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Supplementary Materials for

Targeted exosome coating gene-chem nanocomplex as "nanoscavenger" for clearing α-synuclein and immune activation of Parkinson's disease

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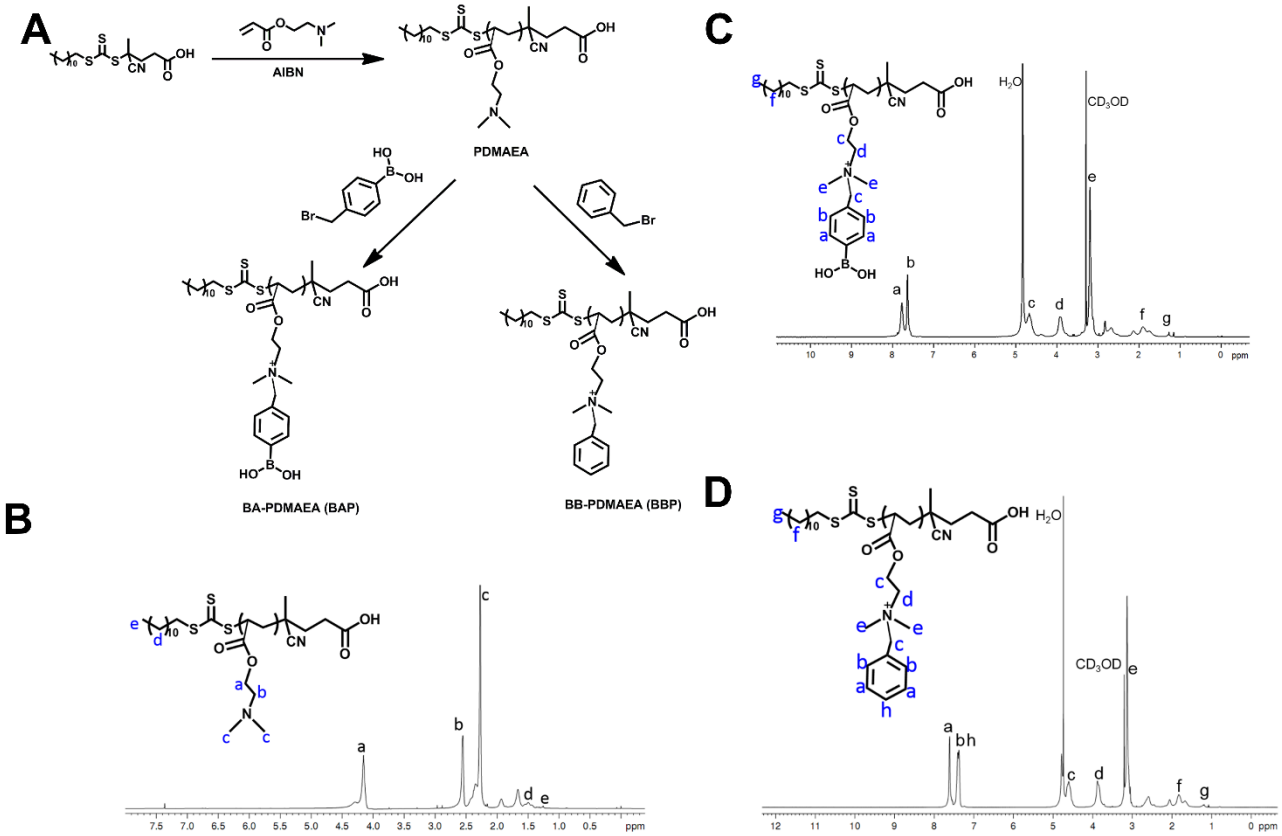

fig. S1. The synthetic routes and characterization of BAP and BBP polymers. (A) The synthetic routes of BAP and BBP polymers. (B) ^{1}H NMR spectra of PDMAEA. (C) ^{1}H NMR spectra of BAP. (D) ^{1}H NMR spectra of BBP.

