

Figure S1 Experimental procedure of APP/PS1 mice feeding and administration protocol.

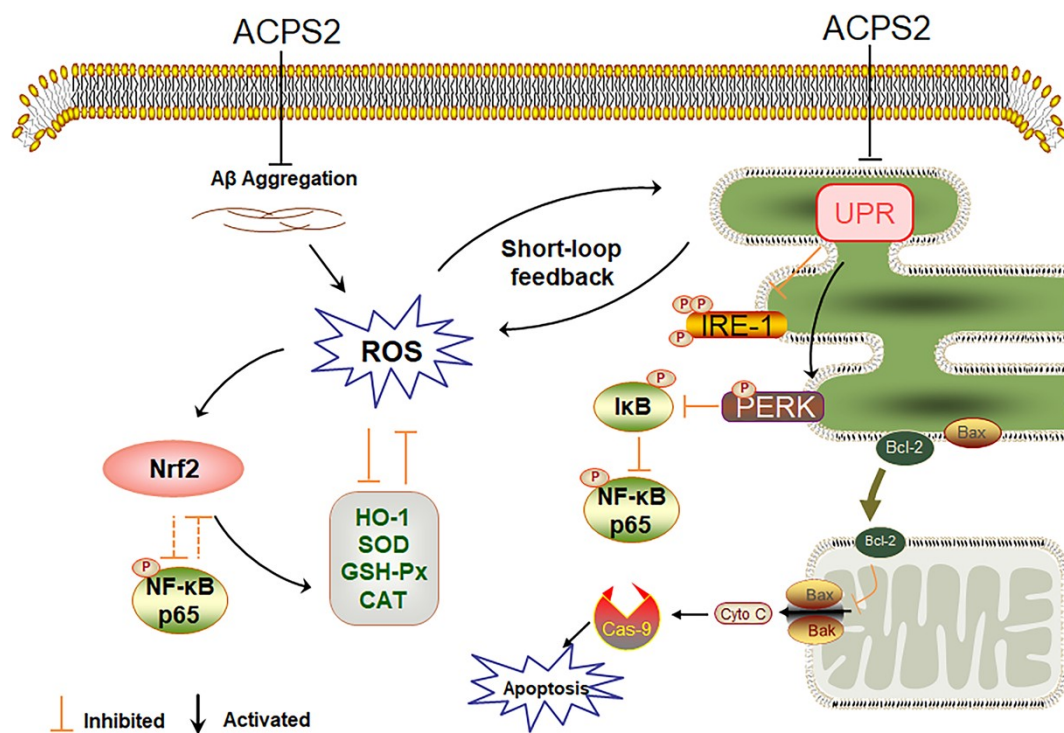


Figure S2 Schematic illustration of putative mechanisms of ACPS2-mediated anti-AD. ACPS2 exerted anti-AD effects by regulating Nrf2 signaling, thereby inhibiting endoplasmic reticulum stress and NF- κ B activation.

Table S1 Primary and secondary antibodies used for Western blotting

| Name | Item number | Molecular Weight (kDa) | Dilution rate |
|--|-------------|------------------------|---------------|
| PERK ^a | bsm-51385m | 122 | 1/1000 |
| P- PERK (Thr982) ^b | DF7576 | 125 | 1/2000 |
| eIF-2 α ^c | 9722s | 38 | 1/1000 |
| P- eIF-2 α (S51) ^c | 9721s | 38 | 1/1000 |
| ATF4 ^a | bs-1531r | 38 | 1/2000 |
| CHOP ^c | 5554s | 27 | 1/1000 |
| IRE-1 ^a | bs-8680r | 105 | 1/2000 |
| P-IRE-1 (S724) ^d | ab48187 | 110 | 1/2000 |
| Bcl-2 ^a | bs-33047m | 26 | 1/500 |
| Cytochrome C ^d | ab133504 | 11 | 1/5000 |
| Caspase-9 ^d | ab25758 | 52 | 1/1000 |
| Cleaved Caspase-9 (Asp353) ^c | 9509s | 37 | 1/1000 |
| Bax ^d | ab32503 | 21 | 1/2000 |
| Bid ^d | ab62469 | 22 | 1/2000 |
| Nrf2 ^d | ab89443 | 68 | 1/2000 |
| Keap1 ^d | ab150654 | 70 | 1/2000 |
| HO-1 ^a | bs-2075r | 32 | 1/1500 |
| T- inhibitor of κ B (I κ B) α^d | ab32518 | 36 | 1/2000 |
| P- I κ B α (S32+S36) ^d | ab12135 | 35.6-40 | 1/500 |
| T- NF- κ B p65 ^d | ab16502 | 64 | 1/2000 |
| P- NF- κ B p65 (S536) ^d | ab86299 | 60 | 1/2000 |
| GAPDH ^e | E-AB-20032 | 37 | 1/2000 |
| Goat Anti-Rabbit (H+L) ^e | E-AB-1003 | \ | 1/4000 |
| Goat-Anti-Mouse (H+L) ^e | E-AB-1001 | \ | 1/4000 |

