The mysteries of neuronal remodeling

Peng Qionglin, Sun Mengshi and Su Xiangbin

2019–11–29

The mysteries of neuronal remodeling

- Axon pruning of mushroom body (MB) γ neurons (PQL)
- Dendrite remodeling of dendritic arborization (da) neurons (SMS)
- Neuronal remodeling of CCAP/Bursicon neurons (SXB)

Axon pruning of mushroom body (MB) γ neurons

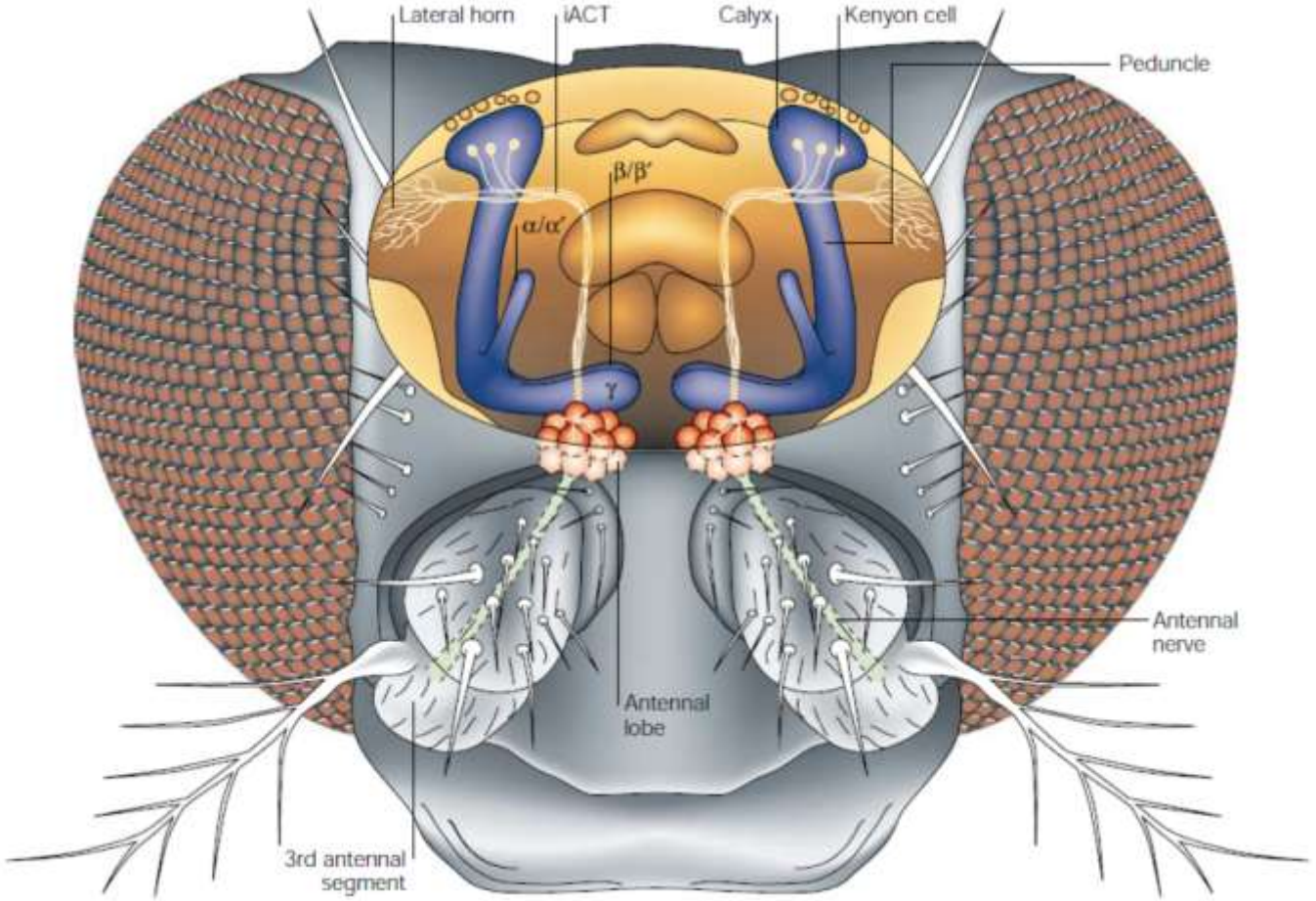
- Overview
- Mosiac analysis
- Development of the *Drosophila* mushroom bodies
- Signaling pathways inducing MB γ neurons pruning

Peng Qionglin

2019-11-29

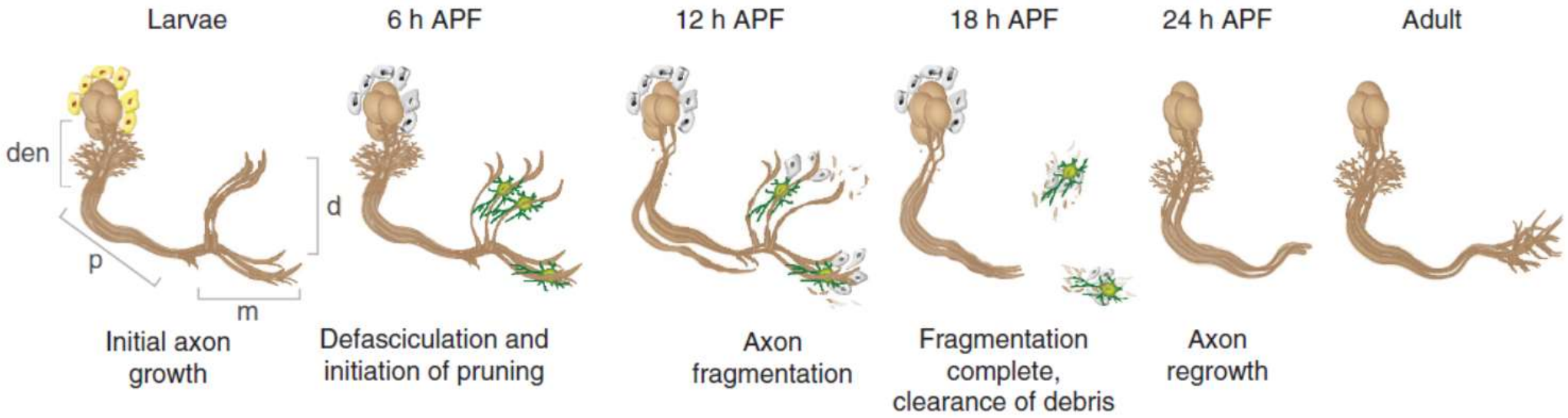
Mushroom bodies (MB)

The insect center for olfactory learning and memory



Heisenberg, M. (2003)

Mushroom body (MB) γ neurons undergo stereotypic remodeling



Yaniv, S. P. and O. Schuldiner (2016)

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Liqun Luo, PhD

Investigator / 2005—Present

Dr. Luo is a professor of biology at Stanford University and a professor of neurobiology by courtesy at Stanford University School of Medicine.

INSTITUTION
Stanford University

The Luo Lab

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CURRENT RESEARCH

Liqun Luo seeks to ur
information and how
developed genetic to
investigate these prob

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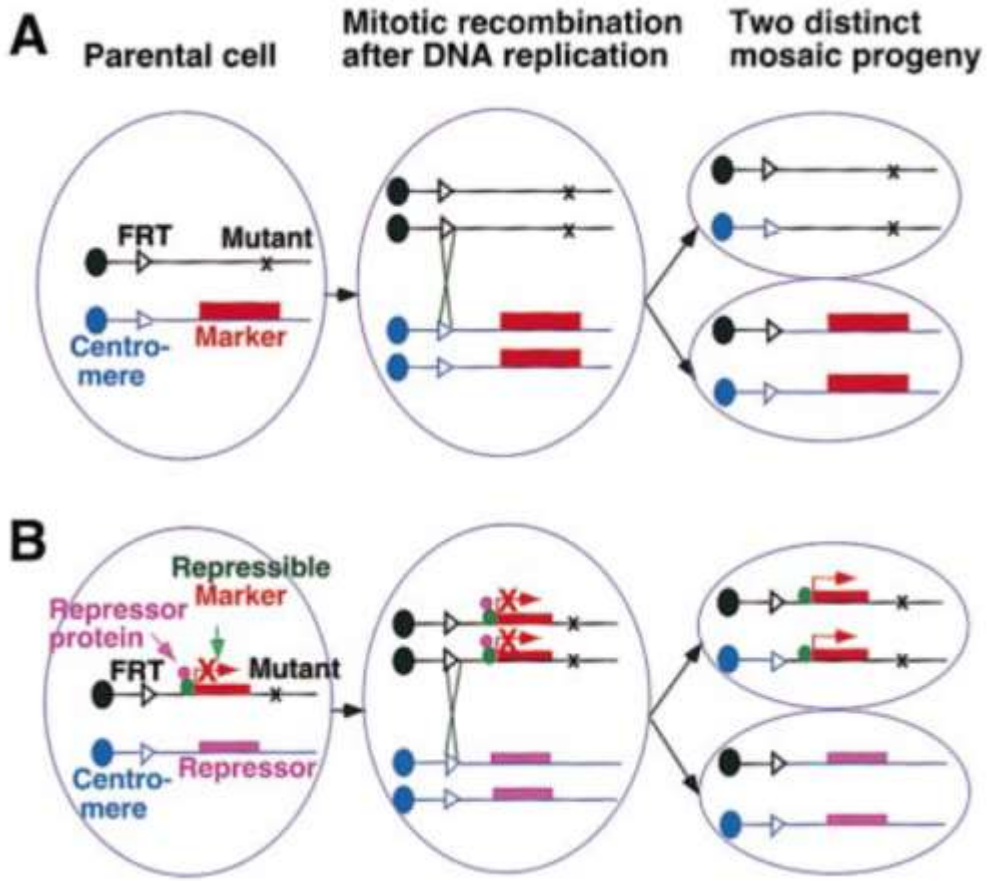
Lee (Tzumin) Lab / We are keen to determine the cellular complexity of the brain, to elucidate how numerous distinct neurons can derive from a limited number of progenitors, and to possibly reengineer the brain for understanding its structure, function and evolution.

Different designs for marking mutant clones in a mosaic organism

Conventional mosaic analysis



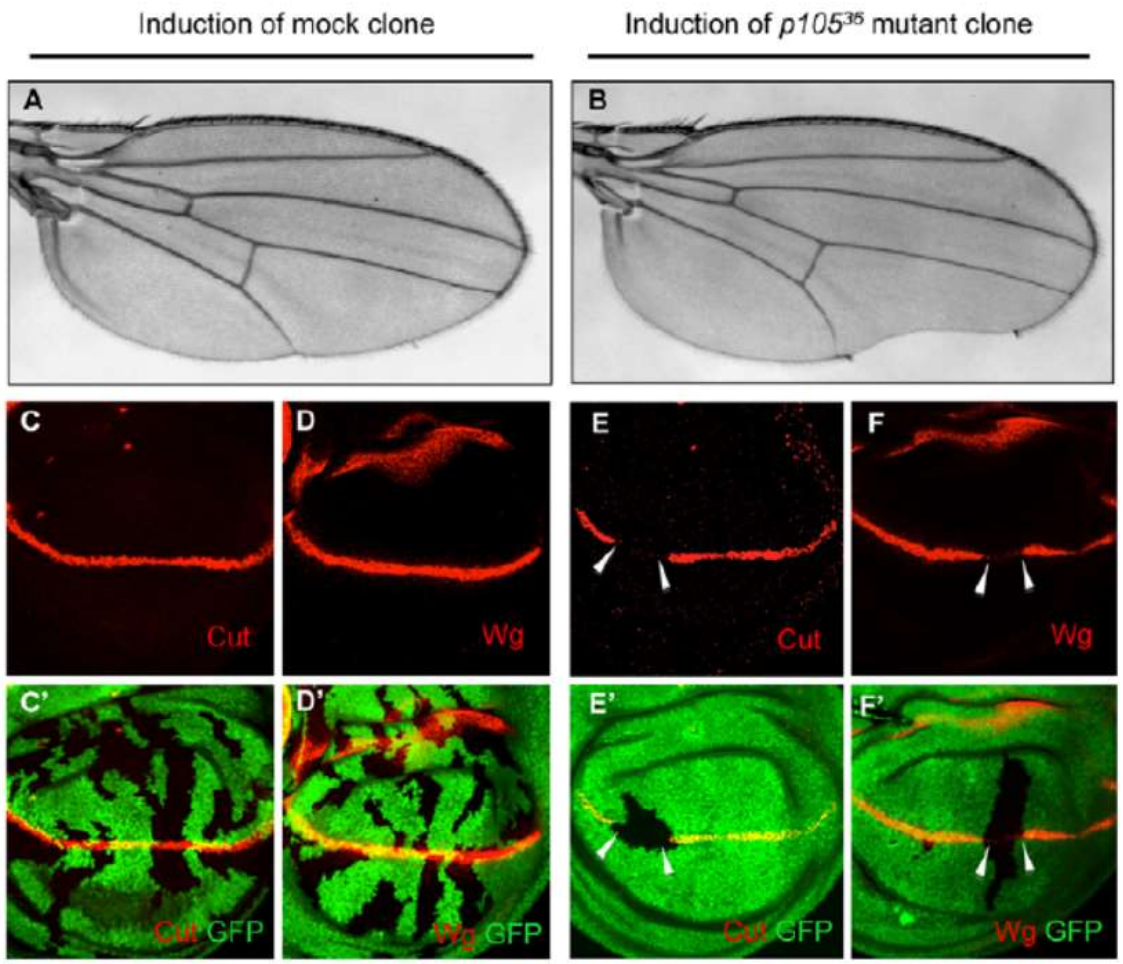
FRT, Mutant, Marker

MARCM (mosaic analysis with a repressible cell marker)

FRT, Mutant, Repressor, repressible Marker

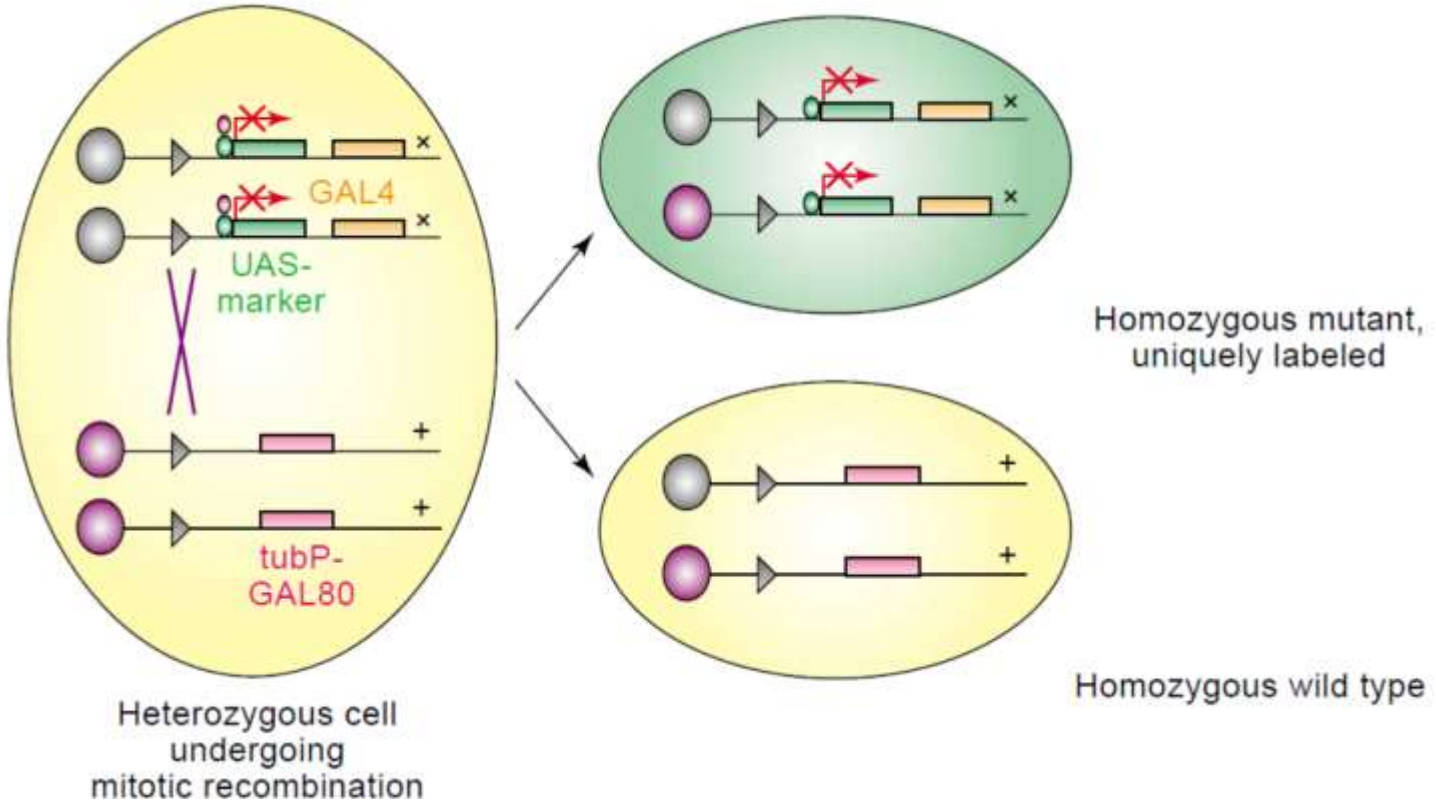
Lee, T. and L. Luo (1999)

Examples-Conventional mosaic analysis



Yu, Z., et al. (2013)

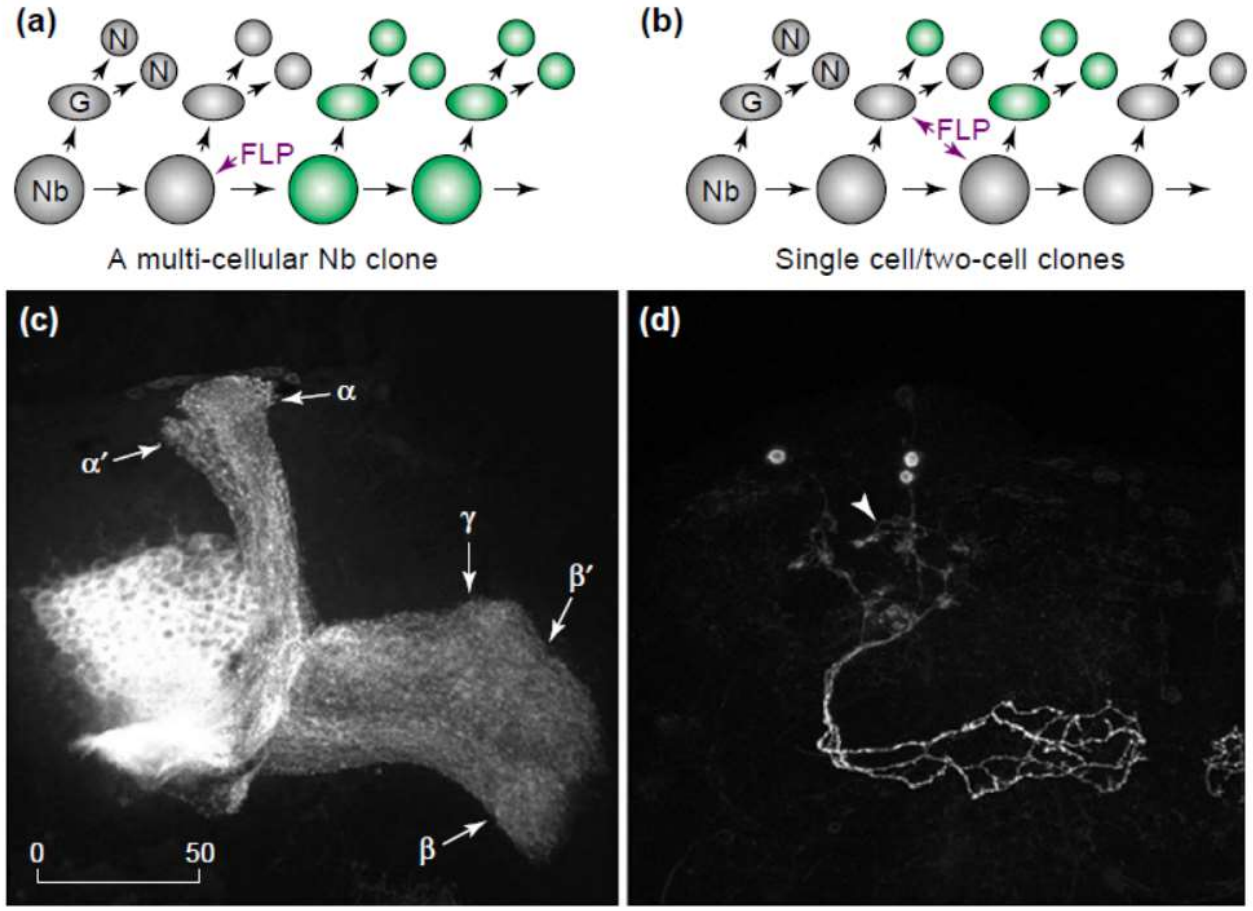
Genetic basis of the mosaic analysis with a repressible cell marker (MARCM) system



Lee, T. and L. Luo (2001)

Examples-MARCM

Cell lineage analysis

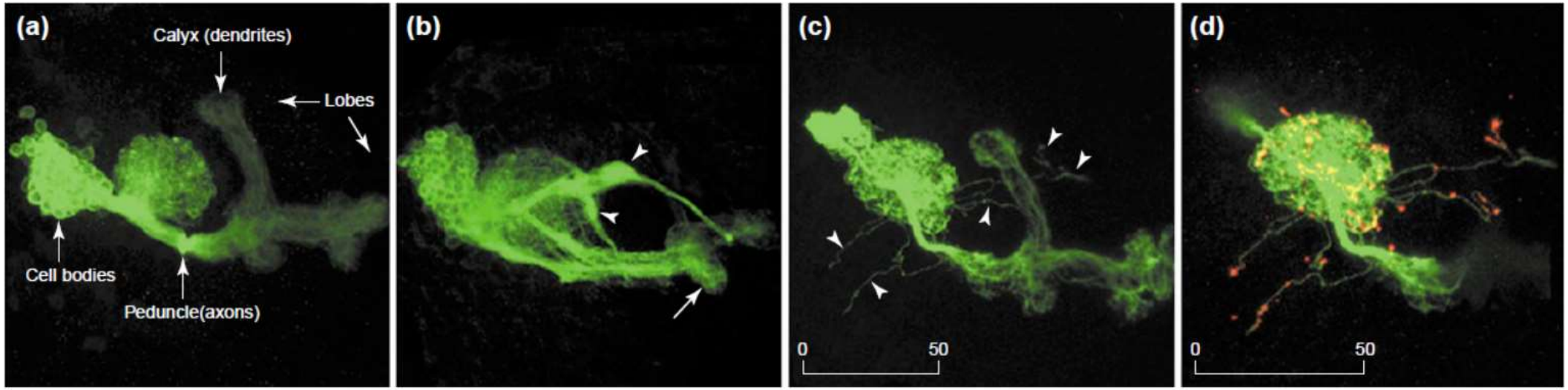


Nb: neuroblast
GMC: ganglion mother cells
N: neurons

Lee, T. and L. Luo (2001)

Examples-MARCM

Functional analysis of candidate pleiotropic genes

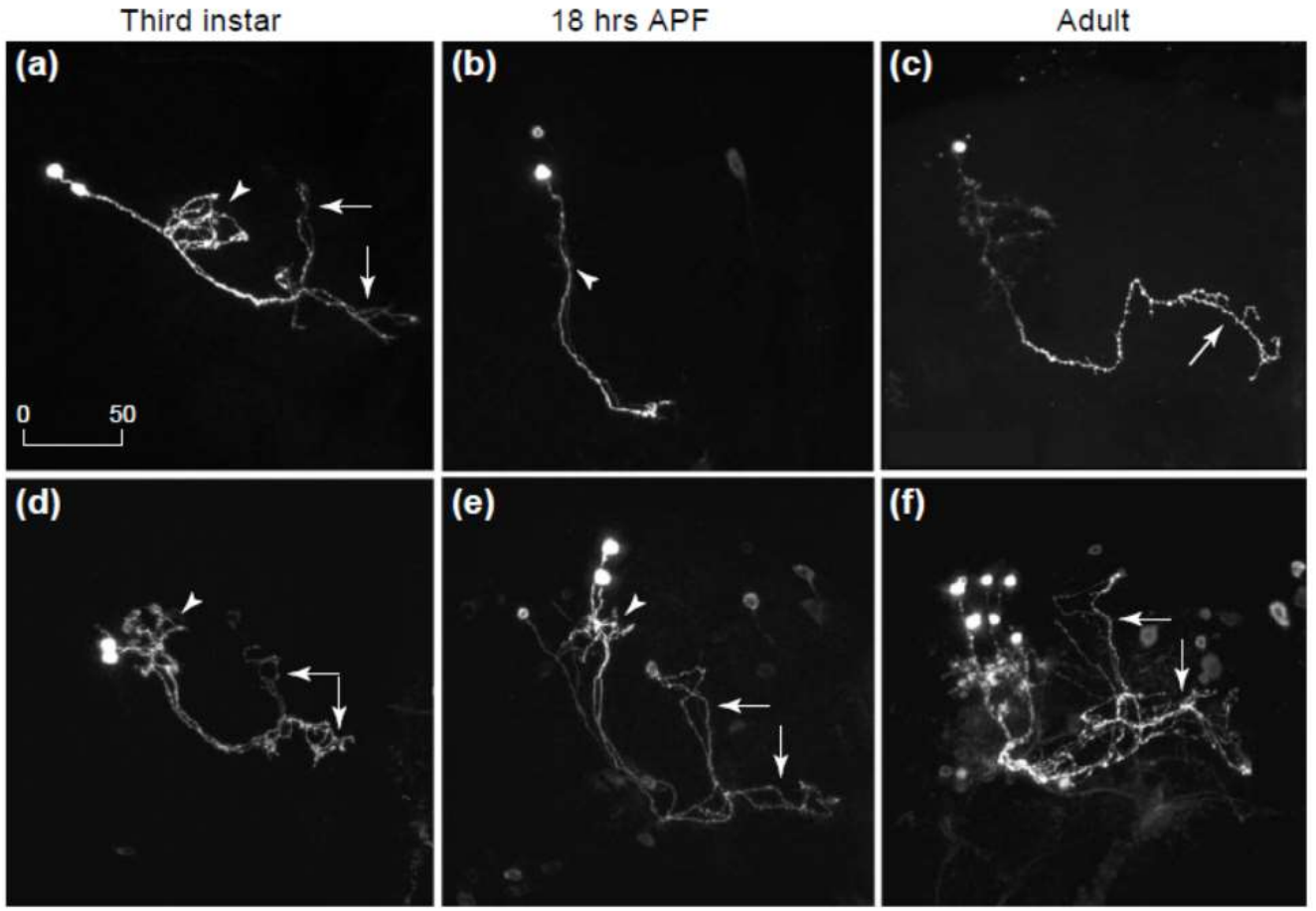


wild-type clone *short stop* mutant clone *RhoA* mutant clone

Lee, T. and L. Luo (2001)

Examples-MARCM

genetic screen to identify new genes

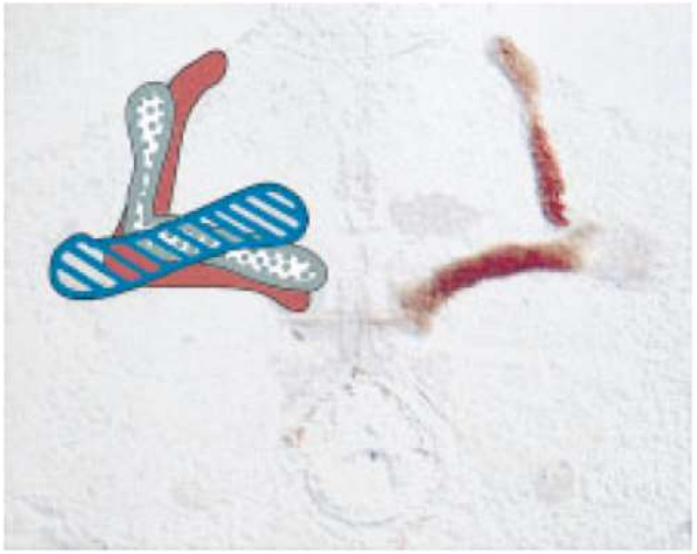


wild type clone

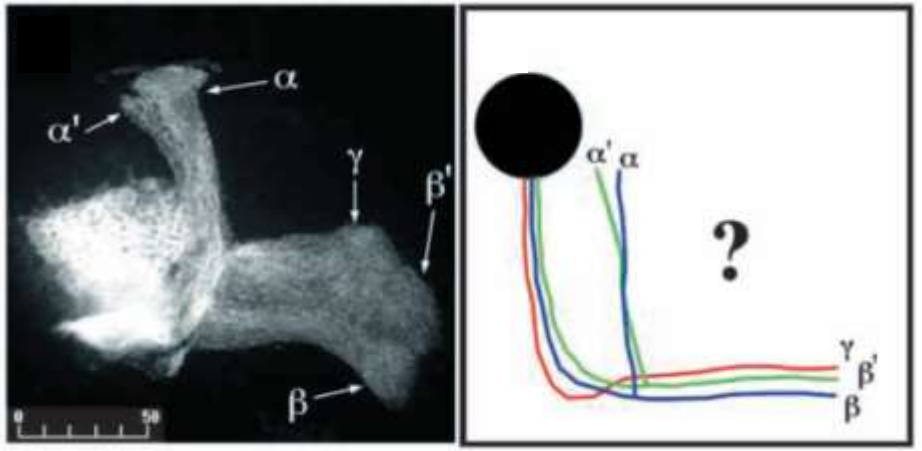
usp mutant clone
ultraspiracle, encoding a co-receptor for the nuclear hormone ecdysone

Lee, T. and L. Luo (2001)

How are three types of MB neurons generated from a single neuroblast ?



