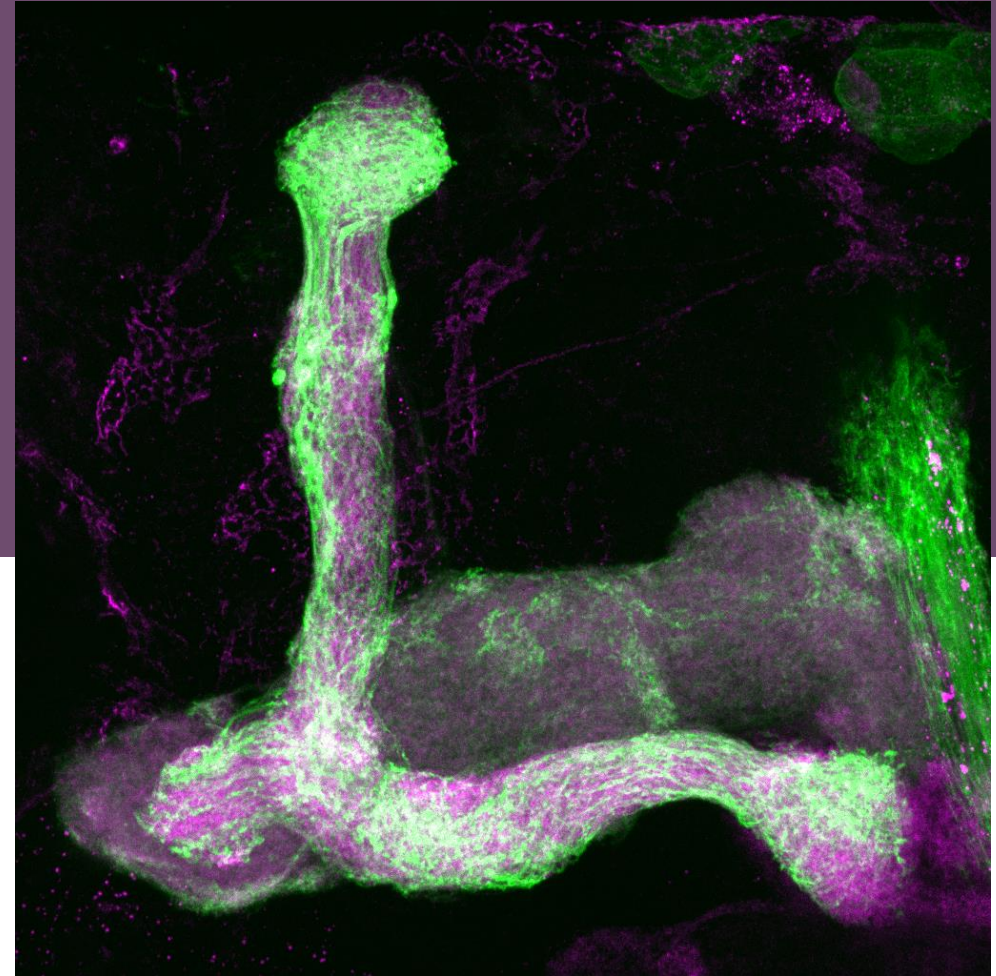


Investigating the mechanisms of DPR12-DIP δ interaction in the *Drosophila* mushroom body during development