^a Antibodies were purchased from Beijing Biosynthesis Biotechnology Co., Ltd. (Beijing, China). ^b Antibody were purchased from Affinity Biosciences. Ltd. (Changzhou, Jiangsu, China). ^c Antibodies were purchased from Cell Signaling Technology (CST) (Shanghai) Biological Reagents Co., Ltd. (Shanghai, China). ^d Antibodies were purchased from Abcam China (Shanghai, China). ^e Antibodies were purchased from Elabscience Biotechnology Co., Ltd. (Wuhan, Hubei, China). Abbreviations: ATF4, activating transcription factor 4; Bax, Bcl-2-Associated X; Bcl-2, B-cell lymphoma-2; Bid, a BH3 domain-only death agonist protein; CHOP, CCAAT enhancer binding protein (C/EBP)-homologous protein; eIF, eukaryotic initiation factor; GAPDH, glyceraldehyde-3-phosphate dehydrogenase; HO-1, Heme Oxygenase -1; IRE-1, inositol-requiring enzyme-1; I κ B, inhibitor of NF- κ B; Keap1, kelch-like ECH-associated protein 1; NF- κ B, nuclear factor-kappa B; Nrf2, nuclear factor erythroid 2-related factor 2; P, phospho; PERK, pancreatic ER kinase.

Table S2 All of the detailed parameters of target cytokines obviously decreased or increased among experimental groups.

| Symbol | fc..WT-APP/PS1 | fc..ACPS2-APP/PS1 | Symbol | fc..WT-APP/PS1 | fc..ACPS2-APP/PS1 |
|---|----------------|-------------------|--------------|----------------|-------------------|
| Upregulated proteins by ACPS2 (Number: 26) | | | | | |
| Sdhd | 2909.7% | 2356.1% | Asns | 193.2% | 182.7% |
| Prkcd | 1663.1% | 1944.1% | Tsg101 | 111.1% | 180.1% |
| Shank3 | 2263.7% | 1580.2% | Synpo | 136.4% | 172.4% |
| Synpr | 847.1% | 722.4% | Mff | 131.1% | 155.7% |
| Pepd | 515.3% | 447.5% | Camk4 | 172.0% | 153.5% |
| Prpsap2 | 529.2% | 404.6% | Crip2 | 140.6% | 147.6% |
| Prrt3 | 387.9% | 367.4% | Ly6h | 133.0% | 140.3% |
| Hnrnpdl | 300.1% | 325.1% | Nebl | 150.2% | 135.2% |
| Phactr1 | 258.6% | 305.8% | Ppp1r1b | 258.2% | 133.9% |
| Nrgn | 178.2% | 274.6% | Srsf3 | 119.7% | 127.1% |
| Huwe1 | 295.2% | 268.9% | Rab5c | 154.9% | 126.9% |
| Ermn | 183.9% | 217.6% | Txnrd1 | 104.7% | 119.5% |
| Dlgap2 | 120.1% | 202.9% | Mink1 | 142.5% | 103.4% |
| Downregulated proteins by ACPS2 (Number: 28) | | | | | |
| Slc4a7 | -98.7% | -99.5% | Fxyd6 | -63.9% | -81.5% |
| Rabep1 | -52.5% | -97.2% | Calu | -86.6% | -81.4% |
| Ckap4 | -85.9% | -94.4% | Pdk3 | -61.6% | -81.4% |
| 2-Mar | -55.0% | -94.3% | Nova2;Nova1 | -89.2% | -79.6% |
| Cops3 | -93.2% | -92.2% | Sar1b | -66.7% | -77.2% |
| Rpl9 | -89.9% | -90.2% | Mlec | -80.6% | -76.5% |
| Vamp1 | -69.0% | -89.1% | Cul2 | -78.6% | -69.8% |
| Rab3c | -80.5% | -88.9% | Cmb1 | -52.2% | -65.7% |
| Banf1 | -82.1% | -88.1% | Ciapin1 | -66.4% | -61.6% |
| Rab18 | -87.9% | -87.6% | Traf3 | -75.4% | -60.6% |
| Bcan | -90.4% | -84.0% | Hbb-b2;Hbbt2 | -98.1% | -56.1% |
| Comtd1 | -80.1% | -83.9% | Pthr2 | -52.5% | -54.6% |
| Echl | -60.7% | -83.8% | Bri3bp | -53.2% | -53.7% |
| Slc16a1 | -88.9% | -82.7% | Alg2 | -71.1% | -51.4% |