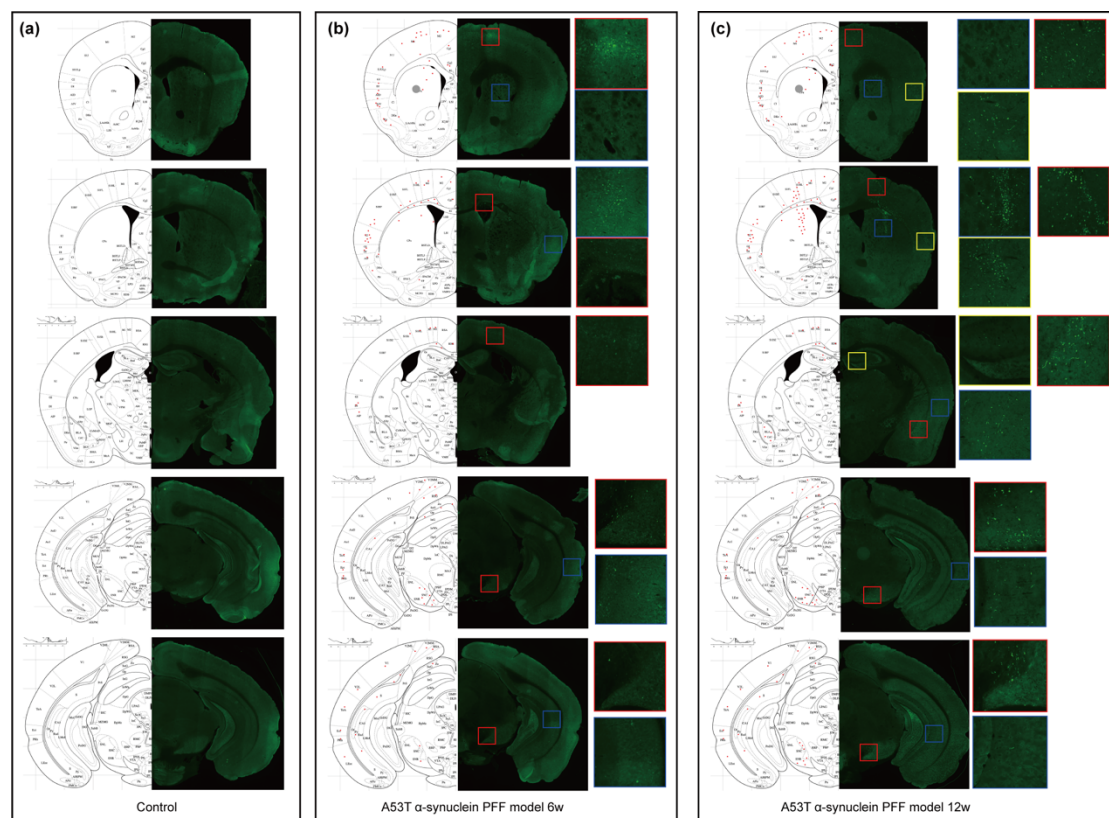


Supplementary Figure 1 Preparation of sonicated α -synuclein PFFs for stereotaxic injections. **Related to Fig. 1.**