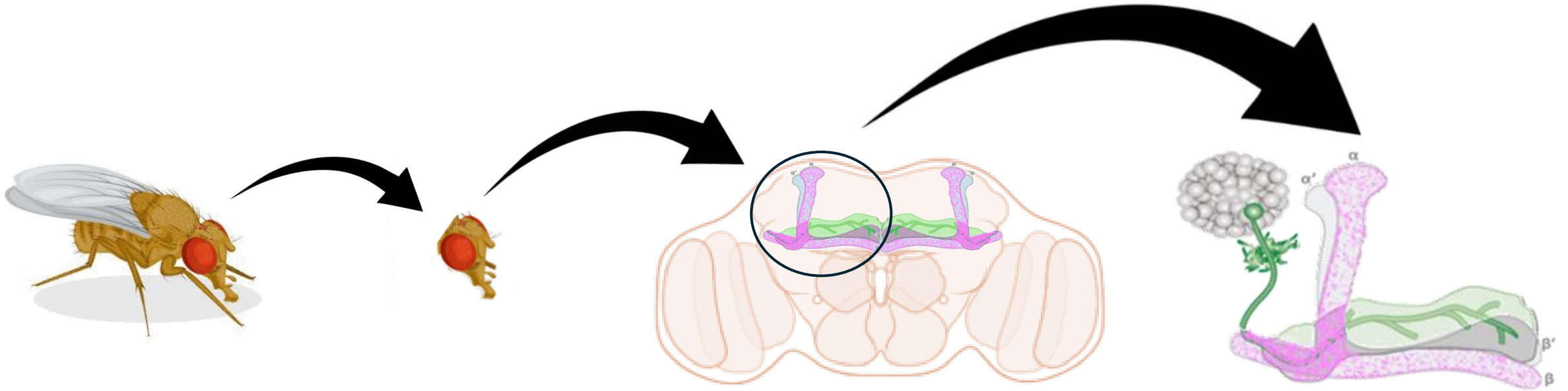
Lior Lin

Rotation at Oren Schuldiner's Lab

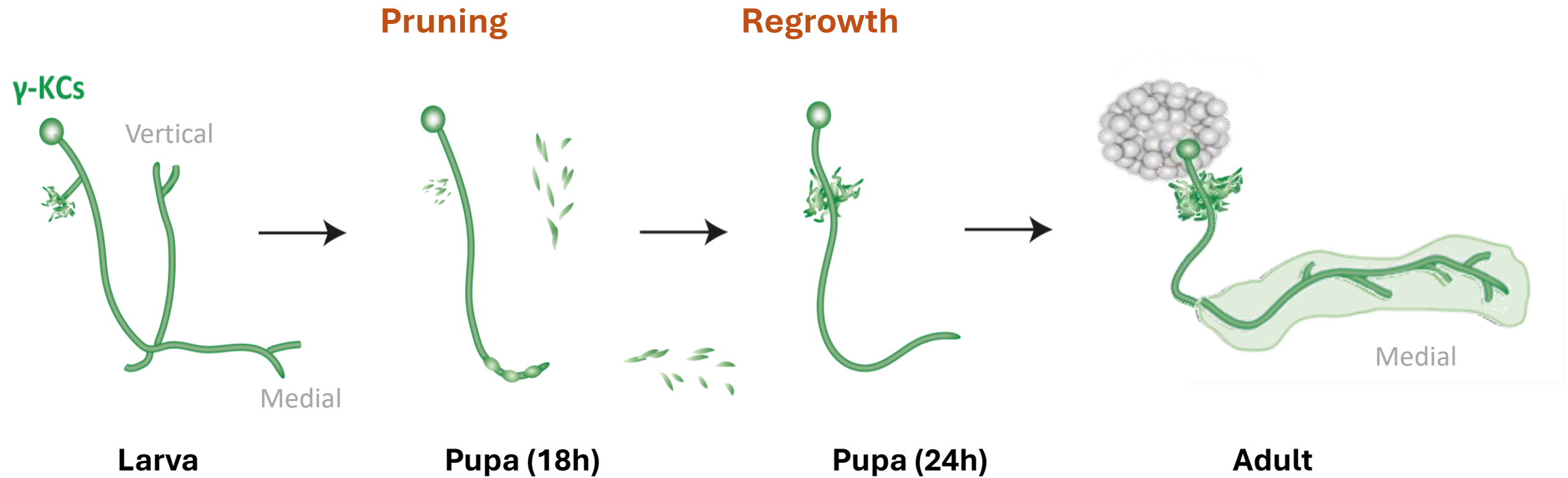
02/05/24



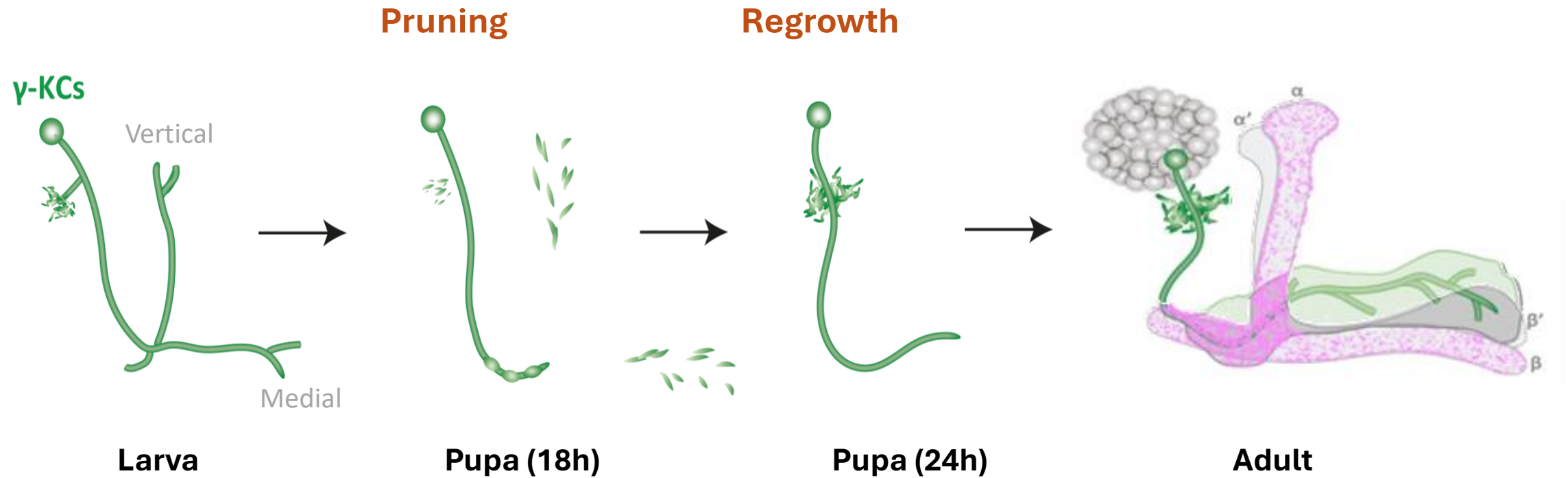
The *Drosophila*'s Mushroom Body



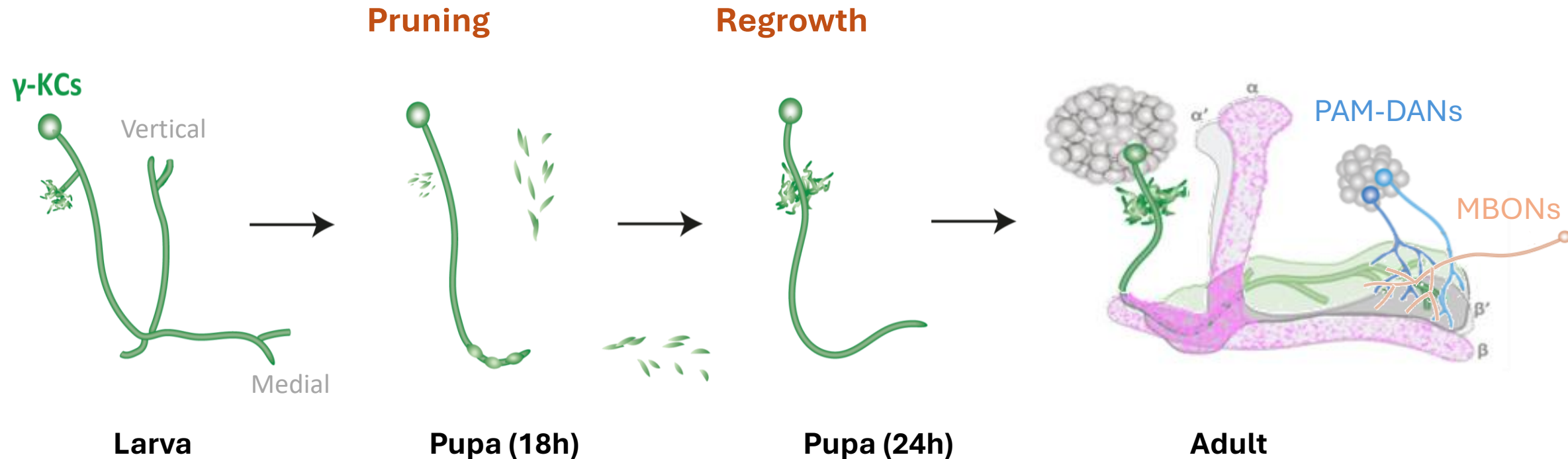
Stereotypical Neuronal remodeling of γ -Kenyon cells in the mushroom body



