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# Supporting Information

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## Supporting Information

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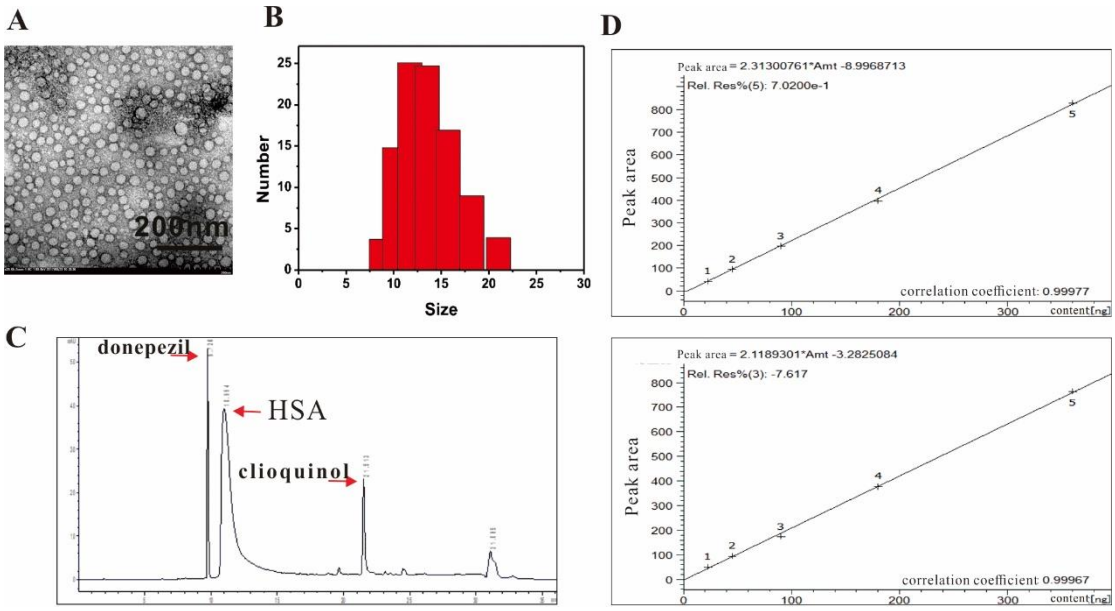


**Figure S1. (**A) TEM images of dcHG NPs (scale bar: 200 nm); and (B) DLS

measurement of dcHG NPs; (C) Absorption spectrum of dcHGT NPs measured by HPLC; (D) Standard curve of donepezil and clioquinol measured by HPLC.