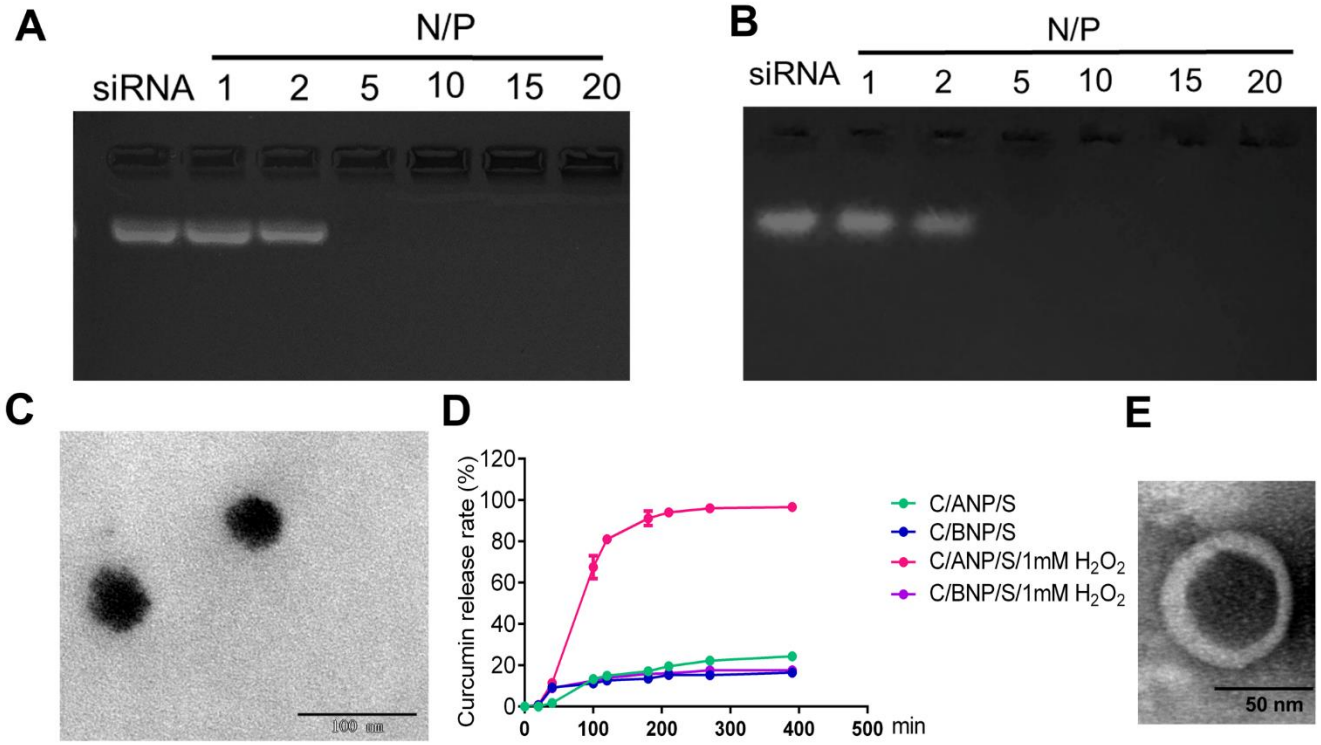

fig. S2. Characterizations of C/ANP/S and exosome. (A) Gel retardation assay of siSNCA at various N/P ratios for C/ANP. (B) Gel retardation assay of siSNCA at various N/P ratios for C/BNP. (C) TEM image of C/ANP/S. (D) Curcumin release rate of NPs. (E) TEM image of exosome.

