## **Supplemental Materials**

**Table List** 

**Table S1** Proteins with significantly different expression levels in proteomics.

Number	Gene. names	Unique.	fc. APP/PS1	fc. APP/PS1+IFY
		peptides	- WT	-APP/PS1
Upregulated proteins by isoforsythiaside (IFY) (Number: 21)				
1	Fgg	2	0.41	1.99
2	mKIAA1101; Oxsr1	2	0.23	3.81
3	Ampd2	7	0.19	4.52
4	Slc25a23	5	0.09	9.46
5	Fn3k	4	0.12	7.64
6	Gmpr	4	0.16	5.83
7	Jam3	4	0.12	8.25
8	Kcna6	2	0.39	2.56
9	Cbx5	3	0.22	5.01
10	Trappc4	3	0.26	4.20
11	Emc1	7	0.19	5.91
12	Crocc	4	0.13	8.59
13	mCG_6739; Rps21	2	0.20	5.90
14	Arl8b	3	0.08	15.23
15	Stk32c	4	0.22	5.50
16	Ube2i	2	0.35	3.45
17	Rab9b	3	0.27	4.67
18	Slc25a10	4	0.65	1.63
19	Ahnak	6	0.22	6.81
20	Wdfy1	6	0.39	3.72
21	Tsr2	3	0.41	4.53
Downregulated proteins by IFY (Number: 4)				
1	Myh11	9	1.53	0.52
2	Rpa1	2	35.80	0.03
3	Mon2	5	2.41	0.60
4	Tmem109	2	3.72	0.54

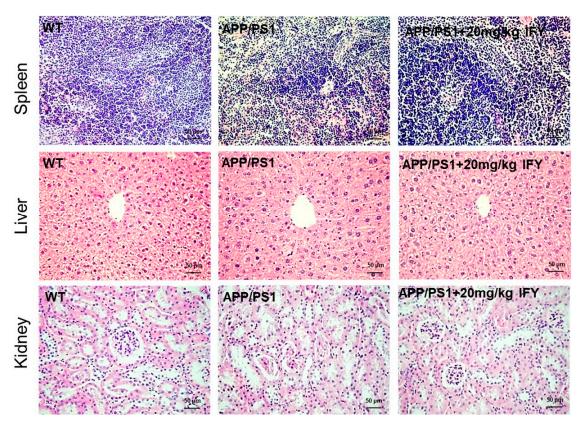
fc. APP/PS1-WT: the ratio of protein between saline-treated APP/PS1mice and WT mice;

fc. APP/PS1+IFY-APP/PS1: the ratio of protein between IFY-treated APP/PS1 mice and saline-treated APP/PS1 mice.

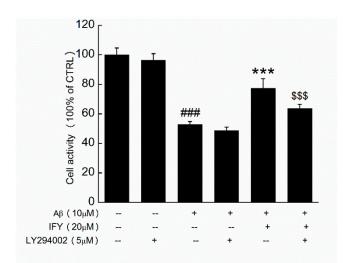
## **Figure List**

Isoforsythiaside (Cas No.: 1357910-26-9) Forsythoside A (Cas No.: 79916-77-1)

**Figure S1.** Chemical structure of (A) isoforsythiaside (Cas NO.: 1357910-26-9) and (B) forsythoside A (Cas No.: 79916-77-1).



**Figure S2.** H & E staining of spleen, liver and kidney tissues (magnification x 20, scale bar: 50 μm; n=3).



**Figure S3.** Cell viability of U251 cells exposed to  $A\beta_{1-42}$  and LY294002 tested by MTT (n=6). IFY significantly increased the viability of  $A\beta_{1-42}$ -treated U251 cells, however, LY294002 blocked down the protective effect of IFY. ###P<0.001 vs. CTRL cells, \*\*\*P<0.001 vs.  $A\beta_{1-42}$ -exposed U251 cells, \$\$\$P<0.001 vs. IFY and  $A\beta_{1-42}$ -exposed U251 cells.

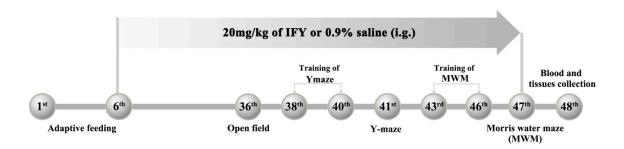


Figure S4. Schematic flow chart of animal experiment.