**Supplementary Figures**

**ALWPs improve cognitive function and regulate Aβ plaque and tau hyperphosphorylation in a mouse model of Alzheimer’s disease**

Youngpyo Nam1,5, Bitna Joo1,4,5, Ju-Young Lee1,Kyung-Min Han1,4, Ka-Young Ryu1, Young Ho Koh2, Jeongyeon Kim1,, Ja Wook Koo1,4, Young-Man We3,\*, Hyang-Sook Hoe1,4,\*

1Department of Neural Development and Disease, Korea Brain Research Institute (KBRI), 61 Cheomdan-ro, Dong-gu, Daegu, Korea, 41068; 2Division of Brain Disease, Center for Biomedical Sciences, Center for Infectious Diseases, Korea National Institute of Health, Osong-eup, Heungdeok-gu, Republic of Korea; 3College of Korean Medicine, Wonkwang University, Iksandae-ro, Iksan, Jeonbuk, Korea, 54538; 4Department of Brain & Cognitive Sciences, Daegu Gyeongbuk Institute of Science & Technology (DGIST), 333 Techno Jungang-daero, Hyeonpung-myeon, Dalseong-gun, Daegu, Korea, 42988. 5These authors contributed equally to this work.

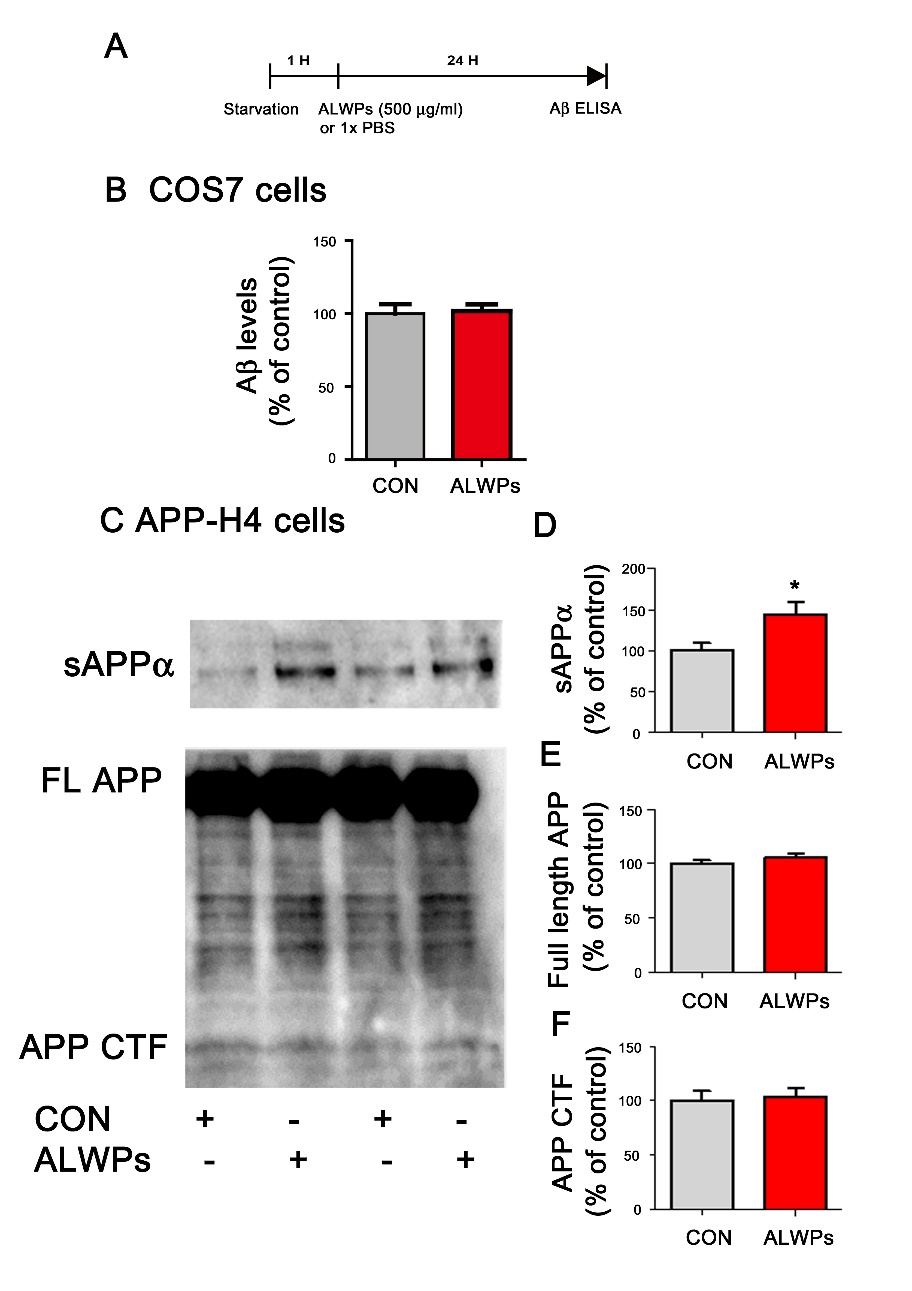
\*Corresponding author

Hyang-Sook Hoe, Ph.D.: Department of Neural Development and Disease, Korea Brain Research Institute (KBRI), 61 Cheomdan-ro, Dong-gu, Daegu, Korea, 41068

E-mail: [sookhoe72@kbri.re.kr](mailto:sookhoe72@kbri.re.kr)

Young-Man We, M.D., Ph.D.: Hyoo Medical Clinic Center, Teheran-ro, Gangnam-gu, Seoul, Korea, 06134

E-mail: [hyooclinic@naver.com](mailto:hyooclinic@naver.com)



**Supplementary Figure. 1.** ALWPs significantly increase secreted APP alpha (sAPP) levels in APP-H4 cells. (A-B) COS7 cells were transiently transfected with a construct expressing human APP for 24 hr and then treated with ALWPs (500 g/ml) or PBS for 24 hr before performing A ELISA (con, n = 16; ALWPs, n = 16). (C) APP-H4 cells were treated with ALWPs (500 g/ml) or PBS for 24 hr, conditioned medium and cell lysates were collected, and western blotting was performed. (D-F) Quantification of data from C (con, n = 24; ALWPs, n = 24). \**p* < 0.05.

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**Supplementary Figure. 2.