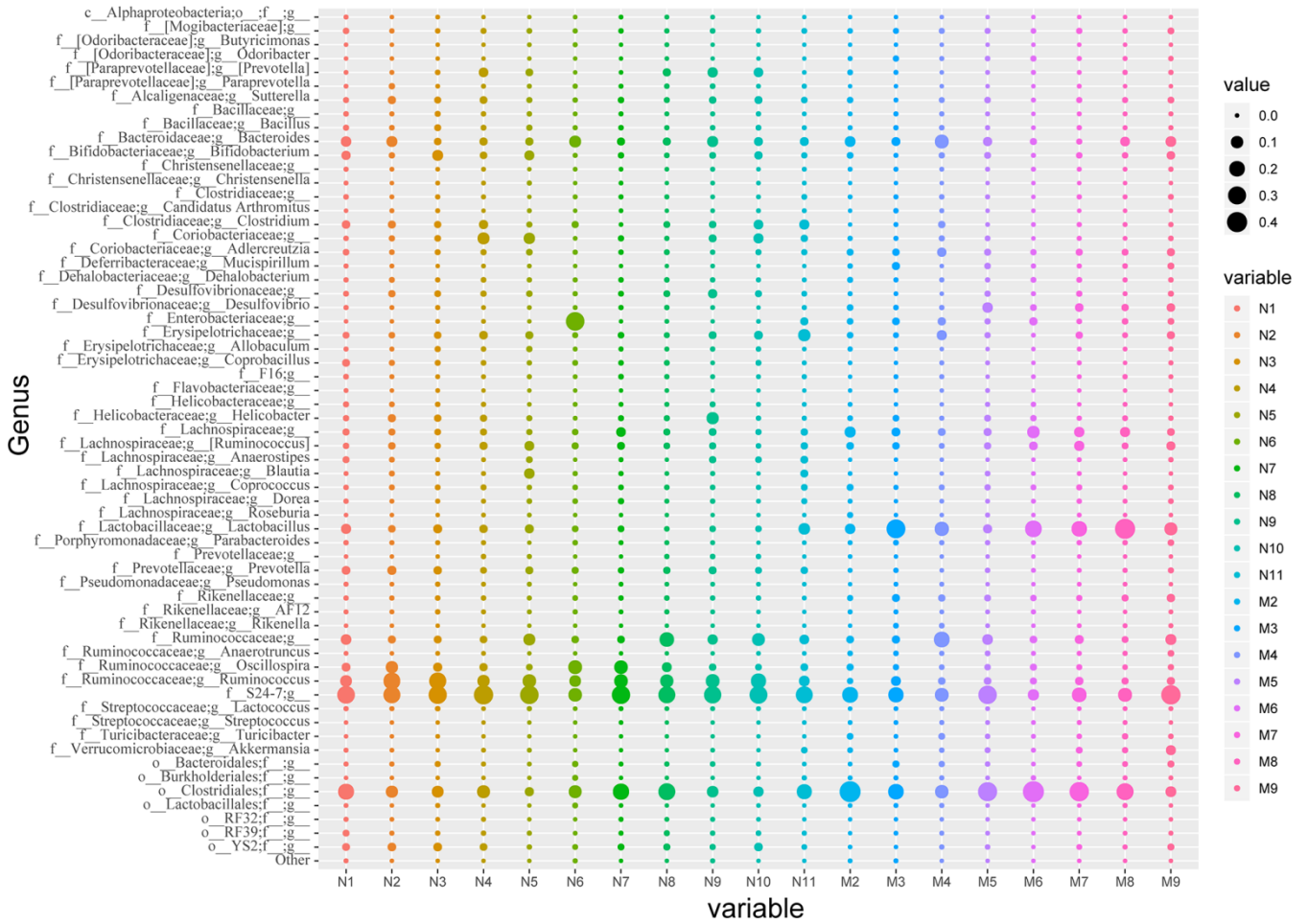