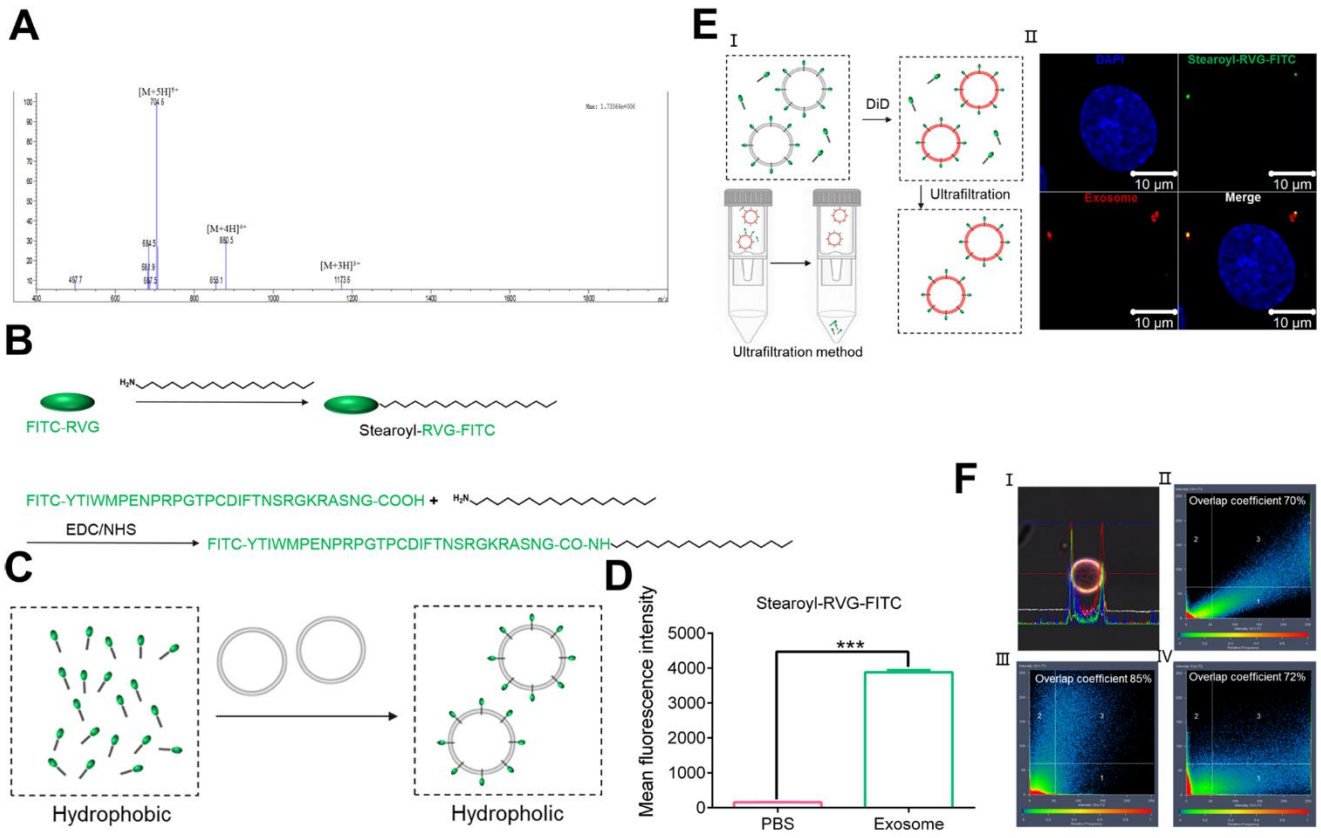

fig. S3. REXO and REXO-C/ANP/S preparation. (A) Mass spectrum of stearoyl-RVG (M.W.=3518.19). Stearoyl-RVG-FITC synthesis. (B) Scheme of stearoy-RVG-FITC synthesis. (I) Reaction formula of stearoyl-RVG-FITC synthesis. (II) Reaction formula of stearoyl-RVG-FITC synthesis. (C) Scheme of stearoyl-RVG-FITC modified exosome preparation. (D) Fluorescence intensity of stearoyl-RVG-FITC in exosome and equal volume PBS after ultrasound method. (E) Stearoyl-RVG-FITC modified exosome characterization. (I) The preparation scheme of DiD labelled exosome with stearoyl-RVG-FITC modification. (II) Confocal images of stearoyl-RVG-FITC modified exosome. (F) Channel analysis of REXO-C/ANP/S confocal images. (I) The confocal image of REXO-C/ANP/S. (II) Overlap analysis of exosome-DiI and curcumin. (III) Overlap analysis of Cy5-siRNA and curcumin. (IV) Overlap analysis of exosome-DiI and Cy5-siRNA. (Ch1-T1: exosome-DiI, Ch2-T2: Cy5-siRNA, Ch1-T3: curcumin, T PMT-T1: Bright field).