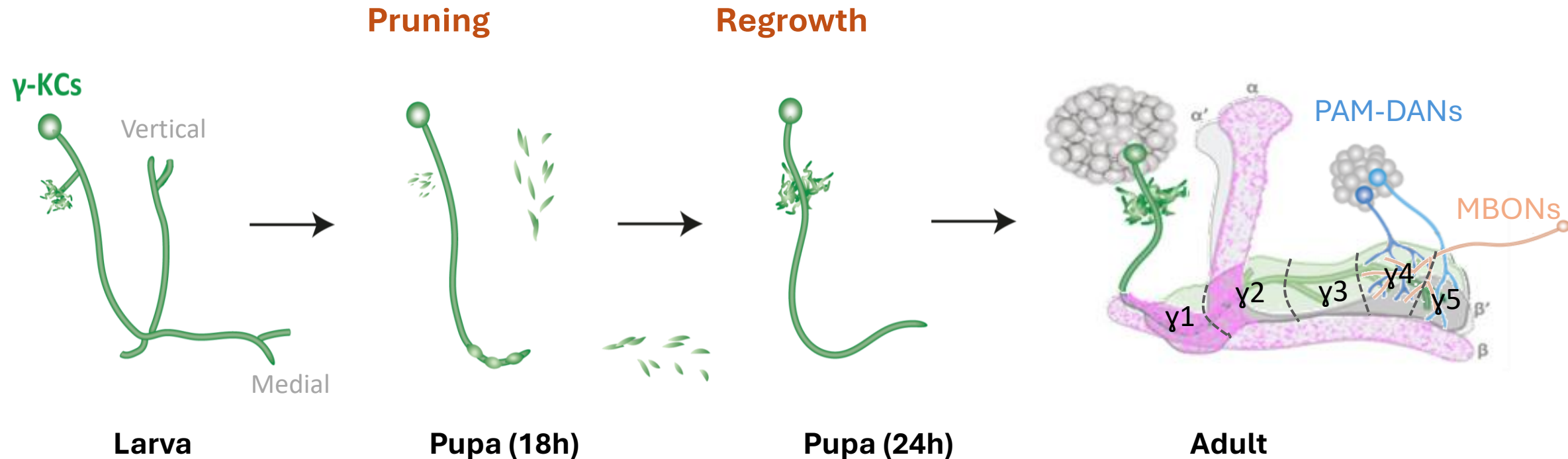
Stereotypical Neuronal remodeling of γ -Kenyon Cells in the mushroom body



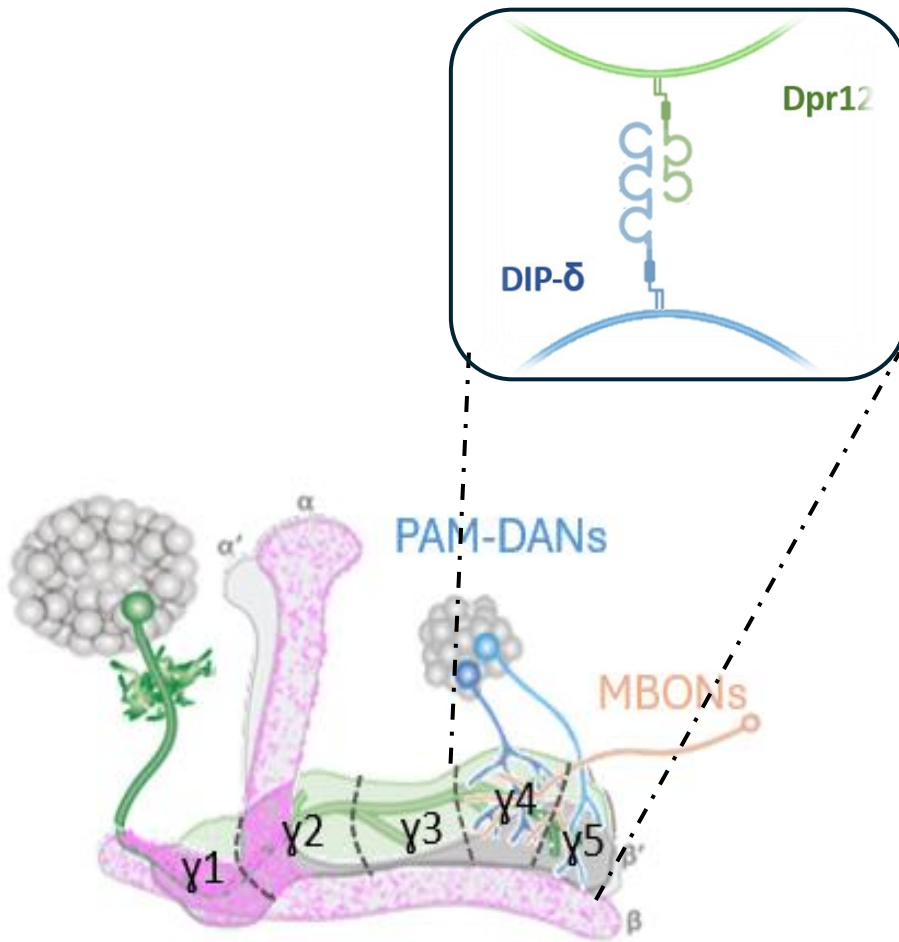
Stereotypical Neuronal remodeling of γ -Kenyon cells in the mushroom body



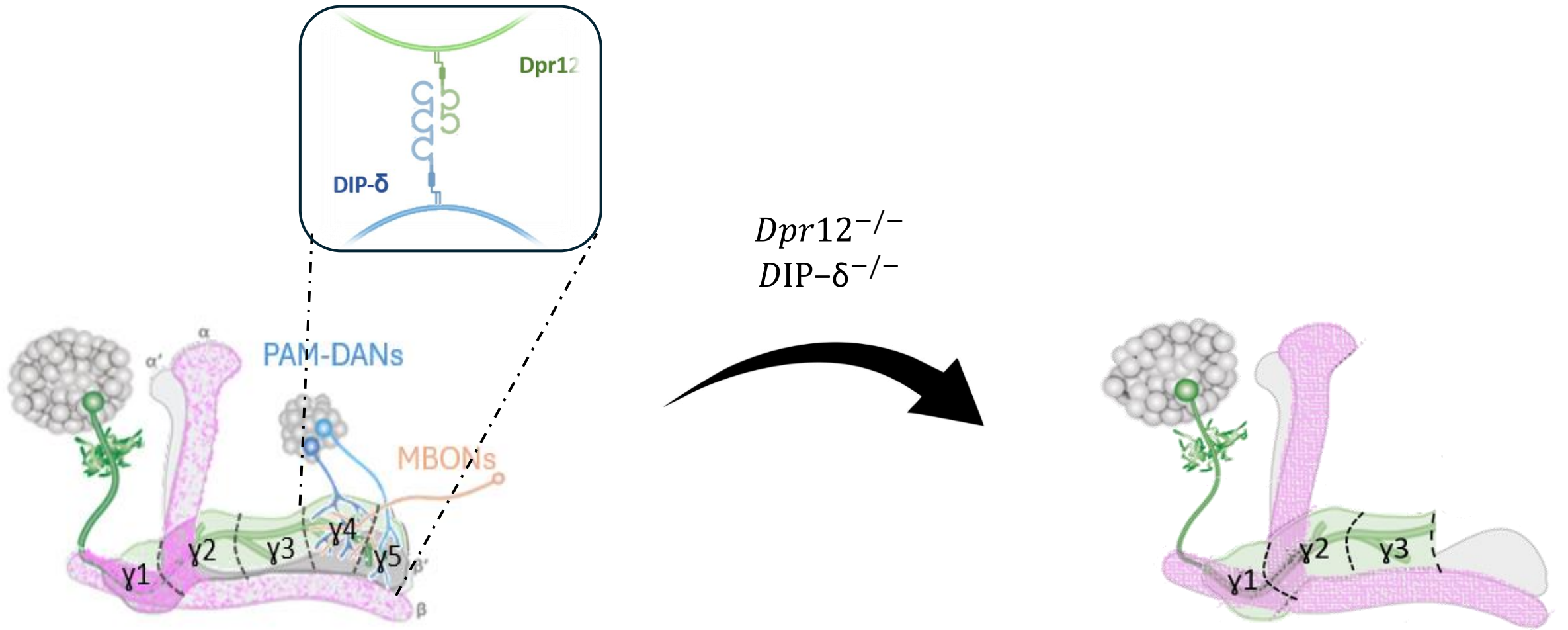
Stereotypical Neuronal remodeling of γ -Kenyon cells in the mushroom body