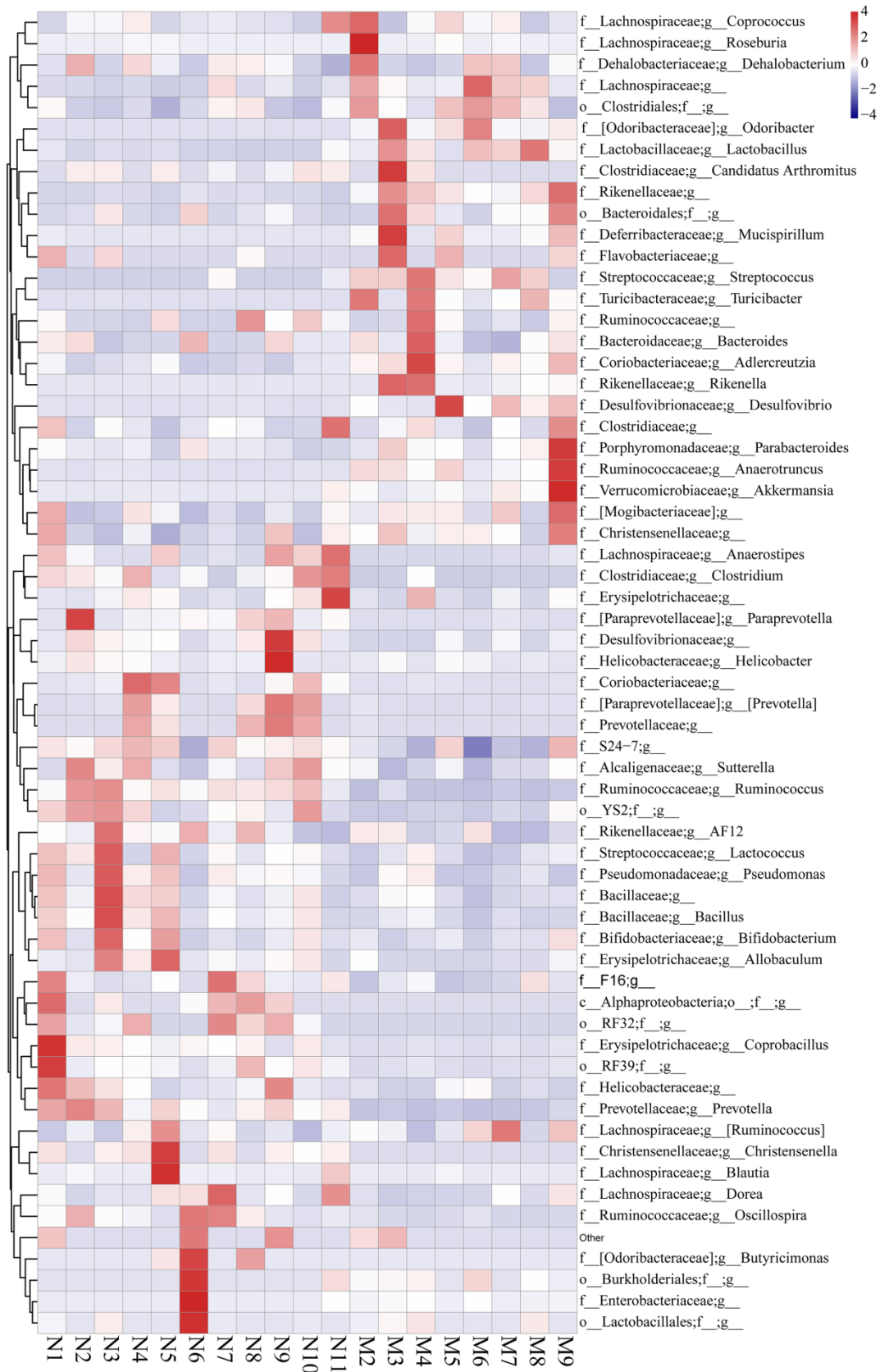