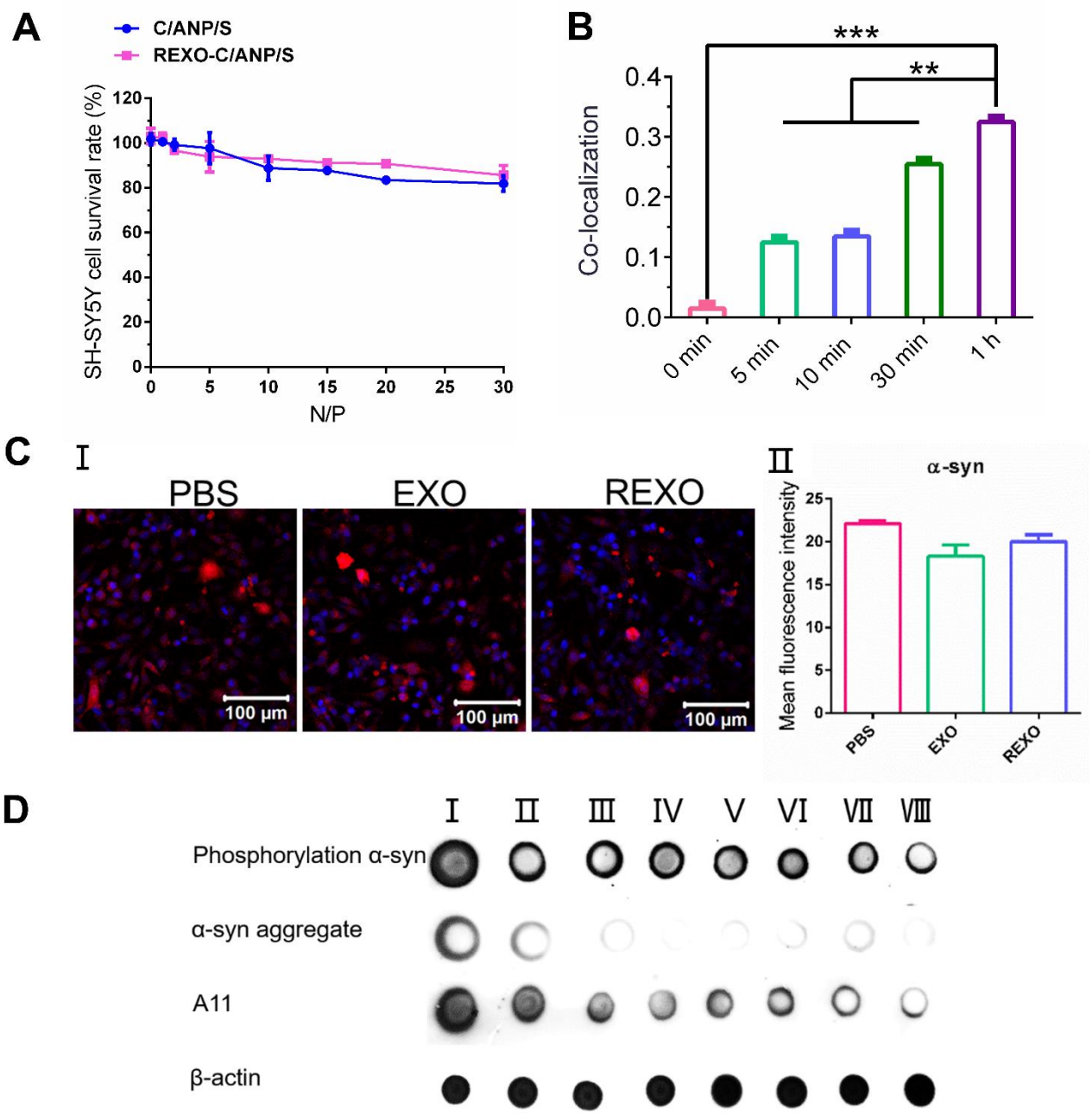

fig. S4. REXO-C/ANP/S treatment *in vitro*. (A) MTT assay of C/ANP/S and REXO-C/ANP/S from N/P ratio of 1 to 30. (B) Co-localization quantitation of SH-SY5Y cells CLSM after NPs incubation in 0 min, 5 min, 10 min, 30 min and 1 h. Cell membrane was labelled with CellMask™ deep red membrane stain and exosome was labelled with DiI. (C) α-Syn-mCherry in cells treated with exosomes. (I) Assessment by CLSM of α-syn-mCherry-SH-SY5Y cells after incubation with exosomes in transwell for 72 h. (II) Quantitative analysis of the α-syn-mCherry. (α-syn-mCherry: red and DAPI: blue). (D) Dot blot of protein in cells incubated with different NPs. (I: PBS; II: Nude C+S; III: C/BNP/S; IV: C/ANP/S; V:

EXO-C/ANP/S; VI: REXO-C/ANP/siNonsense; VII: REXO-ANP/S; VIII: REXO-C/ANP/S). *P < 0.05, **P < 0.01, ***P < 0.001.