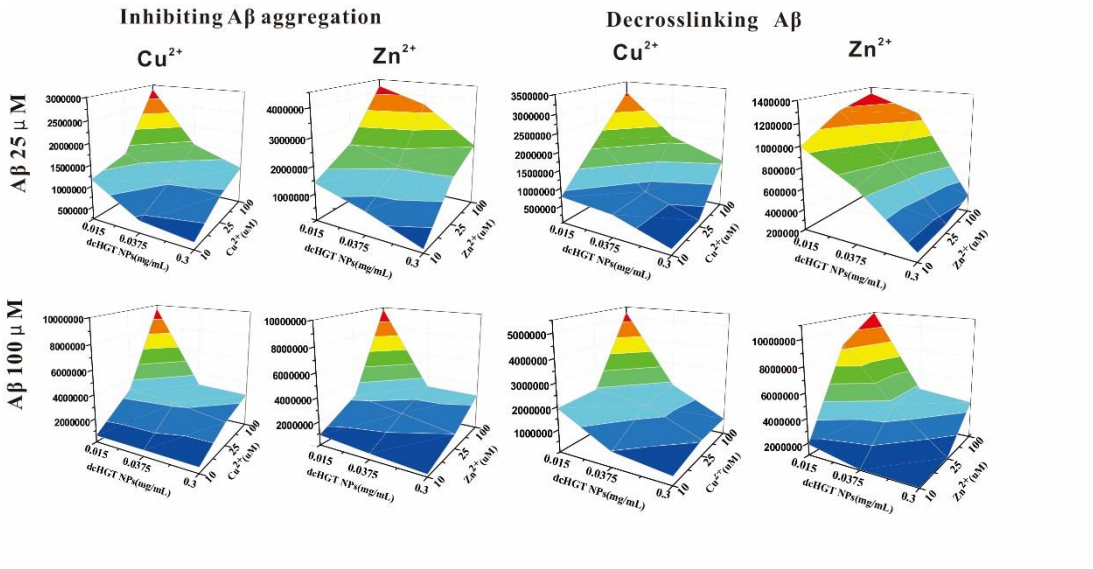


**Figure S2.** 3D color map surface of fluorescence signals in inhibition and disaggregation experiments ([Aβ] = 25,100 μM, [metal ions] = 10-100 μM, and [dcHGT NPs]=0.015-0.15mg/mL). Data are presented as the mean ± SD.

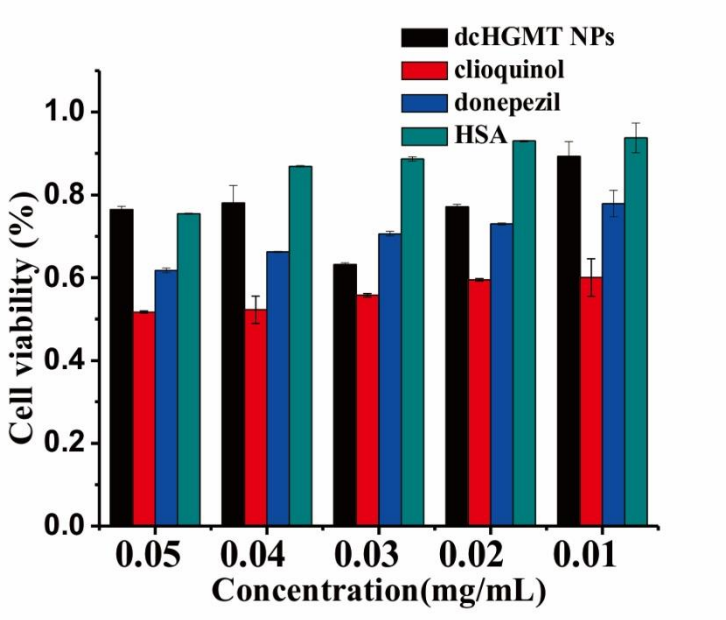

**Figure S3.** Cell viability of BV-2 cells incubated with free donepezil, clioquinol, HSA and dcHGT NPs at various concentrations. Data are presented as the mean ± SD.

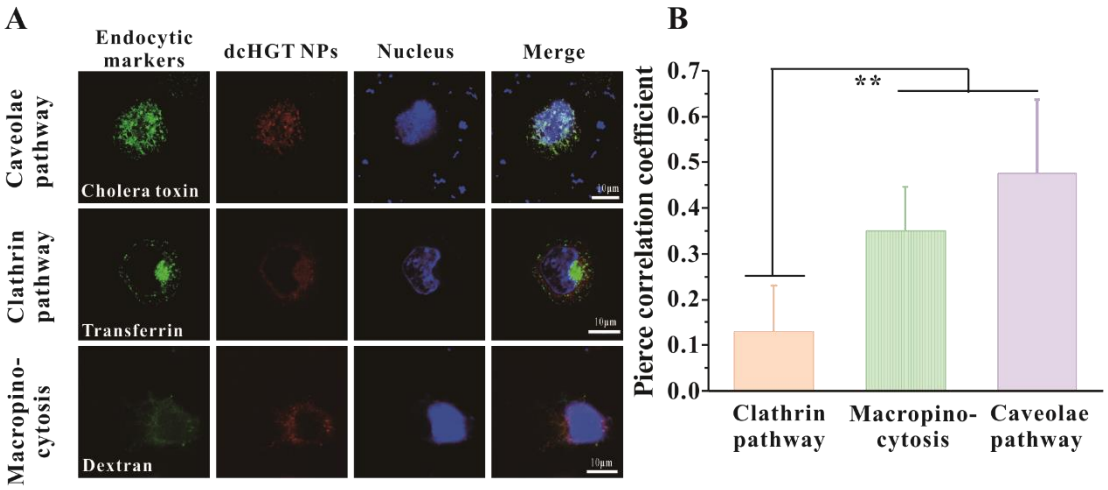


**Figure S4.** Cellular uptake of dcHGT NPs in BV2. (A) Representative images showing the co-localization of dye-labeled dcHGT NPs with endocytic markers by confocal microscopy. The nuclei were stained with Hoechst 33258 (blue). Scar bar, 10 μm. (B) Pearson's correlation coefficient analysis of the co-localization between dcHGT NPs and endocytosis markers in BV2. The quantitative data were obtained through Image J software. Data were expressed as mean ± SD (n = 6). $^{**}P < 0.01$.

