Sutterella | Akkermansia | 0.6 | Positive | Lactobacillus | Ruminococcus | 0.6 | Positive |
| Sutterella | Oscillospira | -0.3 | Negative | Lactobacillus | Akkermansia | -0.5 | Negative |
| Sutterella | Ruminococcus | 0.6 | Positive | Lactobacillus | Lachnospira | -1 | Negative |
| Sutterella | Bacteroides | -0.3 | Negative | Lactobacillus | Odoribacteria | -0.6 | Negative |
|  |  |  |  | Lactobacillus | Oscillospira | 0.4 | Positive |
|  |  |  |  | Lactobacillus | Sutterella | 0.5 | Positive |
| Sutterella | Prevotella | -0.4 | Negative | Odoribacteria | Lactobacillus | -0.6 | Negative |
| Sutterella | Rikenella | -0.6 | Negative | Odoribacteria | Ruminococcus | 0.6 | Positive |
| Rikenella | Sutterella | -0.6 | Negative | Odoribacteria | Rikenella | -0.5 | Negative |
| Rikenella | Bacteroides | 0.6 | Positive | Odoribacteria | Prevotella | 0.6 | Positive |
|  |  |  |  | Odoribacteria | Bacteroides | -0.4 | Negative |
|  |  |  |  | Odoribacteria | Sutterella | -0.5 | Negative |
|  |  |  |  | Odoribacteria | Lachnospira | 1 | Positive |
|  |  |  |  | Lachnospira | Odoribacteria | 1 | Positive |
|  |  |  |  | Lachnospira | Rikenella | 1 | Positive |
|  |  |  |  | Lachnospira | Prevotella | 1 | Positive |
|  |  |  |  | Lachnospira | Bacteroides | 1 | Positive |
|  |  |  |  | Lachnospira | Lactobacillus | -1 | Negative |
|  |  |  |  | Lachnospira | Oscillospira | 1 | Positive |
|  |  |  |  | Lachnospira | Sutterella | 0.6 | Positive |
|  |  |  |  | Lachnospira | Ruminococcus | 0.6 | Positive |
|  |  |  |  | Ruminococcus | Lachnospira | 0.6 | Positive |
|  |  |  |  | Ruminococcus | Odoribacteria | 0.6 | Positive |
|  |  |  |  | Ruminococcus | Lactobacillus | 0.6 | Positive |
|  |  |  |  | Ruminococcus | Rikenella | -0.6 | Negative |
|  |  |  |  | Ruminococcus | Prevotella | 1 | Positive |
|  |  |  |  | Ruminococcus | Oscillospira | 1 | Positive |
|  |  |  |  | Ruminococcus | Akkermansia | -1 | Negative |
|  |  |  |  | Akkermansia | Ruminococcus | -1 | Negative |
|  |  |  |  | Akkermansia | Prevotella | -0.5 | Negative |
|  |  |  |  | Akkermansia | Suterella | -0.5 | Negative |
|  |  |  |  | Akkermansia | Lactobacillus | -0.5 | Negative |
|  |  |  |  | Akkermansia | Bacteroides | -0.5 | Negative |
|  |  |  |  | Akkermansia | Oscillospira | 1 | Positive |
|  |  |  |  | Oscillospira | Akkermansia | 1 | Positive |
|  |  |  |  | Oscillospira | Prevotella | 0.6 | Positive |
|  |  |  |  | Oscillospira | Bacteroides | -0.5 | Negative |
|  |  |  |  | Oscillospira | Rikenella | -0.4 | Negative |
|  |  |  |  | Oscillospira | Lactobacillus | 0.4 | Positive |
|  |  |  |  | Oscillospira | Lachnospira | 1 | Positive |
|  |  |  |  | Oscillospira | Ruminococcus | 1 | Positive |
|  |  |  |  | Oscillospira | Akkermansia | 1 | Positive |
|  |  |  |  | Oscillospira | Sutterella | -0.5 | Negative |
|  |  |  |  | Sutterella | Oscillospira | -0.5 | Negative |