Crittenden, J. R., et al. (1998)



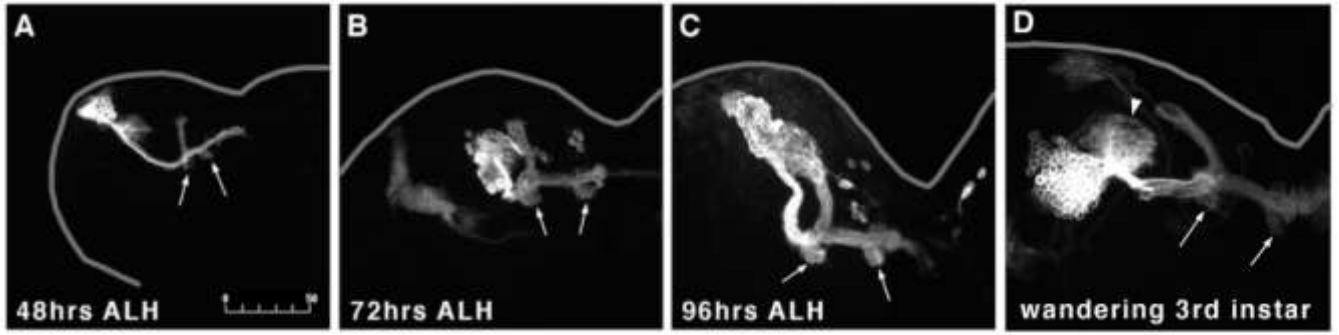
Lee, T., et al. (1999)

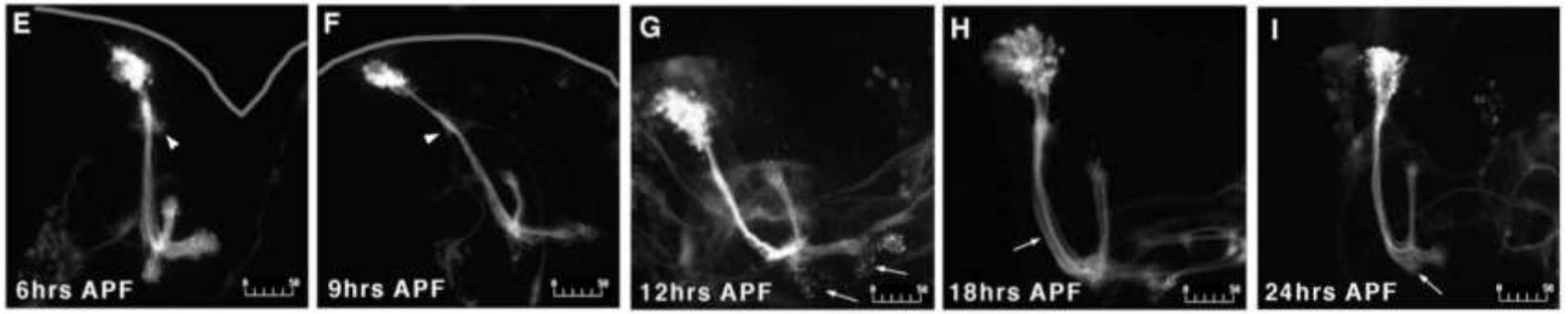
Marking the entire morphology of mushroom body (MB) clones

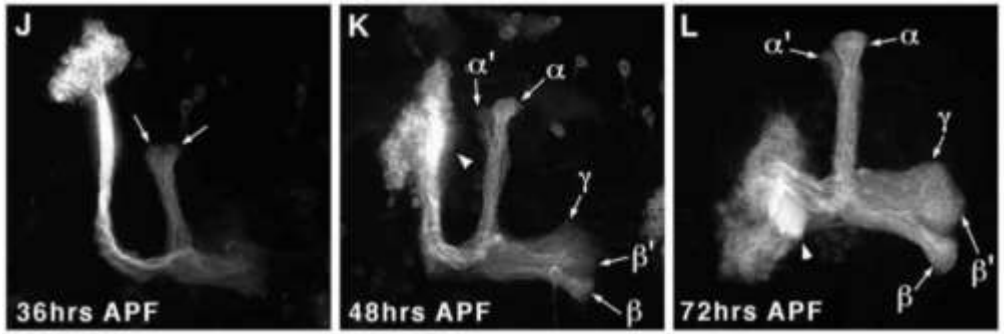
larva

during metamorphosis

pupal stage







NHL: newly hatched larvae

APF: after puparium formation

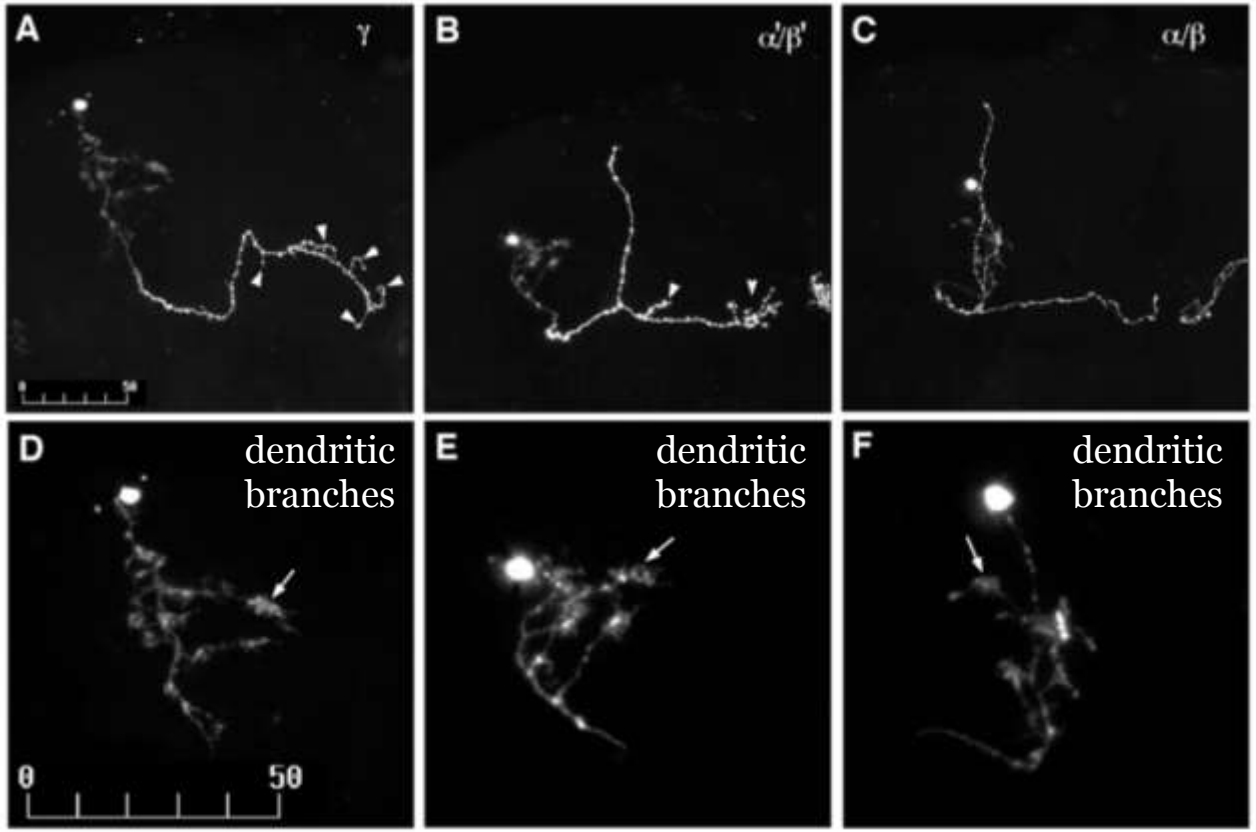
Lee, T., et al. (1999)

Morphological characterization of three types of MB neurons

γ neuron
born during the early larval stage

α/β neuron
born during the late larval stage

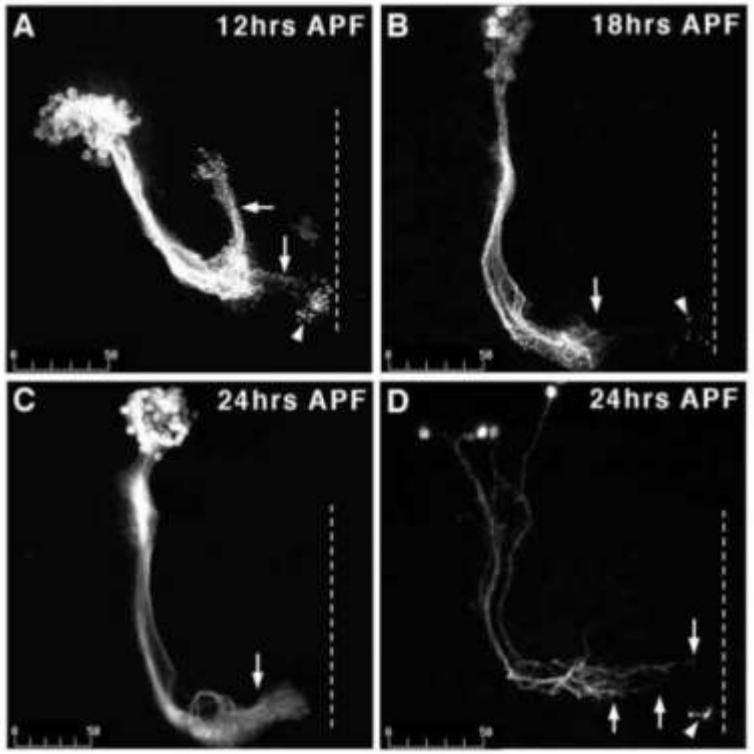
α'/β' neuron
born during the pupal stage



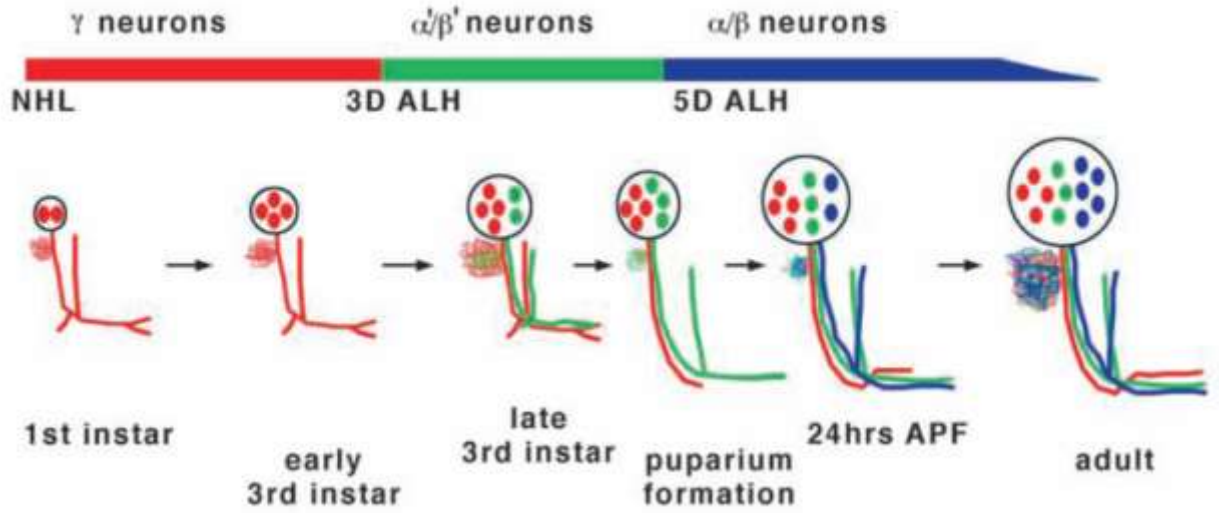
Lee, T., et al. (1999)

Marking the entire morphology of mushroom body (MB) clones

Axon reorganization of γ neurons during metamorphosis



Different behaviors of γ, α'/β' and α/β neurons during metamorphosis

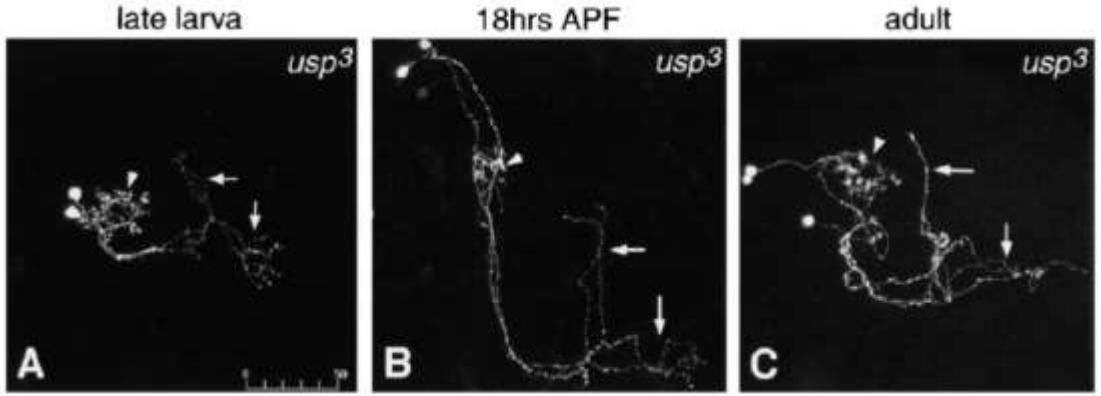


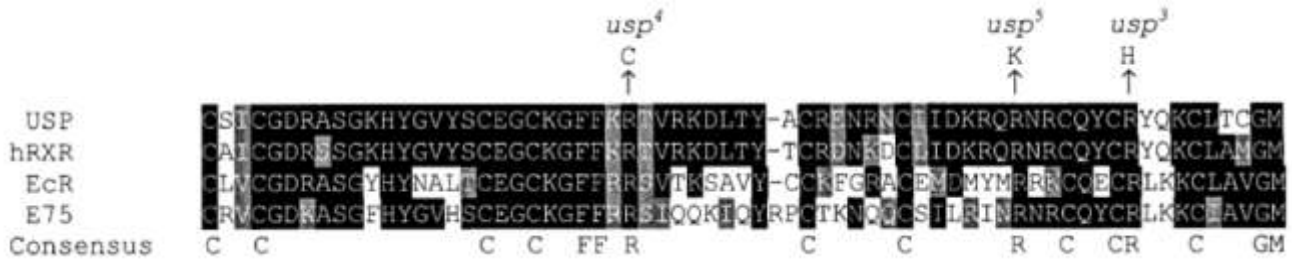
Lee, T., et al. (1999)

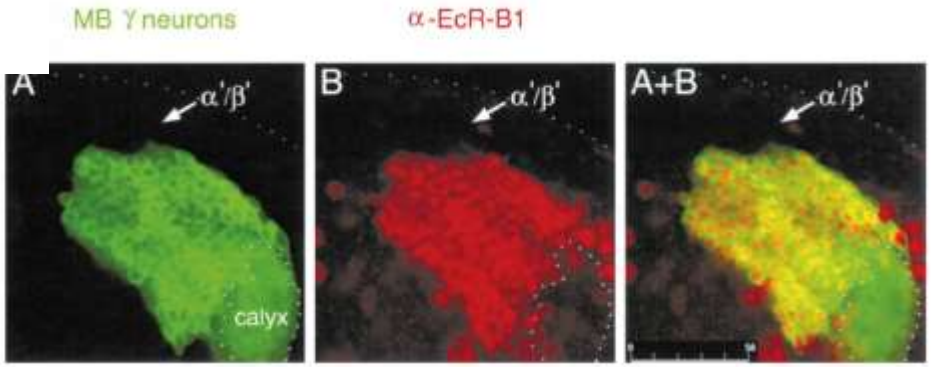
How maturing neurons reorganize their projections?

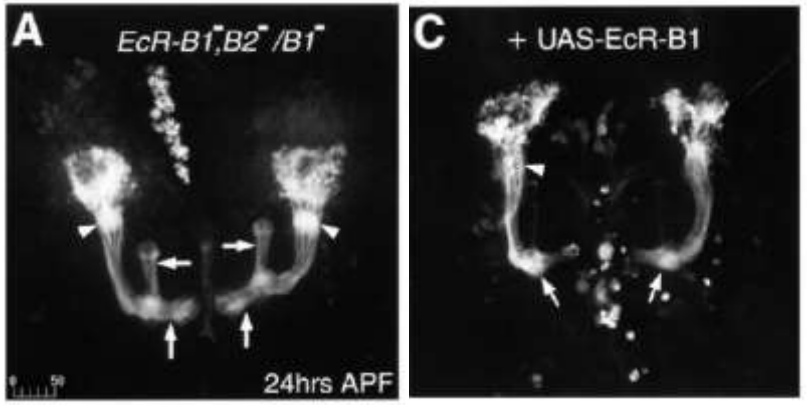
Neuron, Vol. 28, 807–818, December, 2000, Copyright ©2000 by Cell Press

Cell-Autonomous Requirement of the USP/EcR-B Ecdysone Receptor for Mushroom Body Neuronal Remodeling in *Drosophila*









Lee, T., et al. (2000)

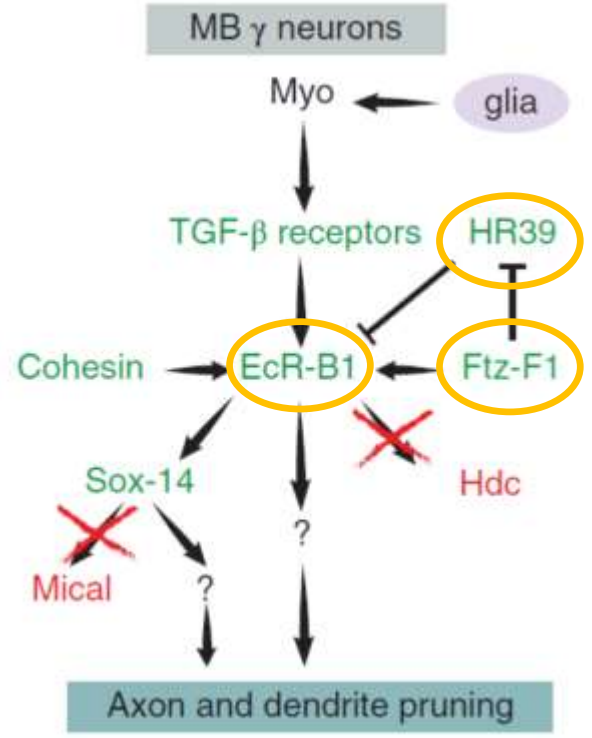
ARTICLES

nature neuroscience

ftz-f1 and *Hr39* opposing roles on *EcR* expression during *Drosophila* mushroom body neuron remodeling

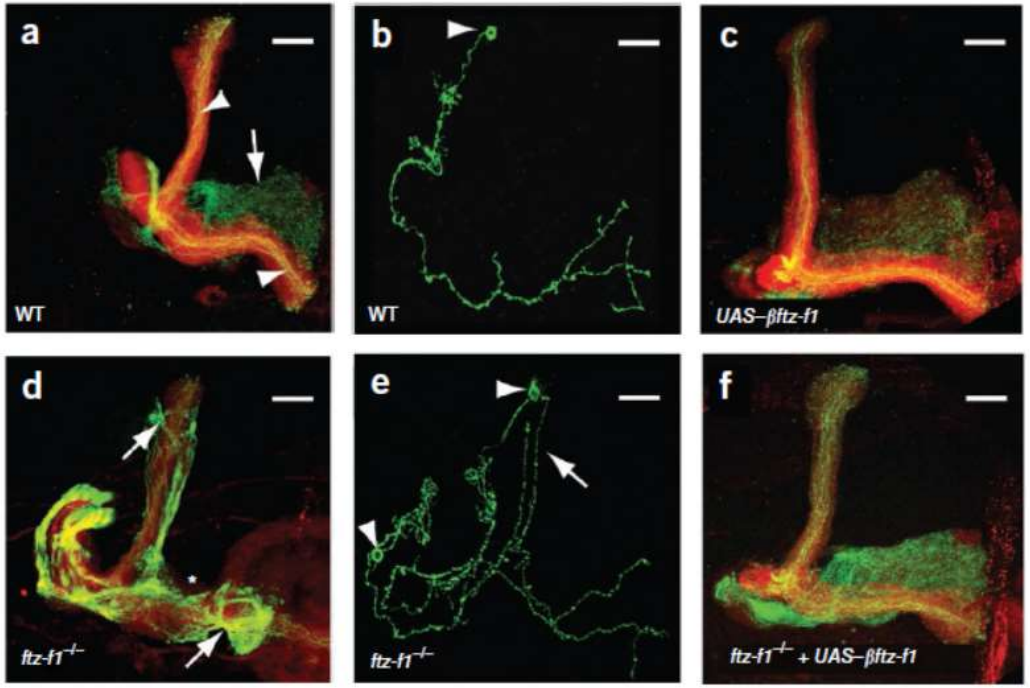
Ana Boulanger[1,5], Christelle Clouet-Redt[1,5], Morgane Farge[1], Adrien Flandre[1], Thomas Guignard[1], Céline Fernando[2–4], François Juge[2–4] & Jean-Maurice Dura[1]

2011

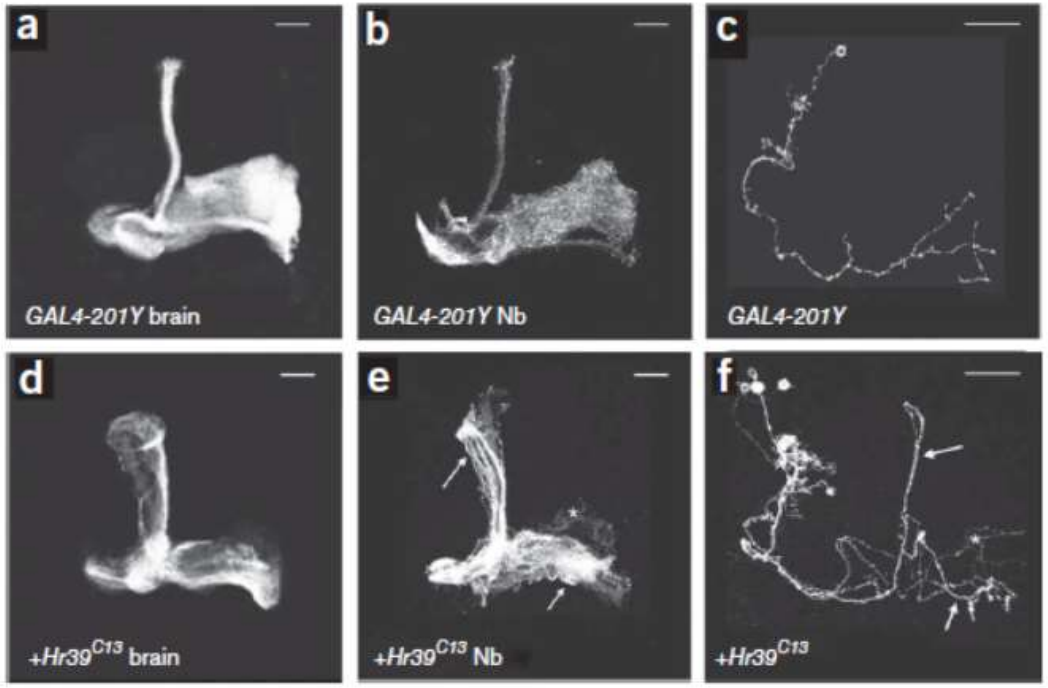


ftz-f1 and *Hr39* opposing roles during MB γ neuron remodeling

βftz-f1 function is required for γ neuron pruning



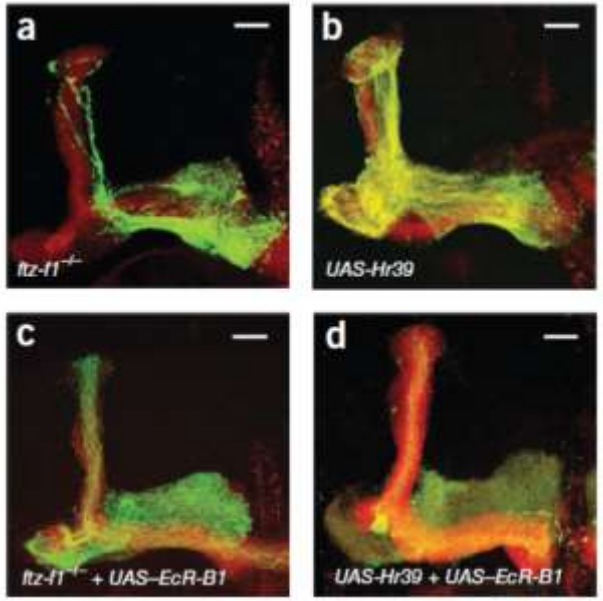
HR39 ectopic expression blocks γ neuron remodeling



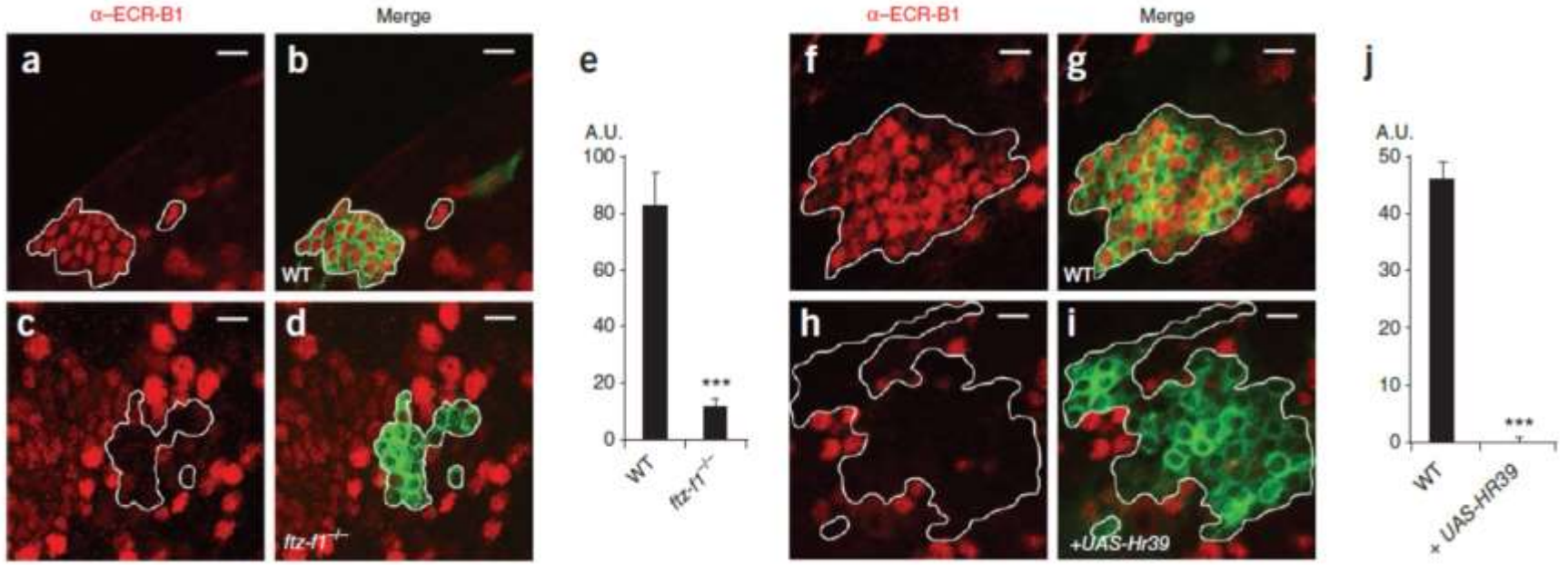
Boulanger, A., et al. (2011)

ECR-B1 is a downstream target of *ftz-f1* and *Hr39*

Forced expression of ECR-B1 rescues *ftz-f1*−/− and HR39 overexpression γ neuronal remodeling defects



Expression of ECR-B1 depends on normal FTZ-F1 and lack of HR39 activity in γ neurons



Boulanger, A., et al. (2011)

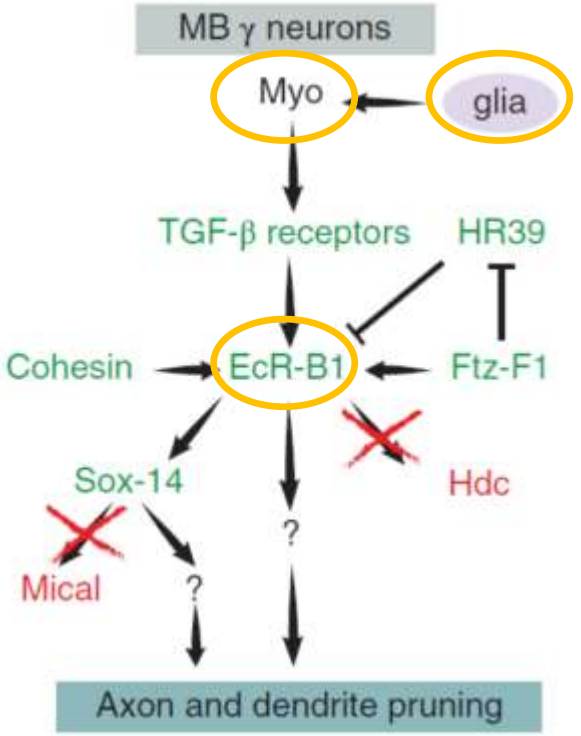
BRIEF COMMUNICATIONS

nature neuroscience

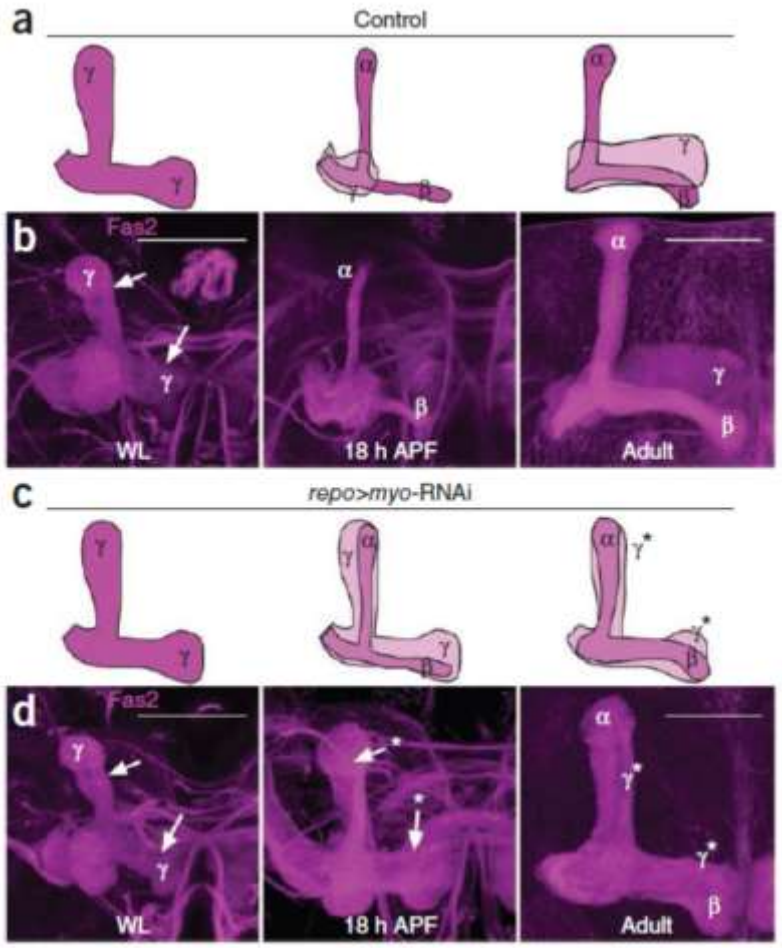
Glia instruct developmental neuronal remodeling through TGF-β signaling

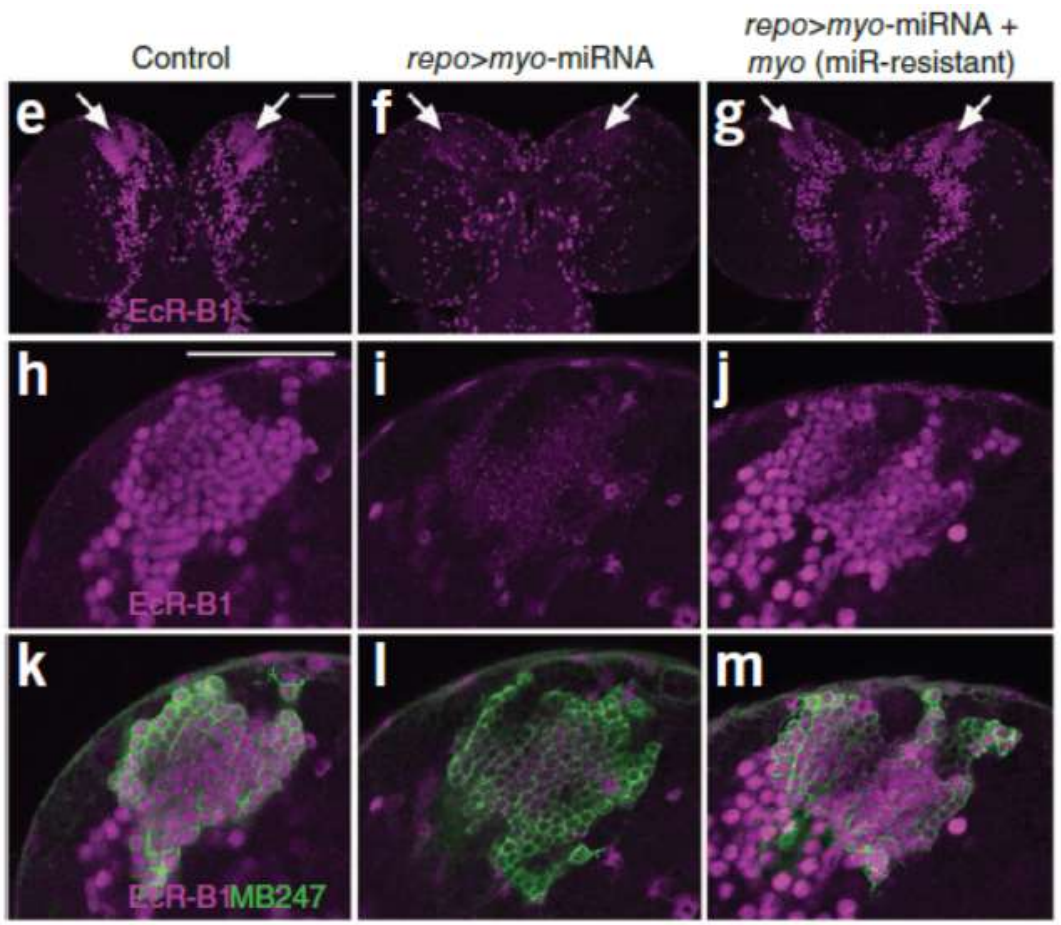
Takeshi Awasaki[1,2], Yaling Huang[1,2], Michael B O'Connor[3] & Tzumin Lee[1,2]

2011



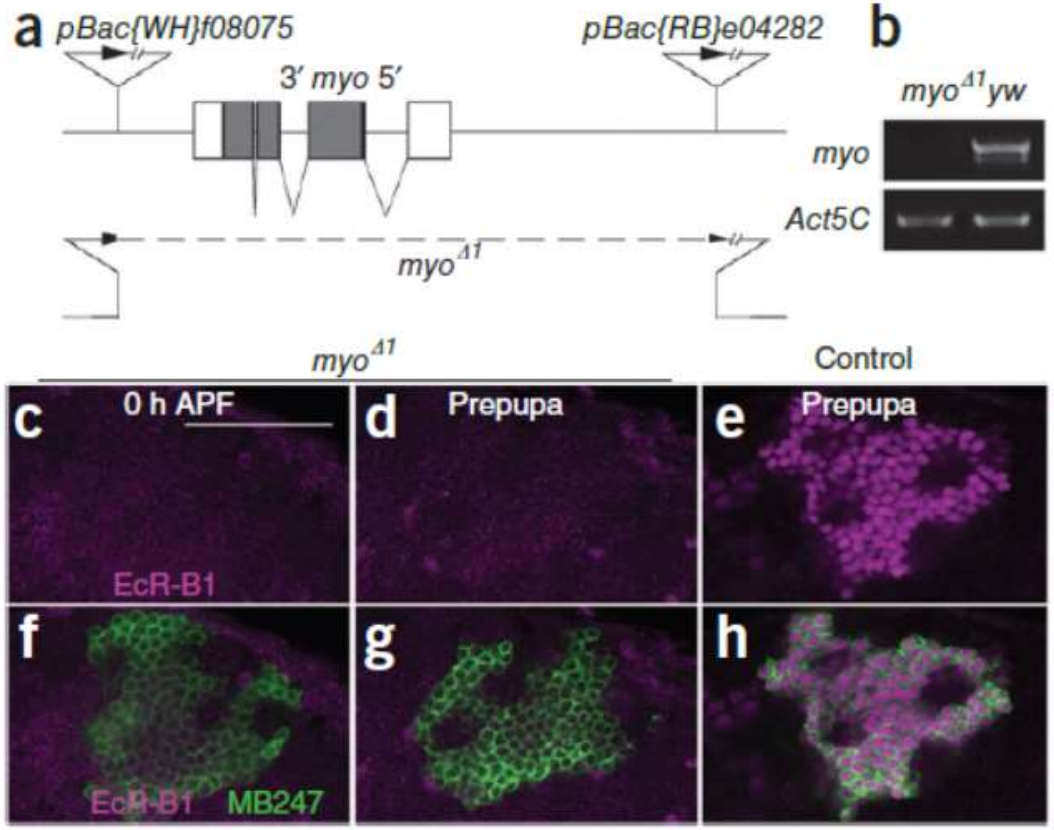
Effect of glial silencing of *myo* on mushroom body remodeling

