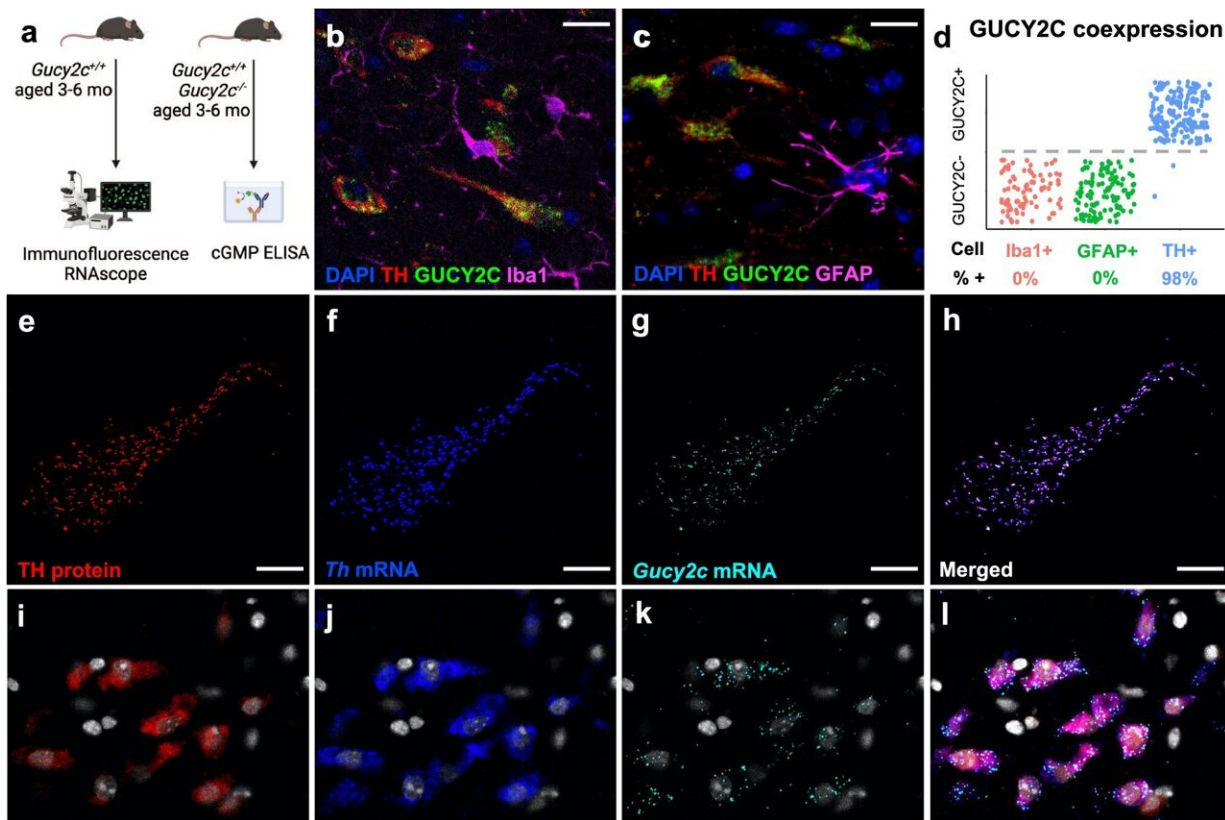


# Gut protein may protect brain cells in Parkinson's disease

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Functional GUCY2C protein and mRNA are expressed by DA neurons within the SNpc. **a** Schematic of mice used for analyses. **b–d** Immunofluorescence staining reveals that guanylyl cyclase C (GUCY2C) protein is expressed in 98% of tyrosine hydroxylase (TH)+ neurons, but not in astrocytes or microglia, in the mouse midbrain ( $n = 3$ ). Scale bars represent 20  $\mu\text{M}$ . **e–l** Combined immunofluorescence and RNAscope identifies high levels of *Gucy2c* mRNA co-expressed with TH protein and mRNA. Scale bars represent 200  $\mu\text{M}$  (**e–h**) or 20  $\mu\text{M}$  (**i–l**). **m** *Gucy2c* mRNA is not expressed by TH-negative cells ( $n = 3$ ). **n**

*Gucy2c* mRNA is expressed at nearly a third of *Th* mRNA levels in DA neurons ( $n = 3$ ) as determined through RNAscope. **o** Treating *Gucy2c*<sup>+/+</sup>(WT), but not *Gucy2c*<sup>-/-</sup>(KO), SNpc with the GUCY2C agonist linaclotide (LIN), but not with inactive peptide control, upregulates intracellular cGMP production ( $n = 9-11$ ). Statistics were calculated using a two-tailed *t*-test (**m**) or a two-way ANOVA with a false discovery rate

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