





Fig. S1 Expression of GFP in adult brains by *elav-GAL4* and *esg-GAL4*. **a** Temperaturecontrolled expression of *Syn* and *GFP* was achieved by co-expression of *esg-GAL4* with a temperature-sensitive version of the GAL4 inhibitor, Gal80^{TS} as described in Fig. 1a. Green: GFP; DG: dark-ground. Scale bar: 50 µm. **b** The number of GFP-positive cells labeled by TH-GAL4 in 28-day old flies. Mean \pm SEM; the *p*-values of survival curves were calculated using log-rank tests (using total fly numbers), and for category graphs using a one-way ANOVA with a Bonferroni multiple-comparison test. **P* < 0.05; ***P* < 0.01; ****P* < 0.001. а









Dpt

1.5

1.2

0.9

0.6

0.3

0.0

UASSYN

Relative gene expression







GF

Fig. S2 Dysbiosis aggravates the pathology of Parkinson's disease in the intestine. **a** Verification of axenia of GF flies. Bacterial load was determined by plating the homogenate of fly midguts with 1: 1,000 dilution on LB agar plates. Representative images are shown. CR: conventionally reared; GF: germ free. **b** The quantification of cell numbers in esg-positive cell clusters in the anterior midgut. **c** Fluorescence intensity of anti-Dlg signals in intestinal cells. d Activation of intestinal immunity by intestinal α -syn was dampened by antibiotics cocktail. Antimicrobial peptide gene expression of middle intestines of 28-day-old *Drosophila* using qPCR. *Dpt, Diptericin; Attc, Attacin C; Drs, Drosocin. n* = 4.



CR

GF

Fig. S3 Intestinal α -syn triggers the DUOX-ROS-JNK pathway. **a** Fluorescence intensity of anti-p-JNK signals in intestinal cells was calculated. n = 60 for each. **b** The percentage of ISC and enterocytes (EC) in total p-JNK-positive cells. n = 236.