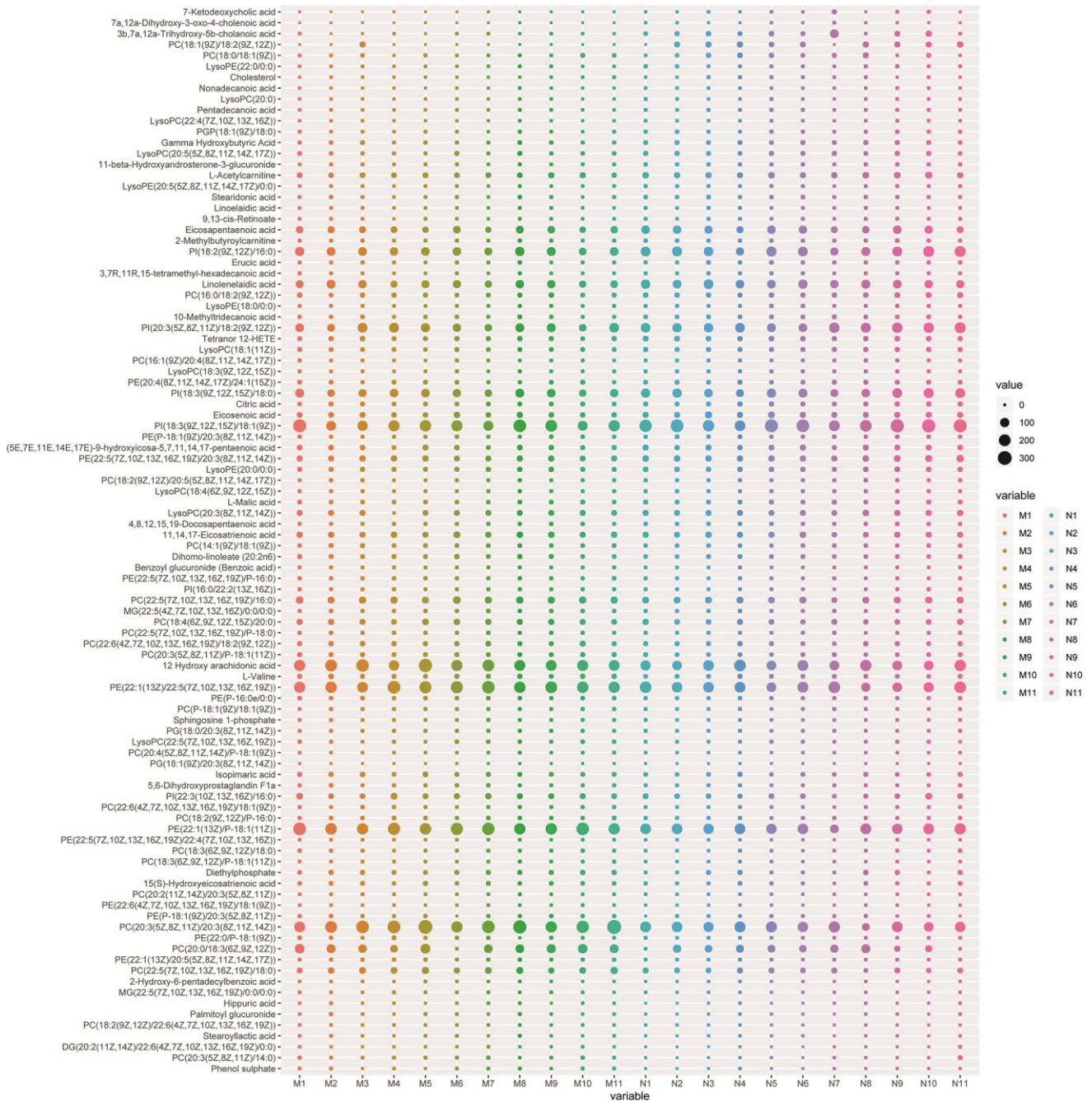
## SUPPLEMENTARY FIGURES



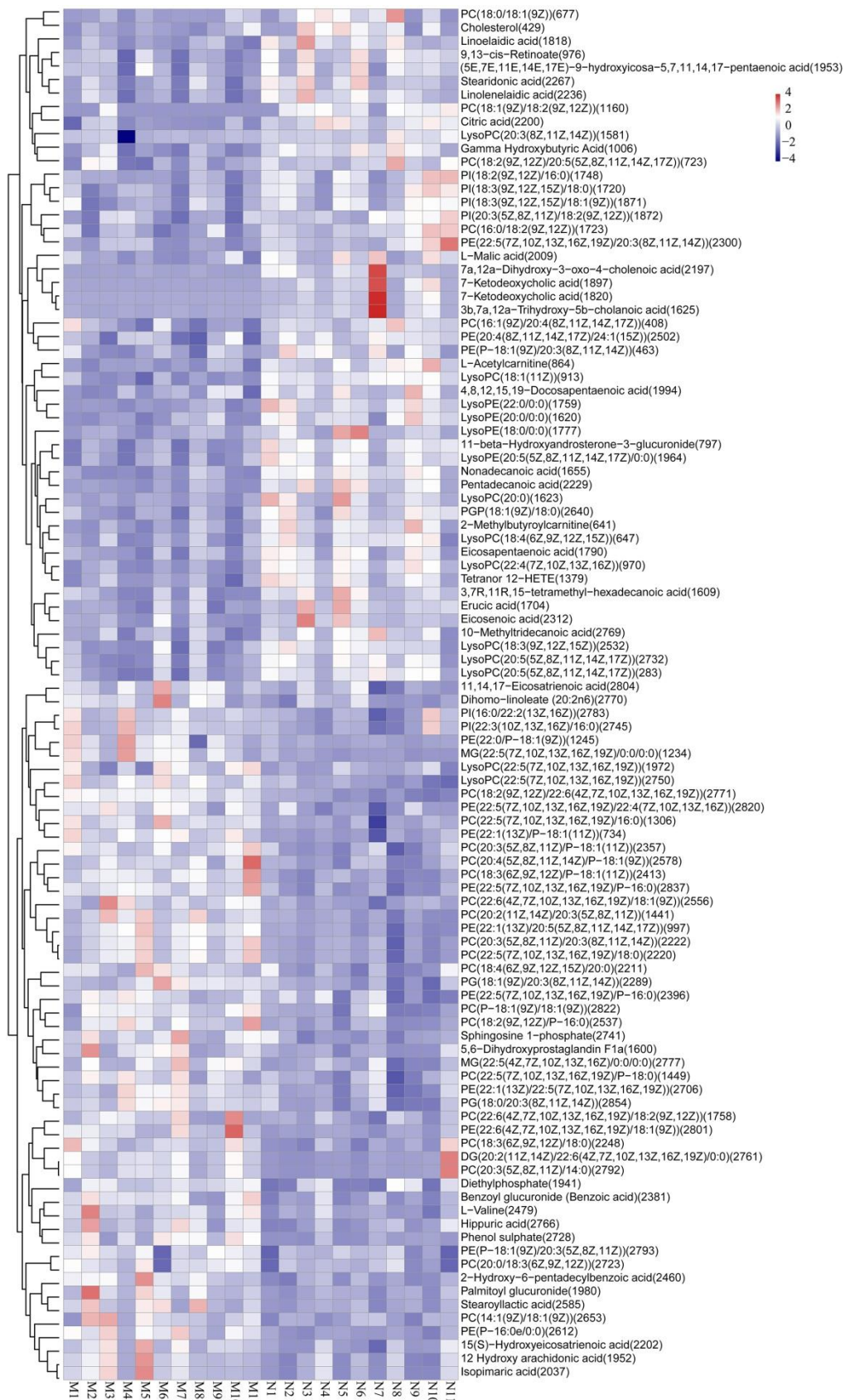
**Supplementary Figure 1A.** Heatmap of gut microbiota in 10-month-old AD-like mice. Data are presented as the means of more than 8 independent experiments.