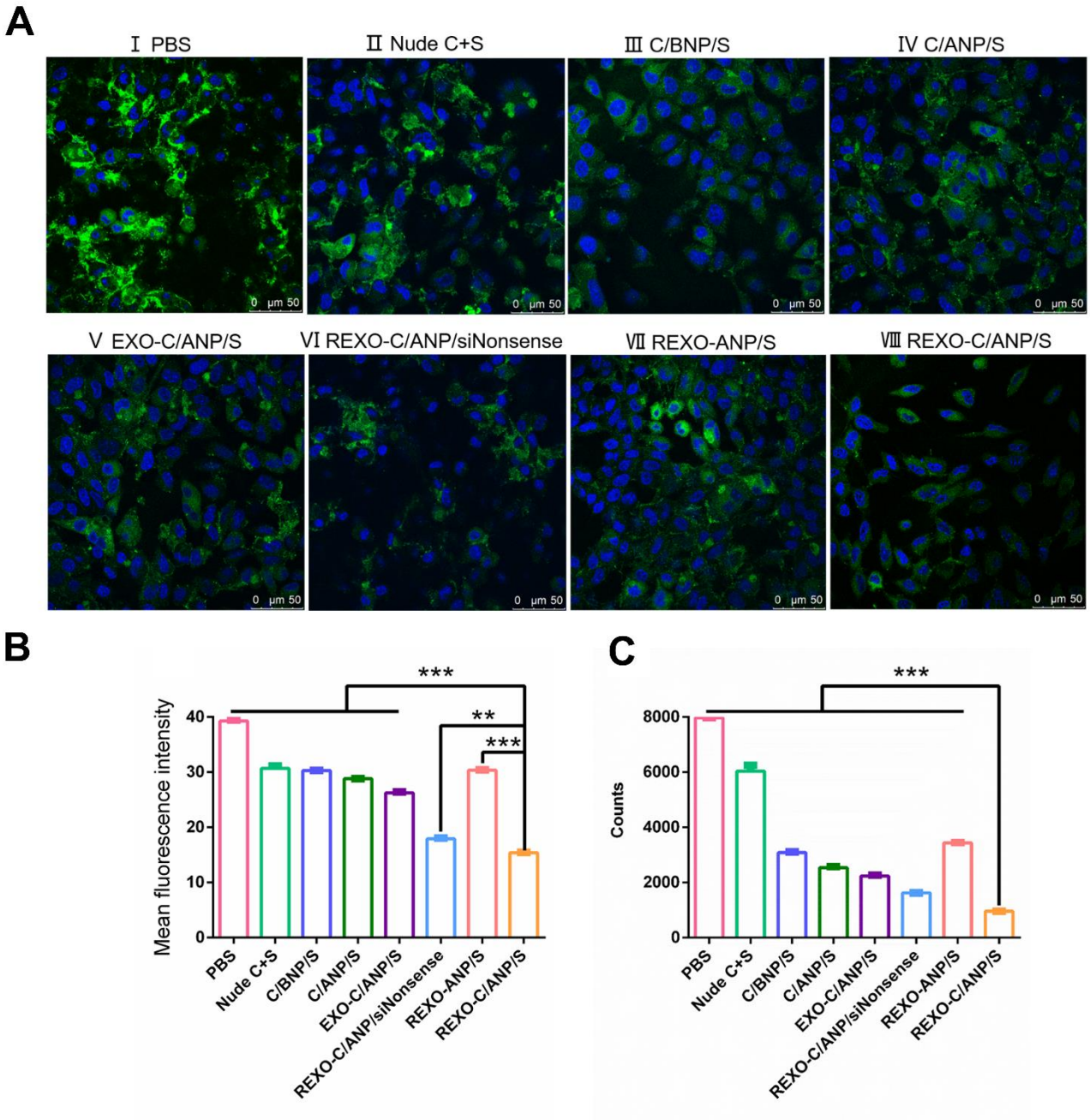

fig. S5. ROS in cells incubated with different NPs in 72 h. (A) ROS images of cells. (B) Mean fluorescence intensity of green color in CLSM images quantitated by Image J. (C) Green area counts in CLSM images quantitated by Image J. (I: PBS; II: Nude C+S; III: C/BNP/S; IV: C/ANP/S; V: EXO-C/ANP/S; VI: REXO-C/ANP/siNonsense; VII: REXO-ANP/S; VIII: REXO-C/ANP/S) *P < 0.05, **P < 0.01, ***P < 0.001.