Dpr12 in γ -Kenyon Cells and DIP- δ in PAM-DANs are required for γ 4/5 formation

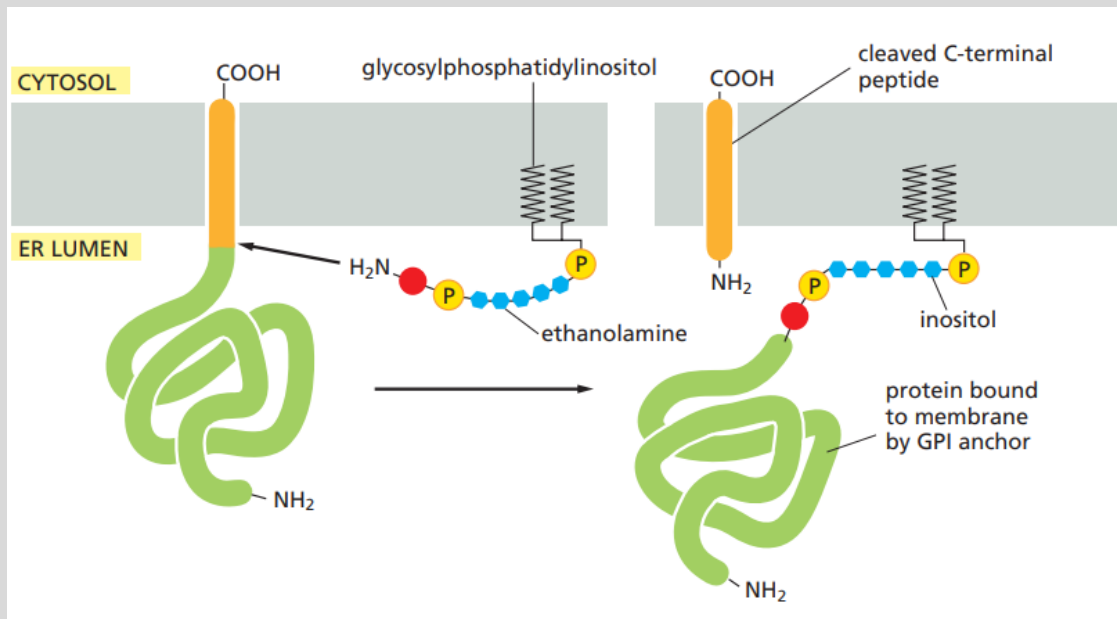


Dpr12 in γ -Kenyon Cells and DIP- δ in PAM-DANs are required for γ 4/5 formation



Dpr12 and DIP- δ are predicted to be GPI-anchored

The attachment of a glycosyl-phosphatidylinositol (GPI) anchor to a protein in the ER



Protein Specificity

Sequence

Dpr12

99.9%

...KFVQRRDHGMYECQVSTPTGIISHFVNLQVWVPEAFILGSGE
LHVDMGSTINLVCIEKSPTPPQYVYWQKNDRLINYVDSRRDITI
ETTPGPRTQSRLIIREPQVTDGNYTCSASNTEPASIYVFSKGD
NMAAISRRKTS**SADRLTHIFRSM LAPCLLLNTVVRHIFLT**

DIP- δ

100%

...QYGDGFGNYRCISKNSLGETEGSIRVYEIPLPSTPSKQVTHTTV
ESRENNIIPSSRNDTTKSLQTDVGYAMKNDLYPGSASSSSSSGGS
SSAASSSSSMQTSALPGGVAGNSLSSMGSKGSLAIGKSTFYTE
RPPNEY**YAASSVAGLLH RALLFGSGIYLTLL**

Ω site

GPI attachment signal

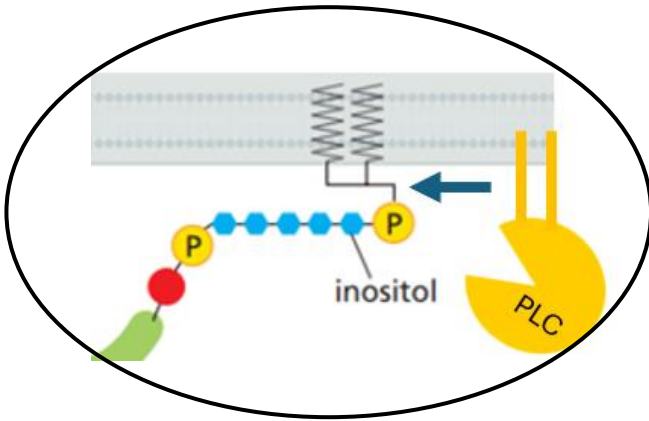
Research objective :

Screen for enzymes that potentially cleave the GPI-anchor
by silencing them in different subsets of neurons

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Phospholipase C (PLC)