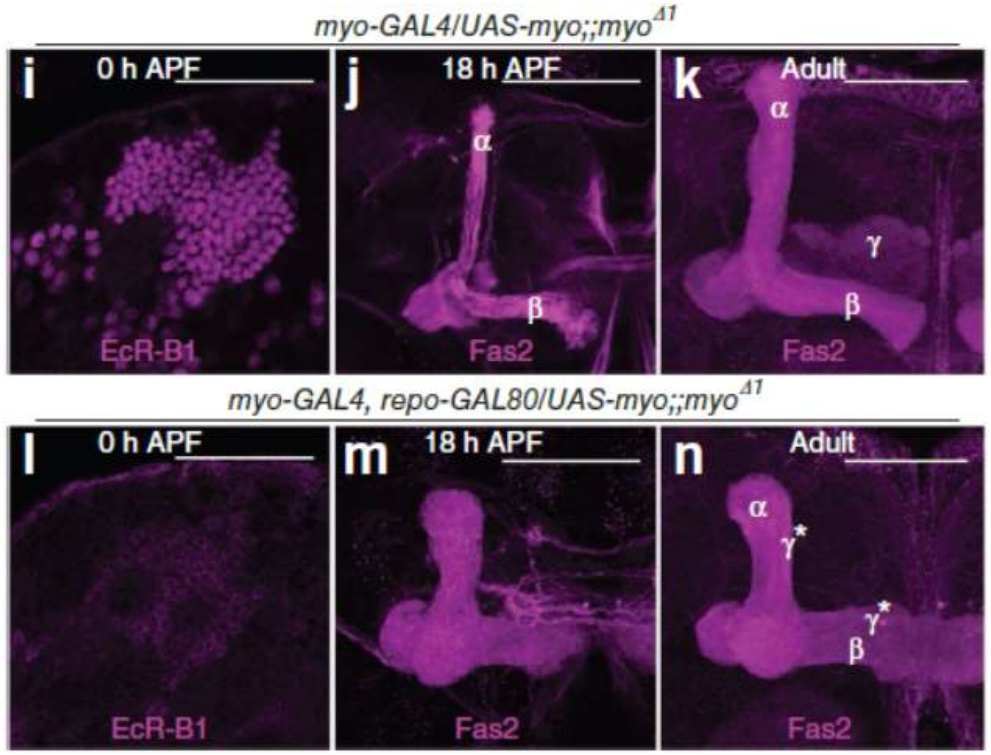




Awasaki, T., et al. (2011)

Effect of *myo* loss of function on mushroom body remodeling





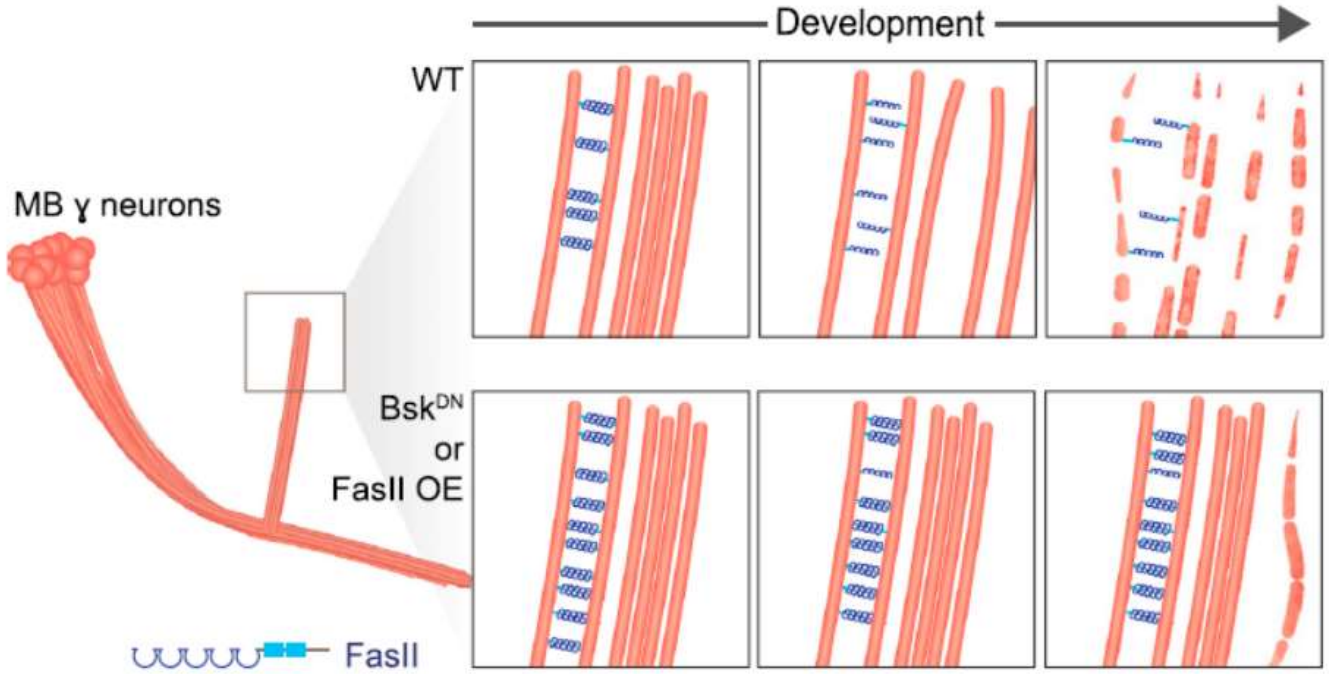
Awasaki, T., et al. (2011)

Article

Neuron

Developmental Axon Pruning Requires Destabilization of Cell Adhesion by JNK Signaling

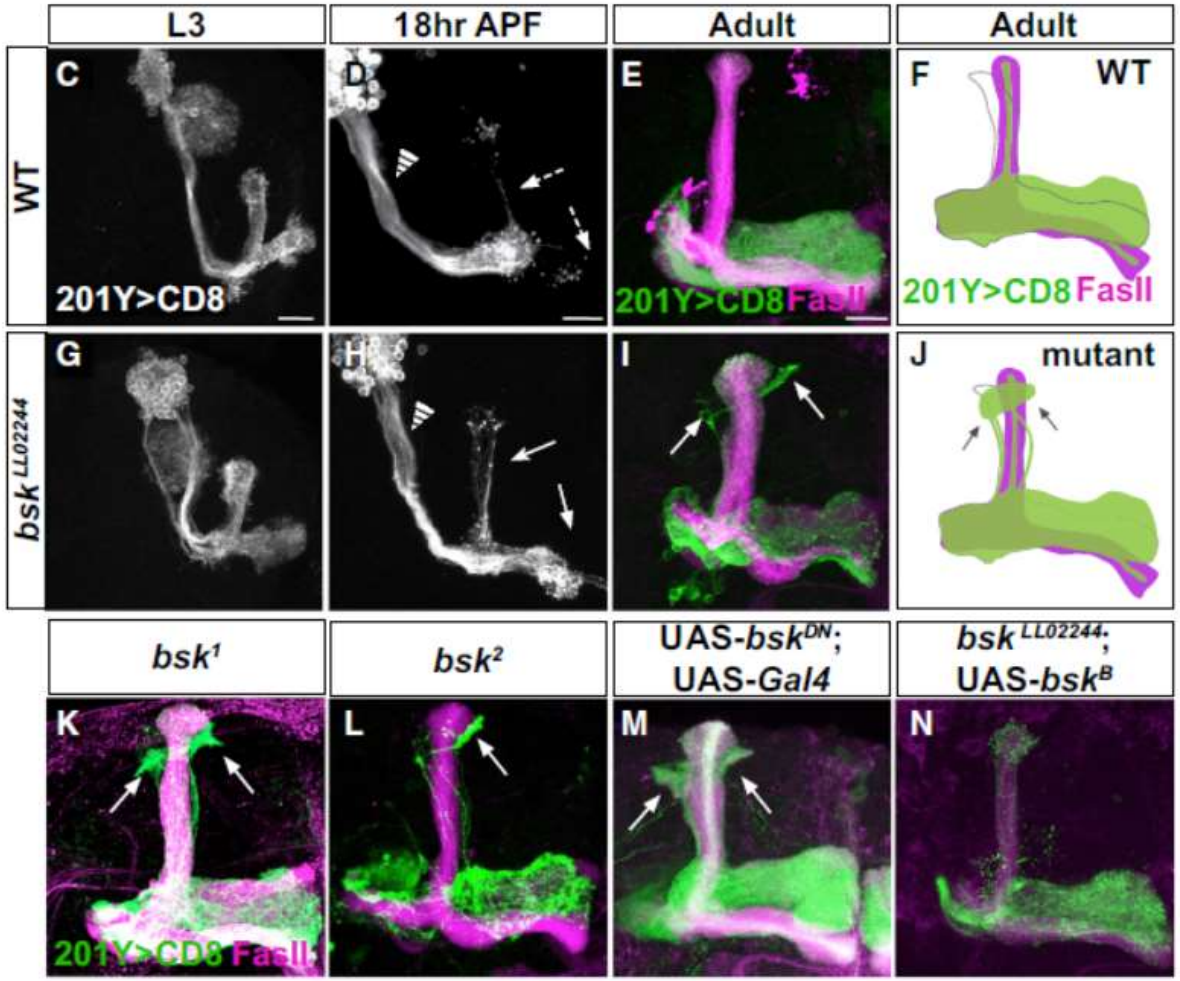
2015



Bsk: *Drosophila* JNK

Fasciclin II: adhesion molecule

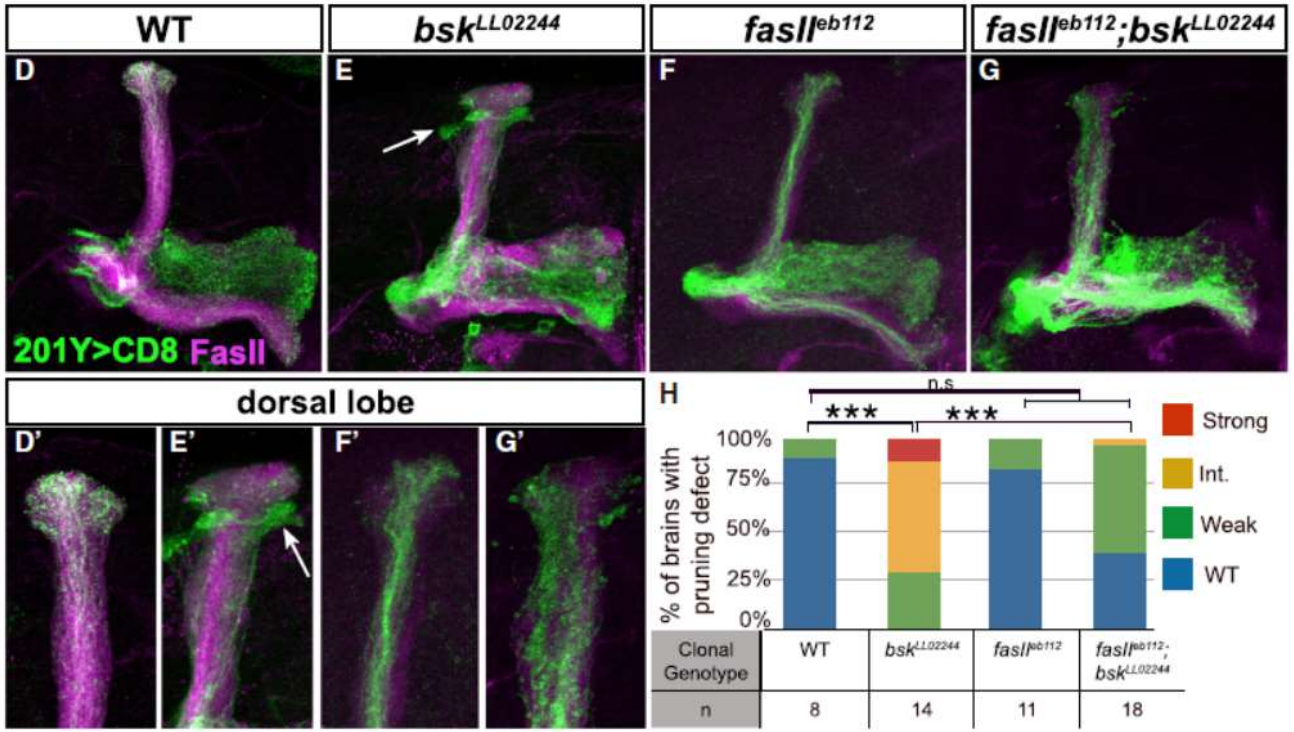
Bsk is required for axon, but not dendrite, pruning of MB γ neurons

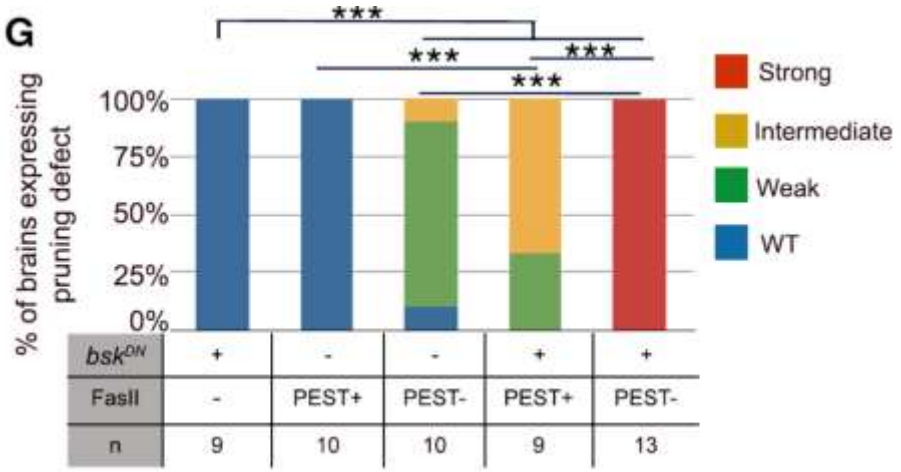


However, canonical JNK targets are not required for MB axon pruning.

Bornstein, B., et al. (2015)

FasII is required to mediate the Bsk pruning defect

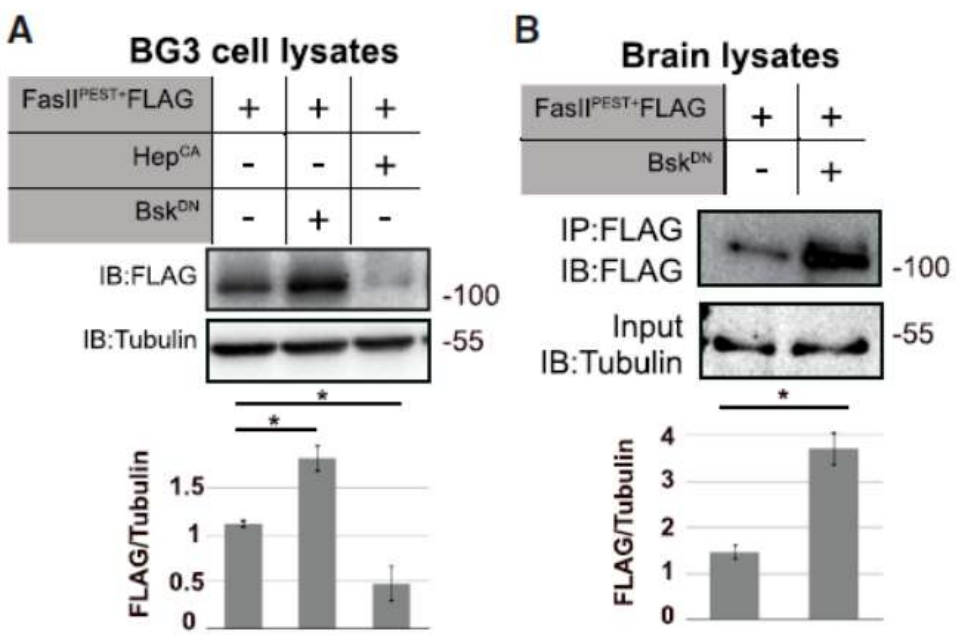


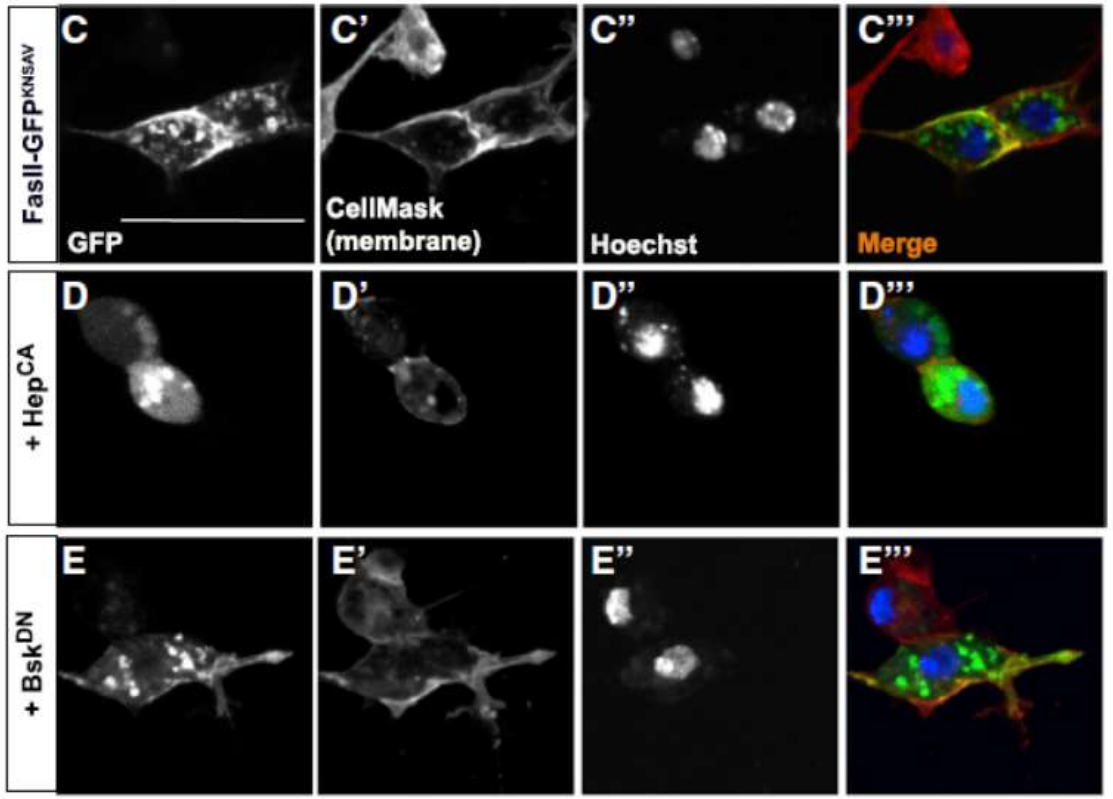


PEST (proline [P], glutamic acid [E], serine [S], and threonine [T]) domain

Bornstein, B., et al. (2015)

Bsk affects FasII stability and membrane localization



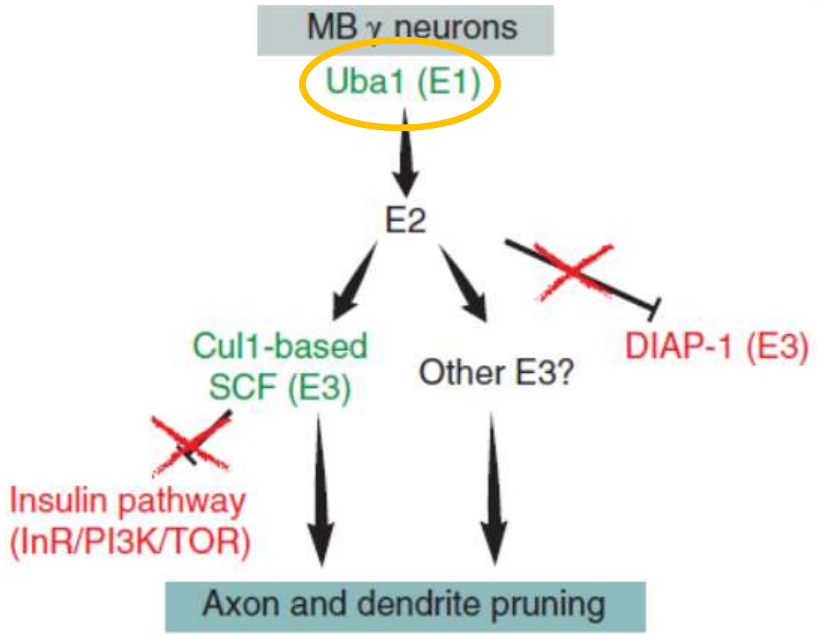


Bornstein, B., et al. (2015)

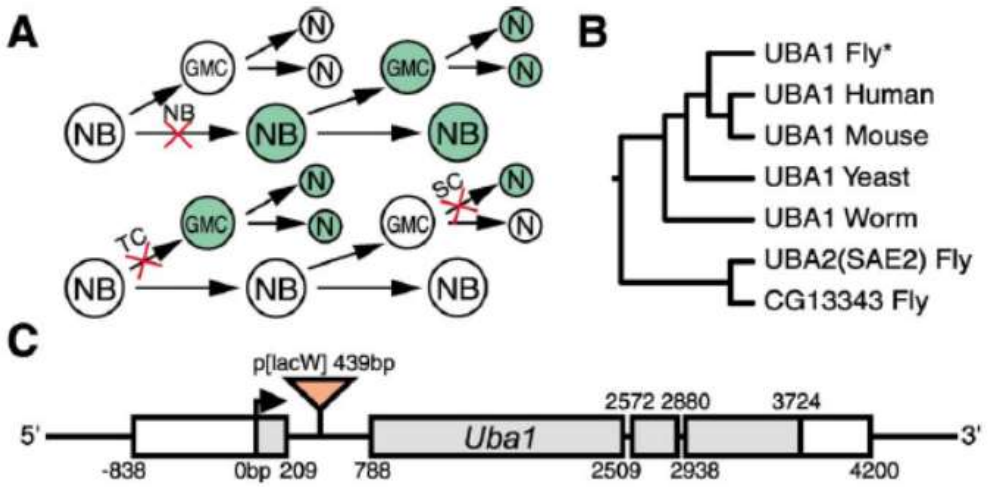
Neuron, Vol. 38, 871–885, June 19, 2003, Copyright ©2003 by Cell Press

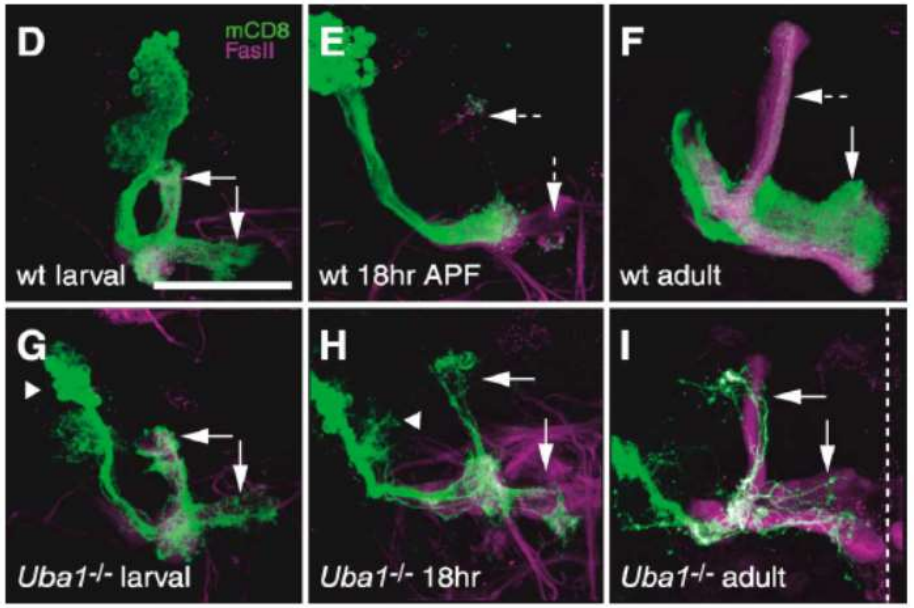
Axon Pruning during *Drosophila* Metamorphosis: Evidence for Local Degeneration and Requirement of the Ubiquitin-Proteasome System

Ryan J. Watts,[1] Eric D. Hoopfer,[1,2] and Liqun Luo[1,2,*]
[1]Department of Biological Sciences
[2]Neurosciences Program
Stanford University
Stanford, California 94305



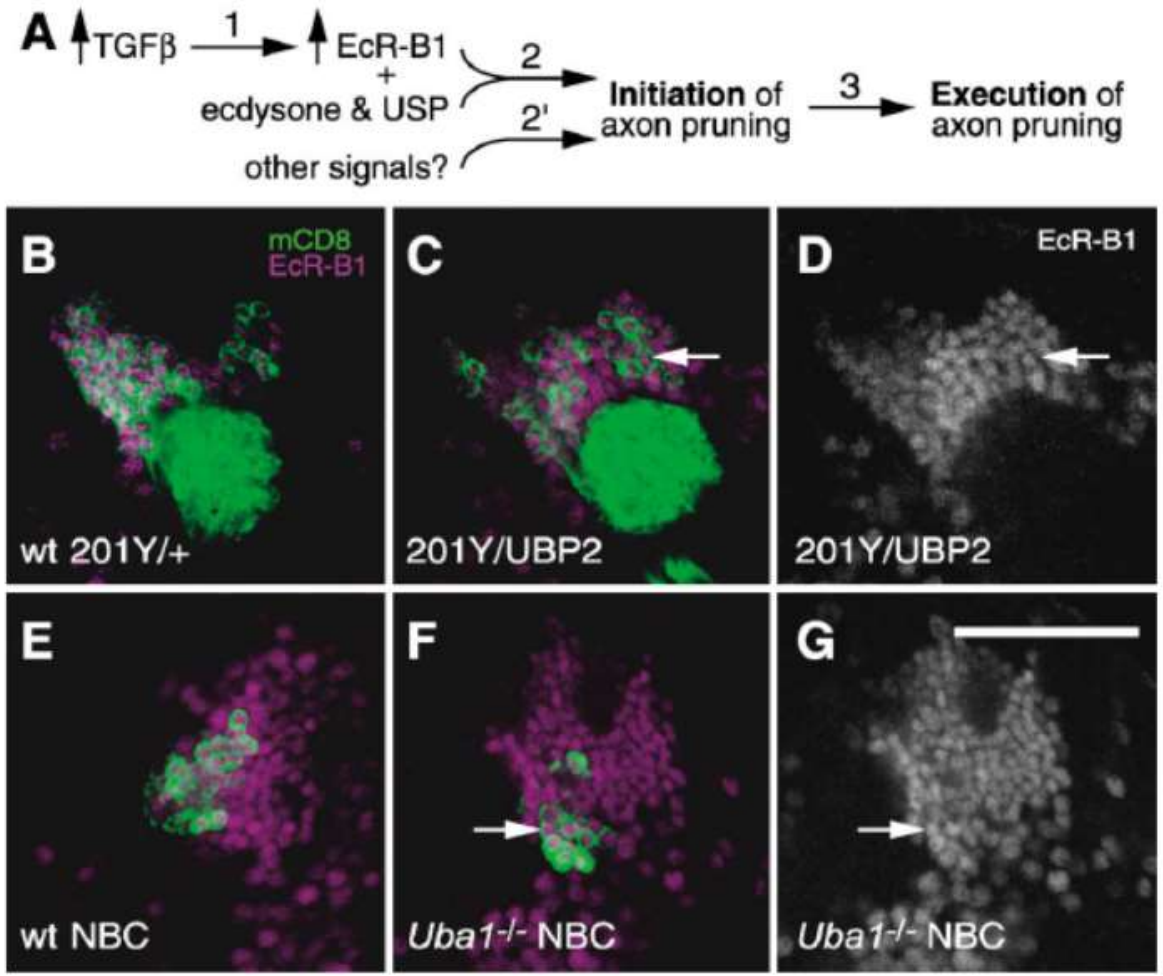
loss-of-function mutations of E1 in MB neurons block axon pruning





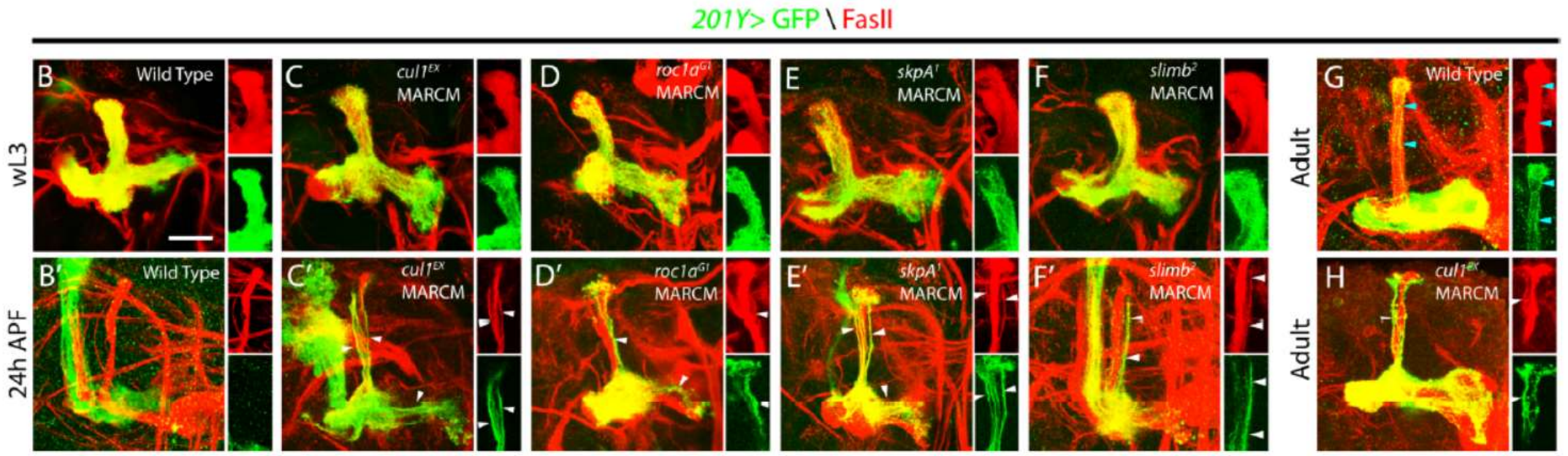
Watts, R. J., et al. (2003)

EcR-B1 expression is unaltered in ubiquitin-proteasome mutants



Watts, R. J., et al. (2003)

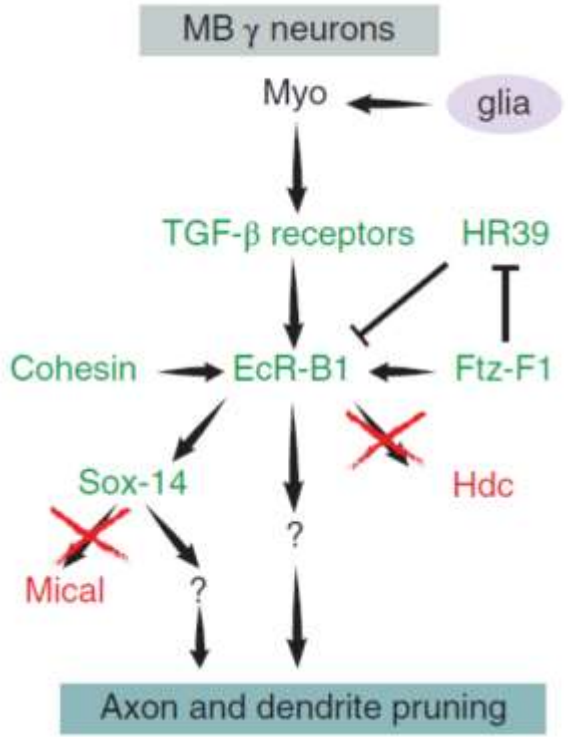
The Cullin-1-based SCF E3 ligase components are required for MB axon pruning



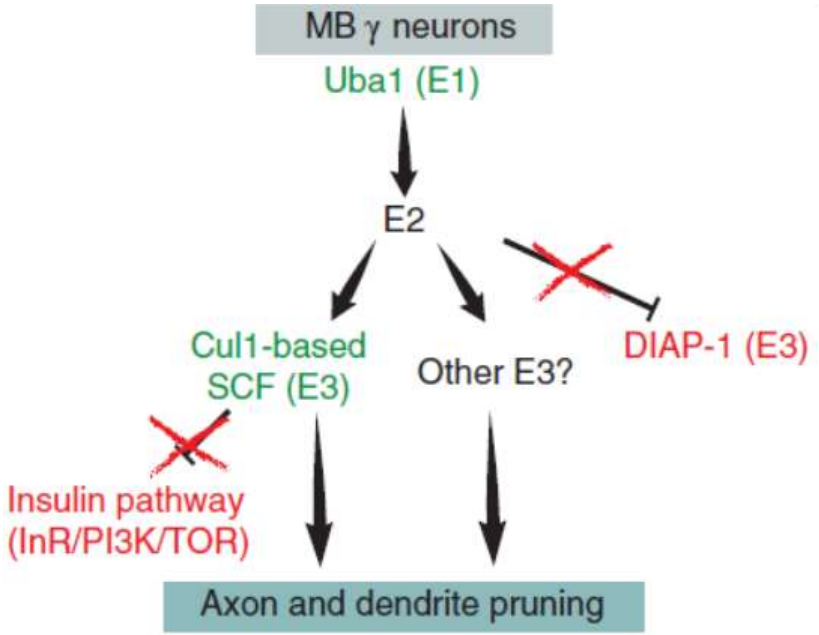
Wong, J. J., et al. (2013)

How maturing neurons reorganize their projections?