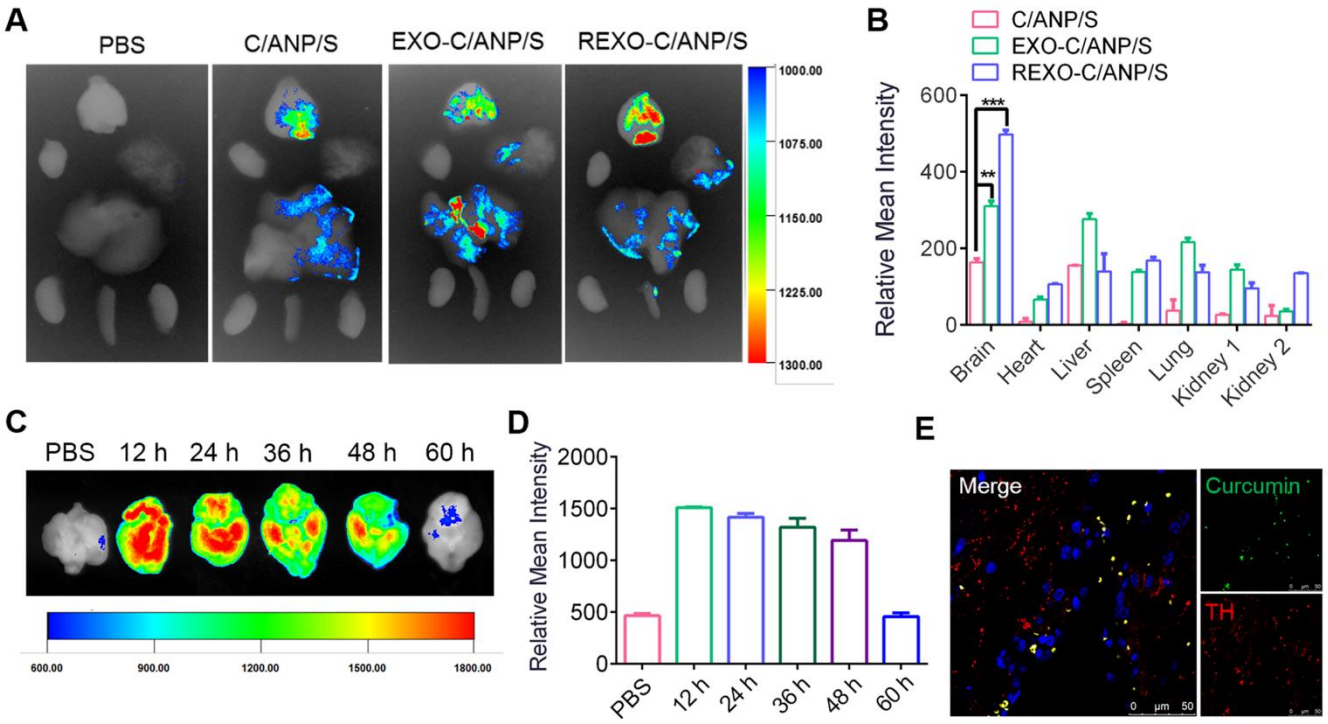

fig. S6. Ex-vivo bioluminescence imaging. (A) Ex-vivo bioluminescence images of C/ANP/S, EXO-C/ANP/S and REXO-C/ANP/S (1 mg/kg curcumin) treated PD mice after 24 h *via* intravenous injection. (B) Quantitation of ex-vivo bioluminescence images in (A). (The relative mean fluorescence intensity was compared with the control organs. Relative mean fluorescence intensity of NP treated mice brain=mean fluorescence intensity of NP treated mice brain - mean fluorescence intensity of 5% glucose solution treated mice brain.). (C) Ex-vivo bioluminescence images of brain from REXO-C/ANP/S (2 mg/kg curcumin) treated PD mice at designed time points after intravenous injection. (D) Quantitation of ex-vivo bioluminescence images in (C). (E) Immunofluorescence staining of brain substantia nigra region from REXO-C/ANP/S (2 mg/kg curcumin) treated PD mice after 12 h *via* intravenous injection. Nuclei: DAPI, blue; dopaminergic neurons: TH, red; curcumin: green. *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.