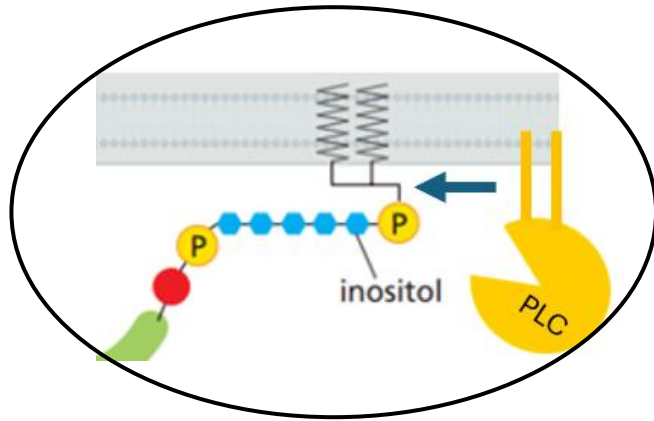


- NorpA
- Small wing (Sl)

Research objective :

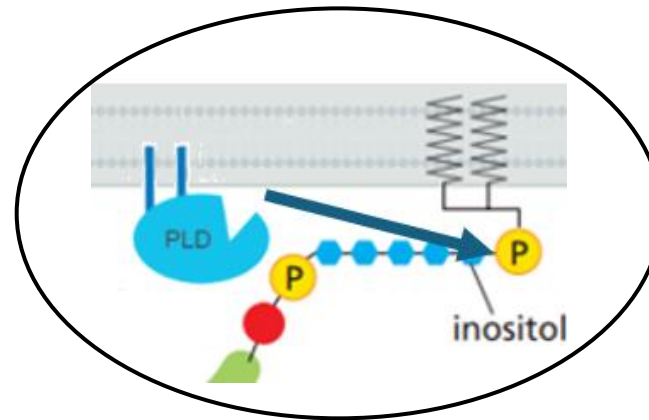
Screen for enzymes that potentially cleave the GPI-anchor by silencing them in different subsets of neurons

Phospholipase C (PLC)



- NorpA
- Small wing (Sl)

Phospholipase D (PLD)

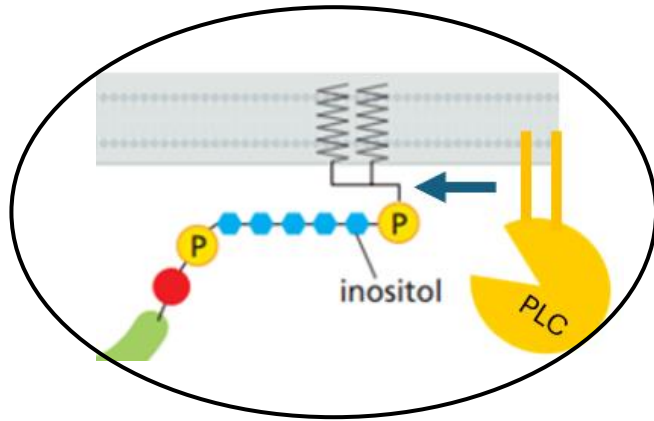


- PLD

Research objective :

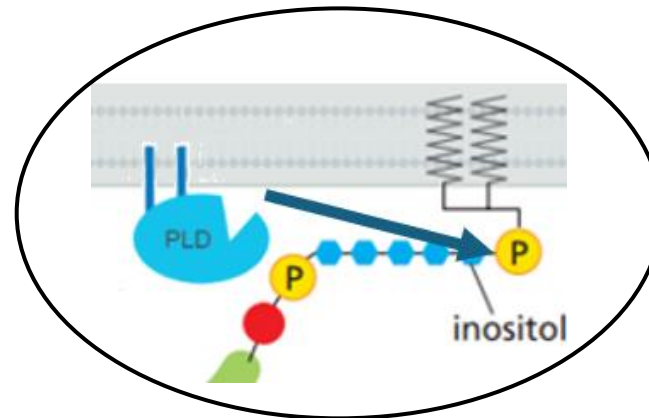
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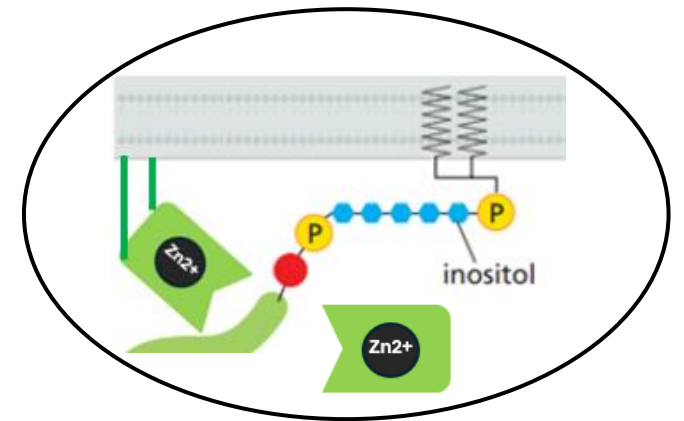
- NorpA
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Phospholipase D (PLD)



- PLD

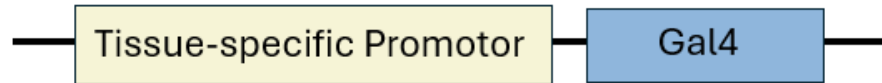
ADAM Family



- Meltrin
 - Kuzbanian
 - Kuzbanian like
 - Tace (ADAM 17)
- } (ADAM 10)

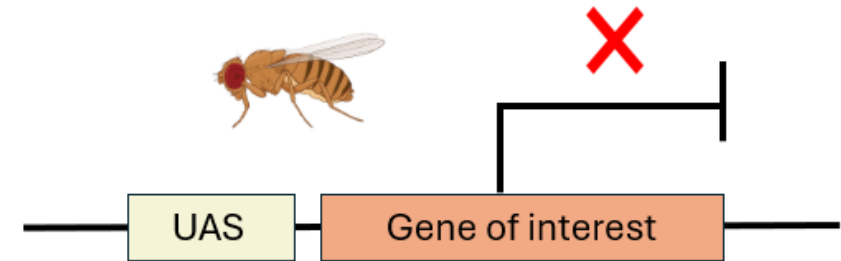
The UAS-Gal4 binary system allows tissue-specific transgene expression