|  |  |  |  | Sutterella | Akkermansia | -0.5 | Negative |
|  |  |  |  | Sutterella | Lachnospira | 0.6 | Positive |
|  |  |  |  | Sutterella | Rikenella | 0.5 | Positive |
|  |  |  |  | Sutterella | Bacteroides | 0.6 | Positive |
|  |  |  |  | Sutterella | Prevotella | 0.4 | Positive |
|  |  |  |  | Sutterella | Odoribacteria | -0.5 | Negative |
|  |  |  |  | Sutterella | Lactobacillus | 0.5 | Positive |
| **Aging Control (Phylum)** | **Aging Probiotic (Phylum)** |
| **Taxon1** | **Taxon2** | **Correlation (p<0.05)** | **Association** | **Taxon1** | **Taxon2** | **Correlation (p<0.05)** | **Association** |
| Firmicutes | Actinobacteria | 1 | Positive | Firmicutes | Bacteroidetes | 1 | Positive |
| Firmicutes | Bacteroidetes | -1 | Negative | Firmicutes | Proteobacteria | 0.6 | Positive |
| Firmicutes | Verrucomicrobia | -0.3 | Negative | Firmicutes | Cyanobacteria | -0.5 | Negative |
| Bacteroidetes | Firmicutes | -1 | Negative | Firmicutes | Verrucomicrobia | 0.6 | Positive |
| Bacteroidetes | Actinobacteria | -0.3 | Negative | Firmicutes | Actinobacteria | -0.3 | Negative |
| Bacteroidetes | Verrucomicrobia | 0.5 | Positive | Bacteroidetes | Firmicutes | 1 | Positive |
| Verrucomicrobia | Bacteroidetes | 0.5 | Positive | Bacteroidetes | Proteobacteria | 0.5 | Positive |
| Verrucomicrobia | Firmicutes | -0.3 | Negative | Bacteroidetes | Cyanobacteria | -0.5 | Negative |
| Verrucomicrobia | Proteobacteria | 0.6 | Positive | Bacteroidetes | Verrucomicrobia | 0.6 | Positive |
| Verrucomicrobia | Actinobacteria | -0.5 | Negative | Bacteroidetes | Actinobacteria | -0.2 | Negative |
| Actinobacteria | Verrucomicrobia | -0.5 | Negative | Actinobacteria | Bacteroidetes | -0.2 | Negative |
| Actinobacteria | Firmicutes | 1 | Positive | Actinobacteria | Firmicutes | -0.3 | Negative |
| Actinobacteria | Bacteroidetes | -0.3 | Negative | Actinobacteria | Proteobacteria | -0.5 | Negative |
| Actinobacteria | Proteobacteria | -0.3 | Negative | Actinobacteria | Cyanobacteria | -0.5 | Negative |
| Proteobacteria | Actinobacteria | -0.3 | Negative | Actinobacteria | Verrucomicrobia | -0.6 | Negative |
| Proteobacteria | Verrucomicrobia | 0.6 | Positive | Verrucomicrobia | Actinobacteria | -0.6 | Negative |
|  |  |  |  | Verrucomicrobia | Bacteroidetes | 0.6 | Positive |
|  |  |  |  | Verrucomicrobia | Firmicutes | 0.6 | Positive |
|  |  |  |  | Verrucomicrobia | Proteobacteria | -0.5 | Negative |
|  |  |  |  | Verrucomicrobia | Cyanobacteria | -0.5 | Negative |
|  |  |  |  | Cyanobacteria | Verrucomicrobia | -0.5 | Negative |
|  |  |  |  | Cyanobacteria | Actinobacteria | -0.5 | Negative |
|  |  |  |  | Cyanobacteria | Bacteroidetes | -0.5 | Negative |
|  |  |  |  | Cyanobacteria | Firmicutes | -0.5 | Negative |
|  |  |  |  | Cyanobacteria | Proteobacteria | -0.3 | Negative |
|  |  |  |  | Proteobacteria | Cyanobacteria | -0.3 | Negative |
|  |  |  |  | Proteobacteria | Verrucomicrobia | -0.5 | Negative |