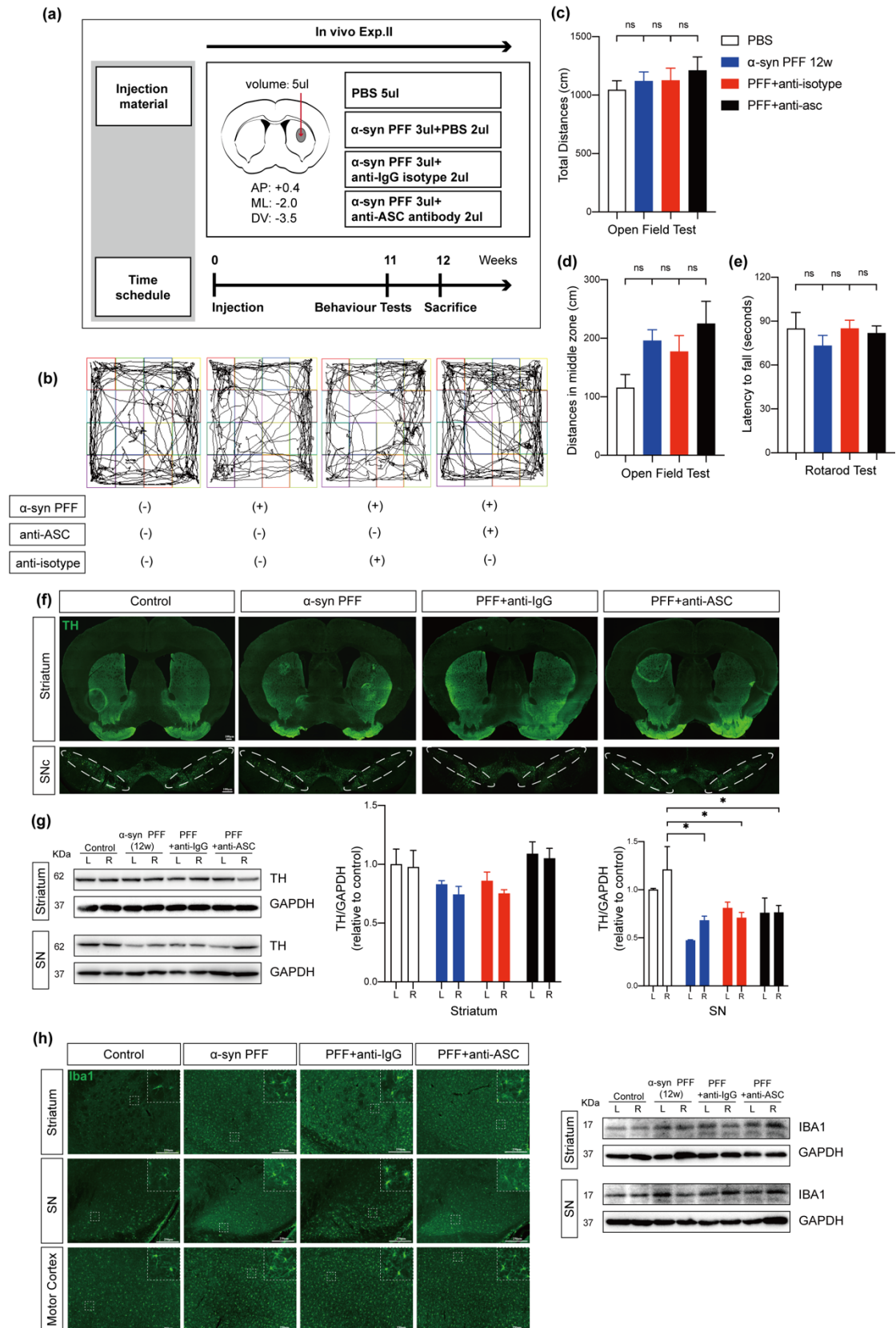
(a, b) Representative TEM images of recombinant human A53T mutant α -synuclein PFFs before and after sonication. Scale bar: 500 nm.



Supplementary Figure 2 Propagation of α -synuclein pathology in the mice brains as PD progresses. **Related to Fig. 1.**