Gal4 Driver Line



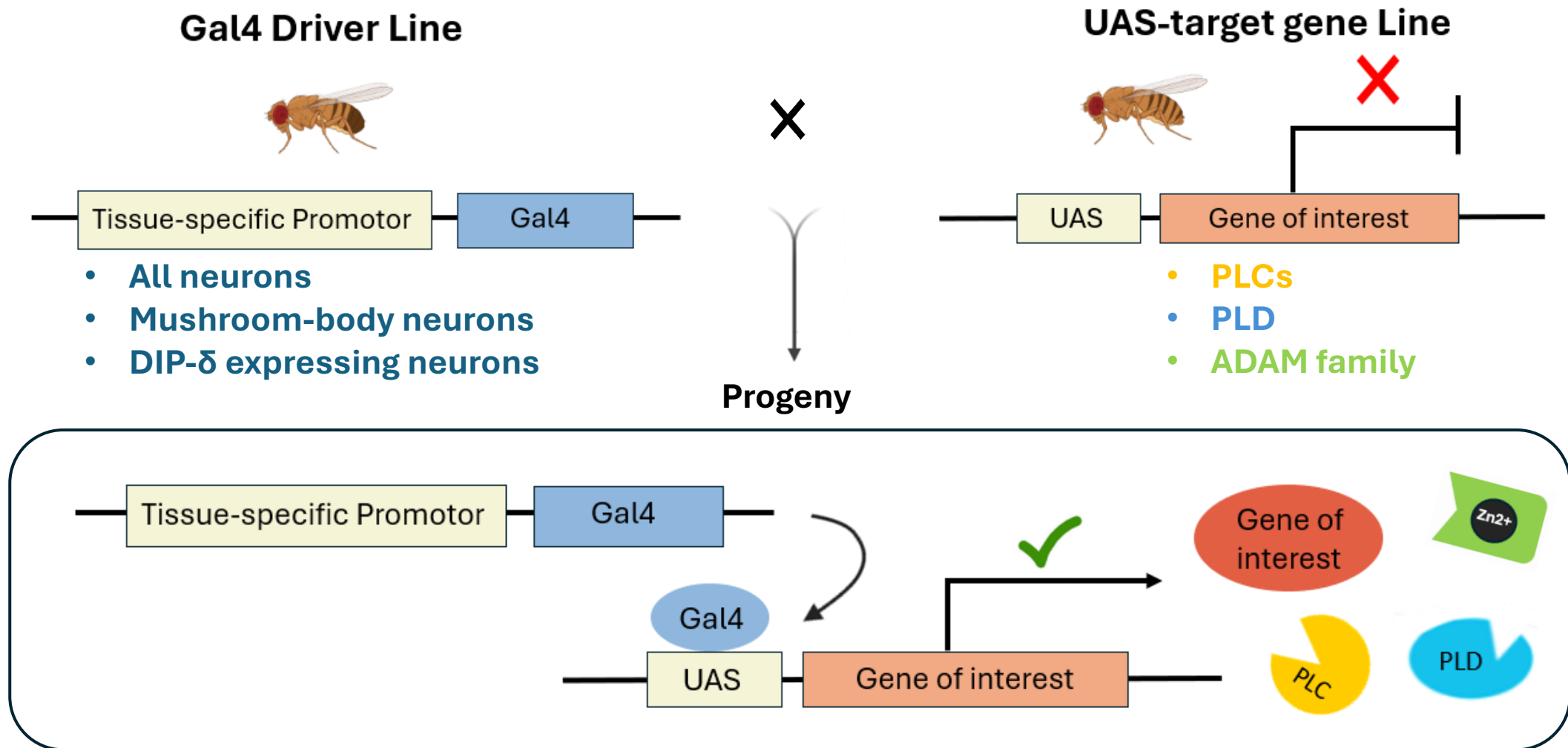
- All neurons
- Mushroom-body neurons
- DIP- δ expressing neurons

UAS-target gene Line



- PLCs
- PLD
- ADAM family

The UAS-Gal4 binary system allows tissue-specific transgene expression



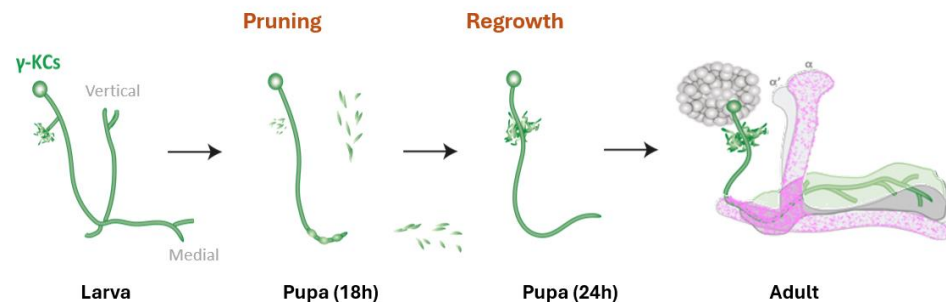
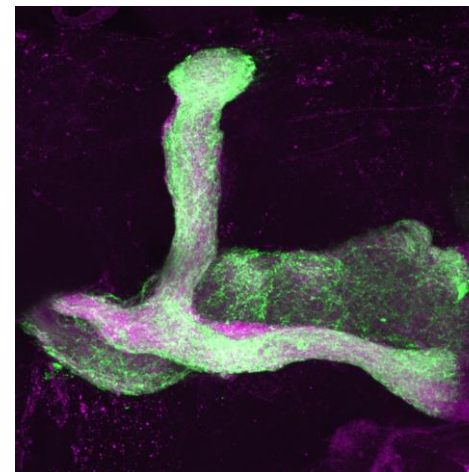
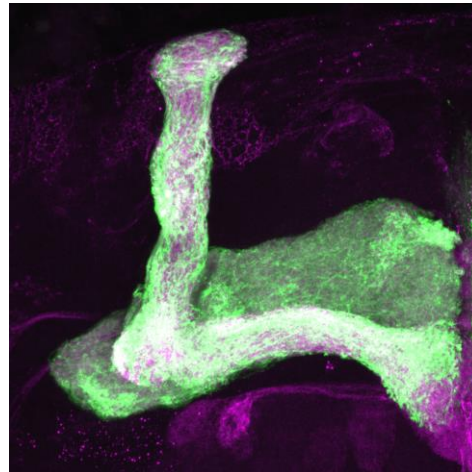
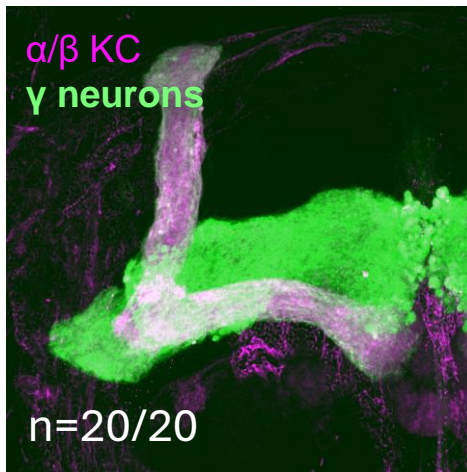
Small wing (Sl) PLC KD in all neurons results in membrane blebbing at the γ -lobe border

