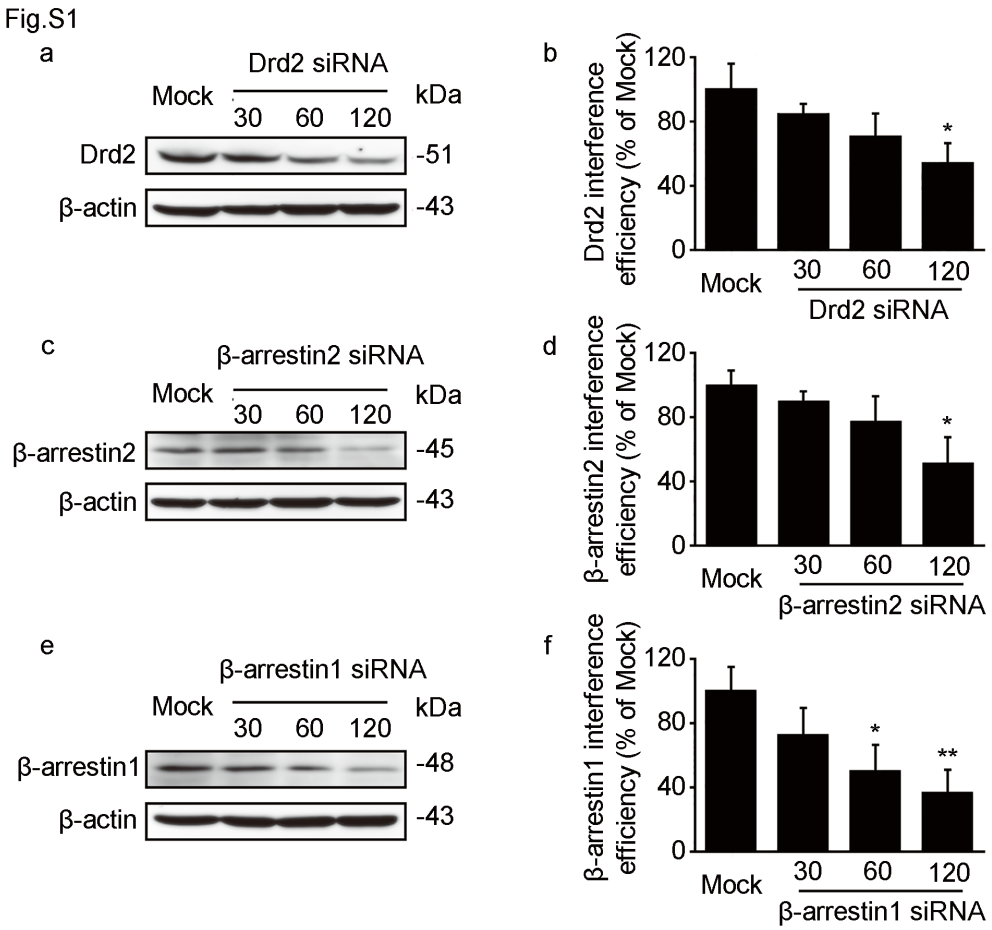

Figure S1. Interference efficiencies of Drd2, β-arrestin2 and β-arrestin1.

(a) Primary astrocytes were transfected with different doses of siRNA targeting the mRNA encoding Drd2 (30, 60, 120 nM) or empty vector. The expression of Drd2 from cell lysates was analyzed by immunoblotting. (b) Densitometric analysis of Drd2. (c) Primary astrocytes were transfected with different doses of siRNA targeting the mRNA encoding β-arrestin2 (30, 60, 120 nM) or empty vector. The expression of β-arrestin2 from cell lysates was analyzed by immunoblotting. (d) Densitometric analysis of β-arrestin2. (e) Primary astrocytes were transfected with different doses of siRNA targeting the mRNA encoding β-arrestin1 (30, 60, 120 nM) or empty vector. The expression of β-arrestin1 from cell lysates was analyzed by immunoblotting. (f) Densitometric analysis of β-arrestin1. $^{*}p<0.05$, $^{**}p<0.01$ vs Con group. Values are means ± SEM. Data are representative of at least three independent experiments.

