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.

7 Kotodesuschelis seid											1												
7= 12= Dihydroxy-3-oxo-4-cholenoic acid =			1	1	1	1	1.1	1											1.1				
3b.7a.12a-Trihydroxy-5b-cholanoic acid =																		1					
PC(18:1(9Z)/18:2(9Z,12Z)) -																	- T						
PC(18:0/18:1(9Z)) -										•				•									
LysoPE(22:0/0:0) -												•	•	•							•		
Cholesterol -				1														1	1				
Nonadecanoic acid =			1	1				1					1			1	1.1		1.1	- 0	1		
Pentadecanoic acid -		- Q.				1		1										1			- 1		
LysoPC(22:4(7Z,10Z,13Z,16Z)) -																							
PGP(18:1(9Z)/18:0) -					•			•			• •	•	•										
Gamma Hydroxybutyric Acid -									•														
LysoPC(20:5(5Z,8Z,11Z,14Z,17Z)) =			1	1							1		1				1	1					
I -Acetulcarnitine -																							
LysoPE(20:5(5Z,8Z,11Z,14Z,17Z)/0:0) -	- 1-																	-	-				
Stearidonic acid -									•												•		
Linoelaidic acid -										•	• •		•										
9,13-cis-Retinoate -	1	1			1	-		1			: :			-	-		1	1	-	-	1		
2-Methylbutyroylcarnitine -																							
PI(18:2(9Z,12Z)/16:0) -																							
Erucic acid -	- F-							-										-					
3,7R,11R,15-tetramethyl-hexadecanoic acid -			•								* *			•									
Linolenelaidic acid -							•	•		•	• •	•	0		•								
PC(16:0/18:2(92,122)) -																1							
10-Methyltridecanoic acid -	- i -	- A -																					
PI(20:3(5Z,8Z,11Z)/18:2(9Z,12Z)) -									•			0		0	0						•		
Tetranor 12-HETE -			•		•		•		•		• •	•	•	•					•	•			
LysoPC(18:1(11Z)) -									•				•	1	•	0							
PG(16:1(9Z)/20:4(8Z,11Z,14Z,17Z)) =	1			1.1		1			-		1 1				1			1			1.1		
PE(20:4(8Z 11Z 14Z 17Z)/24·1(15Z)) =								1														value	
PI(18:3(9Z,12Z,15Z)/18:0) -													•			0						value	
Citric acid -							•			•											•	• 0	
Eicosenoic acid -	-		:	-	-	-	:	-	:	:	: :	-	-	2	-	-	-	-	-	-	-	. 100	
PI(18:3(9Z,12Z,15Z)/18:1(9Z)) =																				•		. 100	
(5E 7E 11E 14E 17E)-9-hydroxyicosa-5 7 11 14 17-pentaenoic acid -																						200	
PE(22:5(7Z,10Z,13Z,16Z,19Z)/20:3(8Z,11Z,14Z)) -																						300	
LysoPE(20:0/0:0) -			•				•	•	•		• •	•	•	•	•				•	•	•		
PC(18:2(9Z,12Z)/20:5(5Z,8Z,11Z,14Z,17Z)) -			•							•			•										
LysoPC(18:4(6Z,9Z,12Z,15Z)) -	1	1	1	1		1		1			: :		:				1	1	1	1	1	variable	
LysoPC(20:3(8Z 11Z 14Z)) -				1																			. NH
4,8,12,15,19-Docosapentaenoic acid -																						- IVII	• •
11,14,17-Eicosatrienoic acid -					•					•	• •	•	•	•	•				•	•	•	• M2	 N2
PC(14:1(9Z)/18:1(9Z)) -	1			1		1		1	:		1 1		1					1	1	1	1	• M3	• N3
Dinomo-Inoleate (20:206) - Benzoul alucuropide (Benzoic acid) -					10.00		1	12										1					
PE(22:5(7Z.10Z.13Z.16Z.19Z)/P-16:0) -	- i -							÷.										1			- <u>1</u>	. IA1+4	• 194
PI(16:0/22:2(13Z,16Z)) -			•						•	•			•							•		• M5	 N5
PC(22:5(7Z,10Z,13Z,16Z,19Z)/16:0) -								•	•	•		•	•	•					•	•	•	 M6 	 N6
MG(22:5(4Z,7Z,10Z,13Z,16Z)/0:0/0:0) -	1					1								2		1	1	1		1	1		
PG(10:4(02,92,122,152)/20:0)=								1														• 1017	• 117