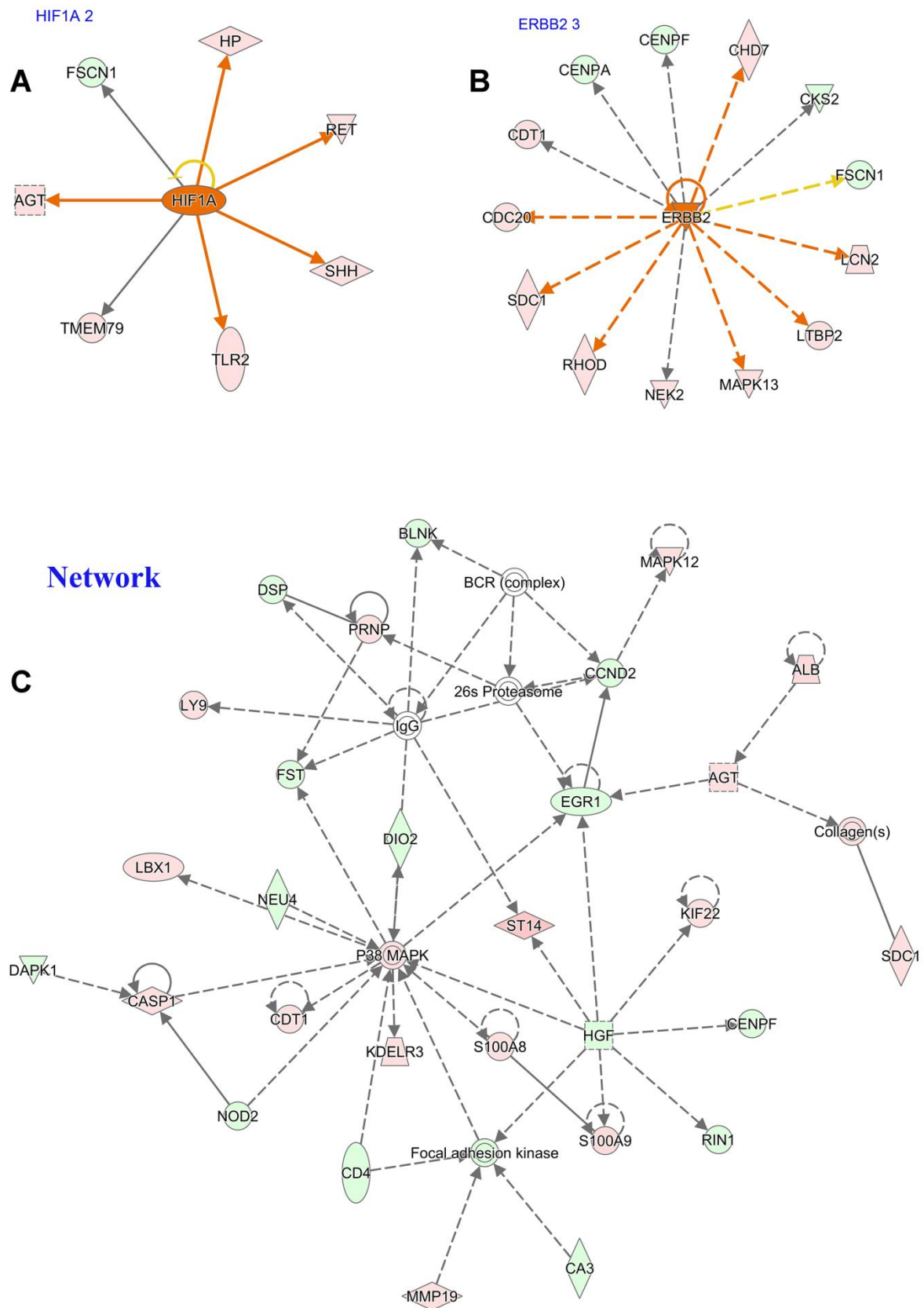
**Supplementary Figure 1B. Heatmap of gut microbiota in 10-month-old AD-like mice.** Data are presented as the means of more than 8 independent experiments.