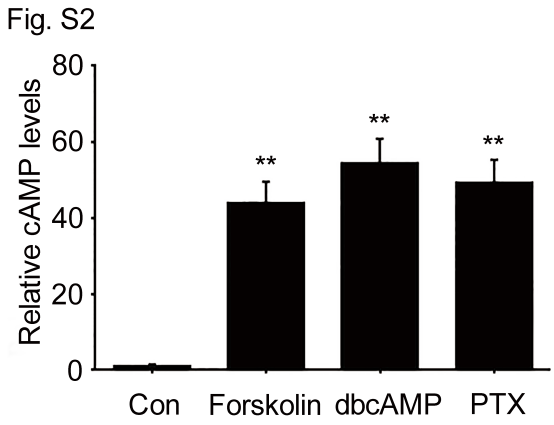

Figure S2. Relative cAMP levels regulated by cAMP up-regulators.

Primary astrocytes were stimulated with 10 μM forskolin, 100 μM dbcAMP or 100 ng/ml PTX for 3h. Culture medium was analyzed for intracellular cAMP levels. $^{**}p<0.01$ vs Con group. Values are means ± SEM. Data are representative of at least three independent experiments.

Fig.S3

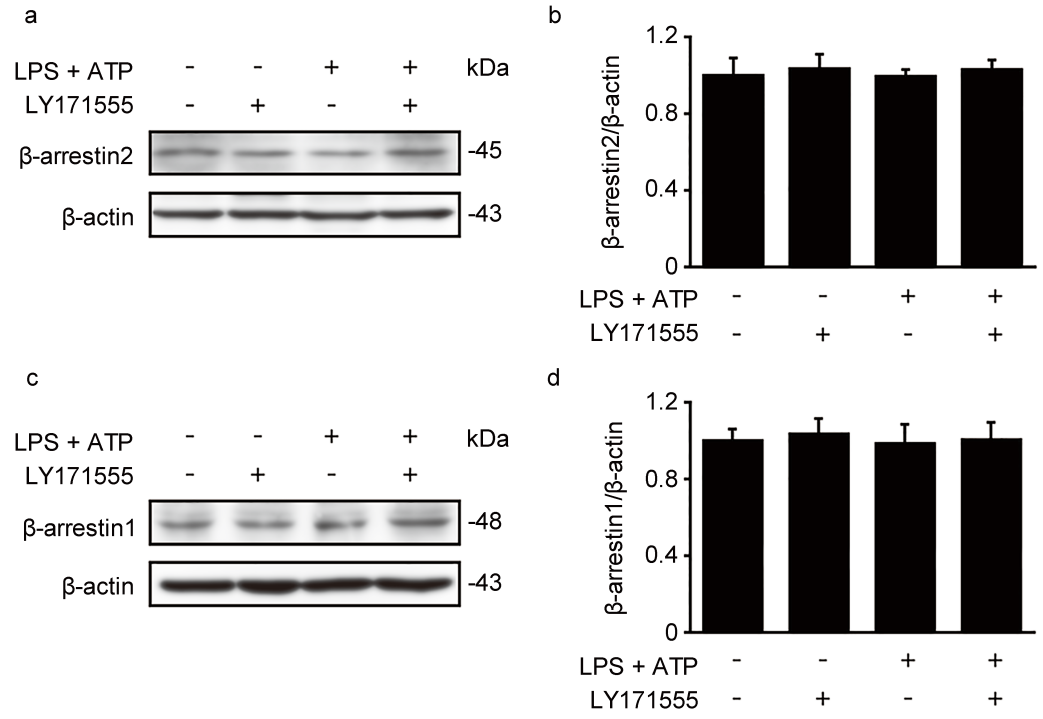

Figure S3. Expressions of Drd2, β-arrestin2 and β-arrestin1 in primary cultured astrocytes.

(a) Expression of β-arrestin2 in primary astrocytes in normal, LY171555 and LPS+ATP treatment conditions analyzed by immunoblotting. (b) Densitometric analysis of β-arrestin2. (c) Expression of β-arrestin1 in primary astrocytes in normal, LY171555 and LPS+ATP treatment conditions analyzed by immunoblotting. (d) Densitometric analysis of β-arrestin1. Values are means ± SEM. Data are representative of at least three independent experiments.

