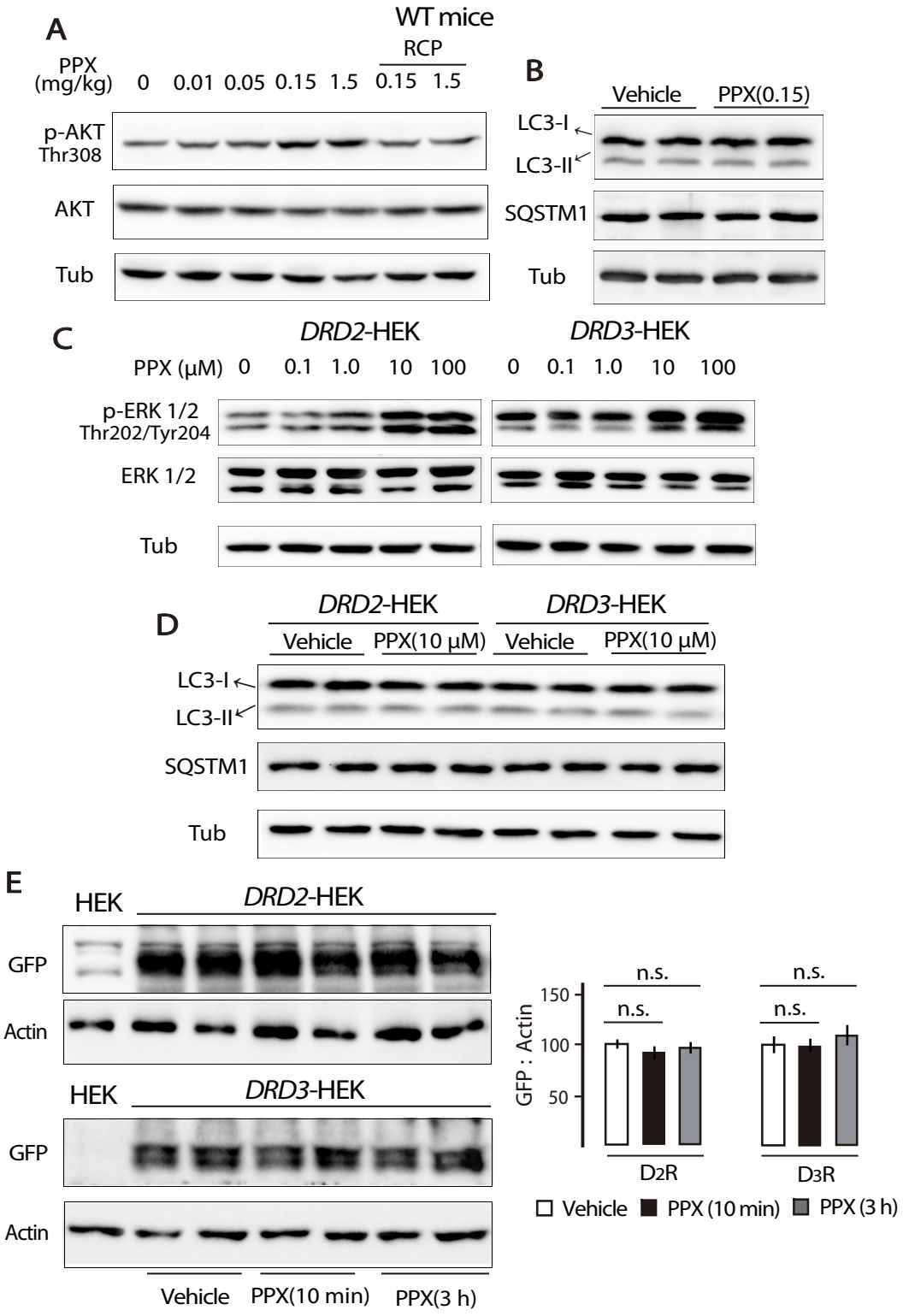