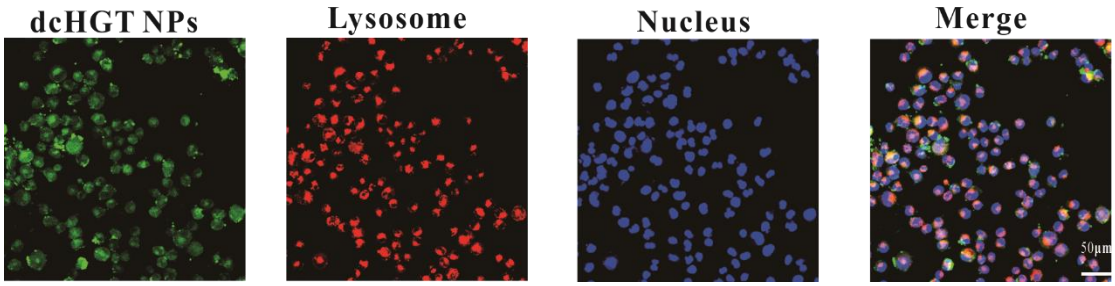


**Figure S5.** Colocalization (yellow) between dcHGT NPs (green) and LysoTracker (red), the indicator of lysosme, after 4 h incubation in BV2. Scar bar, 5 μm.