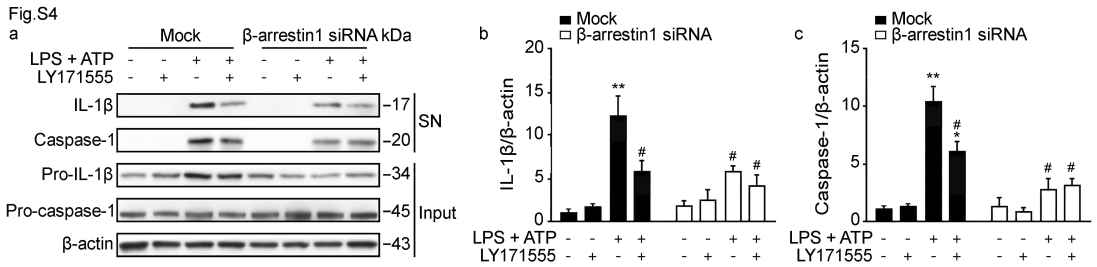

Figure S4. Deficiency of β-arrestin1 has influence on NLRP3 inflammasome activation.

(a) Primary astrocytes were transfected with siRNA targeting the mRNA encoding β-arrestin1 or empty vector. LPS (100 ng/ml) primed-primary astrocytes were treated with LY171555 and then stimulated with ATP (5 mM). IL-1β and caspase-1 from medium supernatants (SN) and pro-IL-1β and pro-caspase-1 from cell extracts (Input) were analyzed by immunoblotting. (b-c) Densitometric analysis of IL-1β and caspase-1. $^{*}p<0.05$, $^{**}p<0.01$ vs Con group. $^{\#}p<0.05$ vs LPS+ATP group. Values are means ± SEM. Data are representative of at least three independent experiments.