57C10-Gal4
All neurons

OK107-Gal4
MB neurons

DIP δ -T2A-Gal4
DIP δ neurons

Sl RNAi



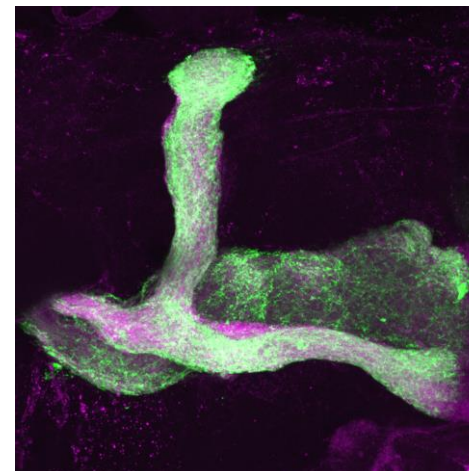
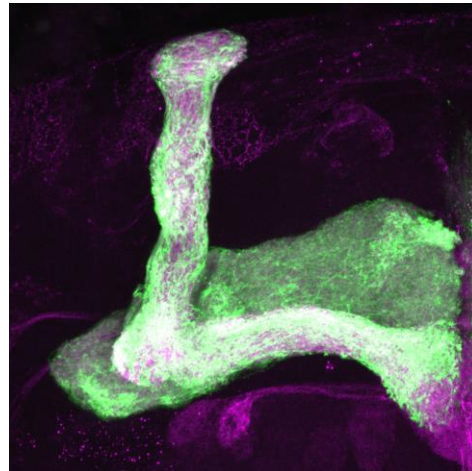
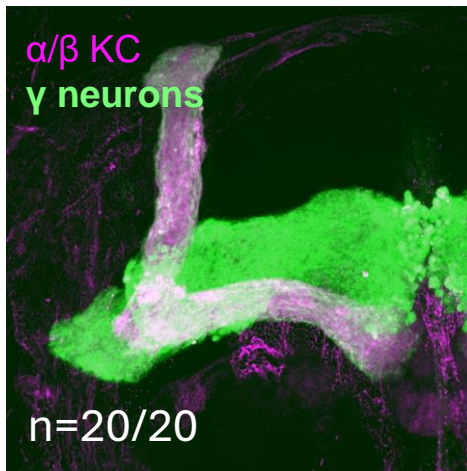
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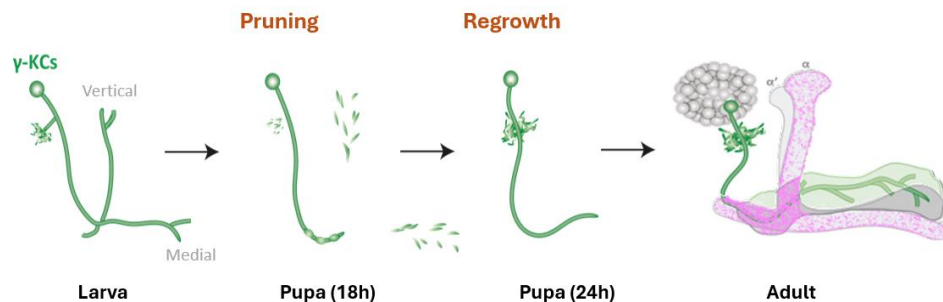
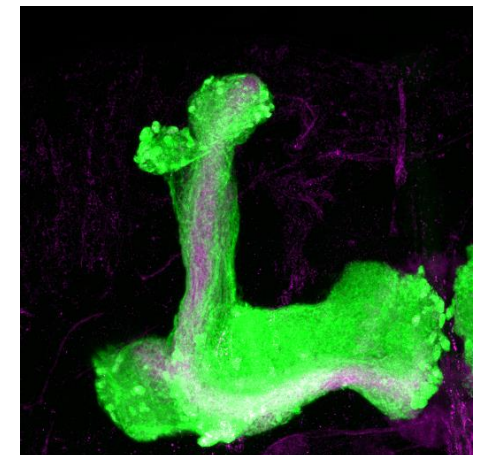
DIP δ -T2A-Gal4
DIP δ neurons

Sl RNAi

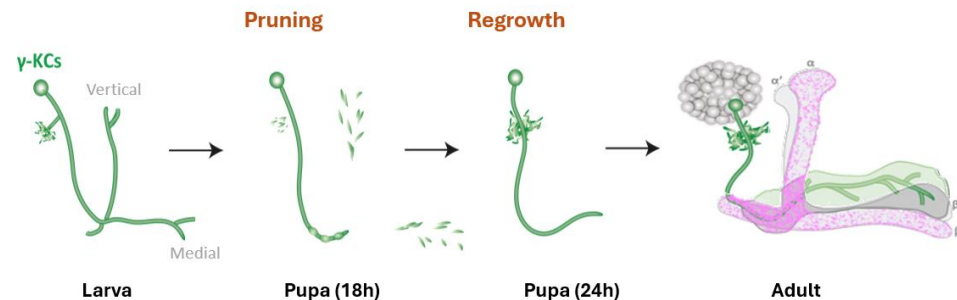
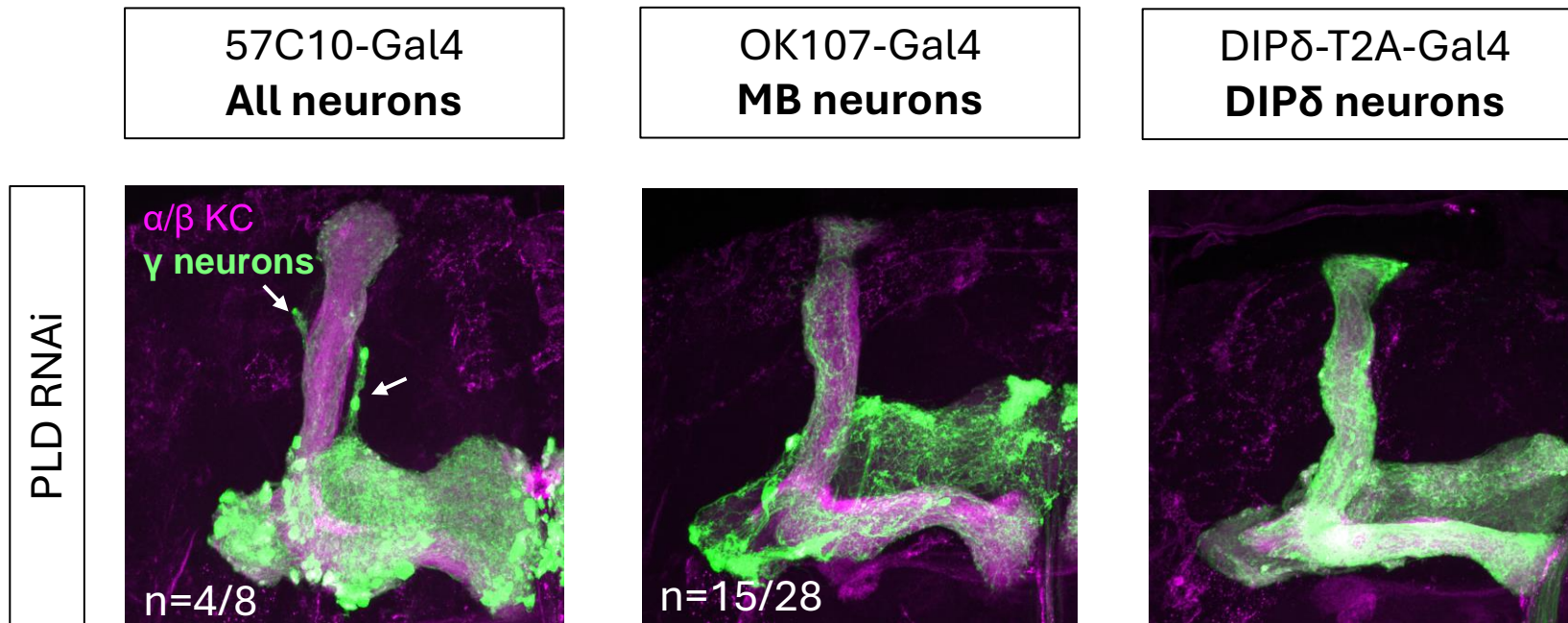