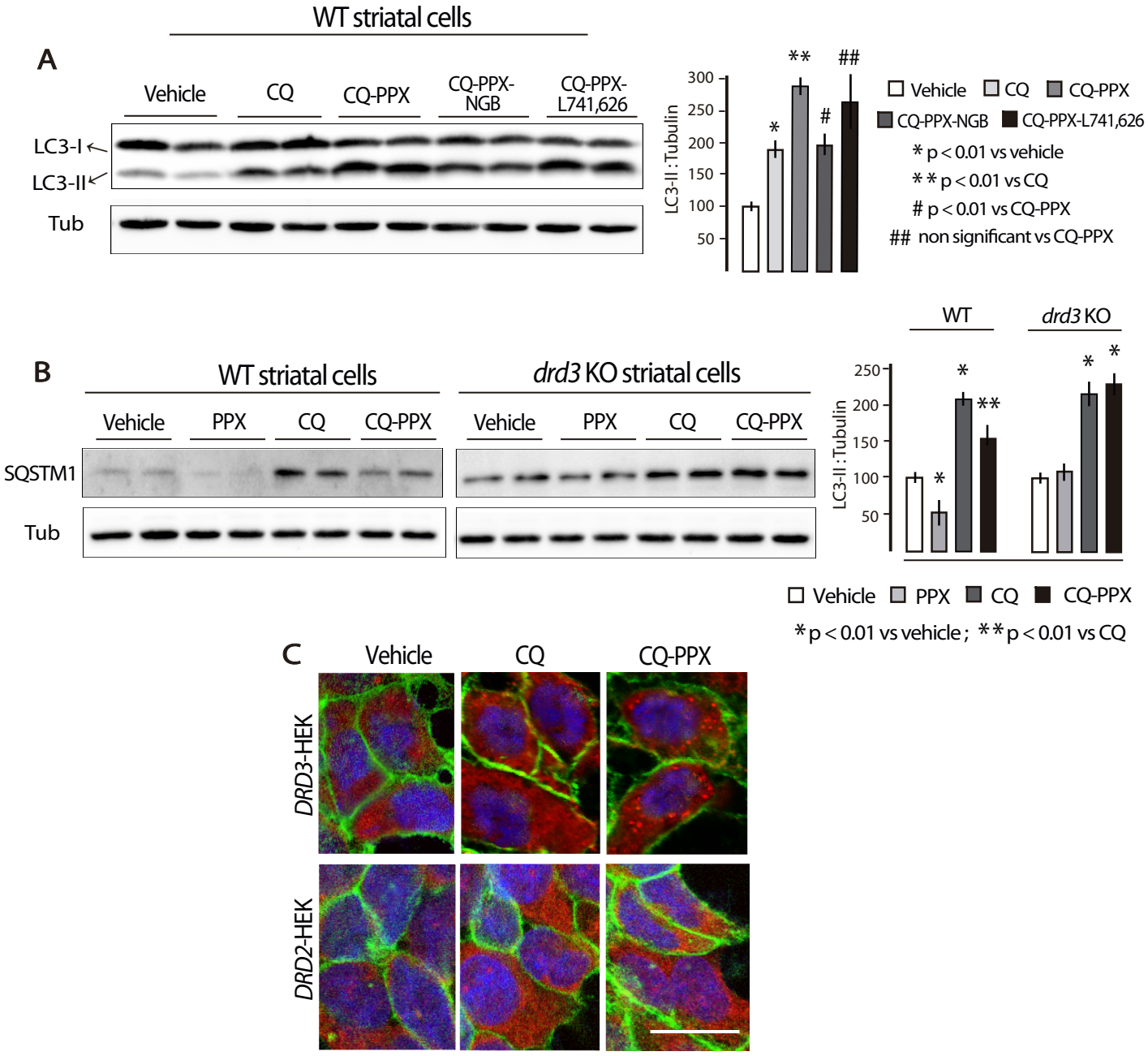
Supplementary Figure 1