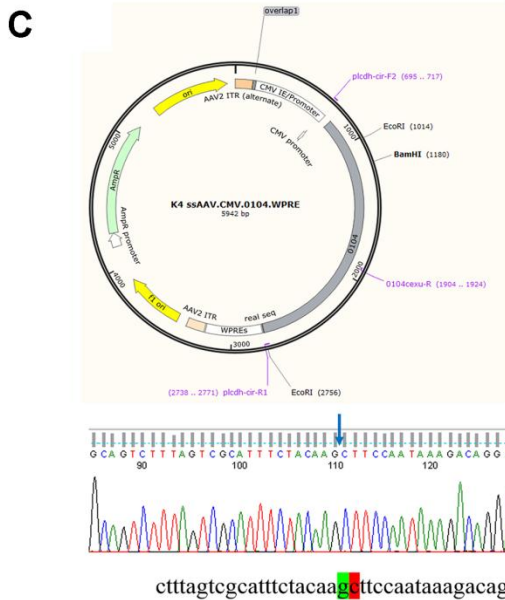
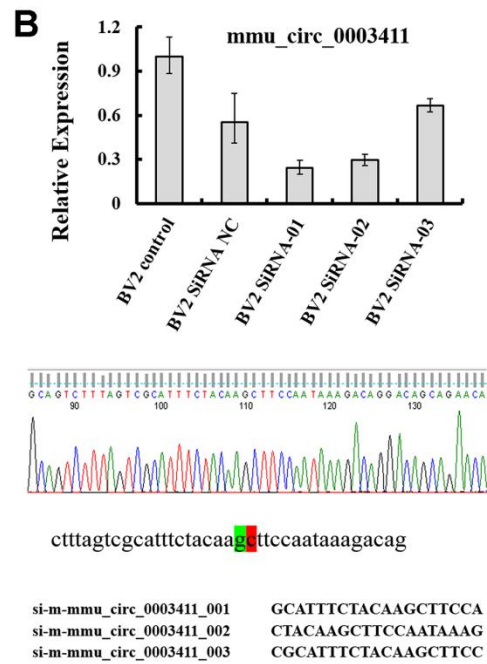
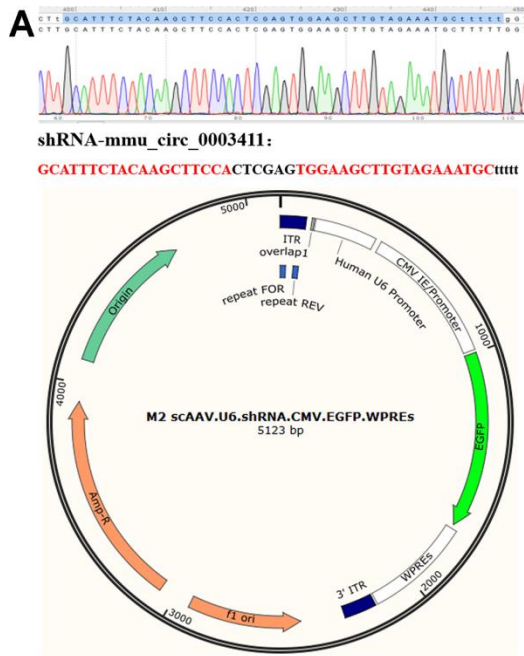
**Supplementary Figure 2A. Heatmap of serum metabolites in 10-month-old AD-like mice.** Data are presented as the means of more than 8 independent experiments.



**Supplementary Figure 2B. Heatmap of serum metabolites in 10-month-old AD-like mice.** Data are presented as the means of more than 8 independent experiments.