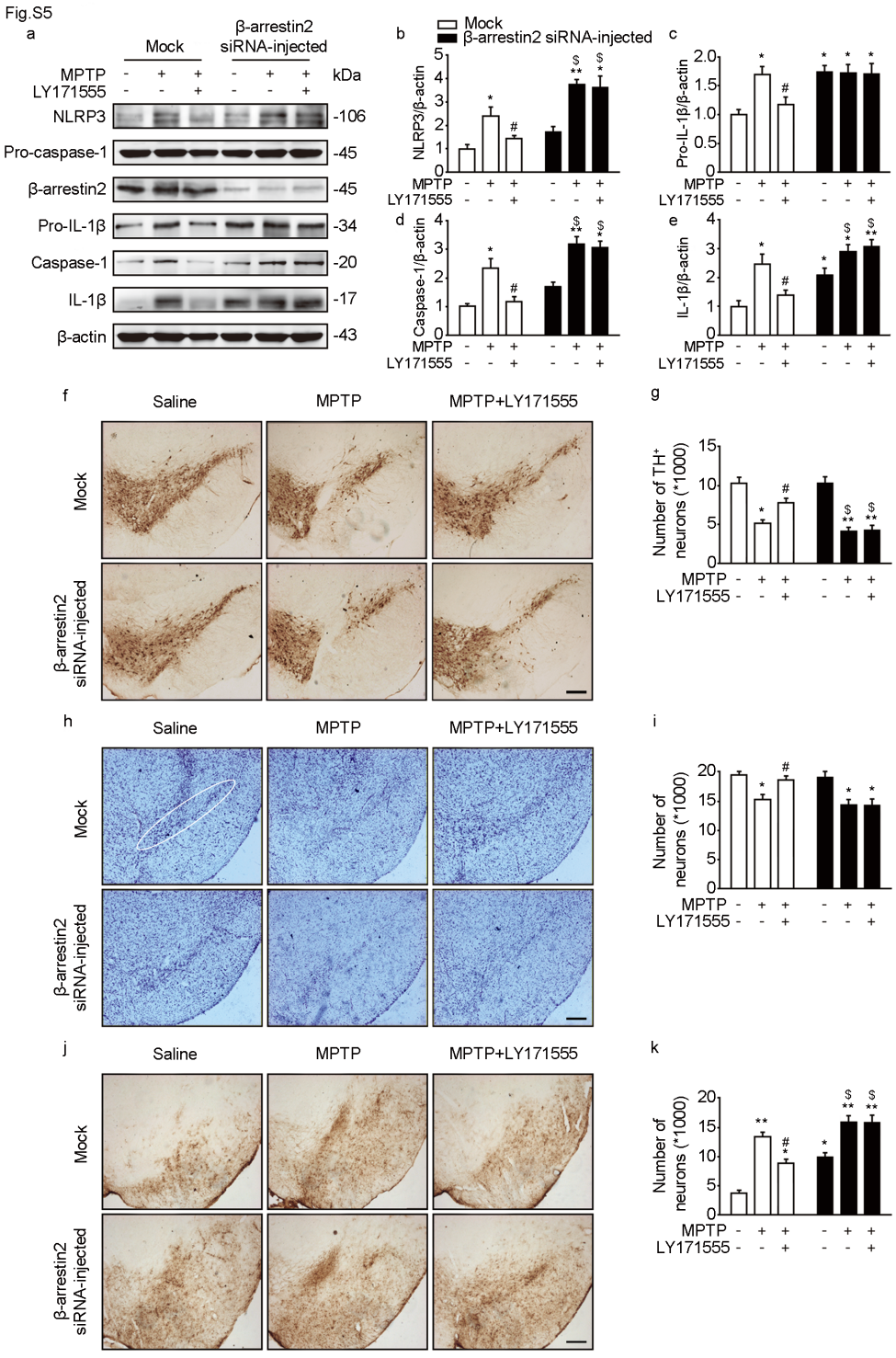

Figure S5. Interference of β-arrestin2 has influence on the anti-inflammatory and neuroprotective effects of Drd2 in MPTP-induced PD mouse model.

(a) WT mice were injected in mesencephalon stereotaxicly with lentivirus targeting the mRNA encoding β-arrestin2 or empty vector. After 10 d, WT and β-arrestin2 siRNA-injected mice were made MPTP (20 mg/kg i.h., q.d., 5 d)-induced-PD model with LY171555 (5 mg/kg i.p., q.d.,11 d) administration or not. NLRP3, pro-caspase-1, caspase-1, pro-IL-1β and IL-1β from mouse

mesencephalon homogenate were analyzed by immunoblotting. (b-e) Densitometric analysis of NLRP3, pro-IL-1β, caspase-1 and IL-1β. (f) Immunohistochemical staining of TH^+ neuron in the SNc. (g) Counting TH^+ neuron in the SNc. (h) Nissl staining of neuron. (i) Counting neuron. (j) Immunohistochemical staining of GFAP in the SNc. (k) Counting GFAP positive astrocytes in the SNc. Scale bar represents 200 μm. $^{*}p<0.05$, $^{**}p<0.01$ vs WT Con group; $^{\#}p<0.05$ vs WT MPTP group; $^{\$}p<0.05$ vs β-arrestin2 siRNA-injected Con group. Values are means ± SEM. Data are representative of six independent experiments.