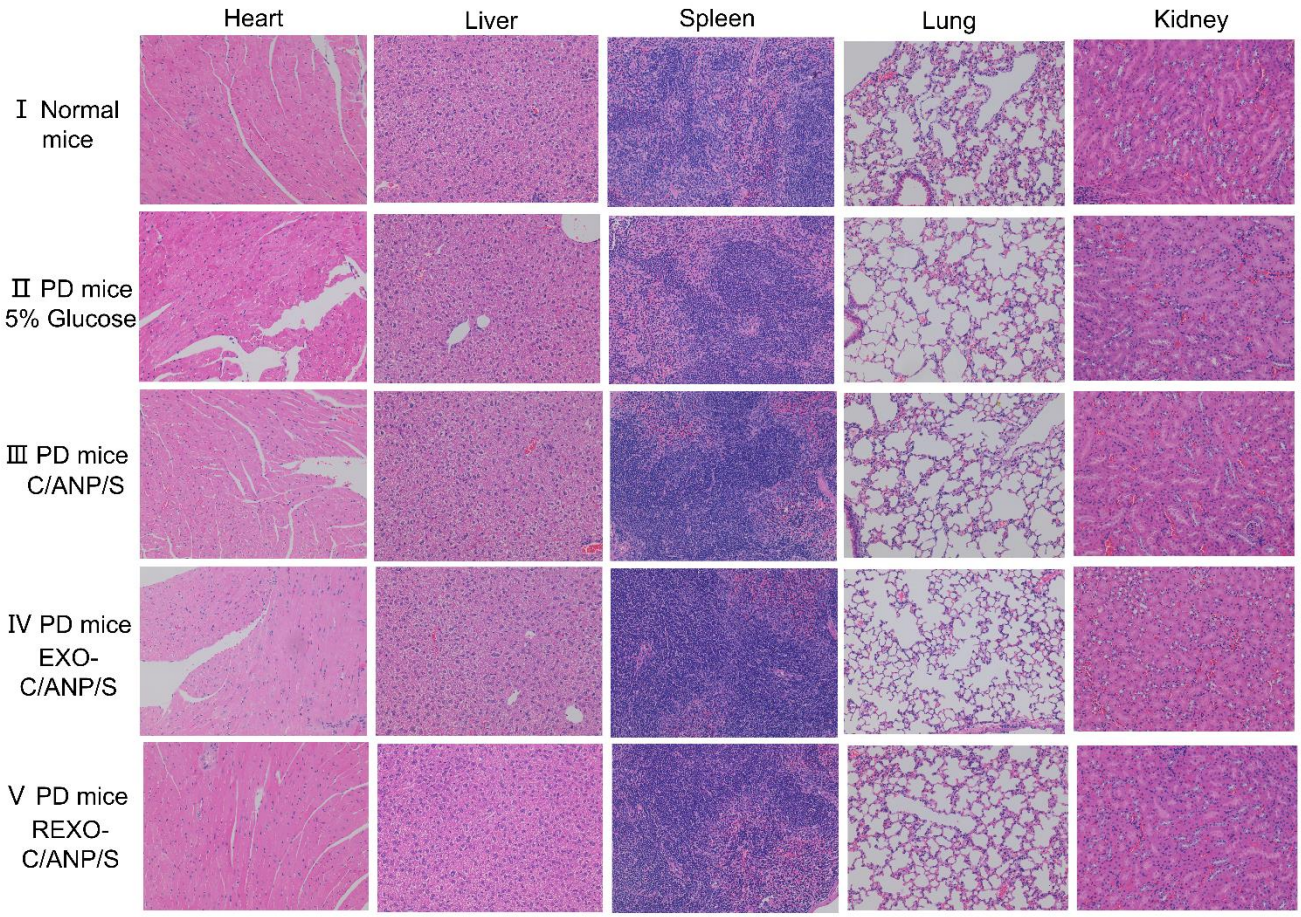

fig. S7. Hematoxylin-eosin (HE) staining of treated mice organs' slices.