PC(22:6(4Z,7Z,10Z,13Z,16Z,19Z)/18:2(9Z,12Z)) -																						 M8 	 N8
PC(20:3(5Z,8Z,11Z)/P-18:1(11Z)) -										•			•								•	• M9	• N9
12 Hydroxy arachidonic acid -	•		•	•		•			•		•	•	•	•	•		•	•	•	•			
L-Valine -	-	-	-	-	-	-	-	-	-	-				-	-	-	-	-	-	-	-	• M10	• N10
PE(22.1(132)/22.5(72,102,132,162,192)) =																						 M11 	 N11
PC(P-18:1(9Z)/18:1(9Z)) =								- A.													1.		
Sphingosine 1-phosphate -					-																		
PG(18:0/20:3(8Z,11Z,14Z)) -			•										•										
LysoPC(22:5(7Z,10Z,13Z,16Z,19Z)) -			•									•	- *										
PC(20:4(52,82,112,142)/P-18:1(92)) -															1			1					
PG(10:1(92)/20:3(02,112,142)) =																		4		1.1			
5,6-Dihydroxyprostaglandin F1a -																							
PI(22:3(10Z,13Z,16Z)/16:0) -										•													
PC(22:6(4Z,7Z,10Z,13Z,16Z,19Z)/18:1(9Z)) -			•	•						•													
PC(18:2(9Z,12Z)/P-16:0) -	÷	-	-		-	-		-	-	÷			-	-			-	-	-	-	-		
PE(22:1(132)/P-10:1(112)) = PE(22:5(77 107 137 167 197)/22-4(77 107 137 167)) =																							
PC(18:3(6Z.9Z.12Z)/18:0) -																		-		-	-		
PC(18:3(6Z,9Z,12Z)/P-18:1(11Z)) -										•		•											
Diethylphosphate -	•						•	•	•	•	• •	۰	•	•				•			•		
15(S)-Hydroxyeicosatrienoic acid -															1		1	1					
PE(22:6(4Z.7Z.10Z.13Z.16Z.19Z)/18:1(9Z)) -																		-					
PE(P-18:1(9Z)/20:3(5Z,8Z,11Z)) -																							
PC(20:3(5Z,8Z,11Z)/20:3(8Z,11Z,14Z)) -	•		•			•	•		•			•	•	0	•	0	•						
PE(22:0/P-18:1(9Z)) -	:	:	:	:	-		-	-	:	-		:	:	:	:	-	-	-		:			
PC(20:0/18:3(6Z,9Z,12Z)) =						1											-				1		
PC(22:5(7Z 107 13Z 16Z 19Z)/18:0) -																							
2-Hydroxy-6-pentadecylbenzoic acid -											· · ·							-					
MG(22:5(7Z,10Z,13Z,16Z,19Z)/0:0/0:0) -																							
Hippuric acid -			1	1	1						1 1		1		1	1		1	1				
Palmitoyl glucuronide - PC(18/2/97 127)/22/6/47 77 107 127 167 197) -	1								-	1			1	1	1	1							
Stearovlactic acid -																							
DG(20:2(11Z,14Z)/22:6(4Z,7Z,10Z,13Z,16Z,19Z)/0:0) -															+								
PC(20:3(5Z,8Z,11Z)/14:0) -										•											•		
Phenol sulphate -	1			1	1				1		1 1	1	1	1	1	1		1	1	1	1		
	M1	M2	M3	M4	M5	M6	M7	M8	M9	M10	M11 N1	N2	N3	N4	N5	N6	N7	N8	N9	N10	N11		
											variable												

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 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)



Supplementary Figure 4. AAV viral transduction system with RNA interference (sicircNF1-419-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.





qPCR primer actin, beta (ACTB), mRNA β-actin-F1 GCTTCTAGGCGGACTGTTAC β-actin-R1 CCATGCCAATGTTGTCTCTT	100bр
mmu_circ_0001239 (Divergent primers) Circ-Zcchc11-F1: 5'- cagcagatgatttgatttgc-3' Circ-Zcchc11-R1: 5'- atattettetttggttcatg-3'	159bp
Sequencing primer Circ-Zcchc11-F2: 5'- ggaagagtgaagctctacag -3' Circ-Zcchc11-R1: 5'- atattettetttggttcatg-3'	282bp

Supplementary Figure 6. AAV viral transduction system with RNA over-expressing mmu_circ_0001239