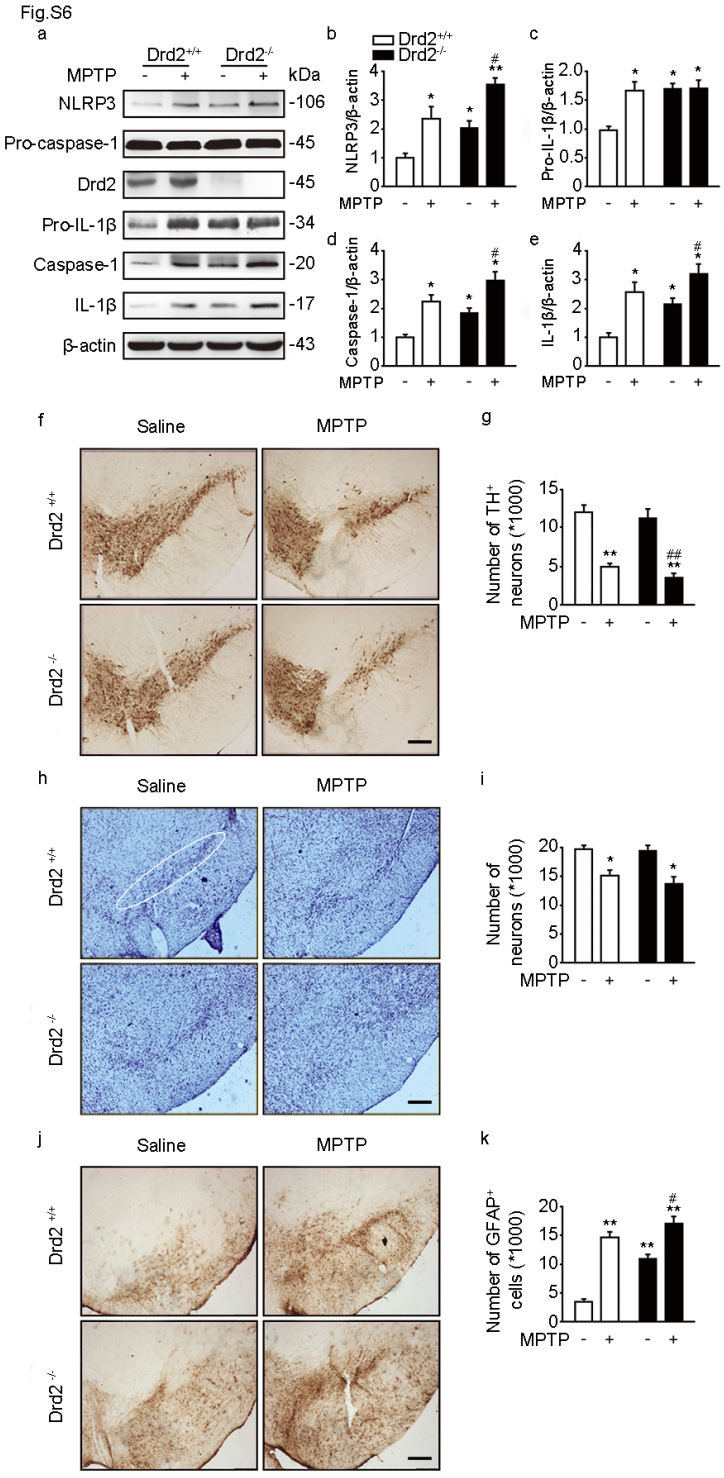

Figure S6. Drd2 agonist has influence on MPTP-induced neuroinflammation.

(a) WT and Drd2$^{-/-}$ mice were made MPTP (20 mg/kg i.h., q.d., 5 d)-induced-PD model. NLRP3, pro-caspase-1, caspase-1, pro-IL-1β and IL-1β from mouse mesencephalon homogenate were analyzed by immunoblotting. (b-e) Densitometric analysis of NLRP3, pro-IL-1β, caspase-1 and IL-1β. (f) Immunohistochemical staining of TH^{+} neuron in the SNc. (g) Counting TH^{+} neuron in the SNc. (h) Nissl staining of neuron. (i) Counting neuron. (j) Immunohistochemical staining of GFAP in the

SNc. (k) Counting GFAP positive astrocytes in the SNc. Scale bar represents 200 μm. $^{*}p<0.05$, $^{**}p<0.01$ vs WT Con group; $^{\#}p<0.05$, $^{\#\#}p<0.01$ vs Drd2$^{-/-}$ Con group. Values are means ± SEM. Data are representative of six independent experiments.

Fig. S7

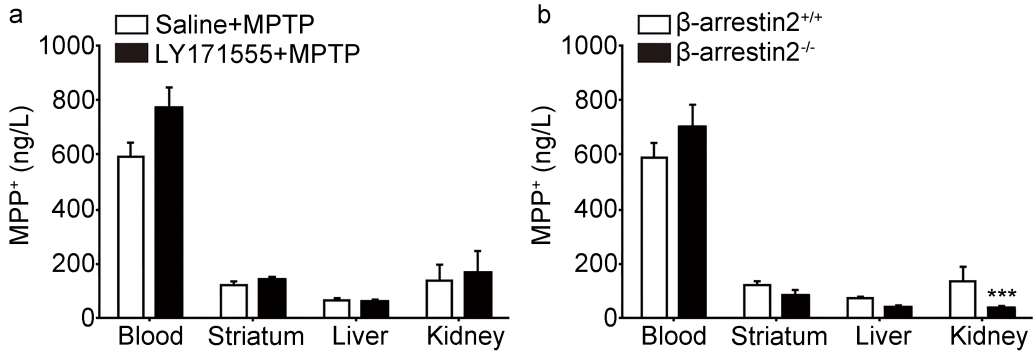

Figure S7. MPP^+ levels detected after MPTP injection.

WT and β-arrestin$2^{-/-}$ mice were sacrificed 90 min after a single dose of MPTP with or without a previous LY171555 injection. MPP^+ levels in blood, striatum, liver and kidney were detected 90 min after MPTP injection by HPLC. $^{***}p<0.001$ vs corresponding β-arrestin$2^{+/+}$ group. Values are means ± SEM. Data are representative of eight independent experiments.