OK107-Gal4

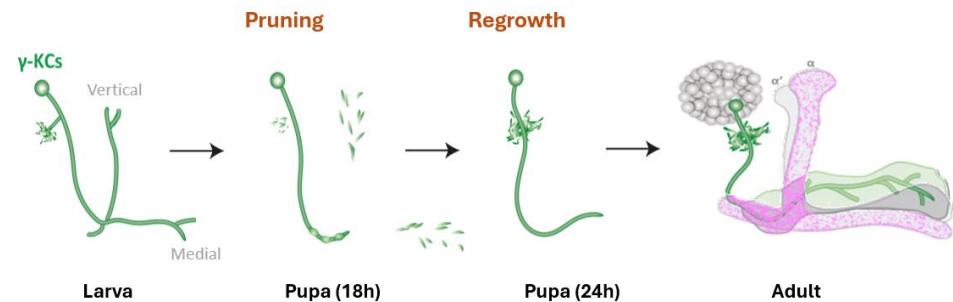
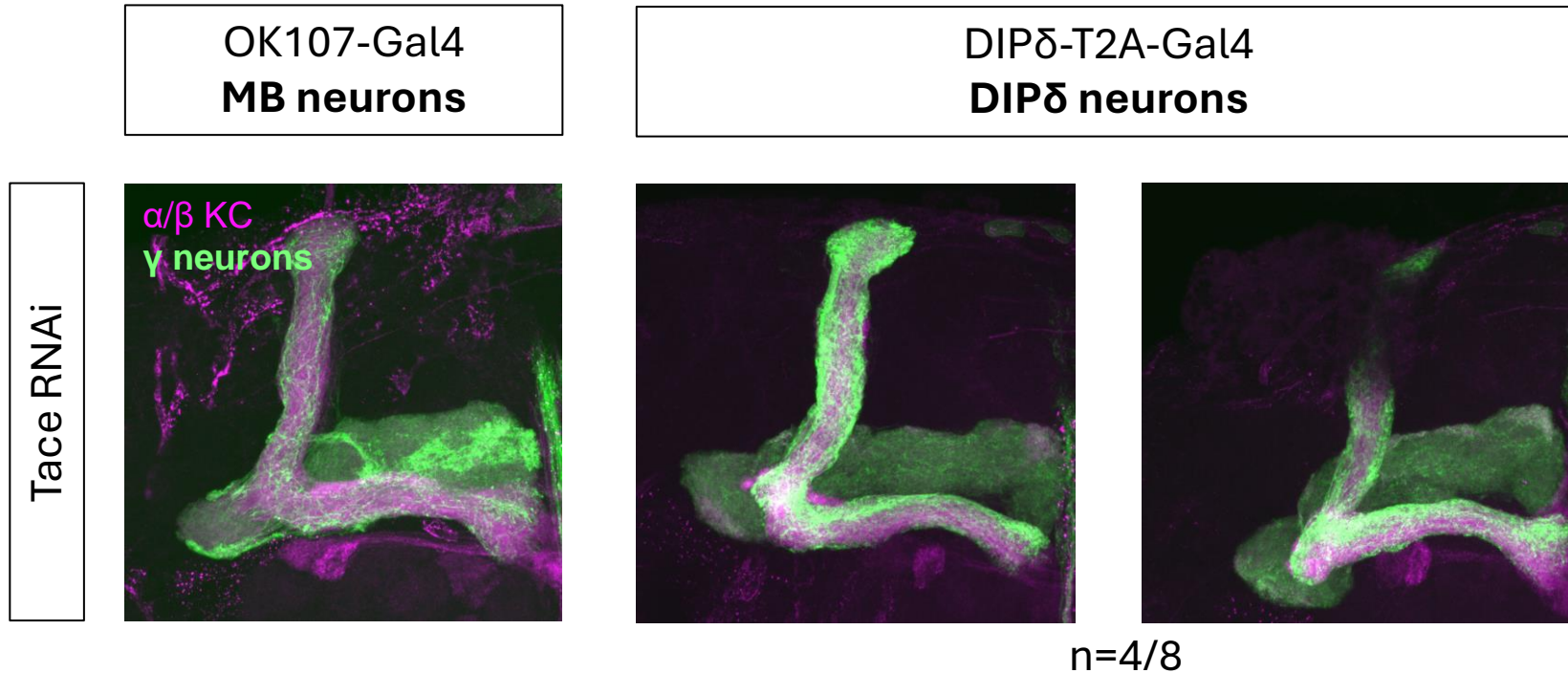
DIP- β RNAi



PLD KD results in membrane blebbing and sparsening of the γ -lobe



Tace (ADAM 17) KD in DIP- δ expressing neurons shows γ -lobe regrowth abnormality



Screen summary

We did not observe a distinct γ -lobe zone formation regrowth defect

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- Some RNAi lines have limited efficiency.
- Post-translation modifications on the GPI-anchor might limit cleavage effectivity.
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We also observed pruning defects and different γ -lobe abnormalities such as membrane blebbing and potentially proliferation defects.

THANK YOU !!