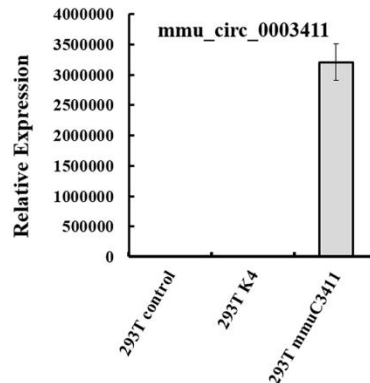
Supplementary Figure 3. The networks of Ingenuity Canonical Pathways (IPA) analysis of differentially expressed mRNAs in the APP/PS1 double transgenic mice brain samples (n=3)



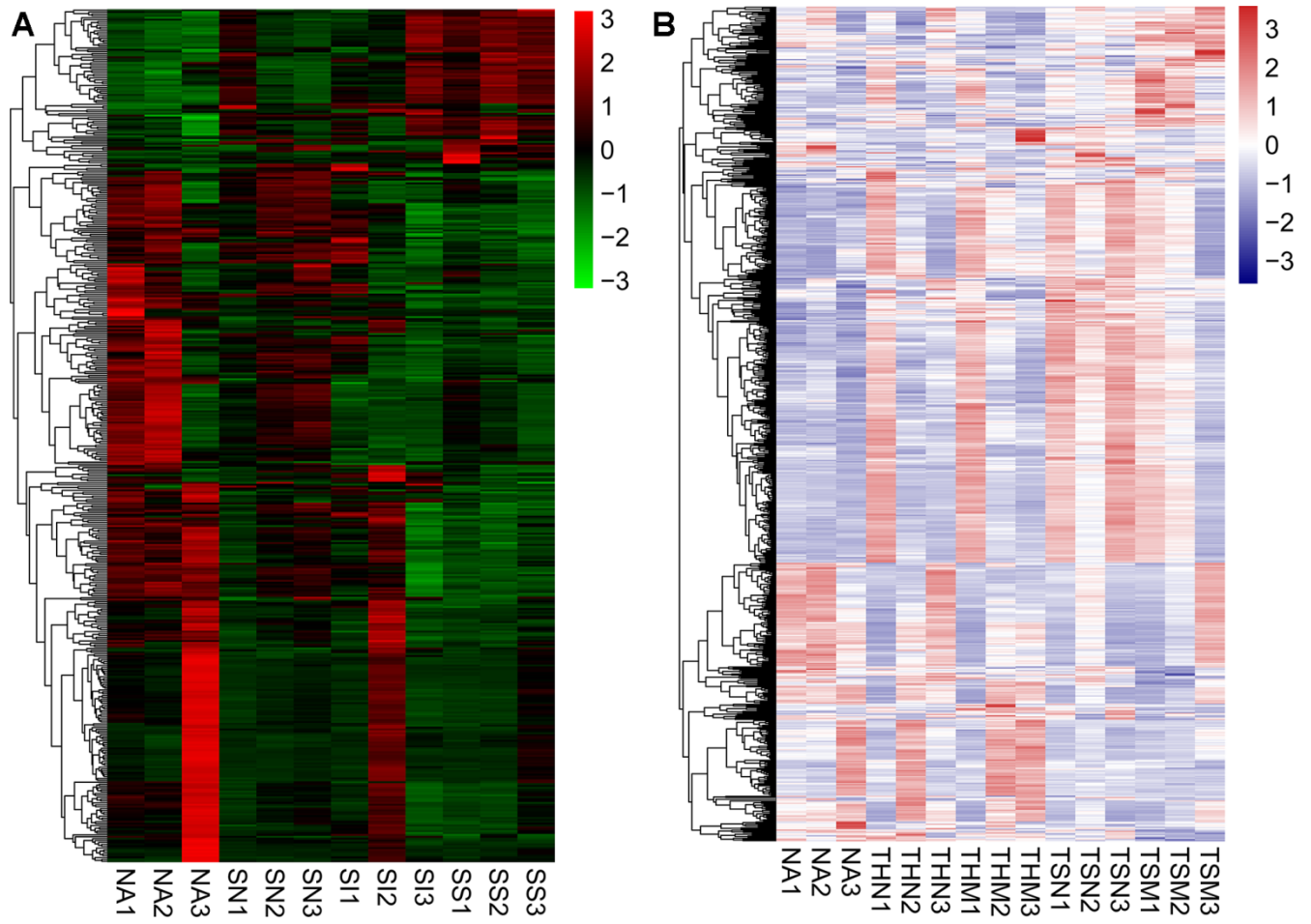
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human-ACTB-R CTCCTAATGTCACGCACGAT  
Product length 250