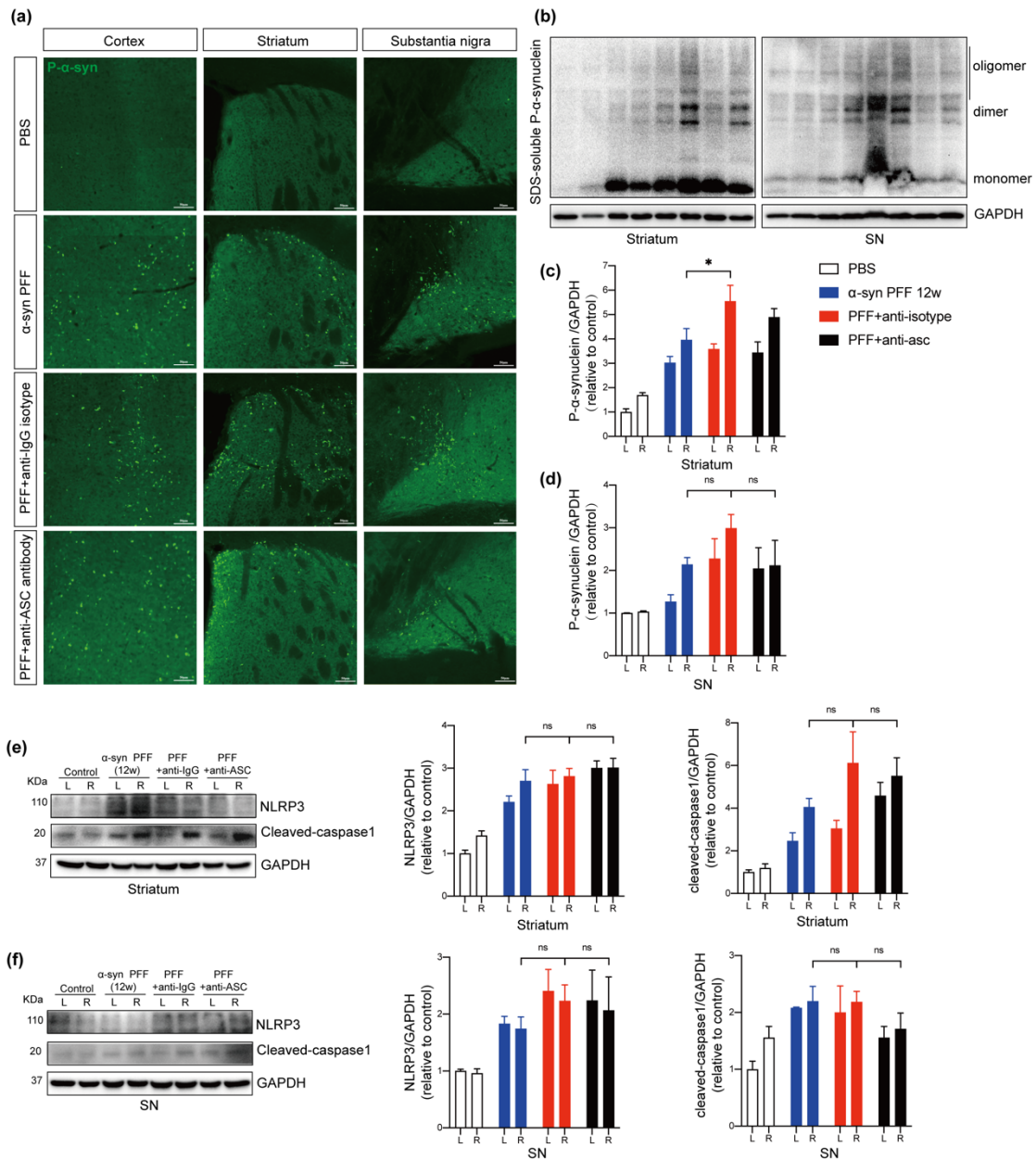
(a-c) Representative immunofluorescence images of P- α -syn (green) in several brain slices of control

mice and PFFs-induced PD mice after six- and twelve- weeks treatment. The colored boxes in images are magnified on the right.



Supplementary Figure 3 No significant protective effects of anti-ASC antibody were found in PFFs-treated PD mice. **Related to Fig. 7.**

(a) Time schedules of the *in vivo* experiment in this study. The number of mice in each group: control group, n = 9; PFF group, n = 9; PFF+anti-IgG group, n = 12; PFF+anti-ASC group, n = 10. (b) Representative images of the tracks of indicated mice in open field test. (c, d) The total distance traveled and distance traveled in middle zone were recorded and analyzed for each mouse. (e) The latency to falling during the rotarod test was recorded and analyzed for each mouse. (f) Representative immunofluorescence staining of TH (green) neurons in the striatum and SNc of mice brains (n = 3-6). White dotted circles indicate the SNc regions. (g) IB analysis and quantification of TH in bilateral striatum and SN of indicated mice (n = 3). (h) Representative immunofluorescence staining of Iba1 (green) in the ipsilateral striatum, SN and motor cortex of mice brains (n = 3-6). White dotted squares show the morphology of microglia after magnification. (i) IB analysis of Iba1 in bilateral striatum and SN of indicated mice (n = 3). Values are presented as mean \pm SEM and are analyzed by one-way or two-way ANOVA followed by Tukey's post hoc test for multiple comparisons. Levels of significance are: *p < 0.05; ns, no significant. Scale bars are as indicated. L, left; R, right; SNc, substantia nigra compacta; SN, substantia nigra.



Supplementary Figure 4 No differences in α -synuclein pathology and NLRP3 inflammasome activation were observed in brain tissues of anti-ASC antibody treated or anti-isotype treated PD mice. **Related to Fig. 7.**

(a) Representative immunofluorescence staining of p- α -syn (green) in ipsilateral striatum, SN and cortex of indicated mice ($n = 3-6$). **(b-d)** IB analysis and quantification of SDS-soluble p- α -syn in bilateral striatum and SN tissues ($n = 3$). **(e, f)** IB analysis and quantification of NLRP3 inflammasome signals in bilateral striatum and SN of indicated mice ($n = 3$). Values are presented as mean \pm SEM and are analyzed by two-way ANOVA followed by Tukey's post hoc test for multiple comparisons. Levels of significance are indicated as follows: * $p < 0.05$; ns, no significant. Scale bar: 50 μ m. L, left; R, right; SN, substantia nigra.