Ecdysone signaling
a major gatekeeper of pruning



Degradation pathways



JNK signaling

FasII

Reference

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- Lee, T., et al. (1999). "Development of the Drosophila mushroom bodies: sequential generation of three distinct types of neurons from a neuroblast." Development **126**(18): 4065-4076.
- Lee, T., et al. (2000). "Cell-autonomous requirement of the USP/EcR-B ecdysone receptor for mushroom body neuronal remodeling in Drosophila." Neuron **28**(3): 807-818.
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- Wong, J. J., et al. (2013). "A Cullin1-based SCF E3 ubiquitin ligase targets the InR/PI3K/TOR pathway to regulate neuronal pruning." PLoS Biol **11**(9): e1001657.
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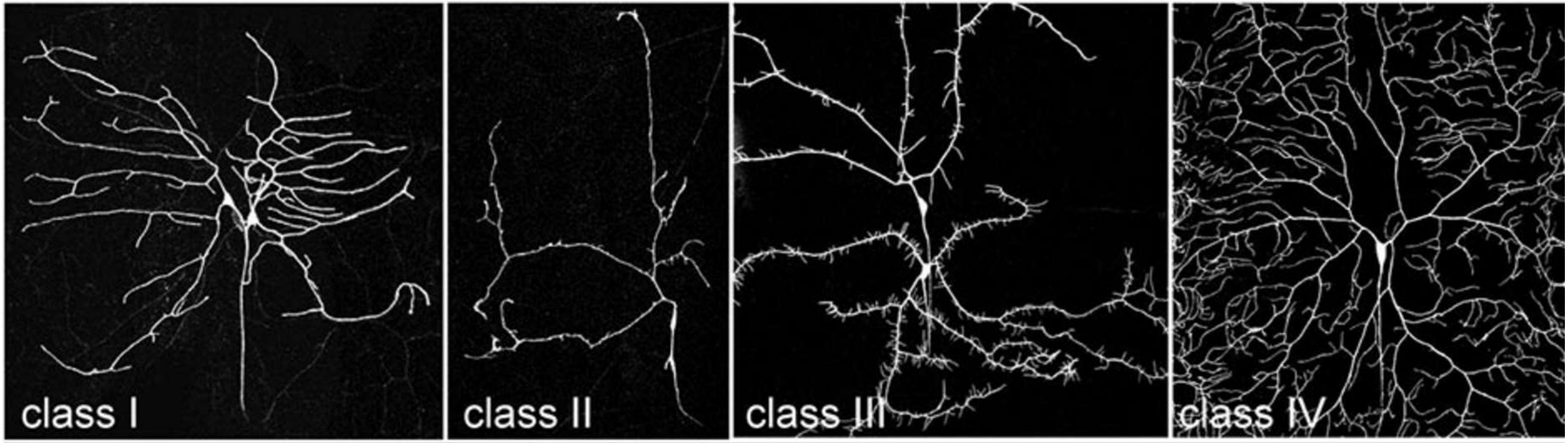
- Yaniv, S. P. and O. Schuldiner (2016). "A fly's view of neuronal remodeling." Wiley Interdiscip Rev Dev Biol **5**(5): 618-635.

Dendrite remodeling of dendritic arborization (da) neurons

Sun Mengshi
2019-11-29

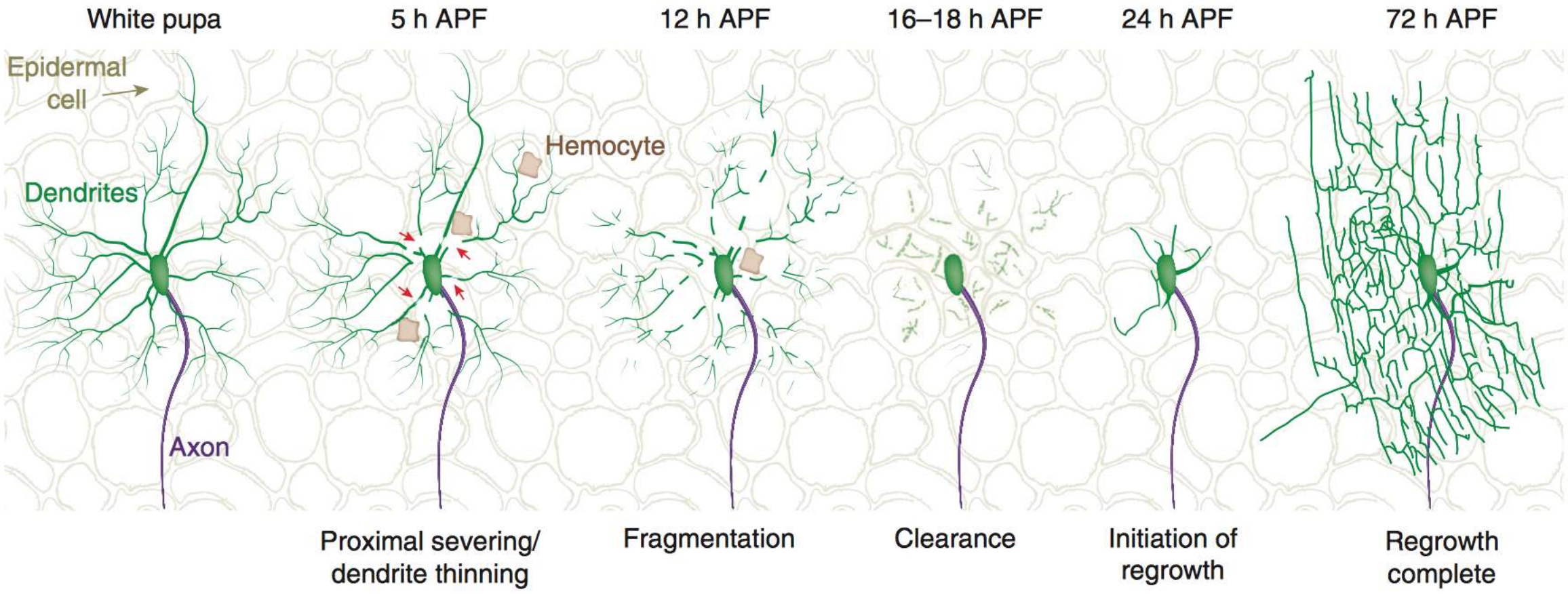
Dendritic arborization (da) neurons



website of Han Lab

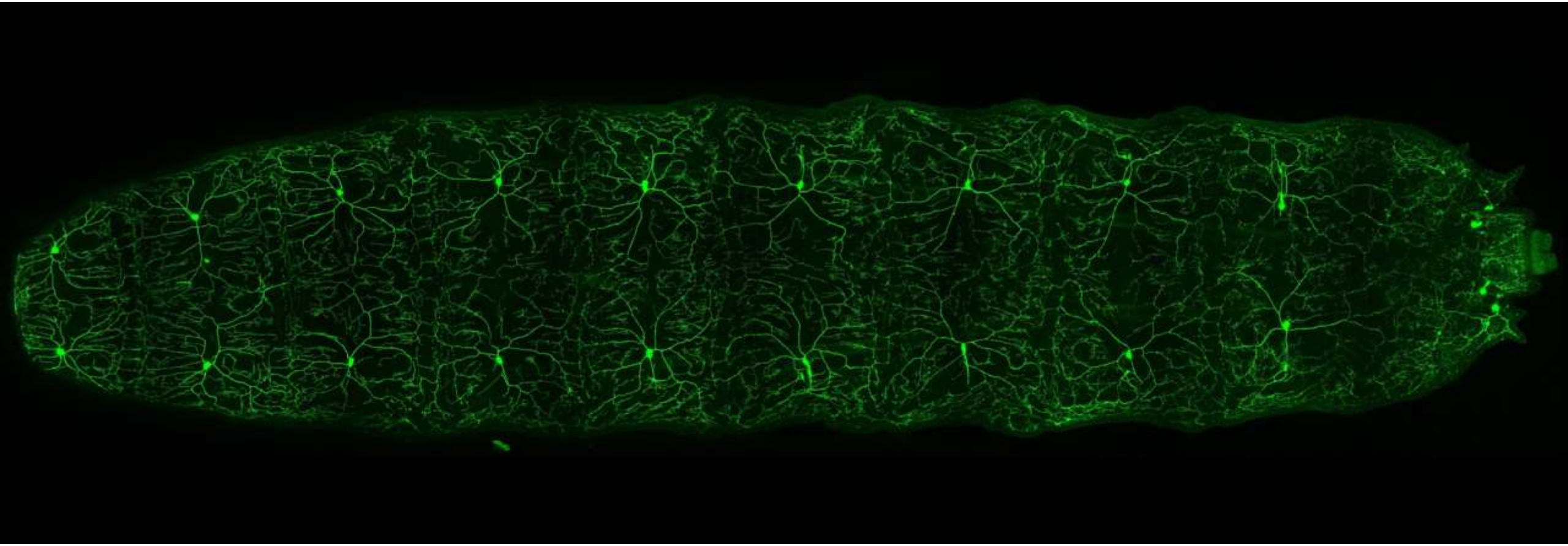
http://han.wicmb.cornell.edu/research/

Dendrite remodeling of da class IV during metamorphosis



Yaniv, S. and Schuldiner, O. 2016.

Green Fluorescent Protein (GFP) expressed in c4da neurons which located in the skin of larvae.



website of Rumbf Lab

http://rumpf.uni-muenster.de/research.html

詹裕农（1946）, 叶公杼（1947）

Fig. 4. The shared office of the authors' lab at UCSF in the early 1980s.

The Jans' Autobiography and Lab History

Select Publications (by year)

2019 2018 2017 2016 2015 2014 2013 2012 2011 2010 2009 2008 2007
2006 2005 2004 2003 2002 2001 2000 1999 1998 1997 1996 1995 1994
1993 1992 1991 1990 1989 1988 1987 1980-1986 1974-1979

2019

- Li, K.X., He. M., Ye, W., Sims, J., Gill, M., Xiang, X., Jan, Y.N., and Jan L.Y. (2019). TMEM 16B regulates anxiety-related behavior and GABAergic neuronal signaling in the central lateral amygdala. Elife. 2019 Sep 4;8. pii: e47106. doi: 10.7554/eLife.47106. PMCID: PMC6746550. [PubMedCentral]
- Wang, L., Simms, J., Peters, C.J., Fontaine, M.T., Li, K., Gill, T.M., Jan, Y.N, and Jan, L.Y. (2019). TMEM16B calcium-activated chloride channels regulate action potential firing in lateral septum and aggression in male mice. J Neurosci. 2019 Jul 18. pii: 3137-18. doi: 10.1523/JNEUROSCI.3137-18.2019. [Epub ahead of print]. PMCID: PMC6733546. [PubMedCentral]
- Ye, W., Han, T.W., He, M., Jan, Y.N., and Jan, L.Y. (2019). Dynamic change of electrostatic field in TMEM16F permeation pathway shifts its ion selectivity. Elife. 2019 Jul 18;8. pii: e45187. doi: 10.7554/eLife.45187. [Epub ahead of print]. PMCID: PMC6690719. [PubMedCentral]
- Feng, S., Dang, S., Han, T.W., Ye, W., Jin, P., Cheng, T., Li, J., Jan, Y.N., Jan, L.Y., and Cheng, Y. (2019). Cryo-EM Studies of TMEM16F Calcium-Activated Ion Channel Suggest Features Important for Lipid Scrambling. Cell Rep. 2019 Jul 9;28(2):567-579.e4. doi: 10.1016/j.celrep.2019.06.023. PMCID: PMC6684876. [PubMedCentral]
- Crottes, D., and Jan, L.Y. (2019). The Multifacted Role of TMEM16A in Cancer. Cell Calcium, doi:10.1016/j.ceca.2019.06.004. [Epub ahead of print]. PMID: 31279157. [PubMedCentral]
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- Wang, T.A., Teo, C.F., Akerblom, M., Chen, C., Tynan-La Fontaine, Greiner, V.J., Diaz, A., Mc-Manus, M.T., Jan, Y.N., and Jan, L.Y., (2019). Thermoregulation via Temperature-dependent PGD2 Production in Mouse Preoptic Area. Neuron May 22. pii: S0896-6273(19)30392-7. doi: 10.1016/j.neuron.2019.04.035. [Epub ahead of print] . PMCID: PMC6639135. [PubMedCentral]
- Zhu, S., Chen, R., Soba, P., and Jan, Y.N. (2019). JNK signaling coordinates with ecdysone signaling to promote pruning of Drosophila sensory neuron dendrites. Development 146(8). pii: dev163592. doi: 10.1242/dev.163592. PMCID: PMC6503988. [PubMedCentral]
- Song, Y., Li, D., Farrelly, O., Miles, L., Li, F., Kim, S.E., Lo, T.Y., Wang, F., Li, T., Thompson-Peer, K.L., Gong, J., Murthy, S.E., Coste, B., Yakubovich, N., Patapoutian, A., Xiang, Y., Rompolas, P., Jan, L.Y., and Jan, Y.N. (2019). The Mechanosensitive Ion Channel Piezo Inhibits Axon Regeneration. Neuron 102:373-389. PMCID: PMC6487666. [PubMedCentral]
- Yadav, S., Younger, S.H., Zhang, L., Thompson-Peer, K.L., Li, T., Jan, L.Y., and Jan, Y.N. (2019). Glial ensheathment of the somatodendritic compartment regulates sensory neuron structure and activity. PNAS 116: 5126-5134. PMCID: PMC6421456. [PubMedCentral]
- Han, T.W., Ye, W., Bethel, N.P., Zubia, M., Kim, A., Li, K.H., Burlingame, A.L., Grabe, M., Jan, Y.N., and Jan, L.Y. (2019). Chemically induced vesiculation as a platform for studying TMEM16F activity. PNAS USA 116:1309-1318. PMCID: PMC6347726 . [PubMedCentral]

Dendrite-specific remodeling of *Drosophila* sensory neurons requires matrix metalloproteases, ubiquitin-proteasome, and ecdysone signaling

Chay T. Kuo, Lily Y. Jan, and Yuh Nung Jan*

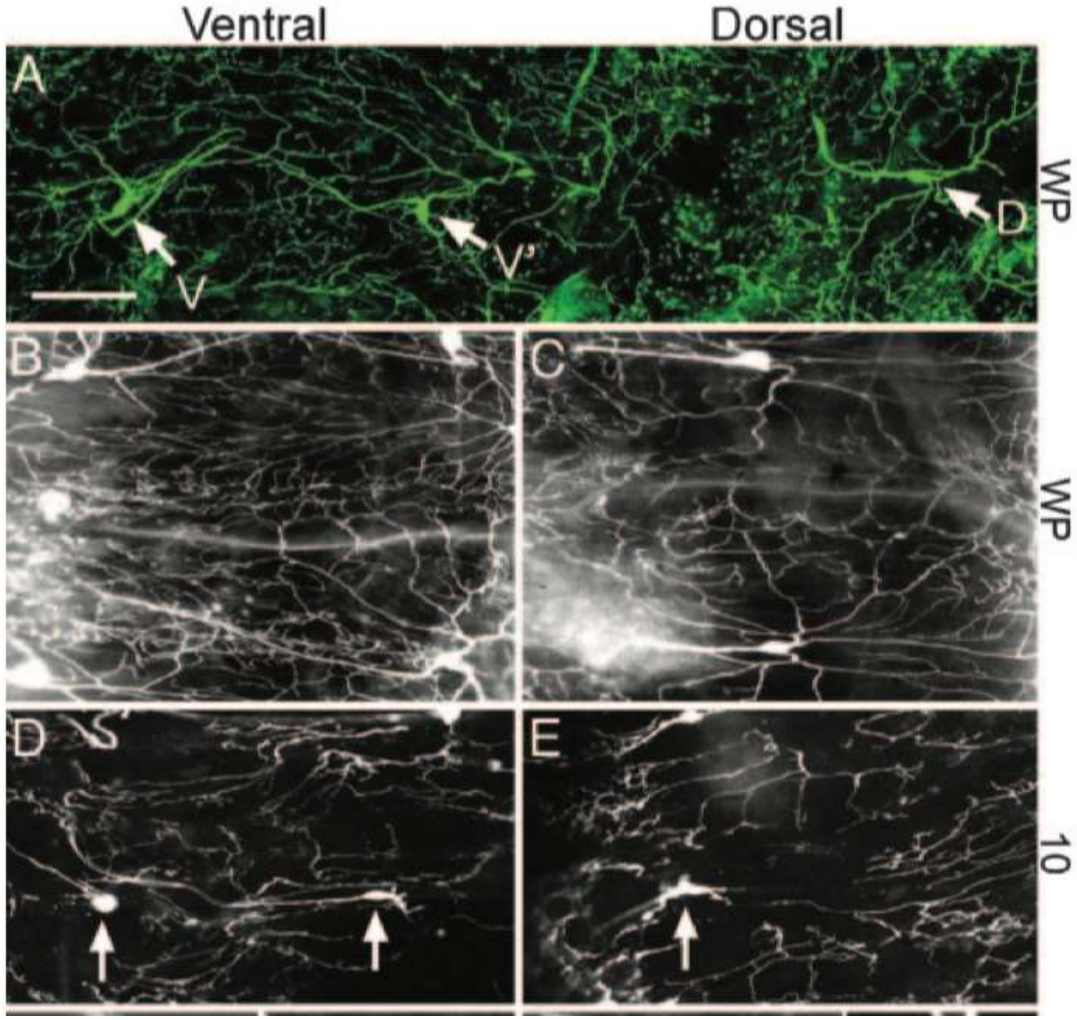
Howard Hughes Medical Institute and Department of Physiology, University of California, 1550 Fourth Street, Room GD484E, San Francisco, CA 94143-0725

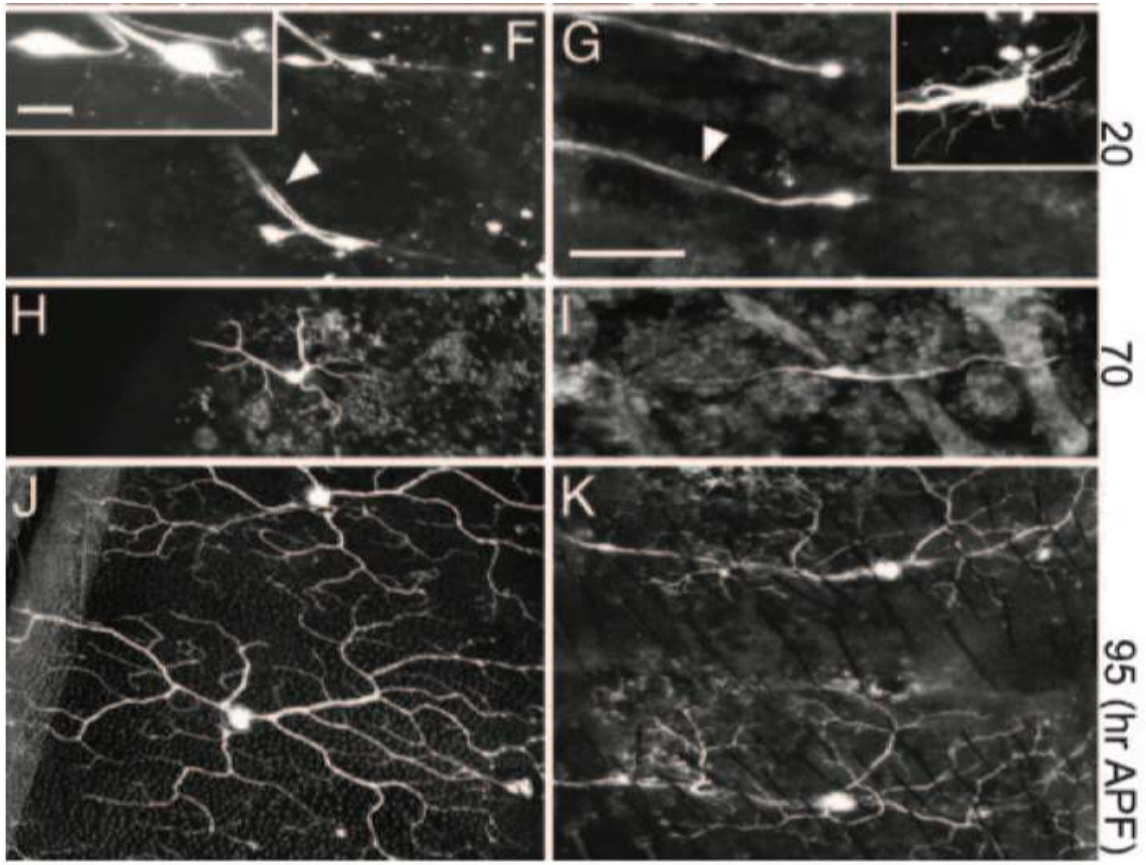
Contributed by Yuh Nung Jan, August 30, 2005

1. **Identify a group of *Drosophila* neurons** that persists through metamorphosis and demonstrates clear reorganization of dendrites.

ppk-Gal4/uas-EGFP : label 3 class IV da (C4da) neurons

2. Dendritic remodeling of C4da neurons during pupariation.





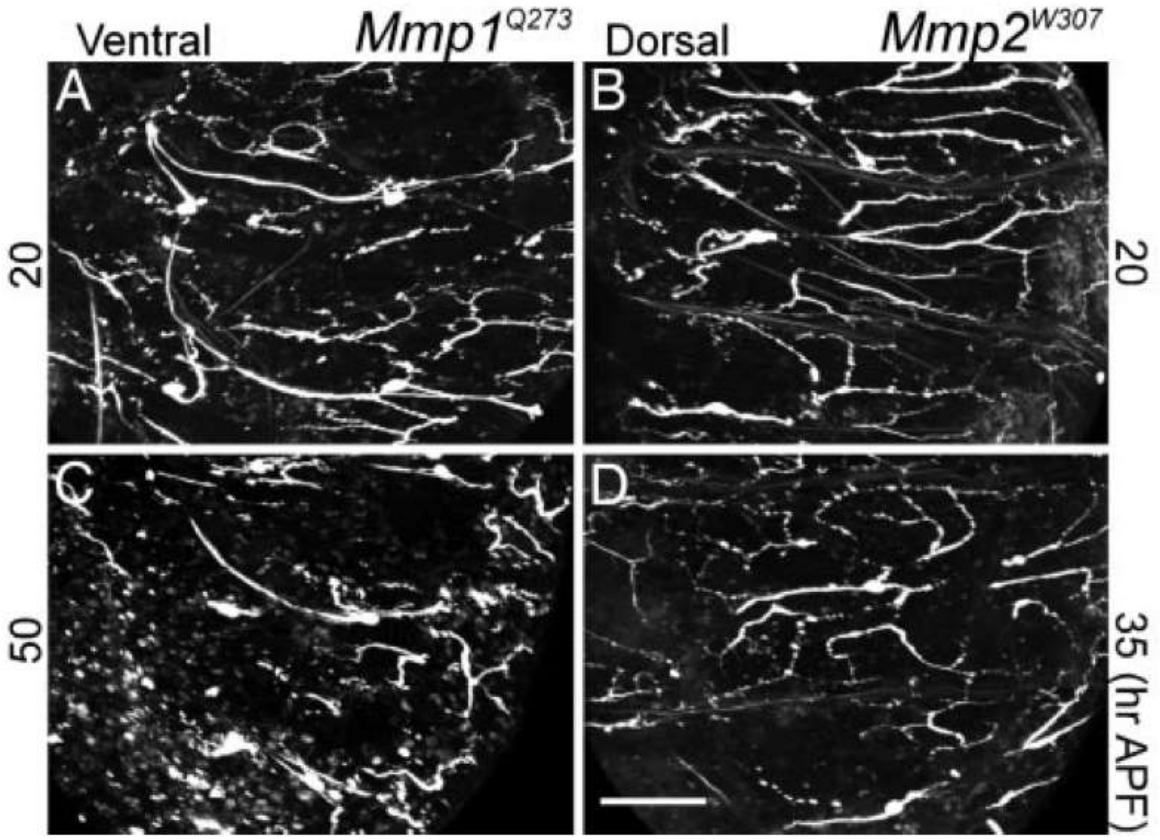
WP: white pupae

AFP: after puparium formation

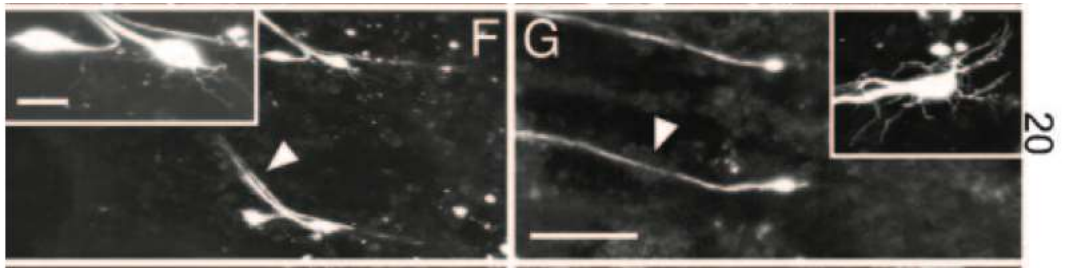
20h APF: larval dendrite removal was complete

3. Whether the degradation of larval dendrites is a result of local tissue remodeling metalloproteinases (Mmp1 and Mmp2) : regulate tissue remodeling during metamorphosis

weaker alleles: Mmp1 ^{Q273} and Mmp2 ^{W307} (survive past head eversion to midpupariation)



WT pupae



Larval dendrites that were severed from the soma remained.

Dendrite degradation defects in Mmp mutants during metamorphosis.

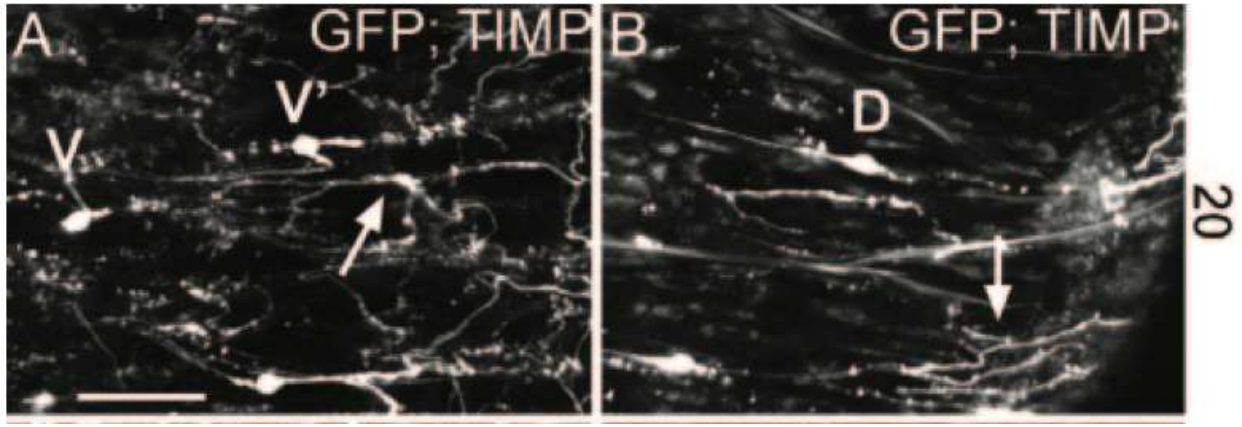
4. To determine the Mmps are extracellular or intracellular signals.

I. functioned site (on the cell / inner the cell)

II. sources (synthesized by either the C4da neurons or surrounding cells)

I. ppk-GAL4>TIMP (tissue inhibitor of metalloprotease)

TIMP：Associates with extracellular membrane surfaces to inhibit Mmp activities



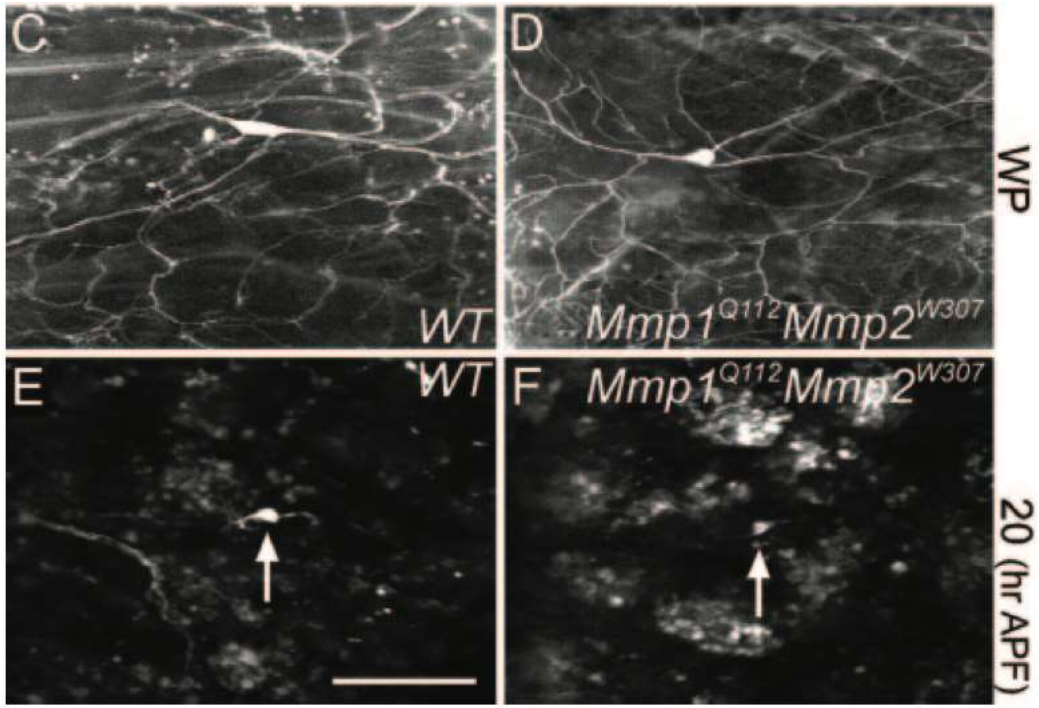
Mmps functioned on the cell surface of dendrites to regulate degradation.