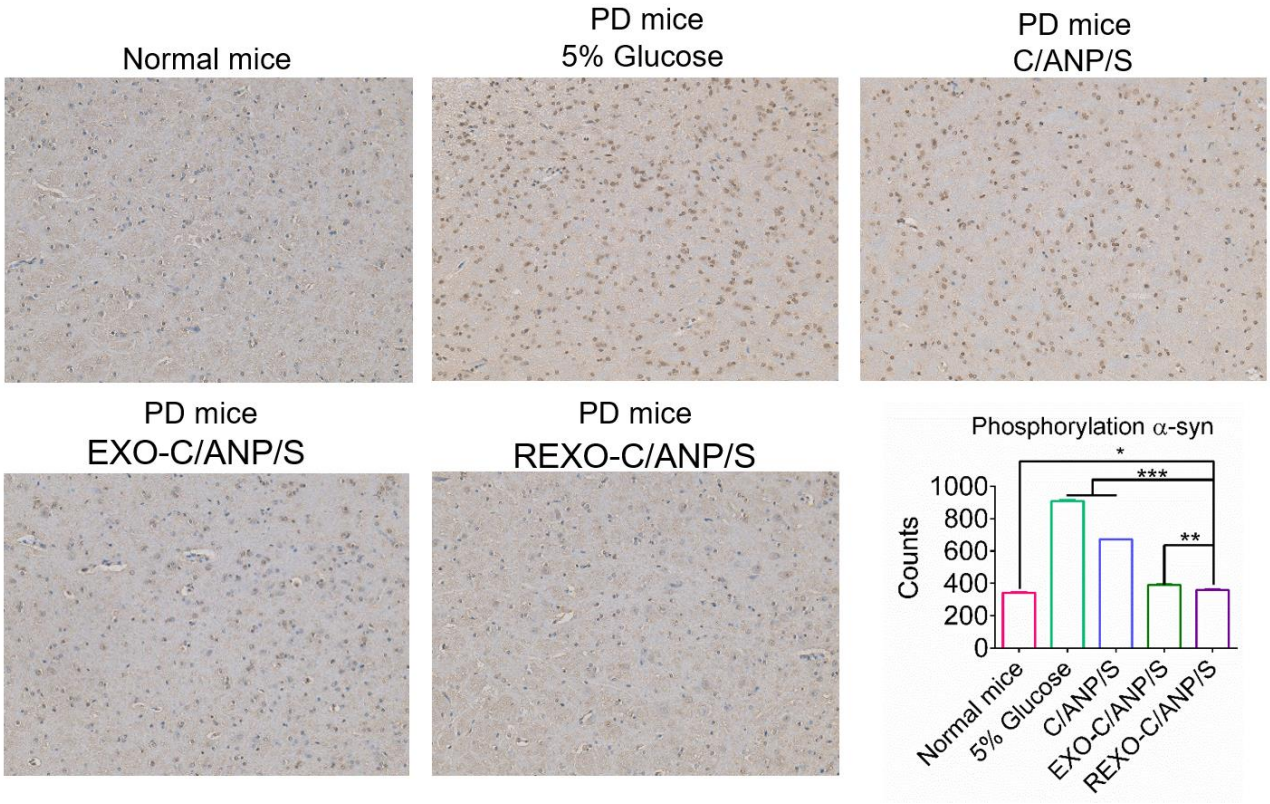

fig. S8. Phosphorylation α-syn immunohistochemistry staining (anti-Phosphorylation α-syn antibody) of brain slides in treated mice SN region. *P < 0.05, **P < 0.01, ***P < 0.001.

Table S1. Sequence information

Name	**Sequence**
RVG29	NH_2-YTIWMPENPRPGTPCDIFTNSRGKRASNG-COOH
Stearoyl-RVG	NH_2-YTIWMPENPRPGTPCDIFTNSRGKRASNG-C18
Stearoyl-RVG-FITC	FITC-YTIWMPENPRPGTPCDIFTNSRGKRASNG-C18
siSNCA	Antisense strand, 5'-UGCUCCUCCAACAUUUGUCTT-3'