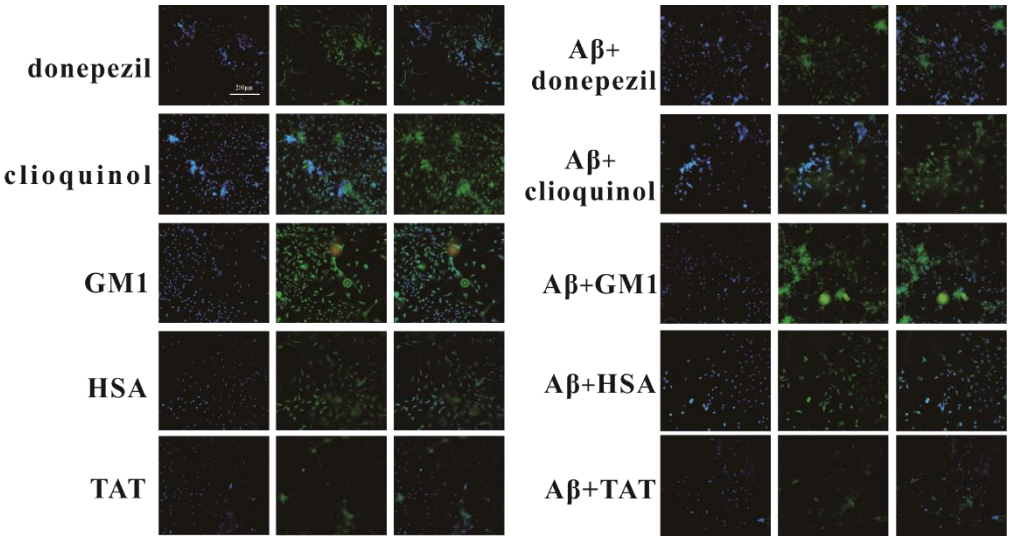


**Figure S6.** Fluorescent morphology images of the primary neurons captured by HCS; Scale bar: 200 μm.

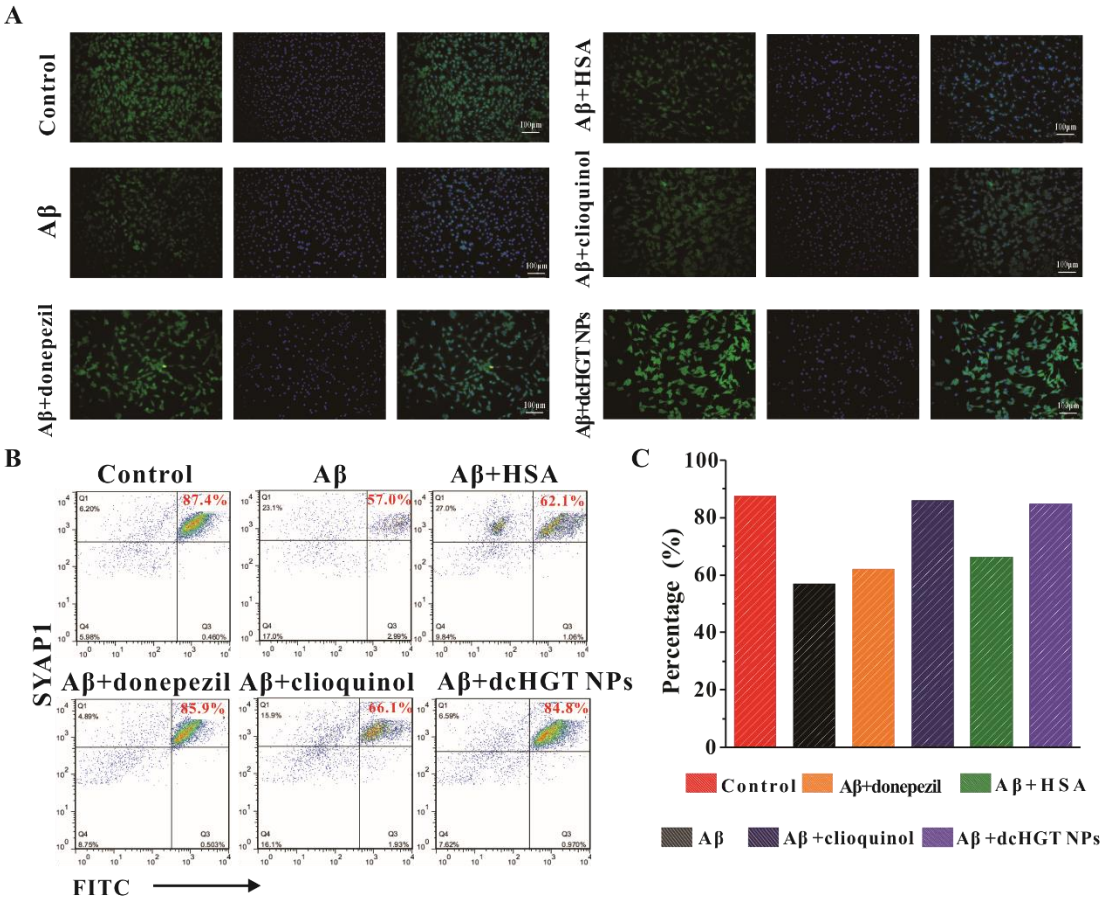


**Figure S7.** Immunofluorescence (A) and flow cytometry (B) were performed to

identificate the expression of synaptophsin (SYAP1) in PC12. (C) Statistical analysis of SYAP1 of PC12 in control, Aβ, Aβ+HSA, Aβ+donepezil, Aβ+clioquinol and Aβ+dcHGT NP groups.