4. To determine the Mmps are extracellular or intracellular signals.

I. functioned site (on the cell / inner the cell)

II. sources (synthesized by either the C4da neurons or surrounding cells)

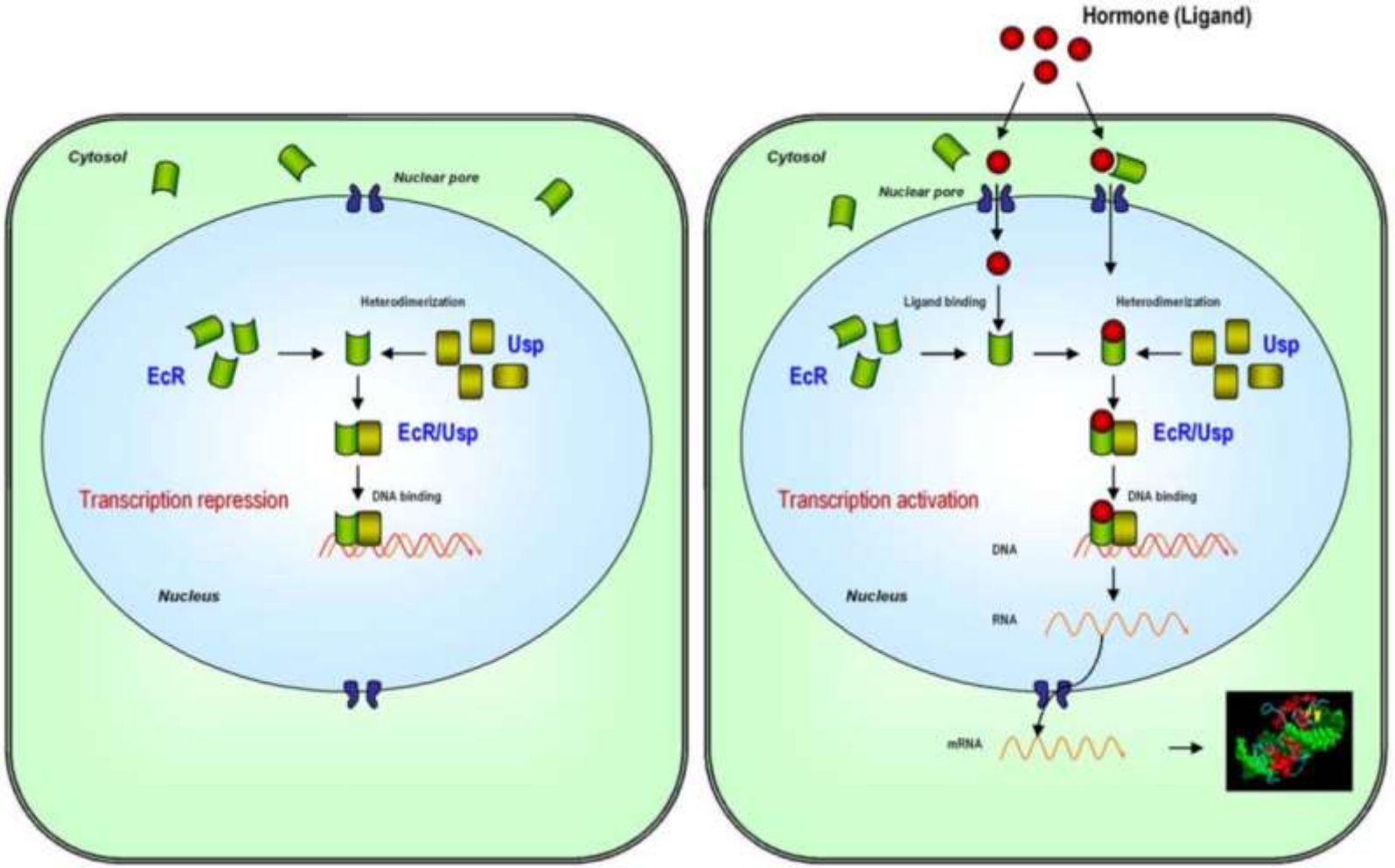
II. MARCM to generate Mmp1 ^{Q112} Mmp2 ^{W307} double mutant C4da clones.



Cell-intrinsic Mmps were not required for dendritic pruning and that extracellular Mmp activity was sufficient for degrading severed larval dendrites during metamorphosis.

5. To look for cell-intrinsic pathways in cleaving larval dendrites.

- Ecdysone, a steroid hormone that regulates much of Drosophila metamorphosis



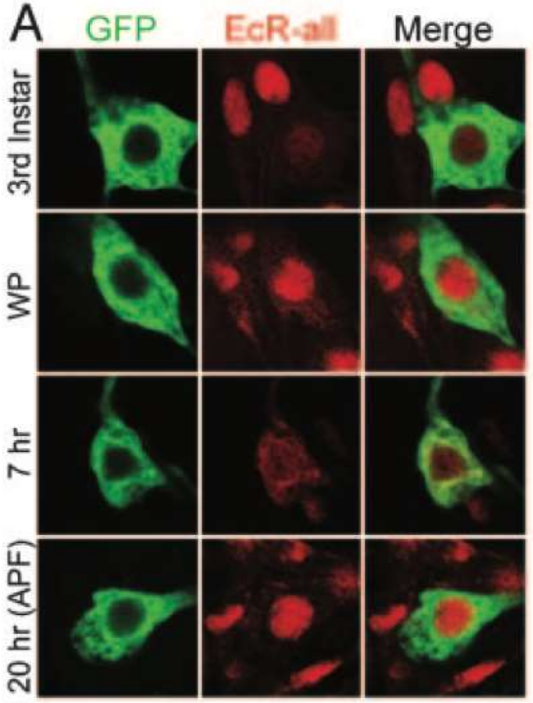
EcR-A,
EcR-B1,
EcR-B2

Functional analysis of ecdysone receptor, Anca Azoitei

5. To look for cell-intrinsic pathways in cleaving larval dendrites.

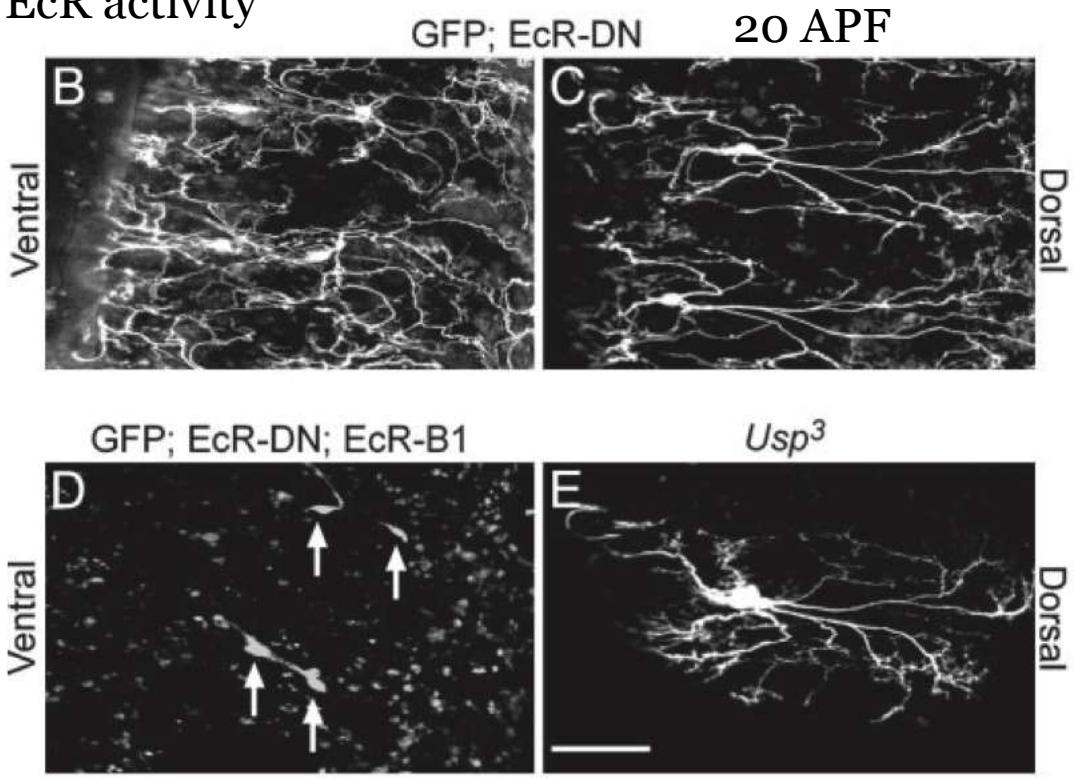
- Ecdysone, a steroid hormone that regulates much of Drosophila metamorphosis

1). Examined EcR expression patterns in C4da neurons



2). To disrupt ecdysone signaling specifically in C4da neurons

Using dominant-negative (DN) EcR proteins to inhibit EcR activity



Rescue

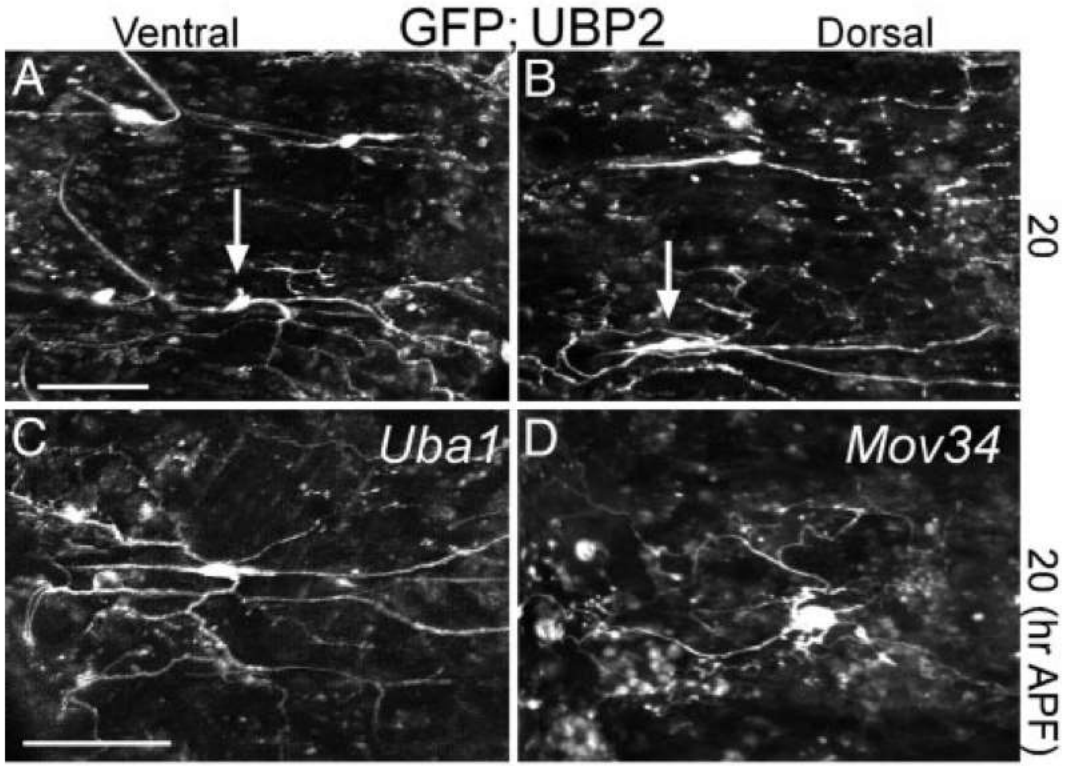
The ecdysone signaling pathway plays an important cell-intrinsic role in initiating dendritic pruning in C4da neurons during metamorphosis.

6. What might be the cellular machineries that carry out dendrite pruning in C4da neurons?

- The protein degradation pathway, the ubiquitin proteasome system (UPS)

ppk-Gal4 > UBP2

a yeast ubiquitin protease which effectively inhibit UPS

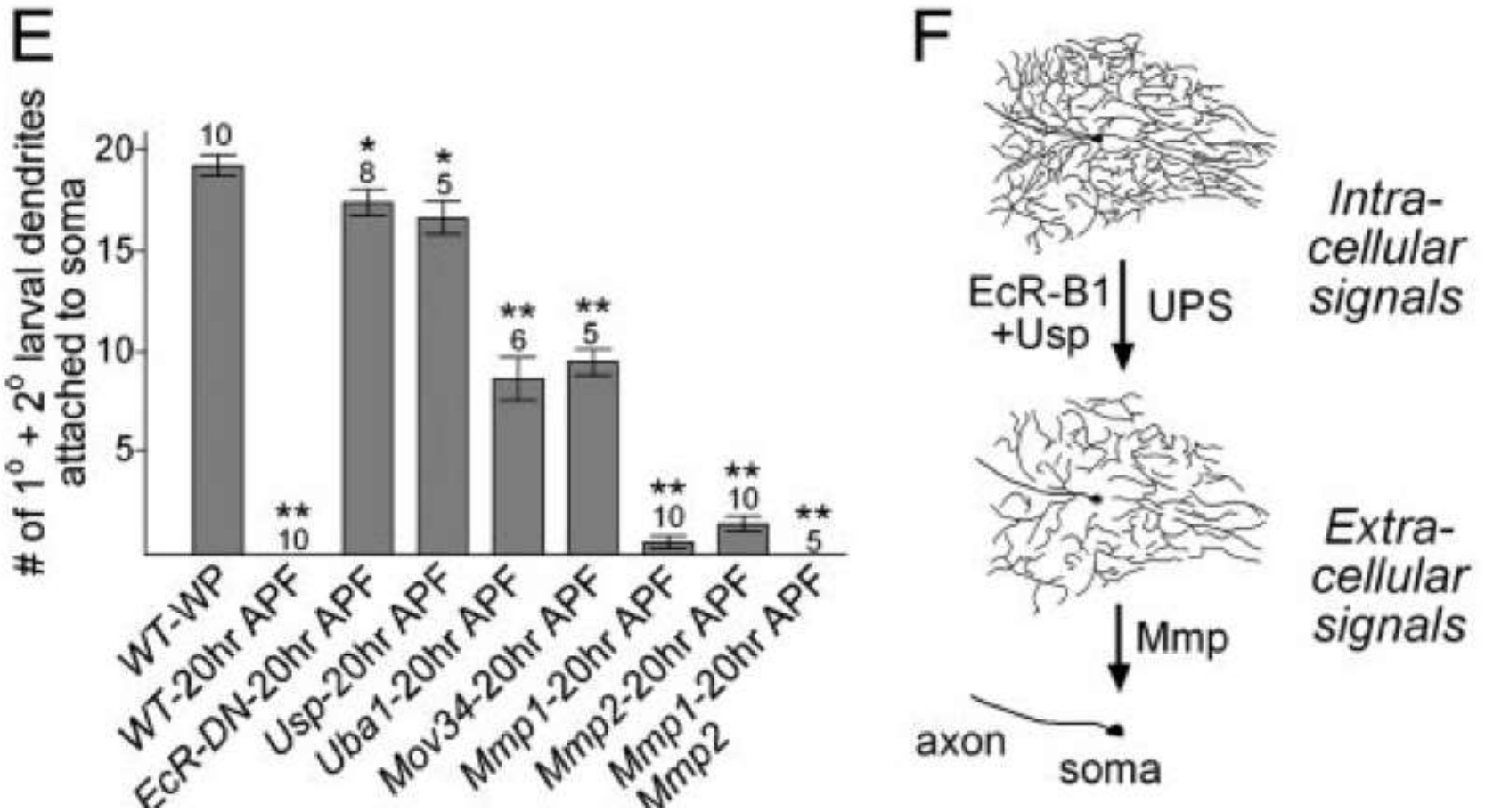


ubiquitin activation enzyme 1 (Uba1)

mutation in the 19S particle of the proteasome (Mov34)

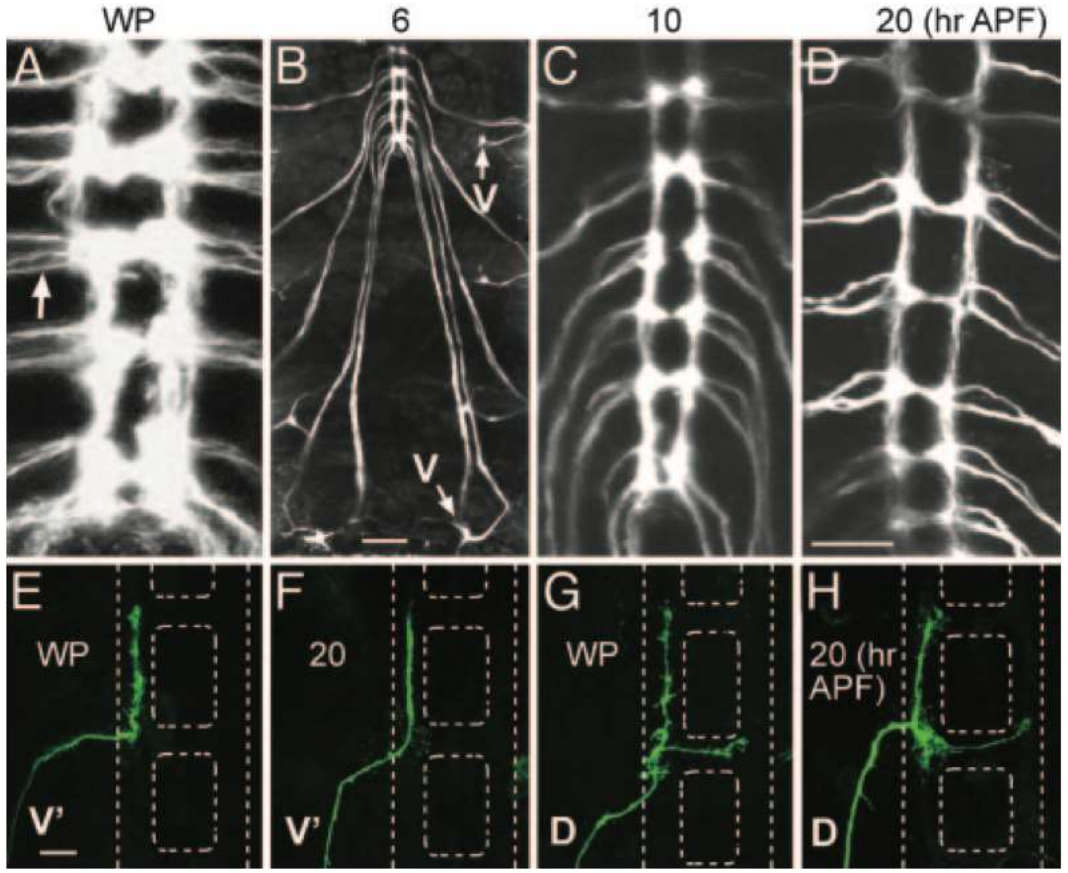
The ubiquitin proteasome system is required for dendrite breakage from neurons.

Dendrite remodeling in C4da neurons starts with signals from ecdysone and UPS that result in the cleavage of larval dendrites from the soma, which then allows for the degradation of severed dendrites by Mmp activity in the extracellular matrix.



7. C4da Neurons Retain Larval Axons During Dendrite Pruning.

Single V' and D C4da neuron clones



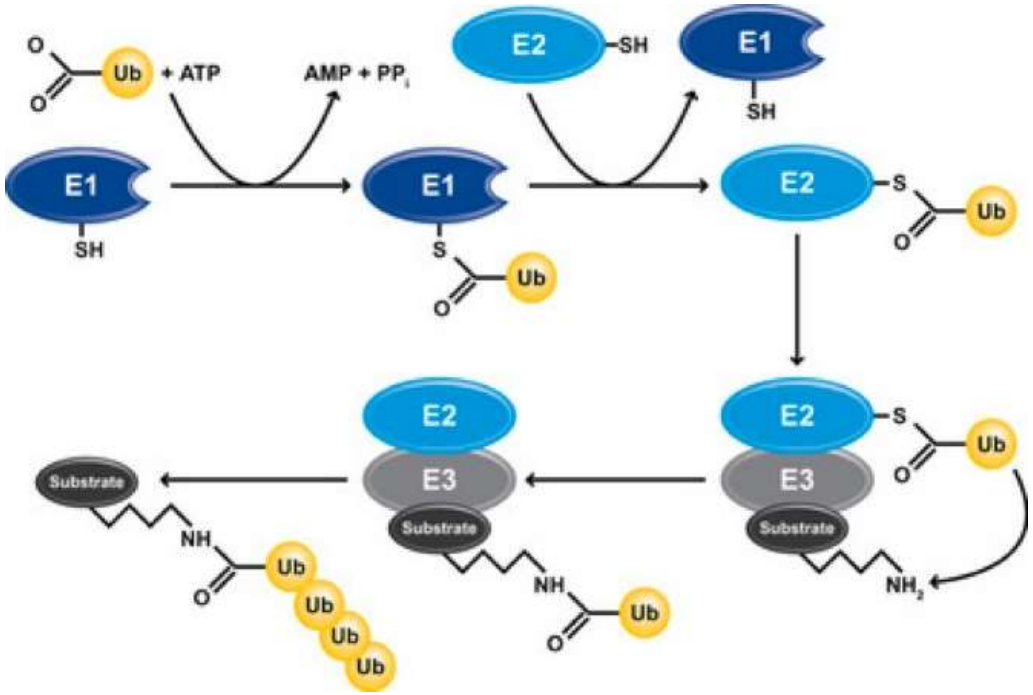
Neuron *51*, 283–290, August 3, 2006 ©2006 Elsevier Inc. DOI 10.1016/j.neuron.2006.07.014

Report

Identification of E2/E3 Ubiquitinating Enzymes and Caspase Activity Regulating *Drosophila* Sensory Neuron Dendrite Pruning

Chay T. Kuo,[1] Sijun Zhu,[1] Susan Younger,[1] Lily Y. Jan,[1] and Yuh Nung Jan[1,*]
[1] Howard Hughes Medical Institute
Departments of Physiology and Biochemistry
University of California, San Francisco
San Francisco, California 94143

E1: the ubiquitin-activating
E2: the ubiquitin conjugating
E3: the ubiquitin ligating

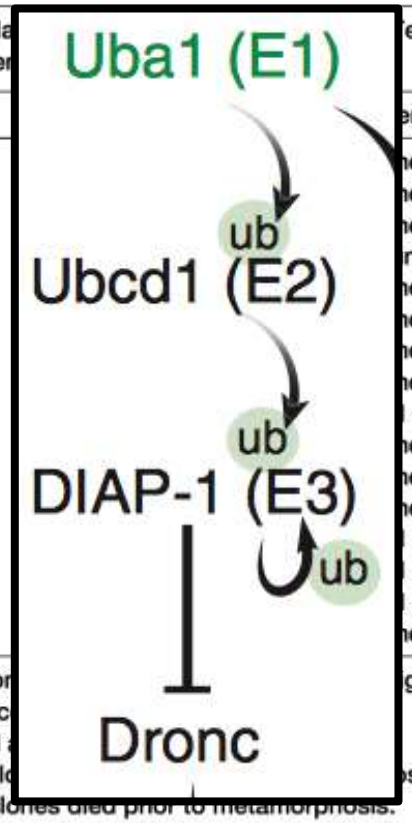


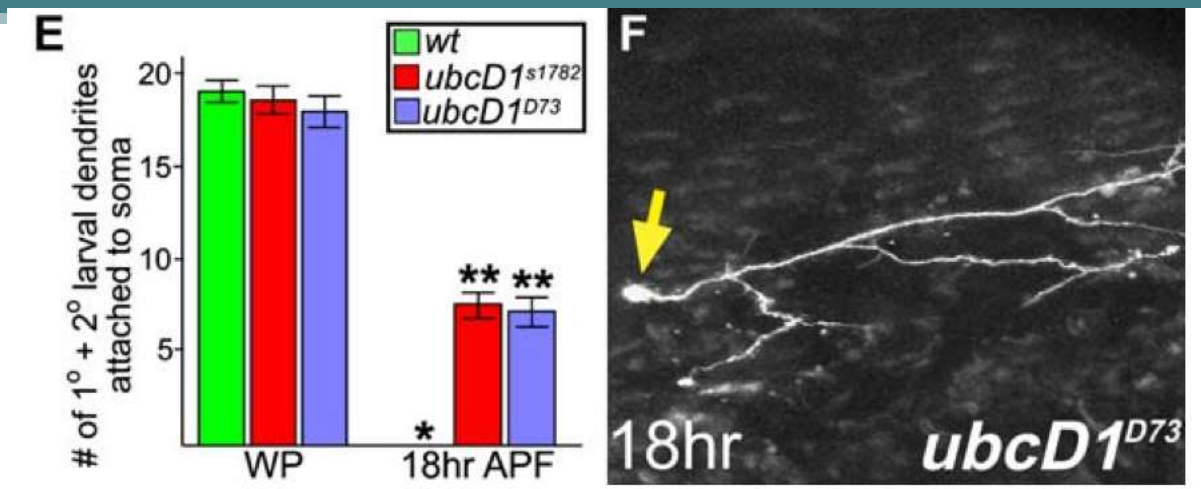
ubiquitination

Table 1. Candida… …ested for C4da Neuron De…

Gene	…enotype
*cbx**	…he
*ubcD2**	…he
*ubcD10**	…he
*ubcD1(eff)**	…ning defect
morgue	…he
*neur**	…he
*su(dx)**	…he
*ari-1**	…he
*ari-2**	…death[a]
*hiw**	…he
*lmg**	…he
parkin	…he
*diap1(th)**	…death[b]
*cul-1(lin19)**	…death[a]
*slmb**	…death[a]
grr1	…he

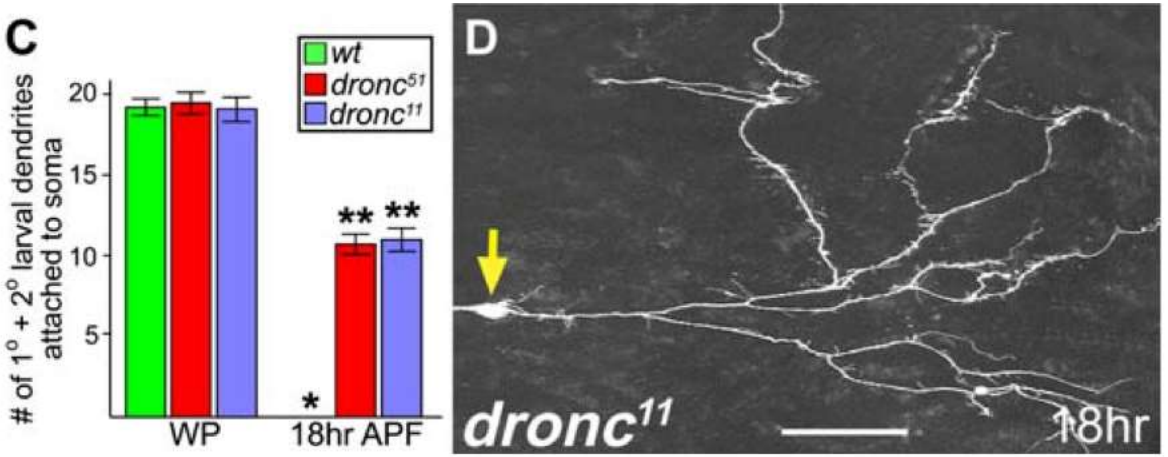
E2, ubiquitin-co… …gase; E3-SCF, ubiquitin ligase c…
* MARCM clonal …
[a] C4da neuron cl… …sis.
[b] C4da neuron clones died prior to metamorphosis.

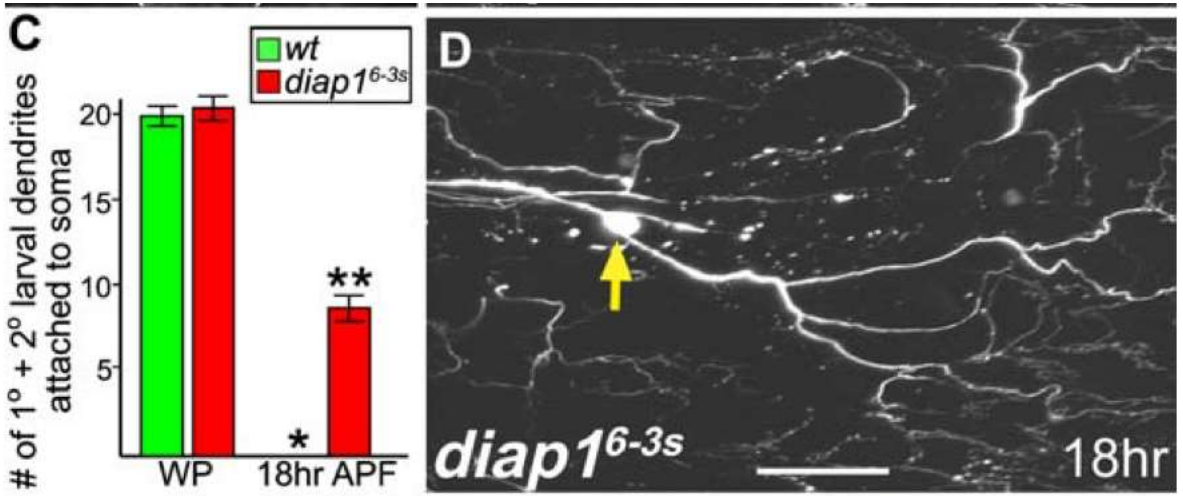




UbcD1 *(effete)* regulates UPS-mediated degradation of the antiapoptotic protein **DIAP1**.

The DIAP1 E3 ubiquitin ligase antagonizes **Dronc caspase** activity.

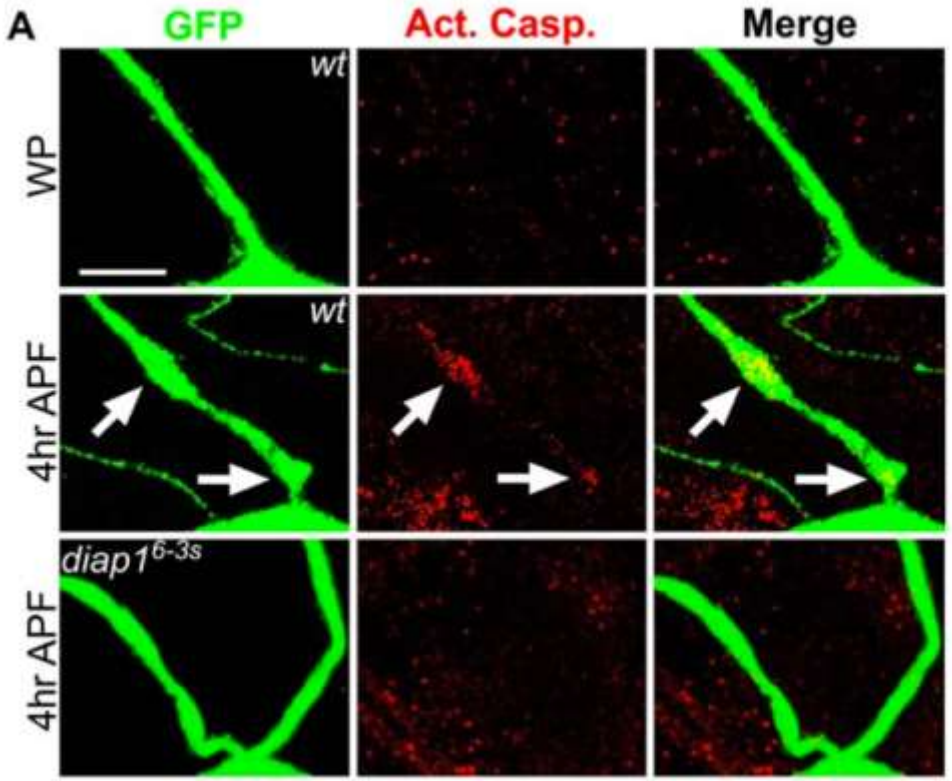


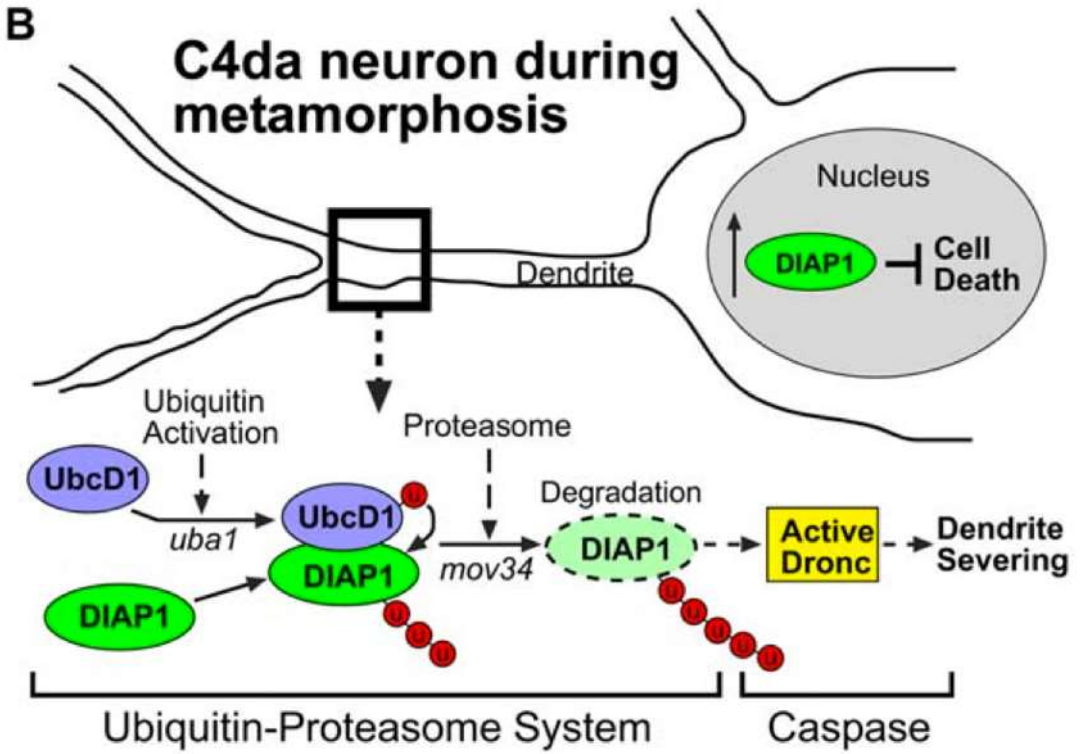


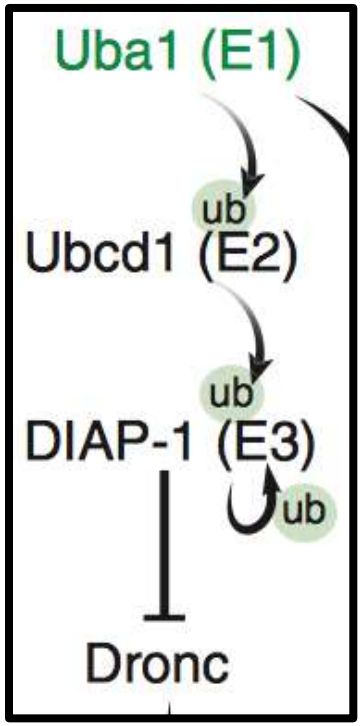
How do the C4da neurons to prune unwanted dendrites without triggering apoptosis?