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Product length 146

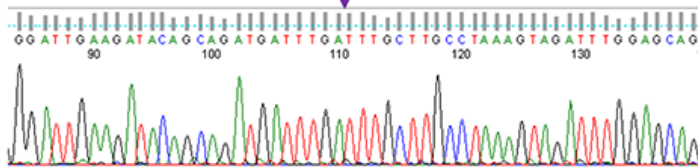
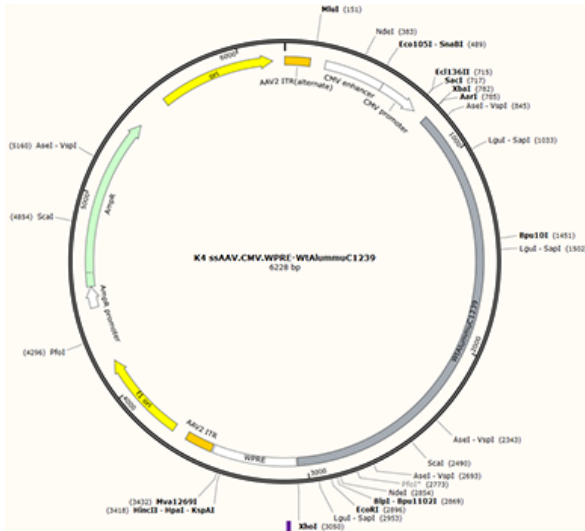
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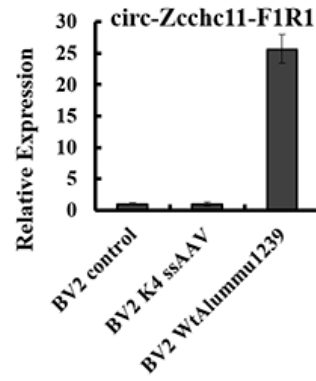
**Supplementary Figure 4.** AAV viral transduction system with RNA interference (*sircNF1-419*-AAV, **A -B**) and separately an over-expressing *circNF1-419* (*sscircNF1-419*-AAV, **C - D**)



**Supplementary Figure 5.** Differential expression mRNAs of the small intestine tissue on the *circNF1-419* treated SAMP8 (A) and KM mice (B). Data are presented as the means of 3 independent experiments.



Splice site: gatacagcagatgattgattgcttgctctaaagtagatt



**qPCR primer**

actin, beta (ACTB), mRNA

β-actin-F1 GCTTCTAGCGGACTGTTAC

β-actin-R1 CCATGCCAATGTTGTCTTT

100bp

**mmu\_circ\_0001239 (Divergent primers)**

Circ-Zcchc11-F1: 5'- cagcagatgattgattgc-3'

Circ-Zcchc11-R1: 5'- atattctctttggtcatg-3'

159bp

**Sequencing primer**

Circ-Zcchc11-F2: 5'- ggaagagtgaagctctacag -3'

Circ-Zcchc11-R1: 5'- atattctctttggtcatg-3'

282bp

Supplementary Figure 6. AAV viral transduction system with RNA over-expressing mmu\_circ\_0001239