|  |  |  |  | Proteobacteria | Actinobacteria | -0.5 | Negative |
|  |  |  |  | Proteobacteria | Bacteroidetes | 0.5 | Positive |
|  |  |  |  | Proteobacteria | Firmicutes | 0.6 | Positive |
| **Aging Control (Genus)** | **Aging Probiotic (Genus)** |
| **Taxon1** | **Taxon2** | **Correlation (p<0.05)** | **Association** | **Taxon1** | **Taxon2** | **Correlation (p<0.05)** | **Association** |
| Prevotella | Rikenella | 1 | Positive | Prevotella | Rikenella | -1 | Negative |
| Prevotella | Sutterella | -0.6 | Negative | Prevotella | Sutterella | -0.6 | Negative |
| Prevotella | Lachnospira | -1 | Negative | Prevotella | Lachnospira | 1 | Positive |
| Prevotella | Oscillospira | -1 | Negative | Prevotella | Oscillospira | 1 | Positive |
| Prevotella | Bacteroides | -0.5 | Negative | Prevotella | Bacteroides | -0.5 | Negative |
| Bacteroides | Prevotella | -0.5 | Negative | Prevotella | Ruminococcus | -1 | Negative |
| Bacteroides | Sutterella | 1 | Positive | Prevotella | Lactobacillus | 1 | Positive |
| Bacteroides | Oscillospira | -1 | Negative | Lactobacillus | Prevotella | 1 | Positive |
| Bacteroides | Lachnospira | 1 | Positive | Lactobacillus | Rikenella | -0.6 | Negative |
| Lachnospira | Bacteroides | 1 | Positive | Lactobacillus | Sutterella | -0.4 | Negative |
| Lachnospira | Sutterella | -0.6 | Negative | Lactobacillus | Dorea | -0.8 | Negative |
| Lachnospira | Prevotella | -1 | Negative | Lactobacillus | Oscillospira | 0.6 | Positive |
| Lachnospira | Rikenella | 1 | Positive | Lactobacillus | Bacteroides | -0.5 | Negative |
| Lachnospira | Oscillospira | 1 | Positive | Lactobacillus | Ruminococcus | -1 | Negative |
| Oscillospira | Lachnospira | 1 | Positive | Ruminococcus | Lactobacillus | -1 | Negative |
| Oscillospira | Prevotella | -1 | Negative | Ruminococcus | Prevotella | -1 | Negative |
| Oscillospira | Bacteroides | -1 | Negative | Ruminococcus | Rikenella | 0.5 | Positive |
| Oscillospira | Sutterella | 1 | Positive | Ruminococcus | Sutterella | -0.3 | Negative |
| Oscillospira | Rikenella | -1 | Negative | Ruminococcus | Dorea | 0.6 | Positive |
| Rikenella | Oscillospira | -1 | Negative | Ruminococcus | Oscillospira | -0.5 | Negative |
| Rikenella | Prevotella | 1 | Positive | Ruminococcus | Bacteroides | 0.6 | Positive |
| Rikenella | Lachnospira | 1 | Positive | Ruminococcus | Lachnospira | 0.8 | Positive |
| Rikenella | Sutterella | -0.6 | Negative | Lachnospira | Ruminococcus | 0.8 | Positive |
| Sutterella | Rikenella | -0.6 | Negative | Lachnospira | Bacteroides | -0.8 | Negative |
| Sutterella | Oscillospira | 1 | Positive | Lachnospira | Prevotella | 1 | Positive |
| Sutterella | Prevotella | -0.6 | Negative | Lachnospira | Rikenella | 0.6 | Positive |
| Sutterella | Lachnospira | -0.6 | Negative | Lachnospira | Sutterella | -0.6 | Negative |
| Sutterella | Bacteroides | 1 | Positive | Lachnospira | Dorea | -0.8 | Negative |