- To look at the subcellular distribution of DIAP1 and Dronc proteins in ppk-EGFP C4da neurons.

An antibody (anti-mammalian caspase 3) that are effective in recognizing activated caspases in Drosophila.





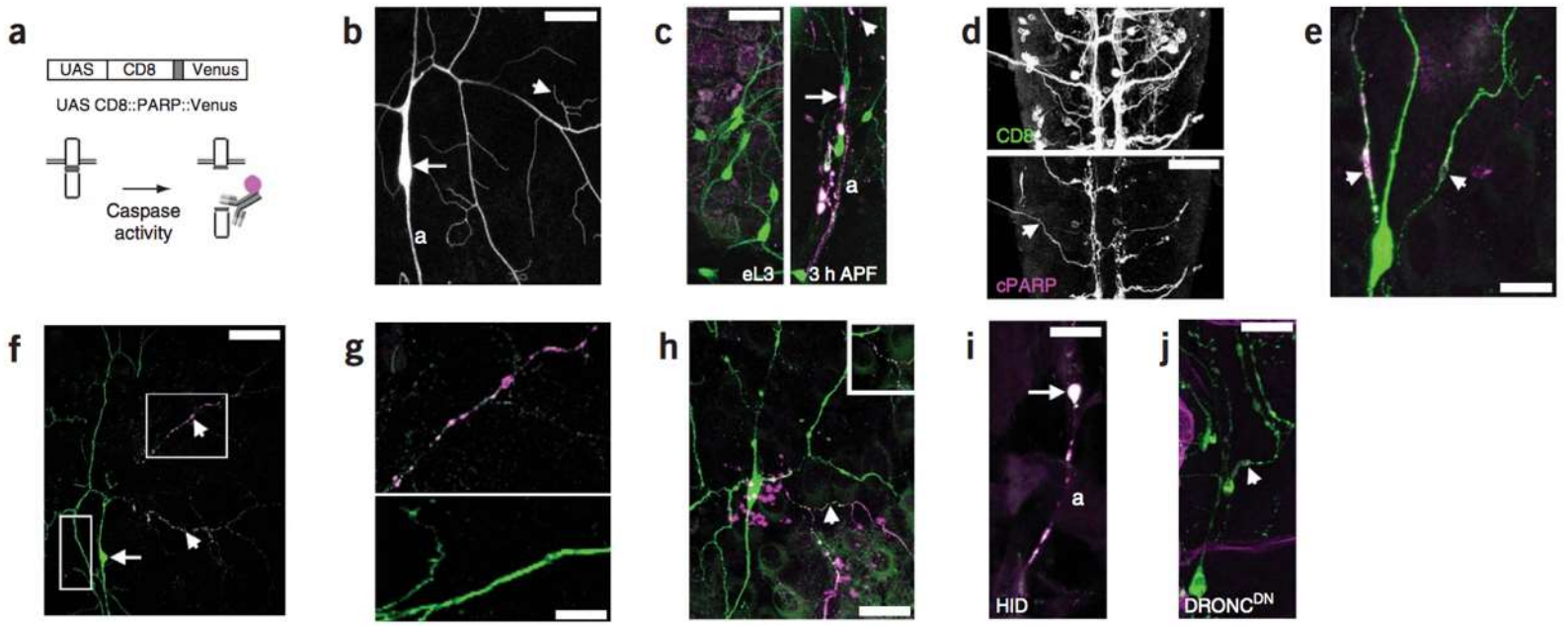


MENU nature neuroscience

Brief Communication | Published: 17 September 2006

Local caspase activity directs engulfment of dendrites during pruning

Darren W Williams, James W Truman



Caspase activation seems to occur after branches are severed and marks them for engulfment by phagocytes.

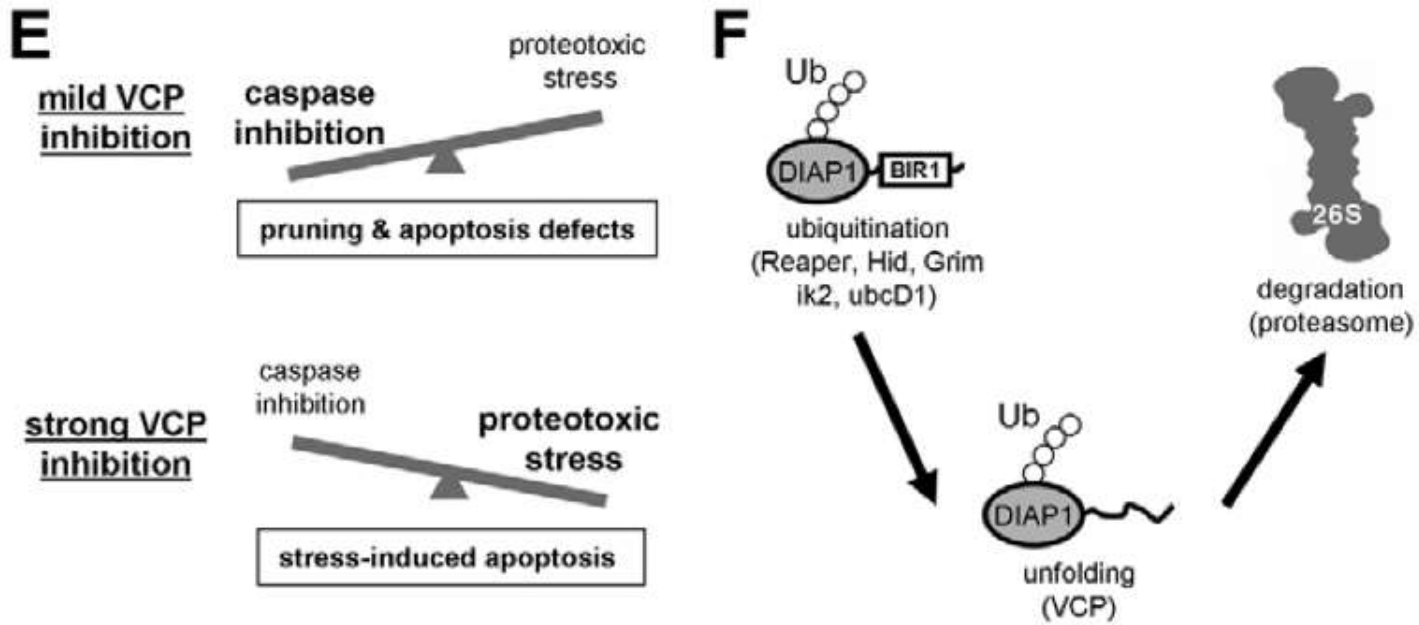
The apoptotic machinery is used for the efficient removal of da sensory neuron dendrites during large-scale pruning

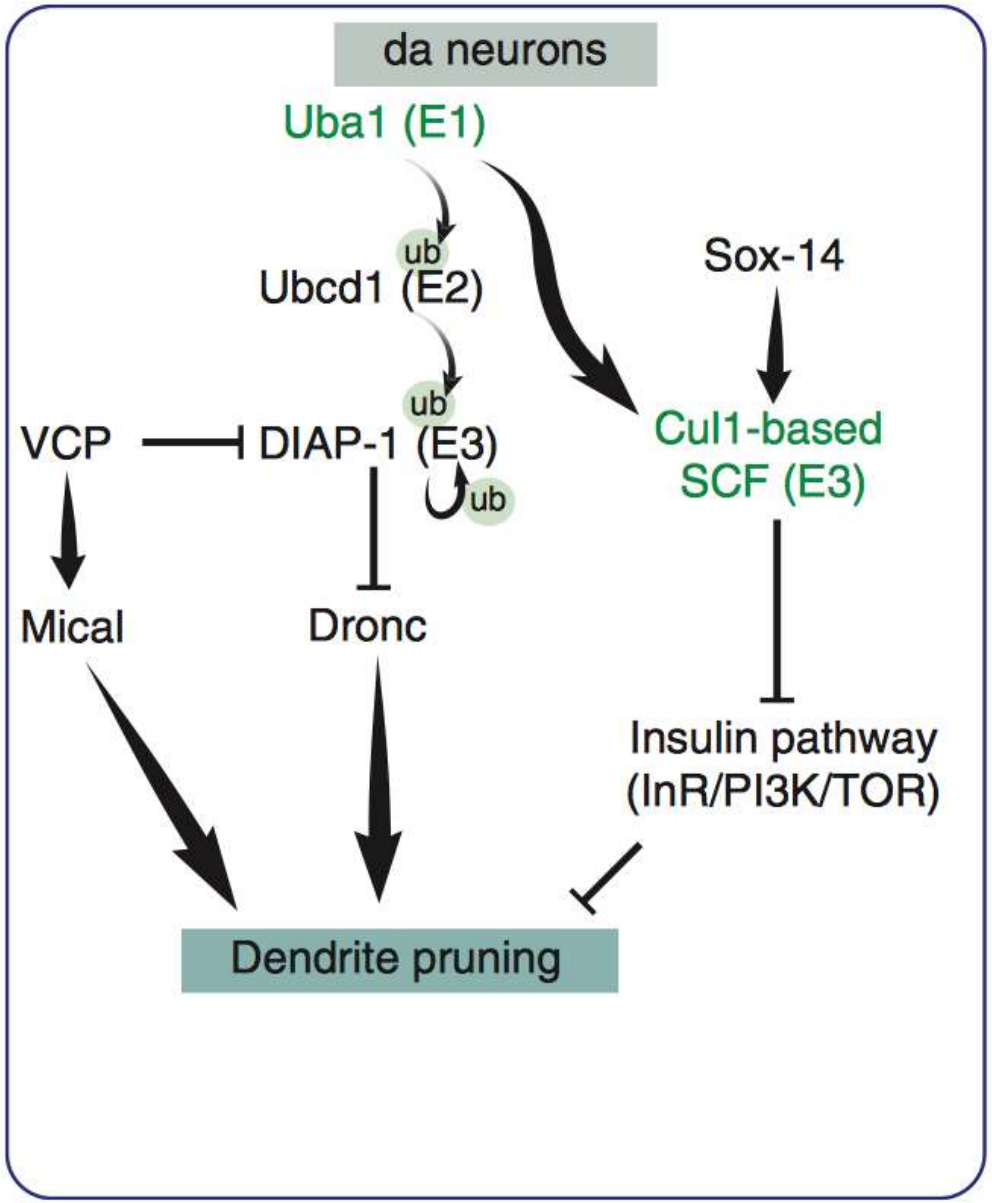
Development 138, 1153-1160 (2011) doi:10.1242/dev.062703

Neuronal remodeling and apoptosis require VCP-dependent degradation of the apoptosis inhibitor DIAP1

Sebastian Rumpf*, Sung Bae Lee*, Lily Yeh Jan and Yuh Nung Jan†

VCP is an abundant AAA ATPase that segregates protein molecules from large cellular structures and thus facilitate the degradation by proteasome.





Yaniv, S. and Schuldiner, O. 2016.

Drosophila IKK-related kinase Ik2 and Katanin p60-like 1 regulate dendrite pruning of sensory neuron during metamorphosis

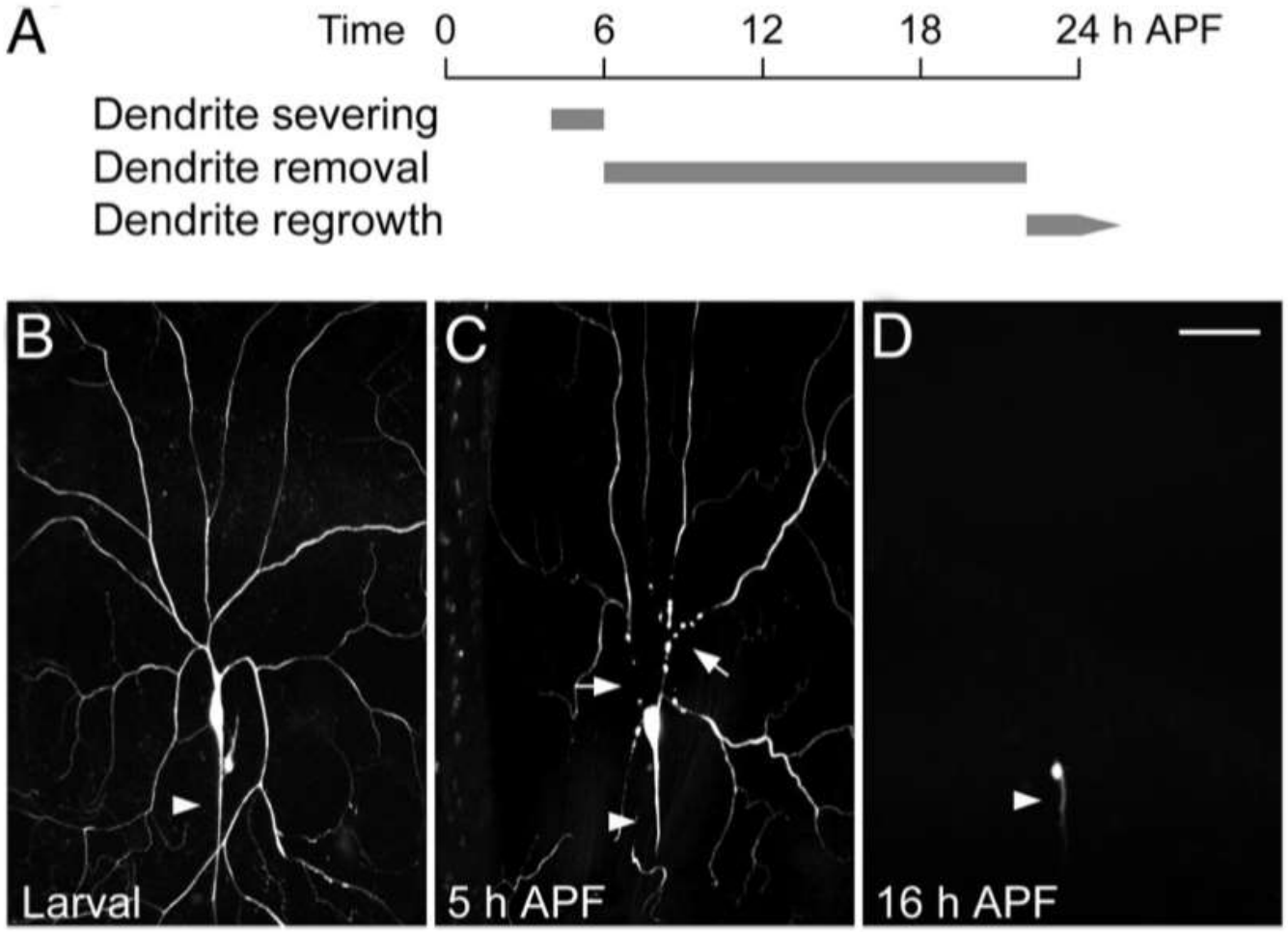
Hsiu-Hsiang Lee, Lily Yeh Jan, and Yuh-Nung Jan[1]

Howard Hughes Medical Institute, Department of Physiology, Biochemistry and Biophysics, University of California, San Francisco, CA 94143

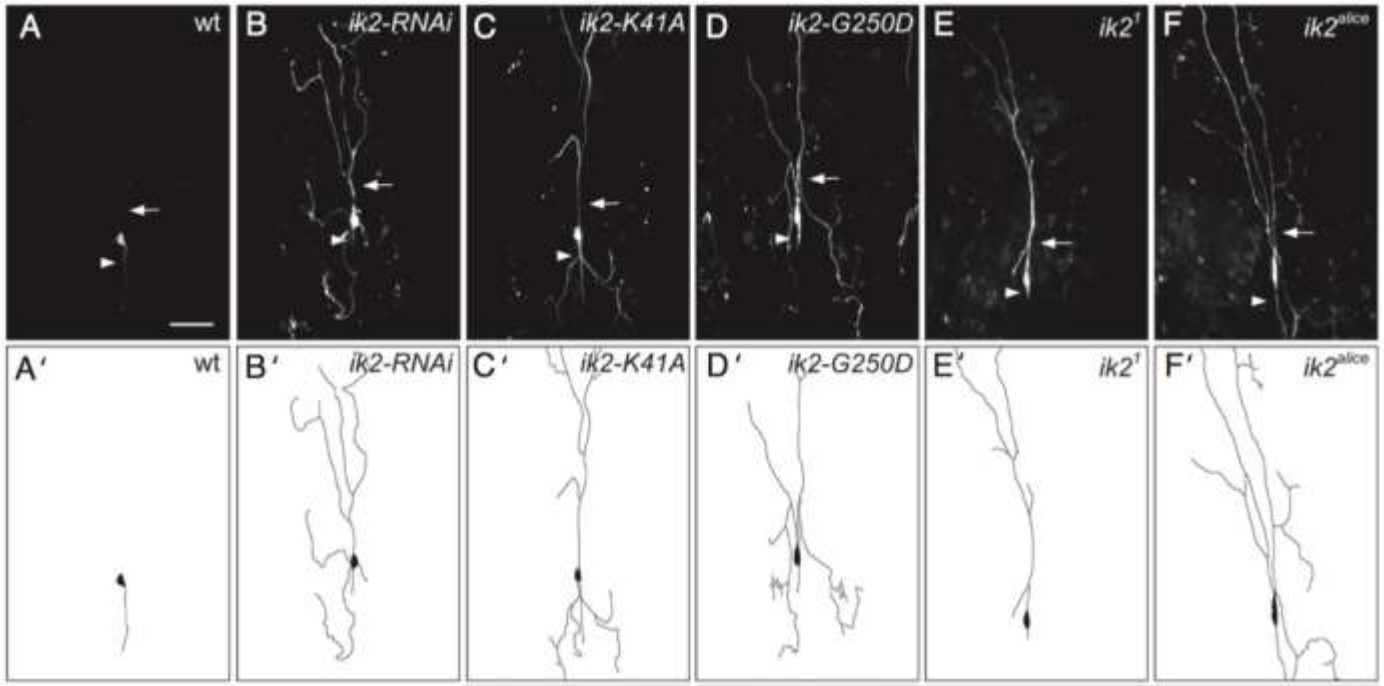
Contributed by Yuh-Nung Jan, February 24, 2009 (sent for review December 30, 2008)

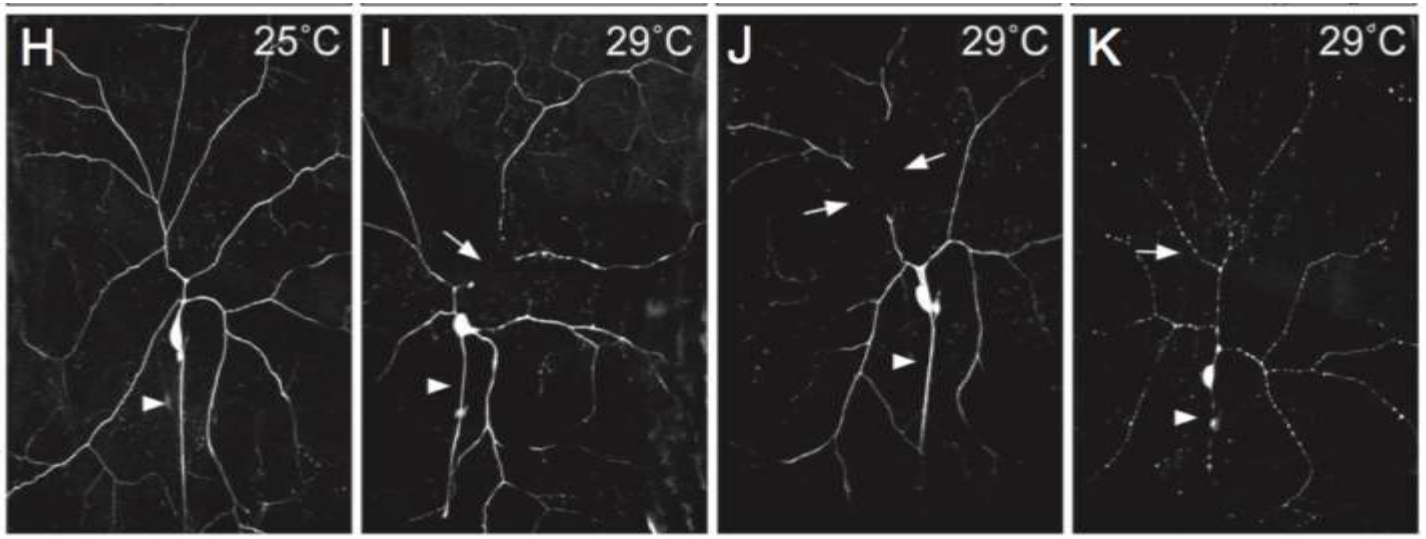
examined the role of Ik2, a non-canonical member of the IκB kinase family that is closely related to the mammalian IKKε/IKKι and TANK binding kinase 1 (TBK1), and functions as an upstream negative regulator of DIAP1 by promoting DIAP1 protein degradation (18, 19).

Sequence of events in the dendrite pruning of *Drosophila* sensory neurons

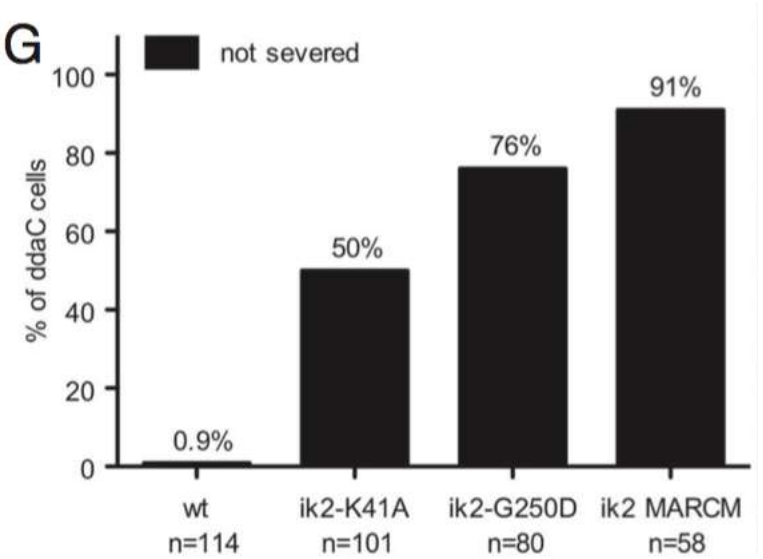


1. Ik2 is essential for dendrite severing during dendrite pruning.





Necessary

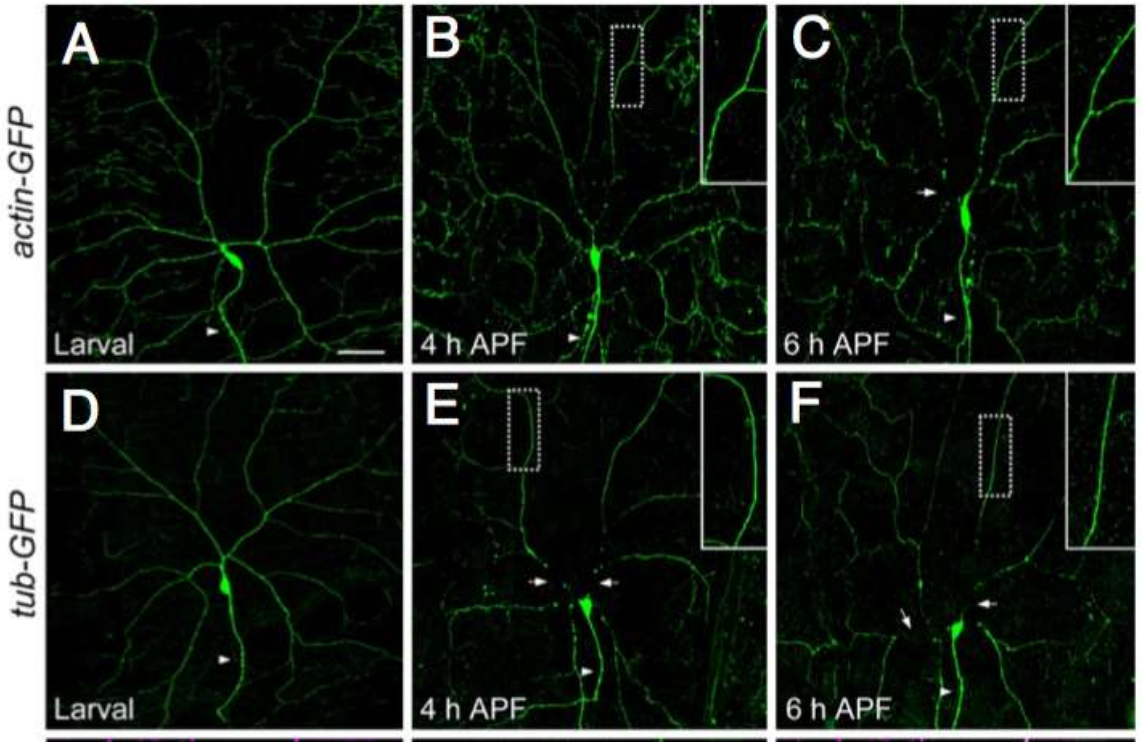


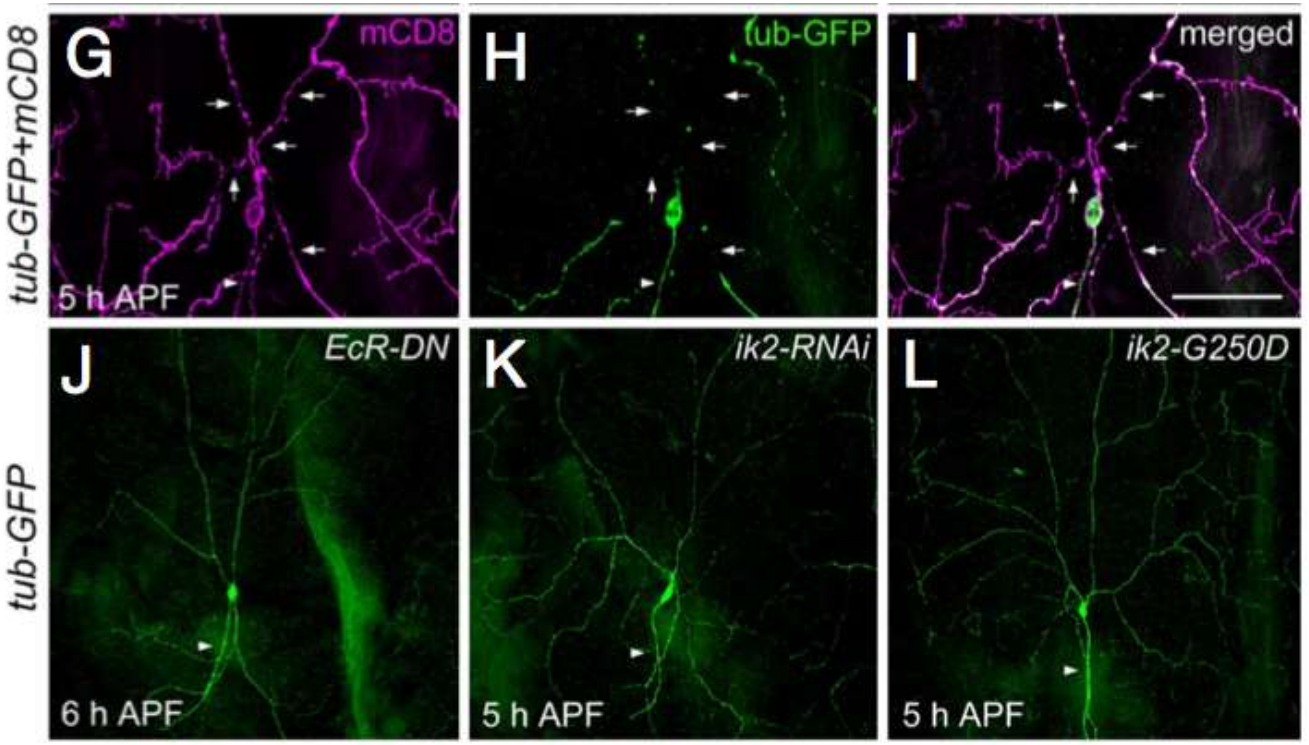
Sufficient

tub-GAL80 ^{ts} ,ppk-eGFP,ppk-GAL4, UAS-ik2

Larvae

2. Localized breakage of microtubule and actin cytoskeletons in the proximal dendrites of ddaC neurons during severing.

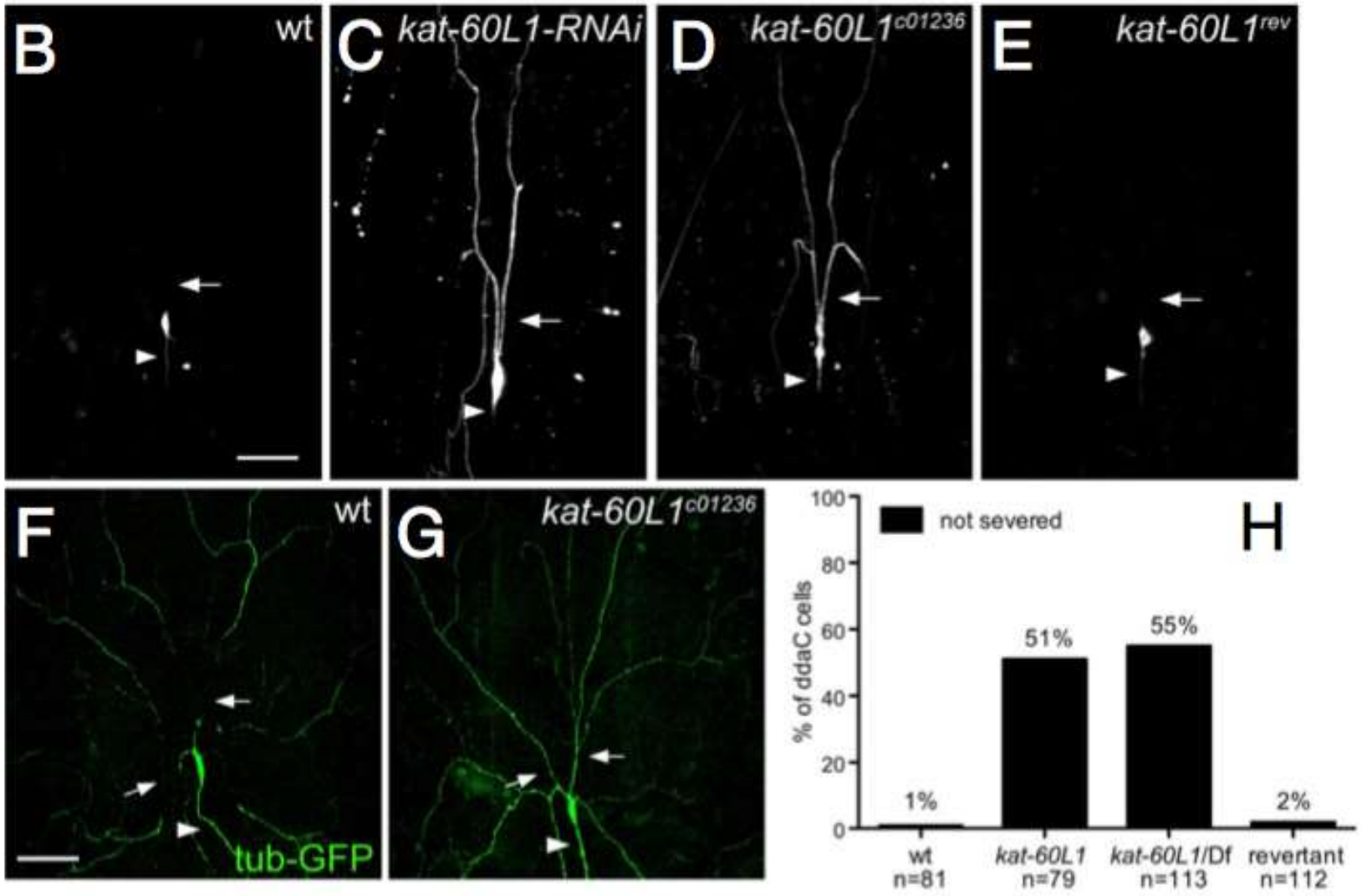


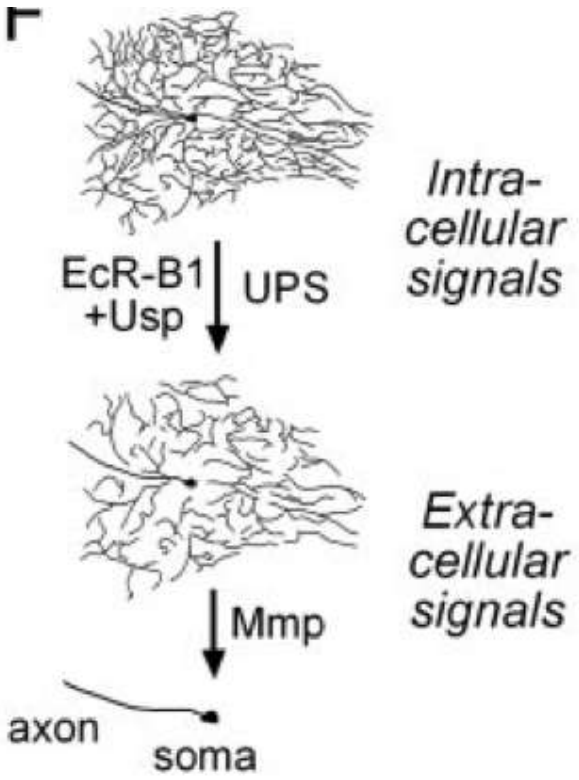


The microtubule and actin cytoskeletons of ddaC neurons are first disrupted in the proximal dendrites before the disconnection of dendritic membrane.