** ALWPs do not alter BACE1 levels in primary hippocampal neurons. (**A**) Primary hippocampal neurons were transfected with GFP plasmid DNA for 24 hr, treated with ALWPs (500 g/ml) or PBS for 24 hr, and immunostained with an anti-BACE1 antibody. (**B**) Quantification of data from A (con, n = 97 dendrites; ALWPs, n = 94 dendrites). (**C**) Primary hippocampal neurons were transfected with GFP plasmid DNA for 24 hr, treated with ALWPs (500 g/ml) or PBS for 24 hr, and immunostained with an anti-NEP antibody. (**D**) Quantification of data from C (con, n = 90 dendrites; ALWPs, n = 90 dendrites). (**E**) 5x FAD mice were orally administered ALWPs (200 mg/kg, p.o.) or PBS daily for 2 weeks and immunostained with an anti-NEP antibody. Representative images of the cortex of 5x FAD mice are shown. (**F**) Quantification of data from E (con, n = 3 mice; ALWPs, n = 3 mice). (**G**) Representative images of the hippocampus of 5x FAD mice are shown. (**H**-**I**) Quantification of data from E (CA1 and DG; con, n = 3 mice; ALWPs, n = 3 mice). \**p* < 0.05, \**p* < 0.001.



**Supplementary Figure 3.** ALWPs regulate dendritic spine morphology in hippocampus CA1 AO dendrites of 5x FAD mice. (**A**-**B**) The cumulative distribution percentage of spine length (A) and spine head width (B) in hippocampal CA1 AO dendrites of 5x FAD mice (n = 8 mice/group, Kolmogorov–Smirnov test). (**C**-**D**) The cumulative distribution percentage of spine length (C) and spine head width (D) in hippocampal CA1 BS dendrites of 5x FAD mice (n = 8 mice/group, Kolmogorov–Smirnov test). (**E**-**F**) The cumulative distribution percentage of spine length (E) and spine head width (F) in cortical layer V AO dendrites of 5x FAD mice (Kolmogorov–Smirnov test). (**G**-**H**) The cumulative distribution percentage of spine length (G) and spine head width (H) in cortical layer V BS dendrites of 5x FAD mice (n = 8 mice/group, Kolmogorov–Smirnov test).

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**Supplementary Figure 4.** ALWPs do not alter Rap signaling pathways. Primary cortical neurons were treated with ALWPs (500 g/ml) or PBS for 24 hr and immunoblotted with anti-PLK2 (**A**-**B**), anti-RapGEF (**C**-**D**), and anti-p-JNK/JNK (**E**-**G**) antibodies (PLK2, n = 4; RapGEF, n = 4; p-JNK, n = 8; JNK, n = 4).