(**A-D**) Dose-response effect of acute pramipexole (PPX) treatment in wild-type (WT) mice and *DRD2*- and *DRD3*-HEK cells. Mice were sacrificed 10 min after a single i.p. injection of 0.01-1.5 mg/kg PPX (**A** and **B**), and cells were treated with 0.1-100 µM PPX for 5 min after 60 min serum starvation (**C** and **D**). AKT phosphorylation at Thr308 and ERK phosphorylation at Thr202/Tyr204 were used as readout of D2R/D3R signalling in mouse striata and cells, respectively [28-30]. Robust phosphorylation was detected at ≥ 0.15 mg/kg PPX in mice (**A**), and at ≥ 10 µM PPX in cells (**C**). AKT phosphorylation in mouse striata was blocked by pre-treatment with the D2R/D3R antagonist raclopride (RCP, 1 mg/kg, i.p., 30 min before PPX). The autophagy markers LC3 and p62 were not altered after acute PPX treatment (**B** and **D**). (**E**) Western-blot for GFP in GFP-*DRD2*-HEK and EGFP-*DRD3*-HEK cells treated with PPX. D2R and D3R expression, as reflected by GFP labeling intensity, were not modified after 10 min and 3 h PPX treatment. n.s, not significant.

Supplementary Figure 2

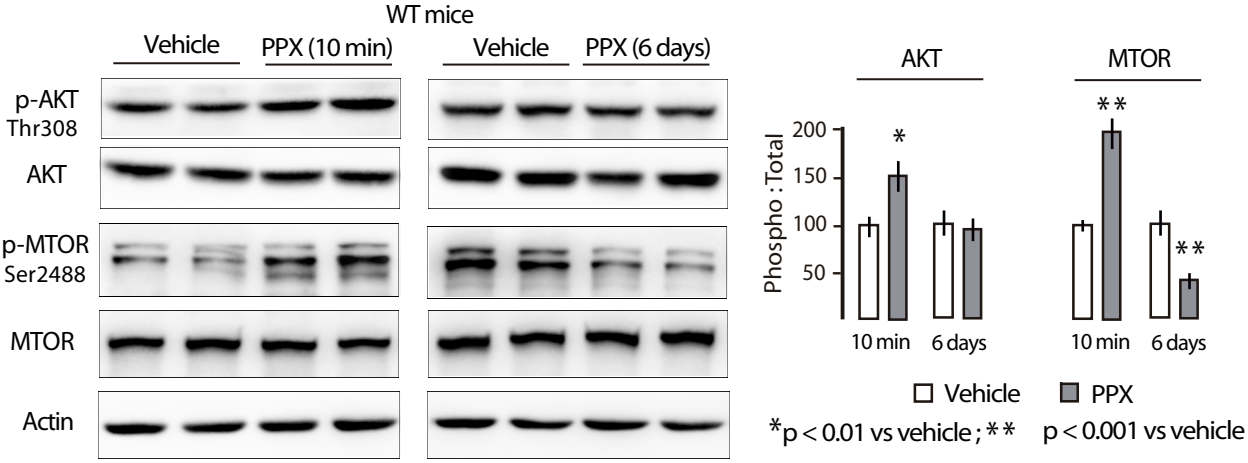


(**A**): Western-blot for LC3 in striatal cells of WT mice. PPX promotes an increase in LC3-II levels in cells pre-treated with chloroquine (compare lanes 3 and 4 [CQ] with lanes 5 and 6 [CQ-PPX]). The increase in LC3-II levels was blocked by co-treatment with the D3R antagonist NGB2904 (CQ-PPX-NGB, lanes 7 and 8) but not by co-treatment with the D2R antagonist L741,626 (CQ-PPX-L741,626, lanes 9 and 10).

(**B**) Western-blot for SQSTM1 in striatal cells of WT- (left) and *drd3* KO mice (right). PPX promotes a decrease in SQSTM1 in WT- but not *drd3* KO mice (PPX, lanes 3 and 4), and the increase in SQSTM1 levels induced by chloroquine was reversed by PPX in WT- but not *drd3* KO mice (compare lanes 5 and 6 with lanes 7 and 8).

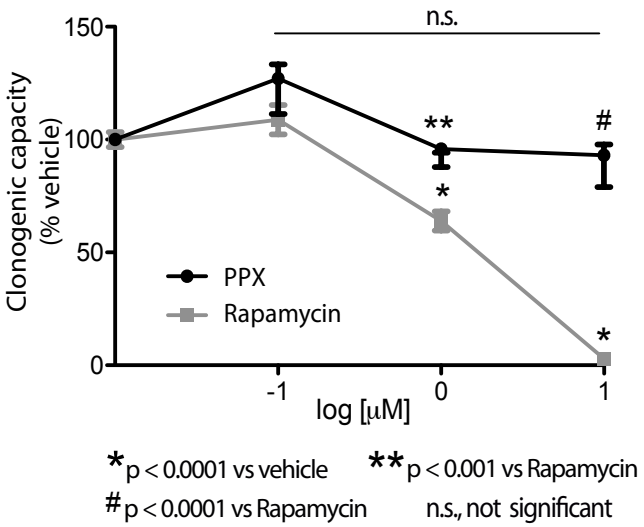
(**C**) Immunofluorescence for LC3 (red) in EGFP-*DRD3*- and GFP-*DRD2*-HEK cells. Chloroquine (20 μM, 3 h; CQ) promoted a slight increase in diffuse LC3 labeling in both *DRD3*- and *DRD2*-HEK cells (compare vehicle and CQ). Consistent with the Cyto-ID assay, after adding PPX (10 μM, 3 h; CQ+PPX), LC3-positive vesicles were detected in *DRD3*- but not in *DRD2*-HEK cells (compare CQ and CQ+PPX). Bar, 10 μm

Supplementary Figure 3



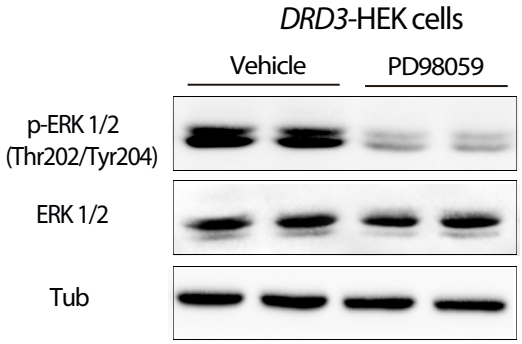
Western-blot for total and phosphorylated forms of AKT at Thr308 (p-AKT) and MTOR at Ser2488 (p-MTOR) in the striatum of WT mice treated with PPX. After 10 min of PPX treatment (left) both kinases were phosphorylated. After 6 days of PPX treatment (right), AKT phosphorylation returned to basal levels but MTOR phosphorylation declined below basal levels.

Supplementary Figure 4



Clonogenic cell survival assay in *DRD3*-HEK cells treated with PPX or rapamycin (0.1-10 μM, 2 weeks). The clonogenic capacity was significantly reduced by rapamycin but not by PPX.

Supplementary Figure 5



Western blot for the total and phosphorylated form of ERK1/2 at Thr202/Tyr204 (p-ERK1/2) in *DRD3*-HEK cells treated with the MEK-ERK1/2 inhibitor PD98059 (25 μM, 1 h). PD98059 promoted a drastic decrease in ERK1/2 phosphorylation.