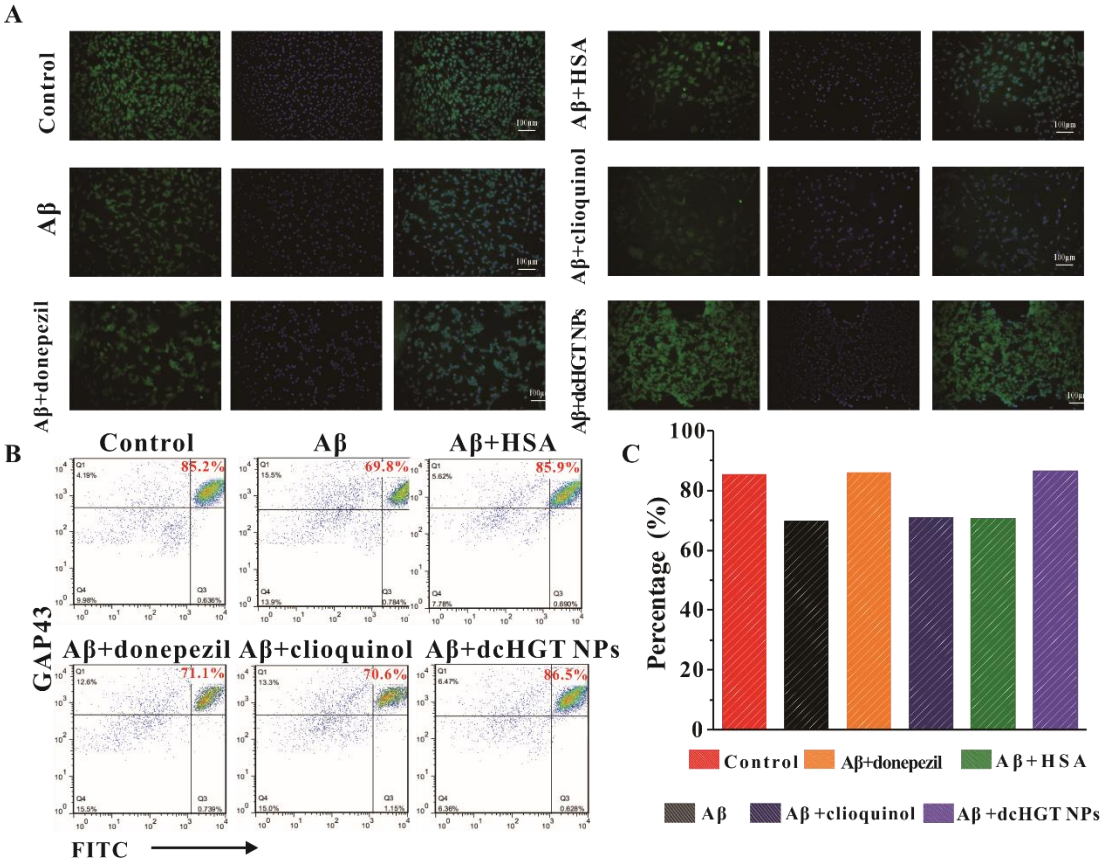


**Figure S8.** Immunofluorescence (A) and flow cytometry (B) were performed to identificate the expression of growth-related protein 43 (GAP43) in PC12. (C) Statistical analysis of GAP43 of PC12 in control, Aβ, Aβ+HSA, Aβ+donepezil, Aβ+clioquinol and Aβ+dcHGT NP groups.

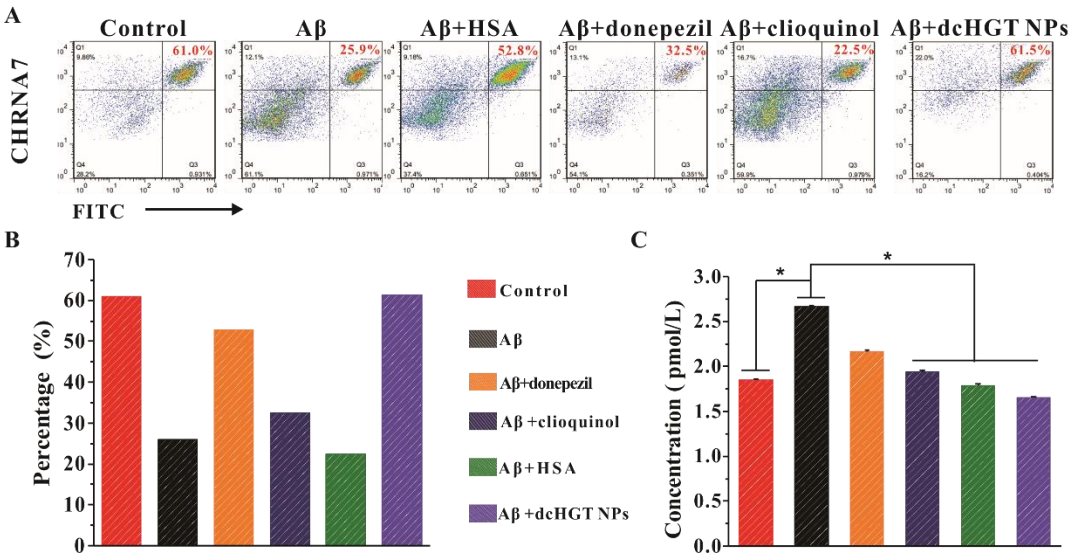


**Figure S9.** (A) Flow cytometry were performed to identificate the expression of neurotype 7 nicotine receptors (CHRNA7) in PC12. (B) Statistical analysis of CHRNA7 of PC12 in control, Aβ, Aβ+HSA, Aβ+donepezil, Aβ+clioquinol and Aβ+dcHGT NP groups. (C) Statistical analysis of the expression of caspase 3 in different groups by ELISA analysis. Data are presented as the mean ± SD. $*P < 0.05$.