|  |  |  |  | Lachnospira | Oscillospira | -1 | Negative |
|  |  |  |  | Oscillospira | Lachnospira | -1 | Negative |
|  |  |  |  | Oscillospira | Prevotella | 1 | Positive |
|  |  |  |  | Oscillospira | Lactobacillus | 0.6 | Positive |
|  |  |  |  | Oscillospira | Ruminococcus | -0.5 | Negative |
|  |  |  |  | Oscillospira | Dorea | -0.4 | Negative |
|  |  |  |  | Oscillospira | Sutterella | -0.8 | Negative |
|  |  |  |  | Oscillospira | Rikenella | -1 | Negative |
|  |  |  |  | Oscillospira | Bacteroides | -0.6 | Negative |
|  |  |  |  | Bacteroides | Oscillospira | -0.6 | Negative |
|  |  |  |  | Bacteroides | Prevotella | -0.5 | Negative |
|  |  |  |  | Bacteroides | Lactobacillus | -0.5 | Negative |
|  |  |  |  | Bacteroides | Ruminococcus | 0.6 | Positive |
|  |  |  |  | Bacteroides | Lachnospira | -0.8 | Negative |
|  |  |  |  | Bacteroides | Dorea | 0.8 | Positive |
|  |  |  |  | Bacteroides | Sutterella | 0.8 | Positive |
|  |  |  |  | Bacteroides | Rikenella | 0.6 | Positive |
|  |  |  |  | Rikenella | Bacteroides | 0.6 | Positive |
|  |  |  |  | Rikenella | Oscillospira | -1 | Negative |
|  |  |  |  | Rikenella | Prevotella | -1 | Negative |
|  |  |  |  | Rikenella | Lactobacillus | -0.6 | Negative |
|  |  |  |  | Rikenella | Ruminococcus | 0.5 | Positive |
|  |  |  |  | Rikenella | Lachnospira | 0.6 | Positive |
|  |  |  |  | Rikenella | Dorea | 0.6 | Positive |
|  |  |  |  | Rikenella | Sutterella | 0.8 | Positive |
|  |  |  |  | Sutterella | Rikenella | 0.8 | Positive |
|  |  |  |  | Sutterella | Bacteroides | 0.8 | Positive |
|  |  |  |  | Sutterella | Oscillospira | -0.8 | Negative |
|  |  |  |  | Sutterella | Prevotella | -0.6 | Negative |
|  |  |  |  | Sutterella | Lactobacillus | -0.4 | Negative |
|  |  |  |  | Sutterella | Ruminococcus | -0.3 | Negative |
|  |  |  |  | Sutterella | Lachnospira | -0.6 | Negative |
|  |  |  |  | Sutterella | Dorea | 0.6 | Positive |
|  |  |  |  | Dorea | Sutterella | 0.6 | Positive |
|  |  |  |  | Dorea | Rikenella | 0.6 | Positive |
|  |  |  |  | Dorea | Bacteroides | 0.8 | Positive |
|  |  |  |  | Dorea | Oscillospira | -0.4 | Negative |
|  |  |  |  | Dorea | Lachnospira | -0.8 | Negative |
|  |  |  |  | Dorea | Lactobacillus | -0.8 | Negative |
|  |  |  |  | Dorea | Ruminococcus | 0.6 | Positive |

**Figure S1**: Bacterial taxa identified to be differentially abundant by linear discrimination analysis (LDA) effect size (LEfSe, log LDA > 2.0) analysis in all the 4 samples at phylum level (**A**) and genus level (**B**). The values are shown as the mean ± SEM. \*Significant differences with p <0.05.



**Figure S2**. Summary of co-occurrences and co-exclusion analysis between young and aging mice at the phylum and genus levels in fecal (**A-B**) and mucosal (**C-D**) cecal (**E-F**). (YC) Young control group, (YP) young probiotic group, (AC) aging control group and (AP) aging probiotic group.