3. RNAi screen on candidate molecules with microtubule-severing or -destabilizing activities

CG1193





nature neuroscience

Article | Published: 01 November 2009

A genetic pathway composed of Sox14 and Mical governs severing of dendrites during pruning

Daniel Kirilly, Ying Gu, Yafen Huang, Zhuhao Wu, Arash Bashirullah, Boon Chuan Low, Alex L Kolodkin, Hongyan Wang & Fengwei Yu

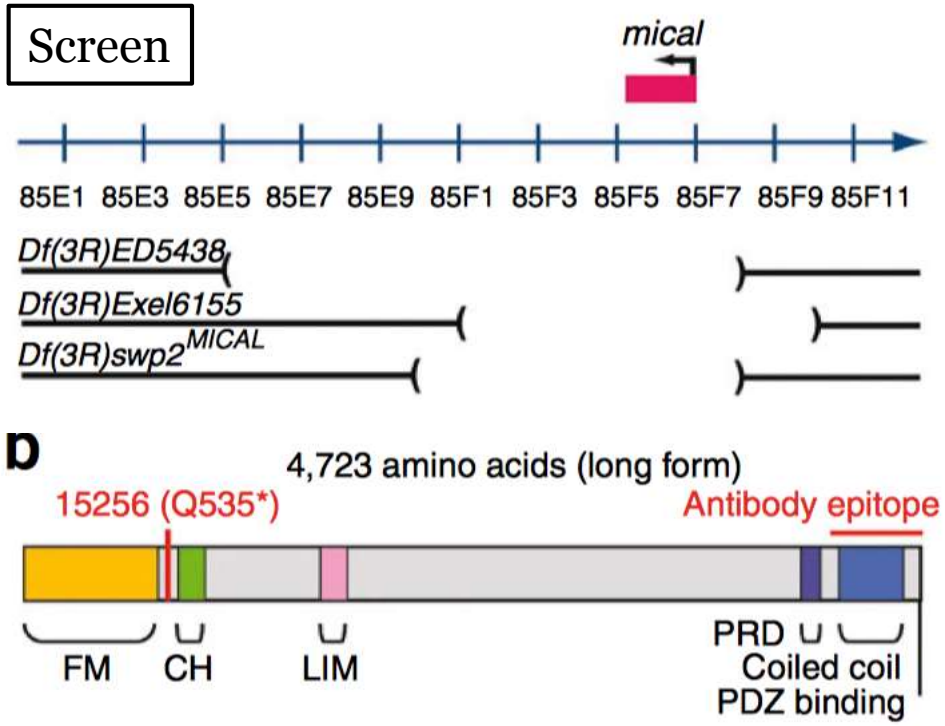
Nature Neuroscience **12**, 1497–1505(2009) | Cite this article

Kuo, C., Jan, L. and Jan, Y. 2005.

Screen the downstream of EcR/Usp via RNAi from previous microarray analyses.

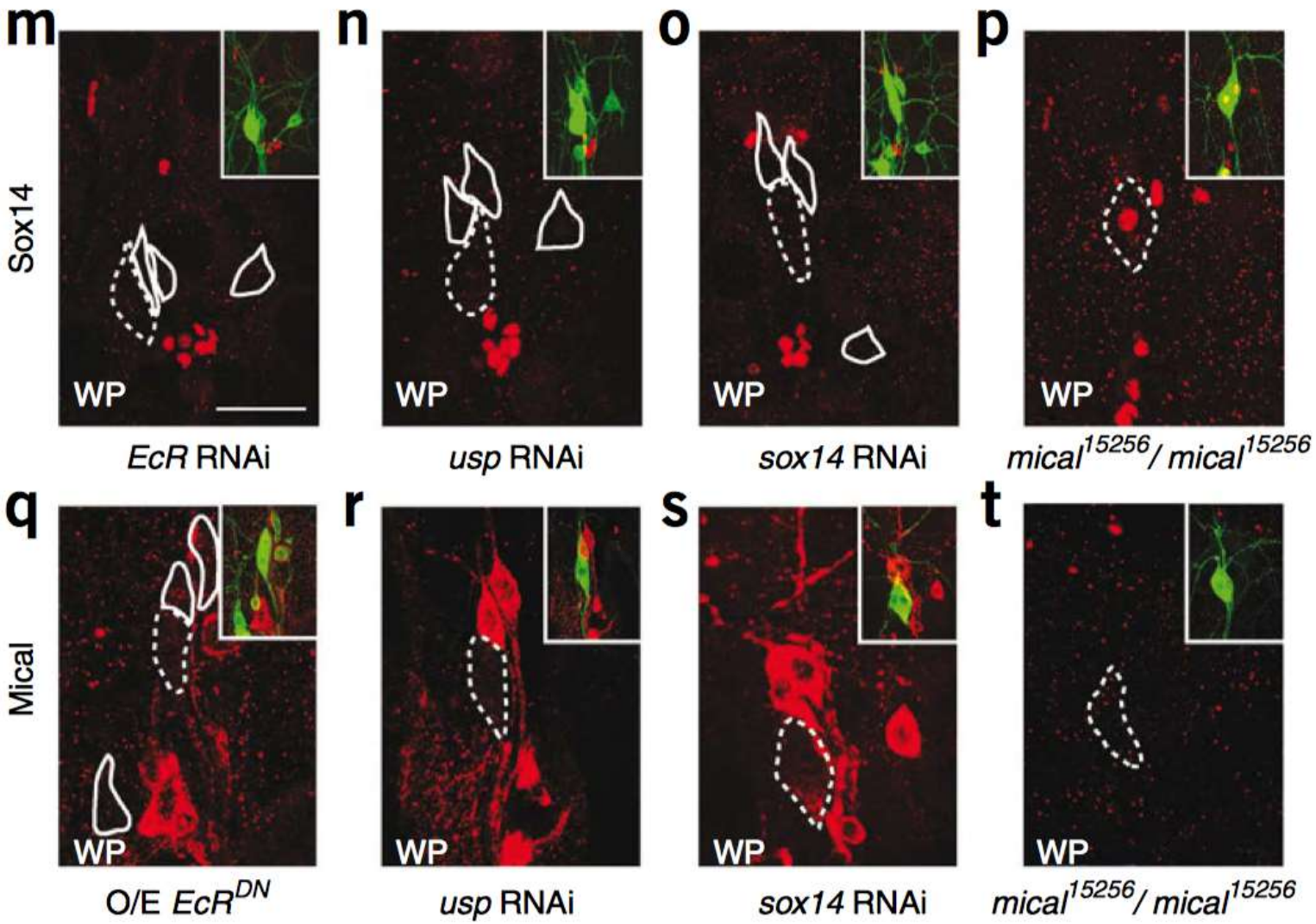
-The transcription factor Sox14 mediates dendrite severing

Screen

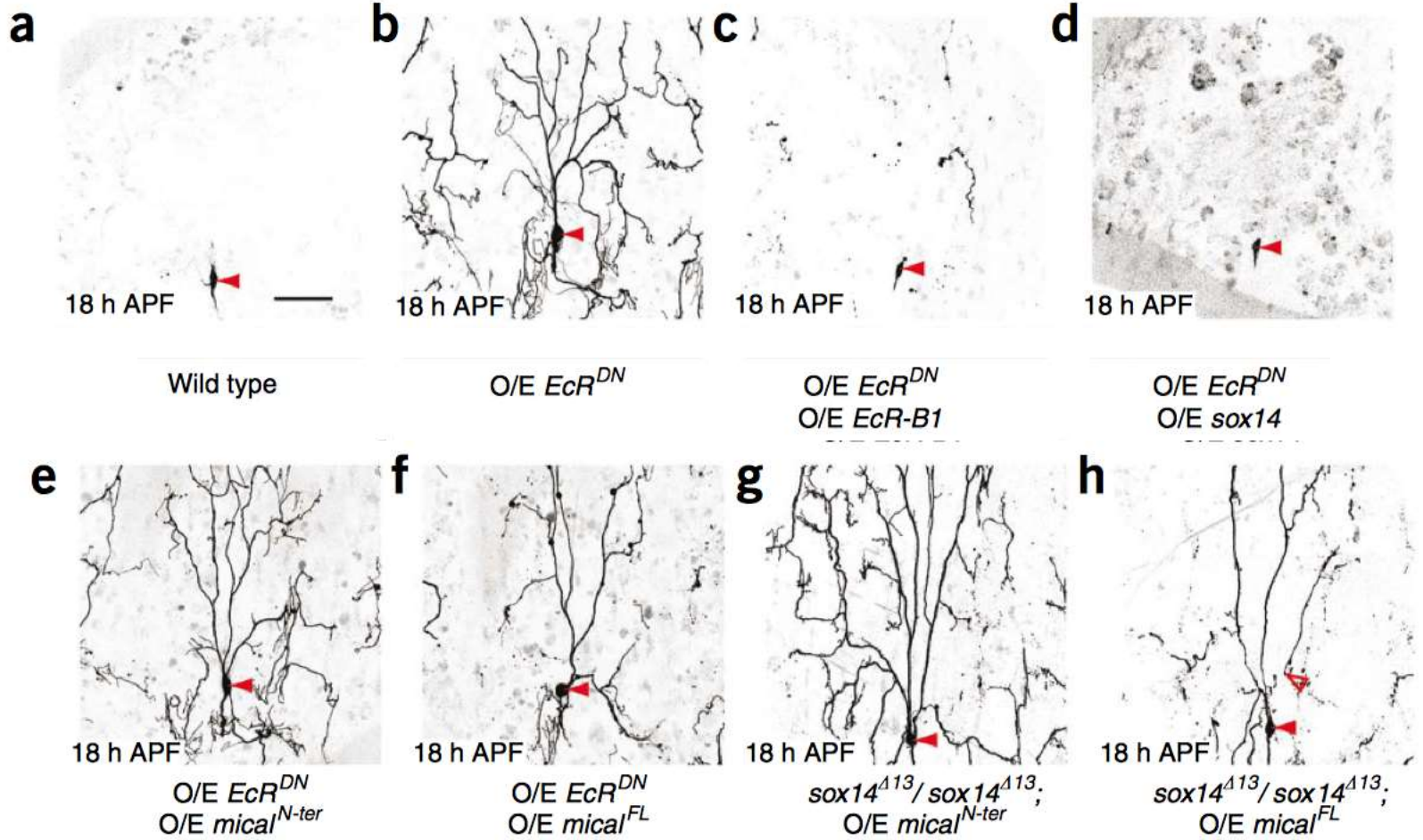


-Mical, encoding an actin-severing enzyme，promotes dendrite severing

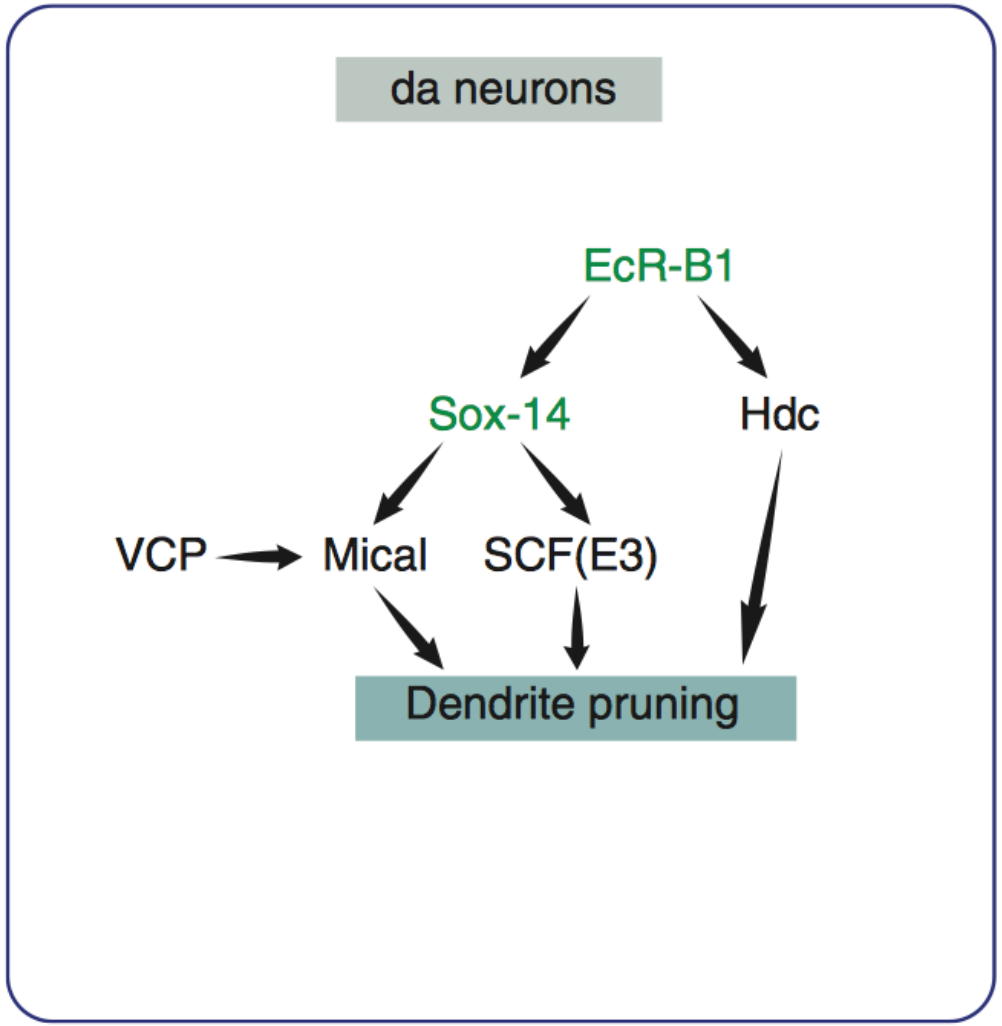
Mical and Sox14 are downstream targets of EcR/Usp



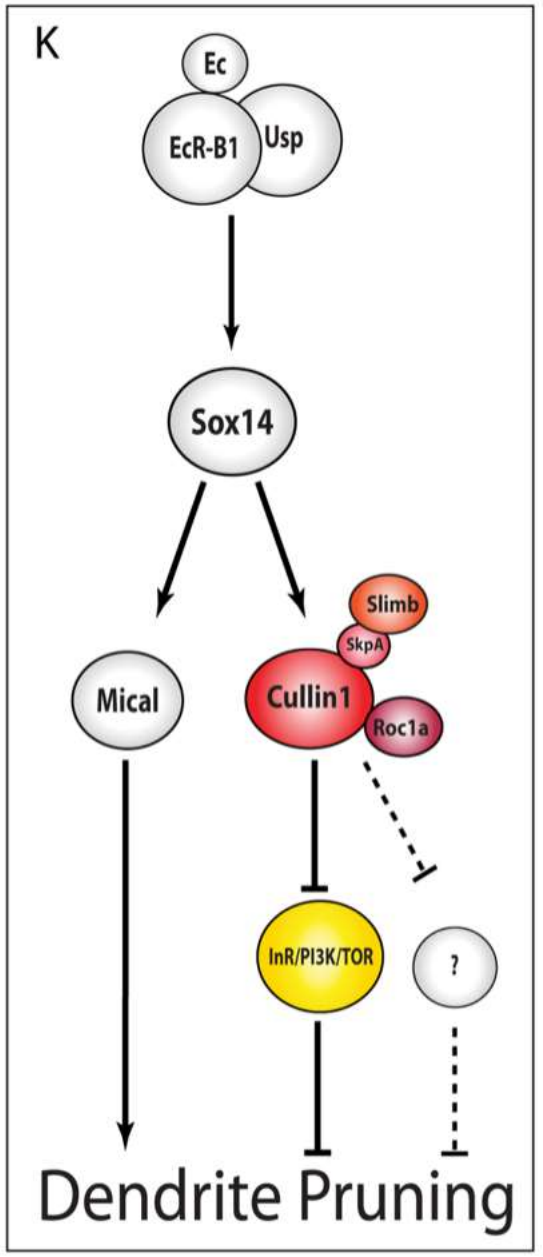
Mical acts downstream of EcR-B1 and Sox14 during severing.



full-length Mical (Mical FL)
N-terminal portion of Mical (Mical N-ter)



Yaniv, S. and Schuldiner, O. 2016.



Wong, J. et al. 2013.

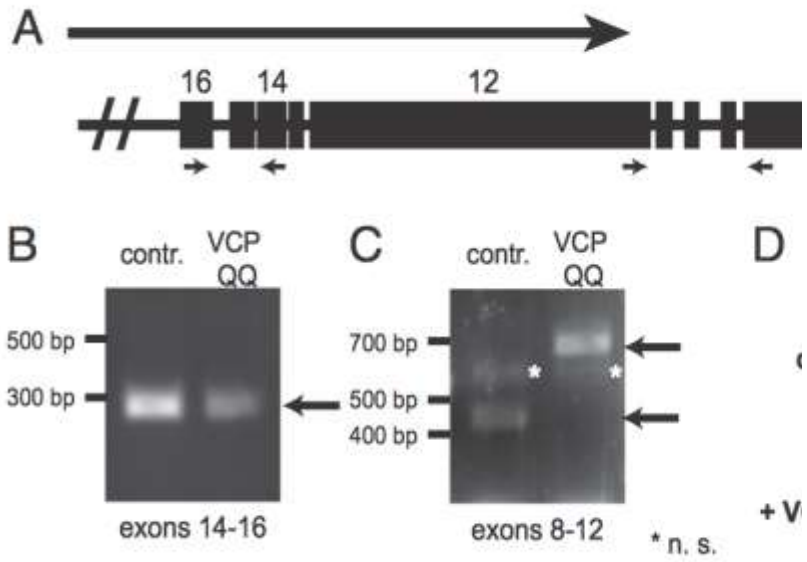
PNAS

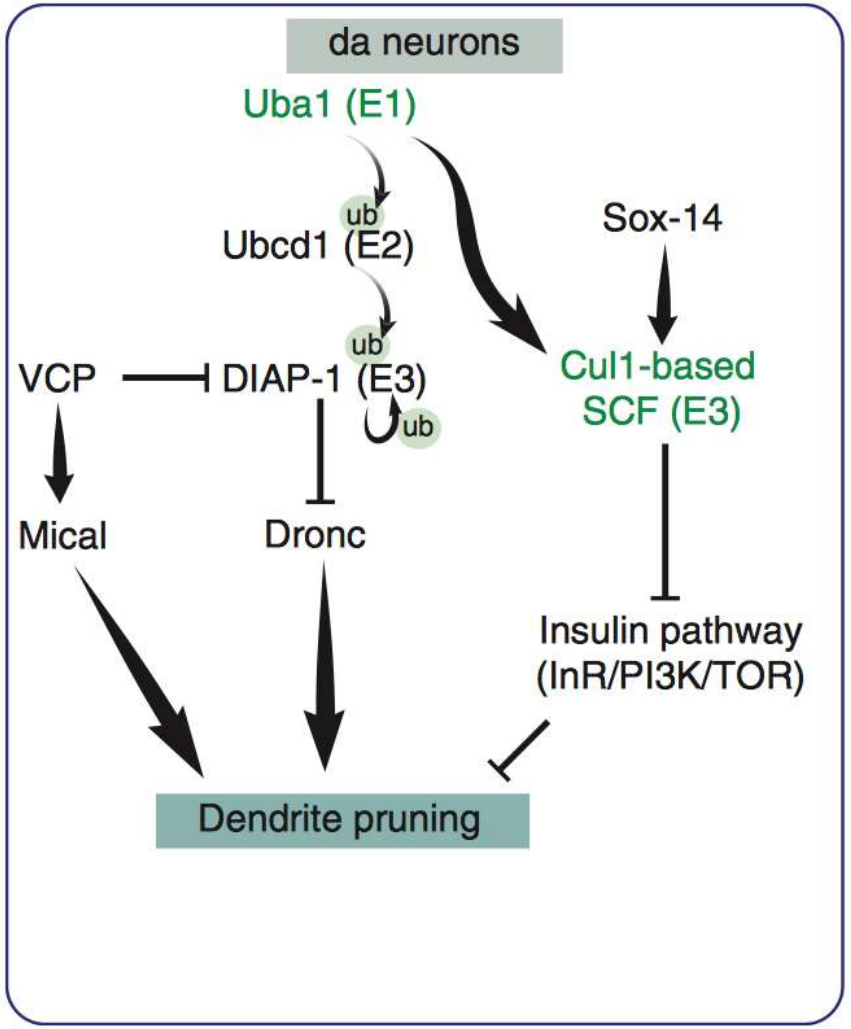
Drosophila Valosin-Containing Protein is required for dendrite pruning through a regulatory role in mRNA metabolism

Sebastian Rumpf[a,b,c,1,2], Joshua A. Bagley[a,b,c], Katherine L. Thompson-Pe
Robert B. Beckstead[d], Lily Yeh Jan[a,b,c], and Yuh Nung Jan[a,b,c,2]

[a]Howard Hughes Medical Institute and Departments of [b]Physiology and [c]Biochemistry, Univers
Department, University of Georgia, Athens, GA 30602

Contributed by Yuh Nung Jan, April 16, 2014 (sent for review December 20, 2013)





MICAL mRNA is misspliced upo

17086 • The Journal of Neuroscience, November 28, 2012 • 32(48):17086–17096

Development/Plasticity/Repair

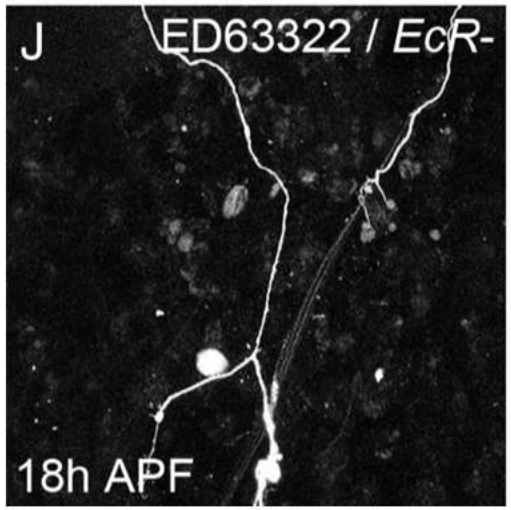
An Interaction Screen Identifies *headcase* as a Regulator of Large-Scale Pruning

Nicolas Loncle and Darren W. Williams
Medical Research Council Centre for Developmental Neurobiology, King's College London, London SE1 1UL, United Kingdom

To isolate novel regulators:

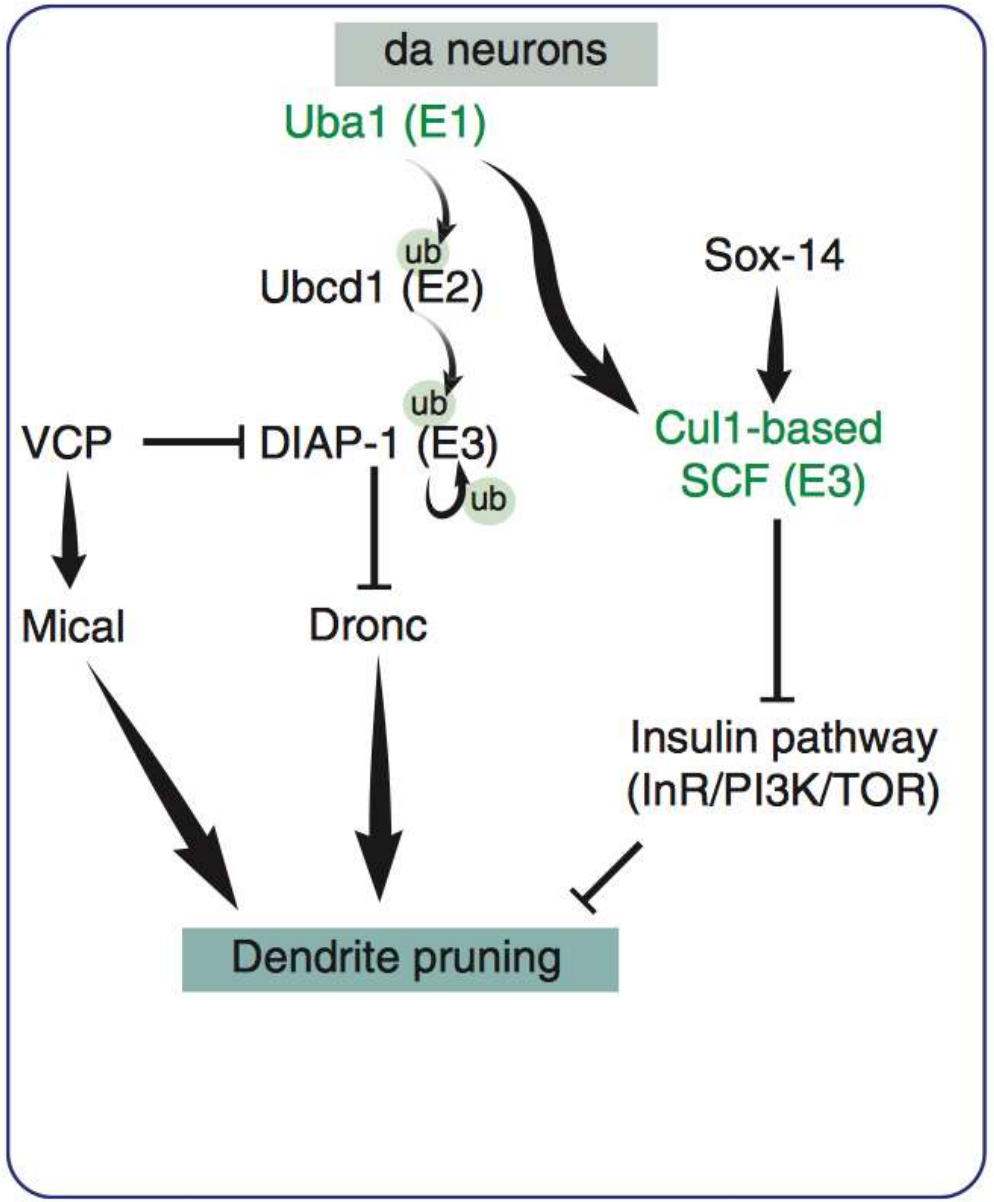
EcR M554fs, ppk-GAL4-CD8::GFP

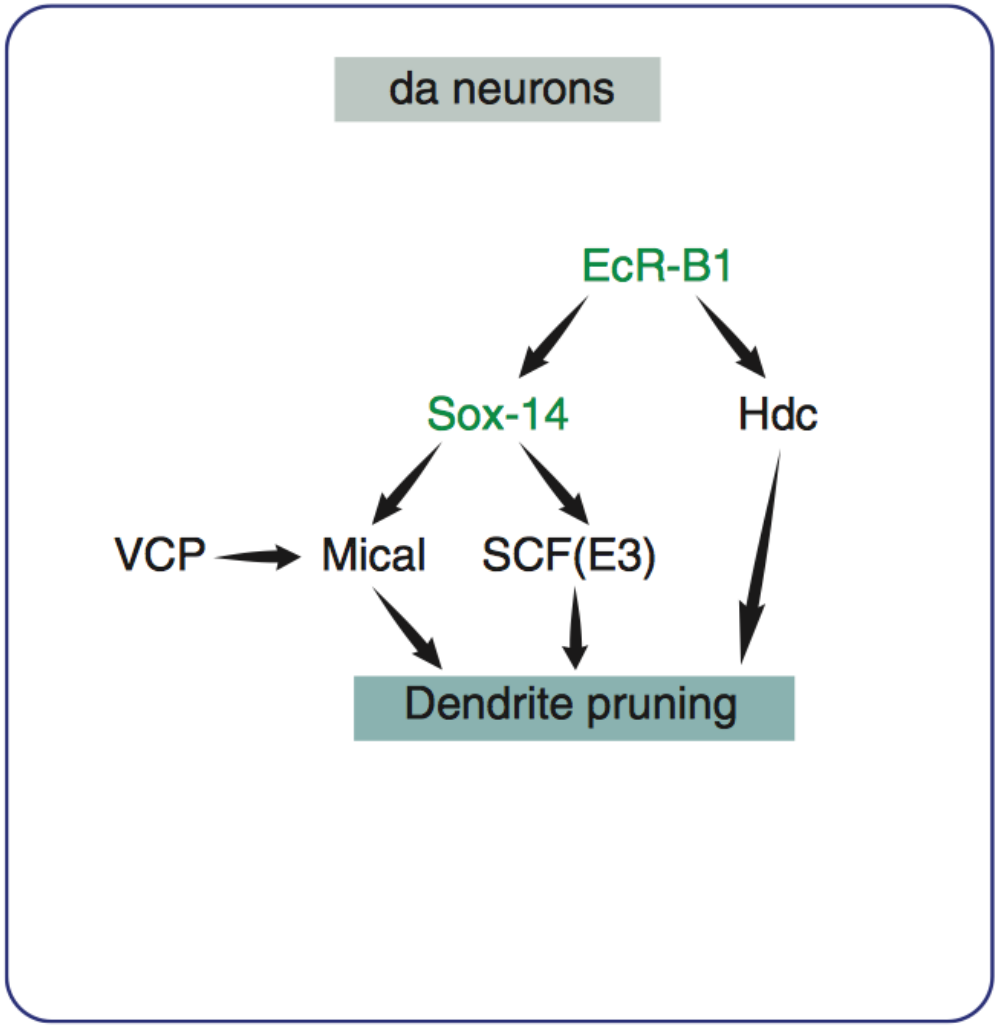
Df(3R) _____



Df(3R)ED6332

headcase


da neurons
Uba1 (E1)
ub
Ubcd1 (E2)
Sox-14
ub
VCP
DIAP-1 (E3)
ub
Cul1-based
SCF (E3)
Mical
Dronc
Insulin pathway
(InR/PI3K/TOR)
Dendrite pruning


da neurons
EcR-B1
Sox-14
Hdc
VCP
Mical
SCF(E3)
Dendrite pruning

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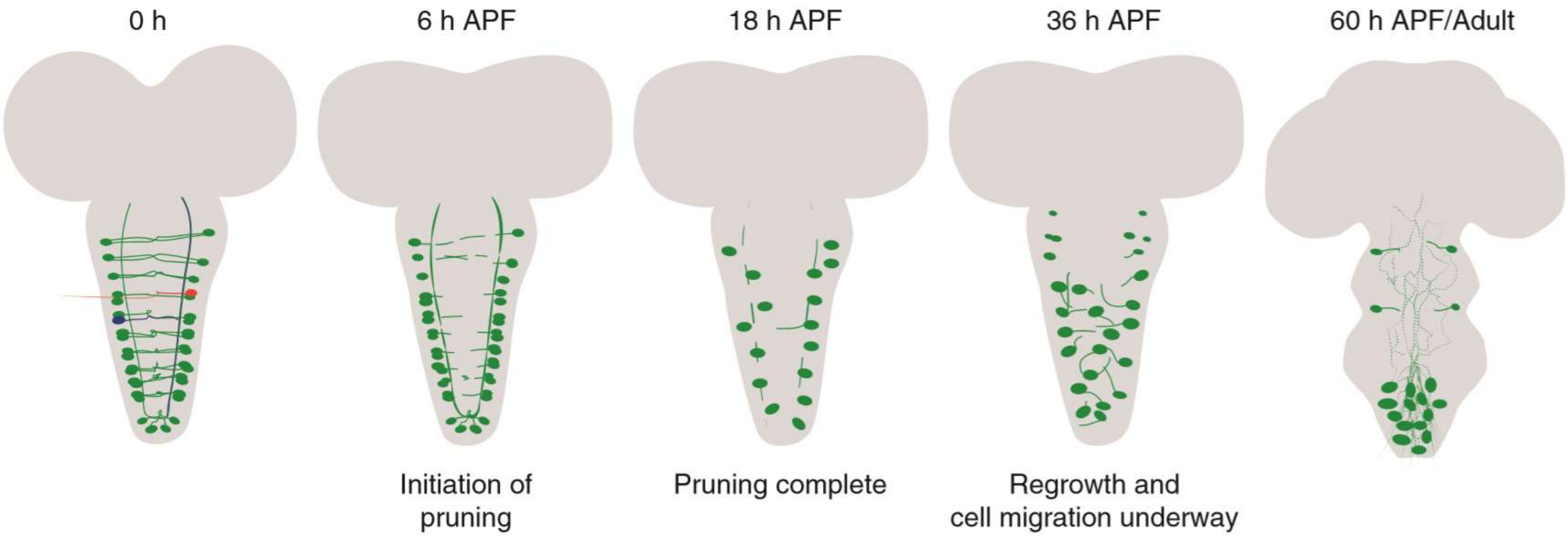
[9] Wong, J., Li, S., Lim, E., Wang, Y., Wang, C., Zhang, H., Kirilly, D., Wu, C., Liou, Y.-C., Wang, H. and Yu, F. 2013. A Cullin1-based SCF E3 ubiquitin ligase targets the InR/PI3K/TOR pathway to regulate neuronal pruning. *PLoS biology*. 11, 9 (2013), e1001657.
[10]Yaniv, S. and Schuldiner, O. 2016. A fly's view of neuronal remodeling. *Wiley interdisciplinary reviews. Developmental biology*. 5, 5 (2016), 618–35.