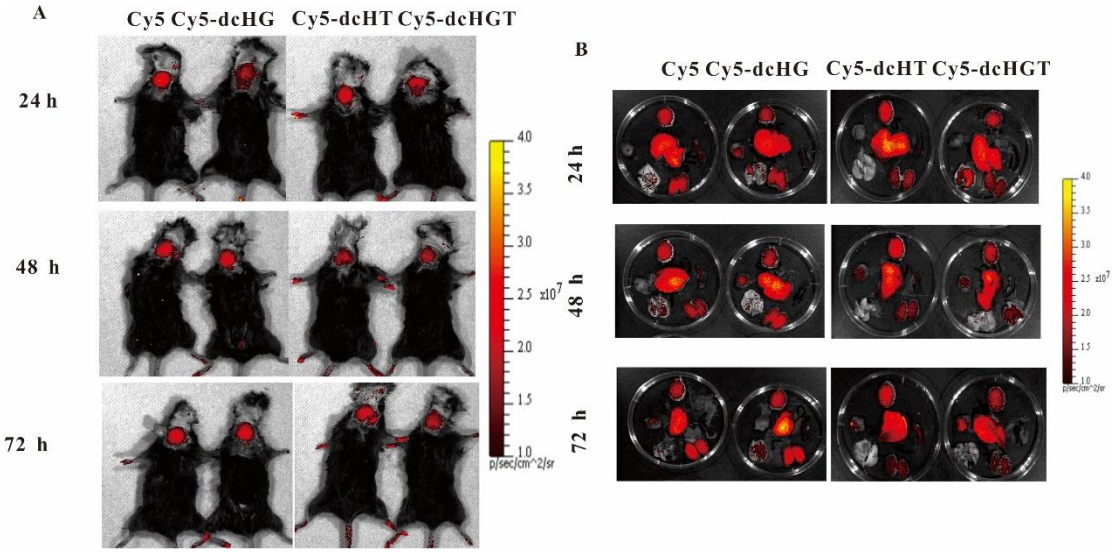


**Figure S10.** (A) In vivo fluorescence imaging at 24h, 48h and 72h after nasal administration of Cy5, Cy5- dcHG NPs, Cy5- dcHT NPs and Cy5- dcHGT NPs; (B) Ex vivo fluorescence images of brain and other tissues at 24h, 48h and 72h after

administration.

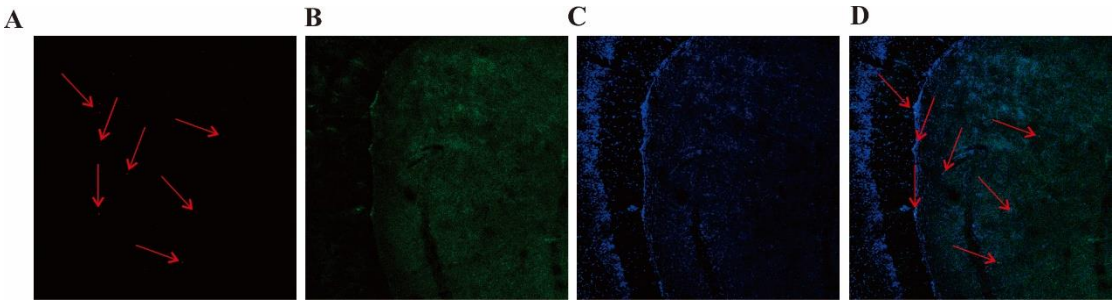


**Figure S11.** Fluorescence imaging of brain slices at 96h after nasal administration with Cy5-dcHGT NPs; (A) Cy5-dcHGT NPs, (B) immunofluorescent primary neurons, (C) DAPI, (D) merge images.