Neuronal remodeling of CCAP/Bursicon neurons

Su Xiangbin
2019-11-29

CONTENTS

Remodeling of CCAP/Bursicon neurons during metamorphosis



Shiri P. Yaniv and Oren Schuldiner. 2016

Questions

1, Morphological changes of CCAP during neuronal remodeling.

2, The spatio-temporal regulation of CCAP during neuronal remodeling.

1), Molecular mechanism of CCAP neuron remodeling.

2), Initial signals for CCAP neuron remodeling.

3), CCAP neurons located correctly during migration.

……

PART 1 Review of CCAP/Bursicon neurons

- CCAP/Bursicon neurons

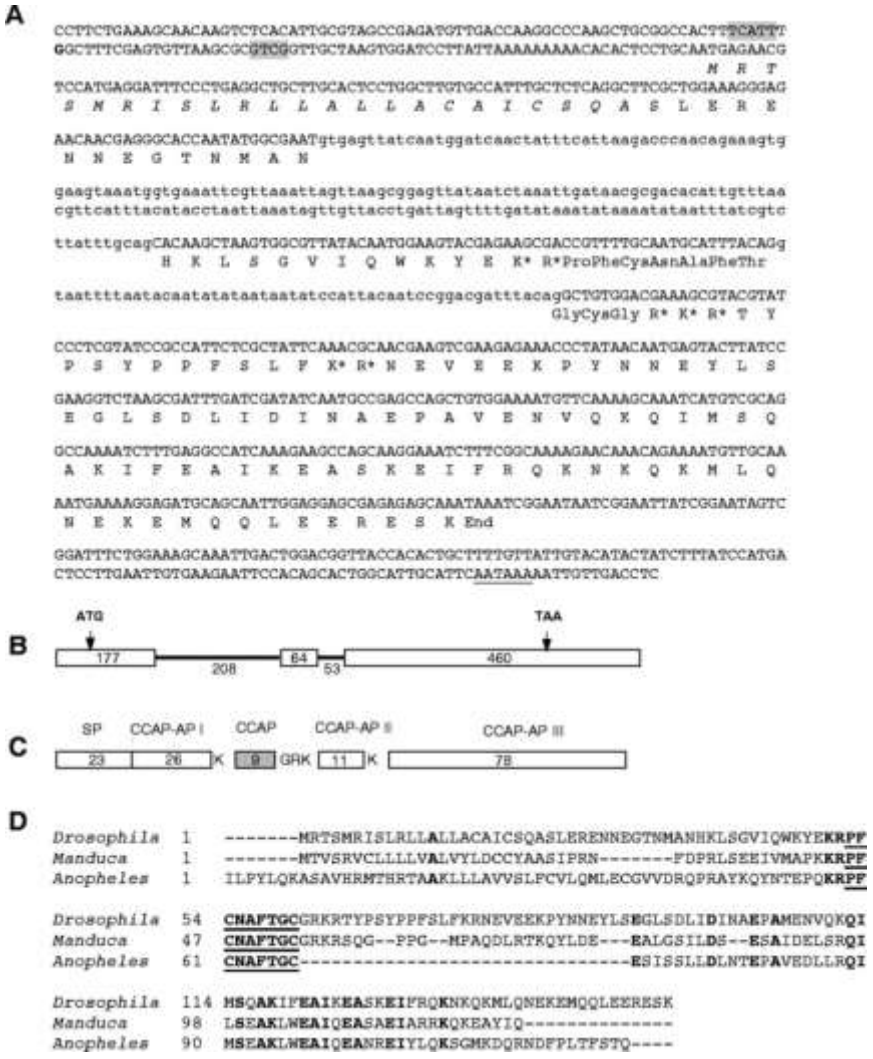
  Crustacean cardioactive peptide (CCAP) expressing neurons

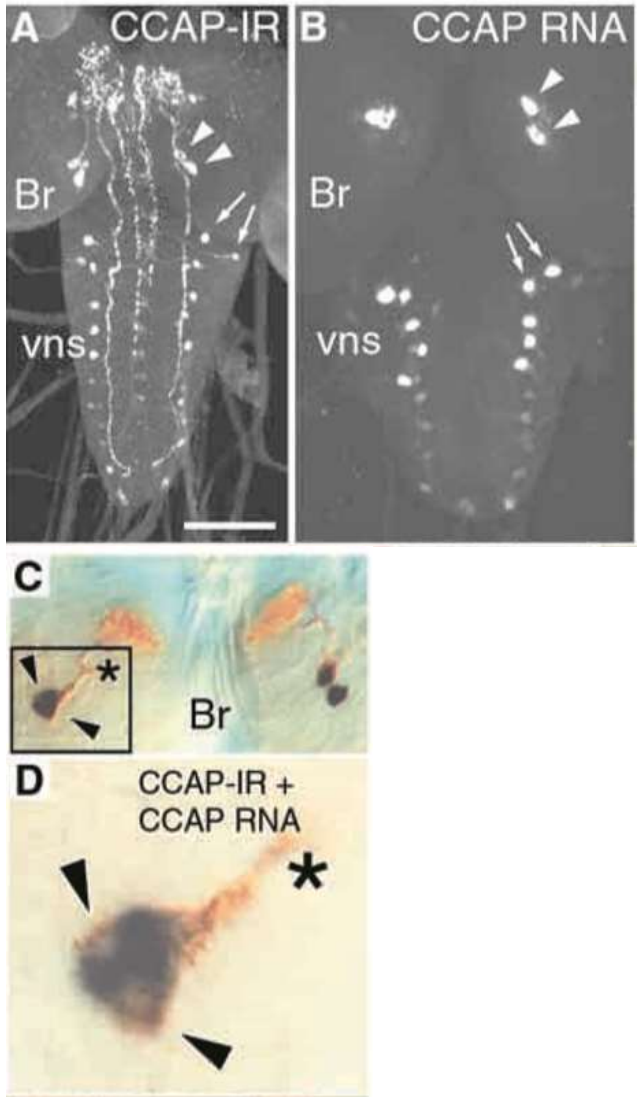
- Located in the ventral nerve cord

- Two major types

  Interneurons and efferent neurons

Structure of CCAP gene and Expression of CCAP RNA in CCAP neurons

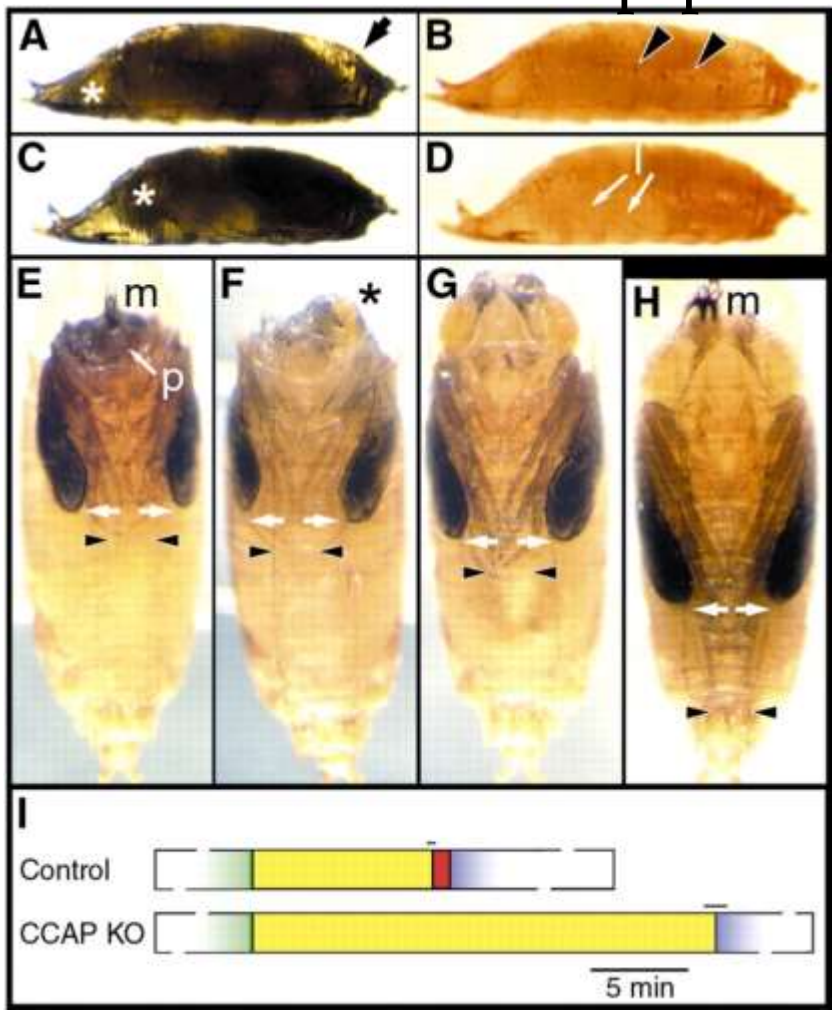




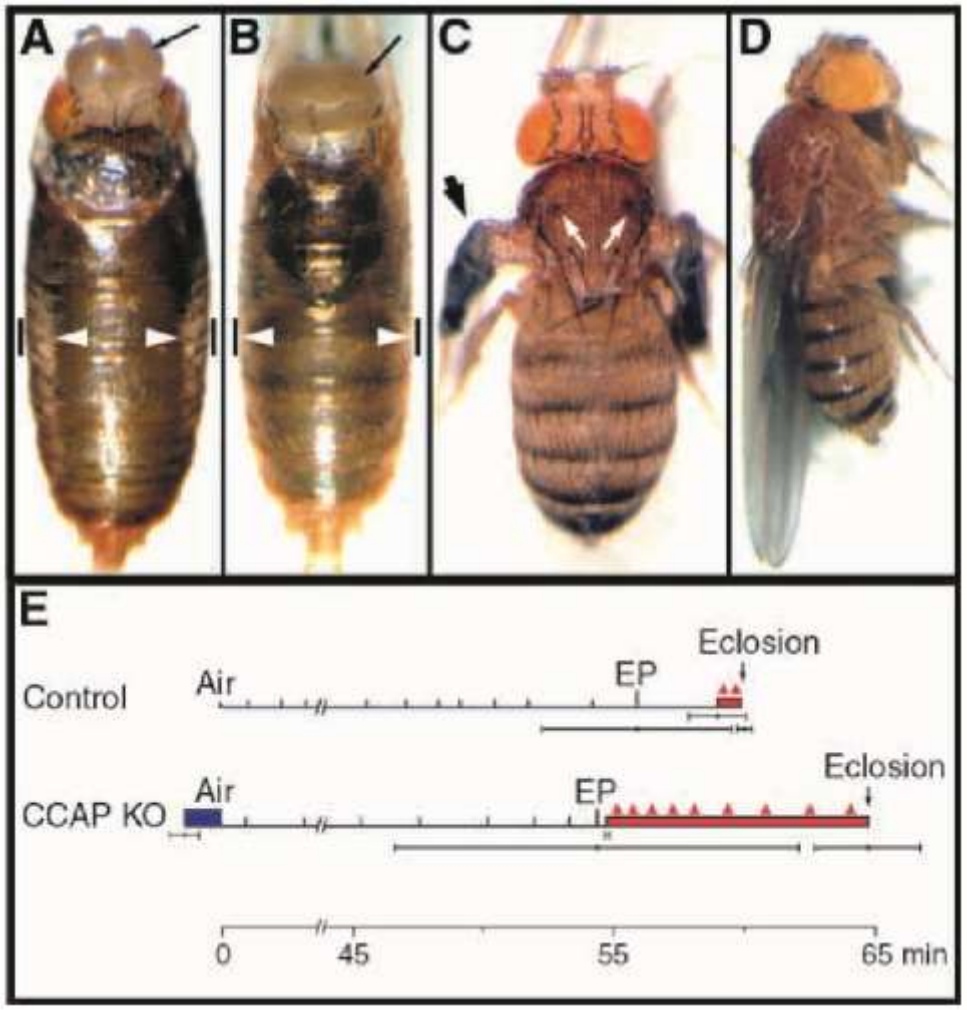
Park JH, et al. Development. 2003

Function of CCAP/Bursicon neurons

1) Targeted ablation of CCAP neurons causes failures of pupation



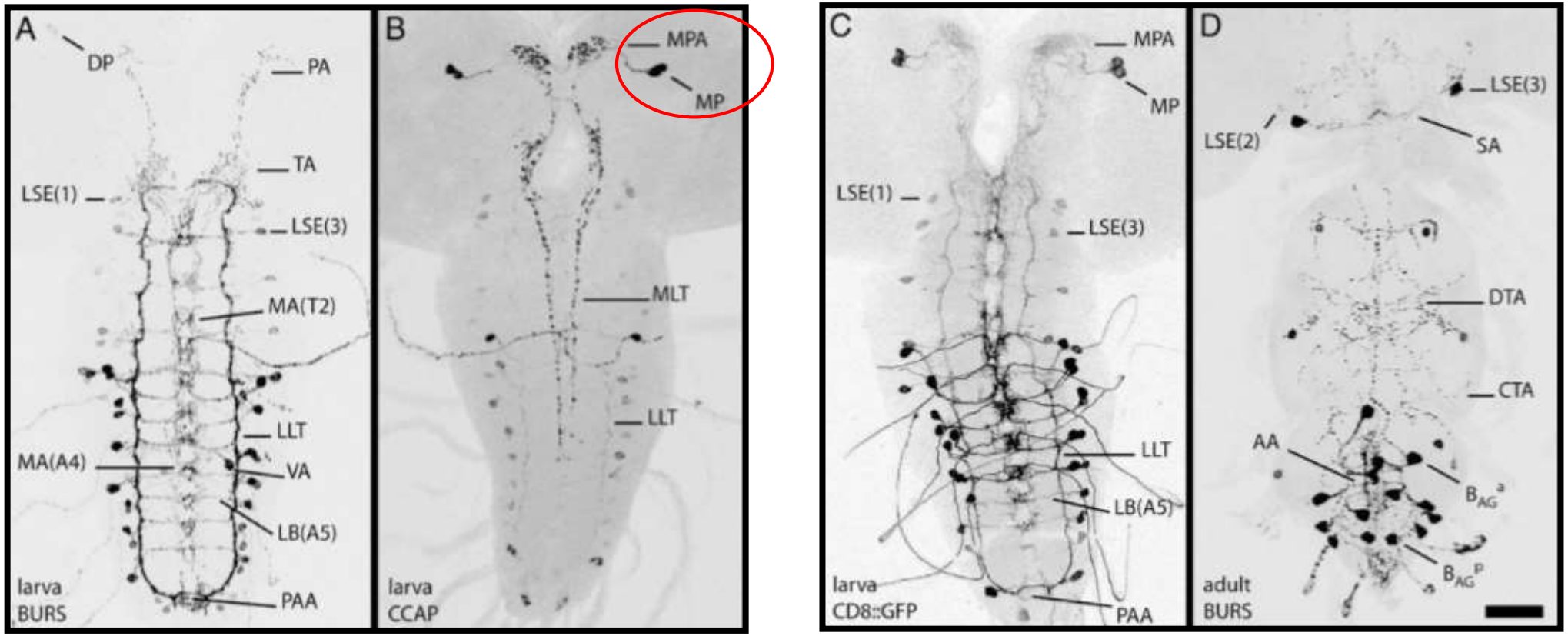
2) Targeted ablation of CCAP neurons causes defects at eclosion and in post-



Park JH, et al. Development. 2003

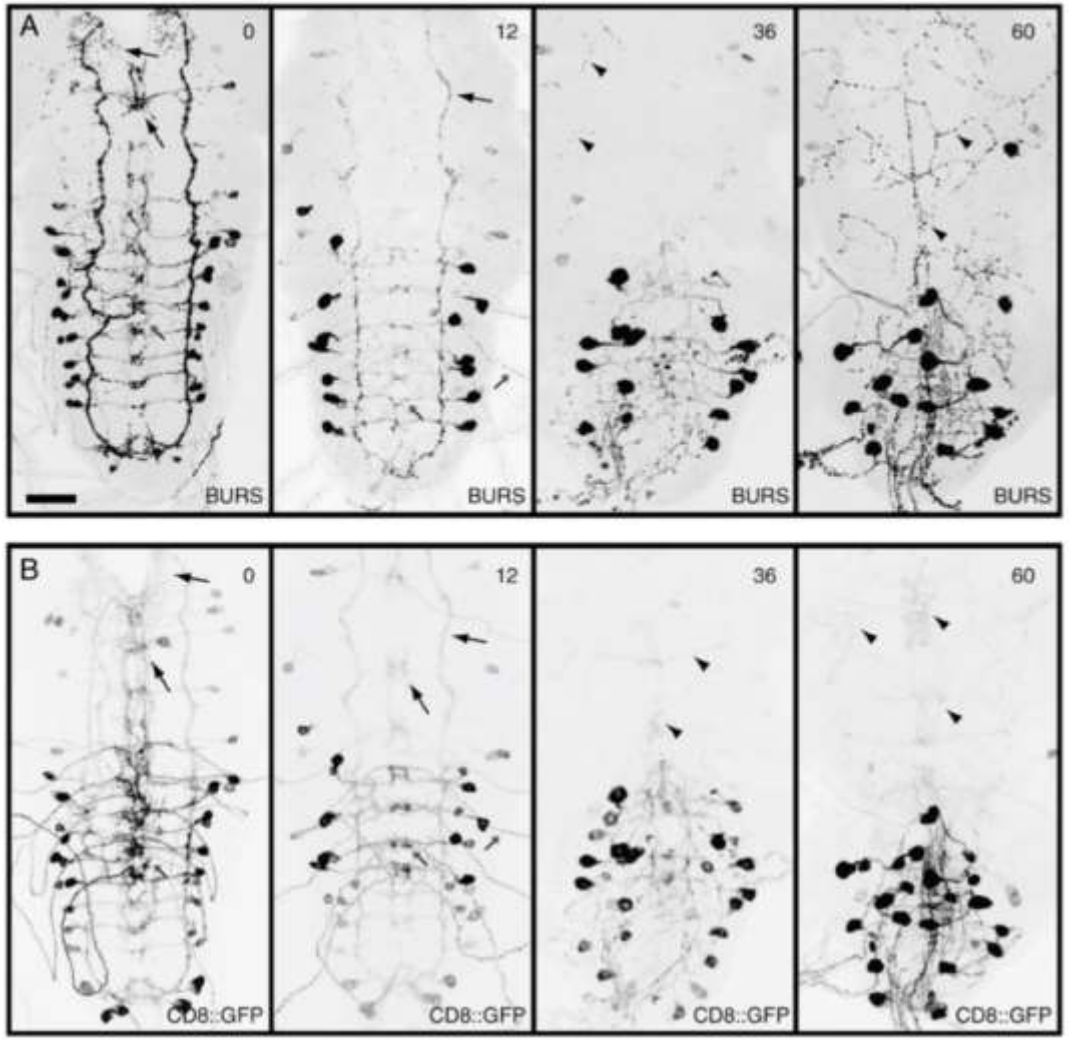
PART 2 Morphological changes of CCAP/Bursicon during neuronal remodeling

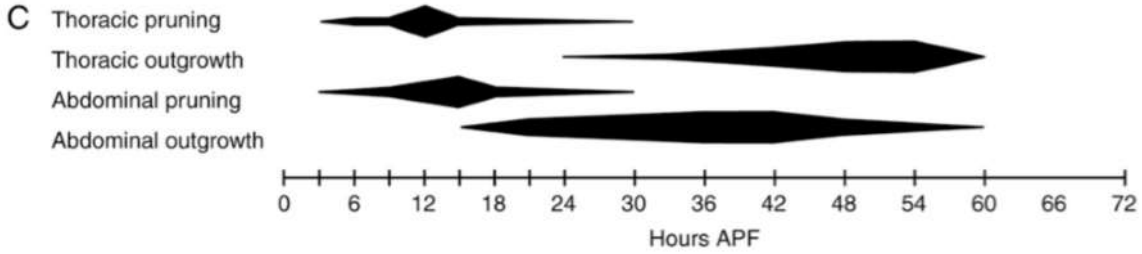
Staining patterns and morphologies of the CCAP/bursicon neurons



Tao Zhao, et al. Genetics. 2008

Remodeling of the CCAP/bursicon neurons during metamorphosis

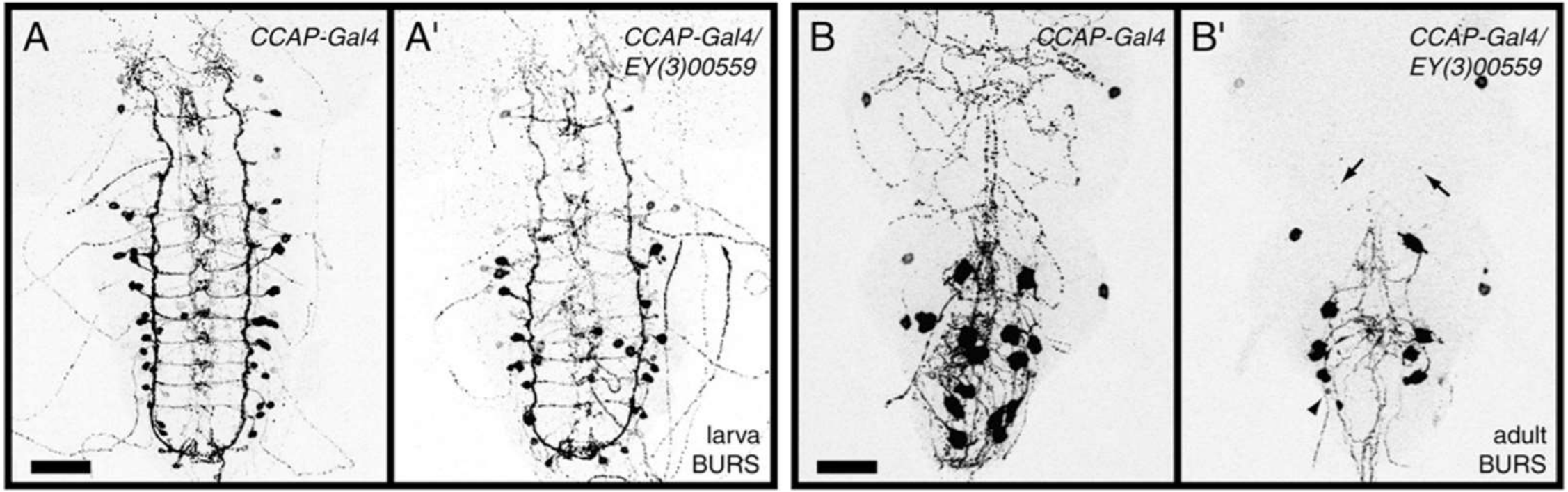




Tao Zhao, et al. Genetics. 2008

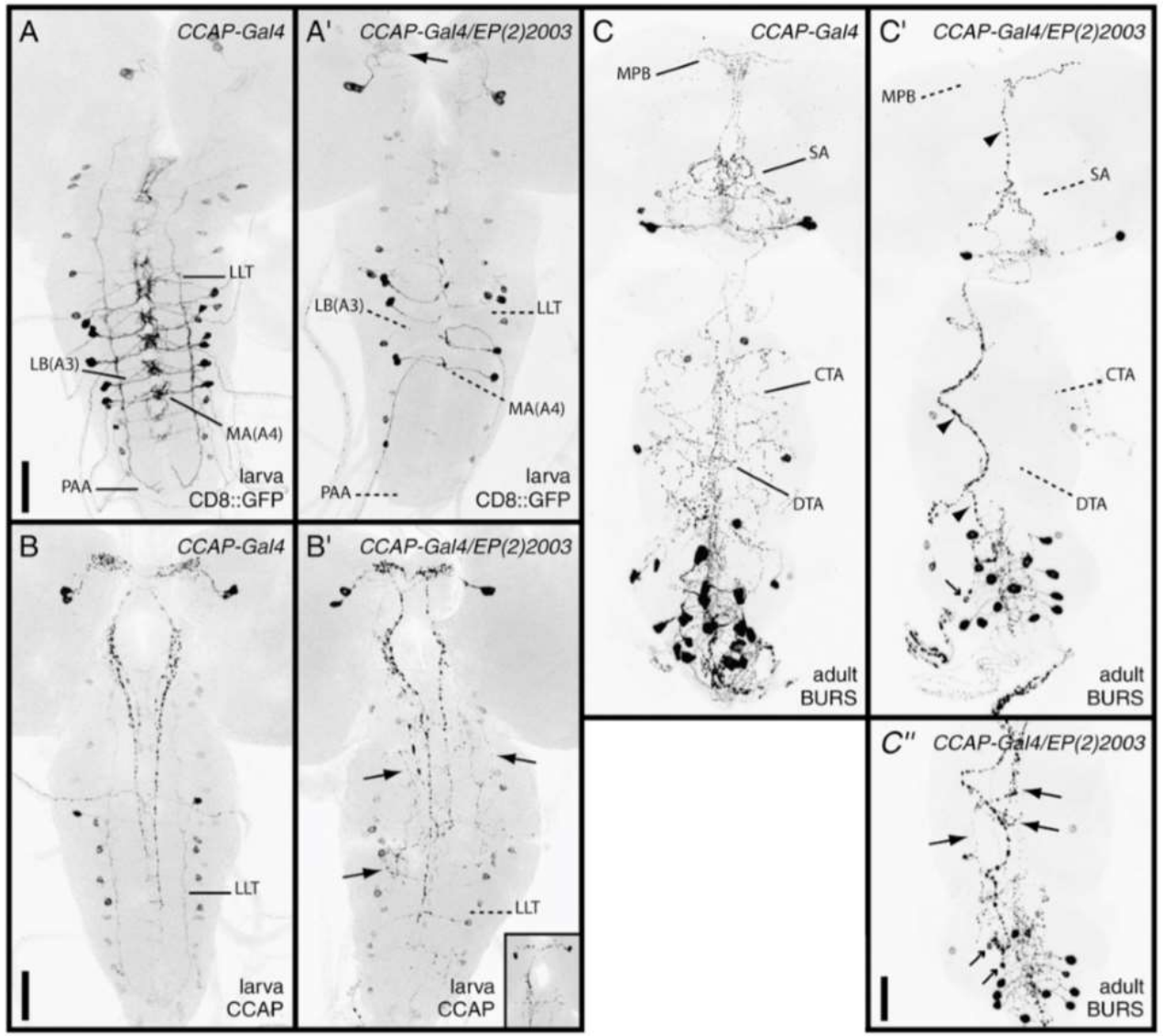
PART 3 Mechanisms involved in CCAP/Bursicon neuron remodeling

GOF of klar resulted in specific loss of adult-specific bursicon-immunoreactive neurites and loss of six to eight CCAP/bursicon cell somata



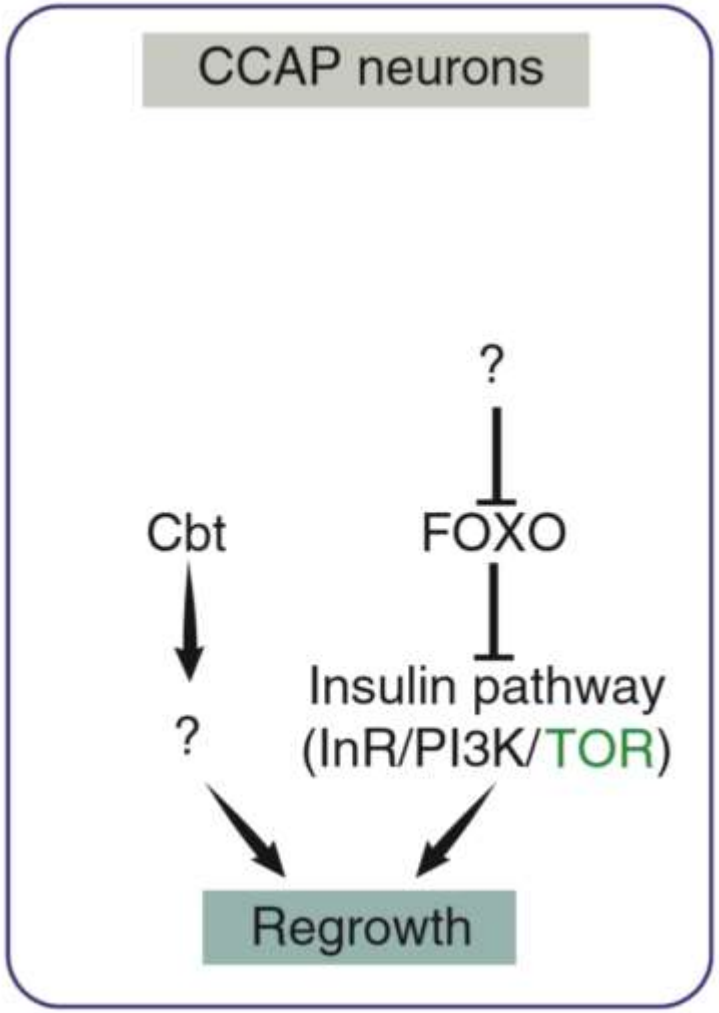
Tao Zhao, et al. Genetics. 2008

GOF of Ptr produced neurite pathfinding defects in larval CCAP/bursicon neurons.

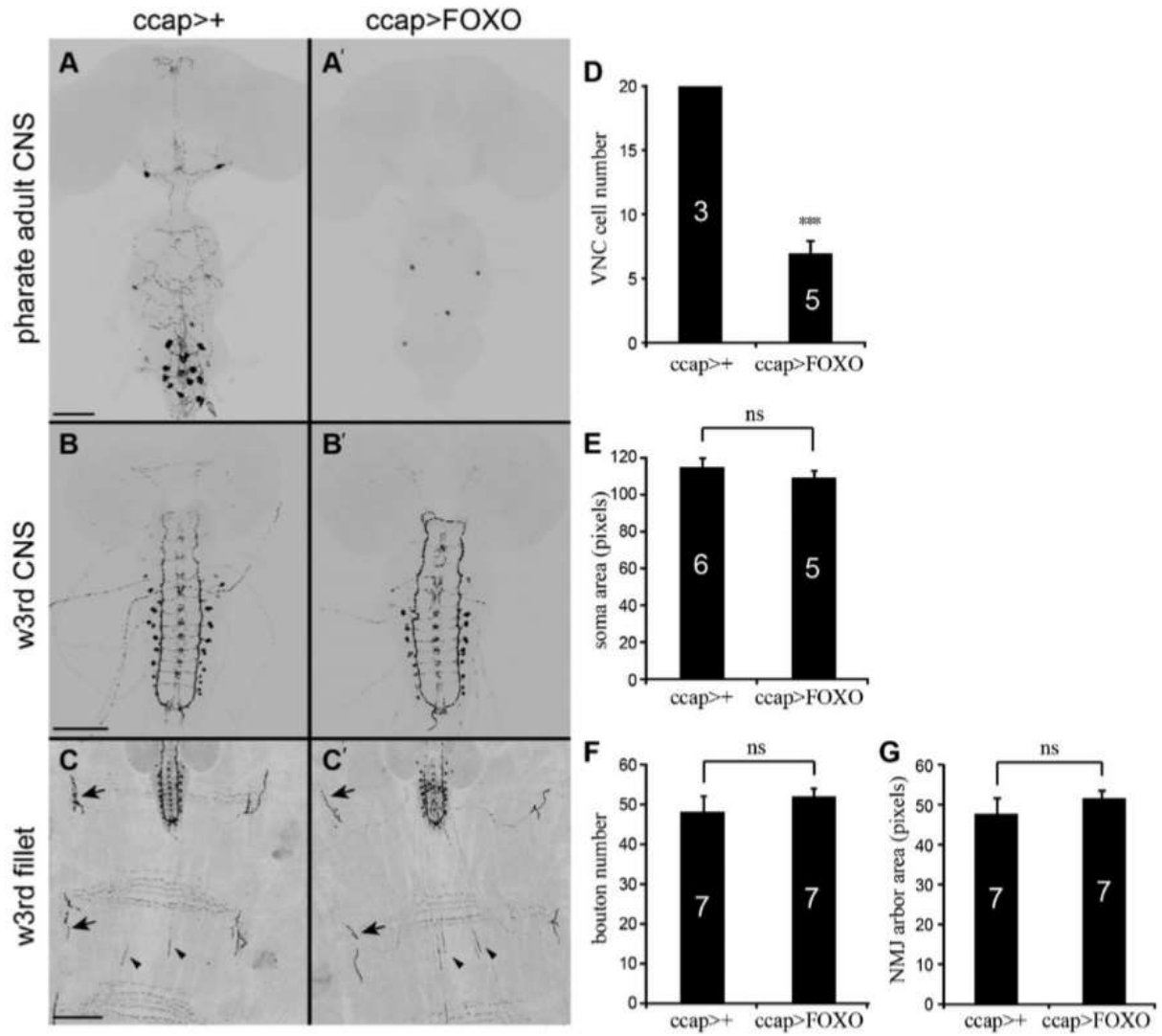


Tao Zhao, et al. Genetics. 2008

Insulin signaling regulates neurite growth during metamorphic neuronal remodeling

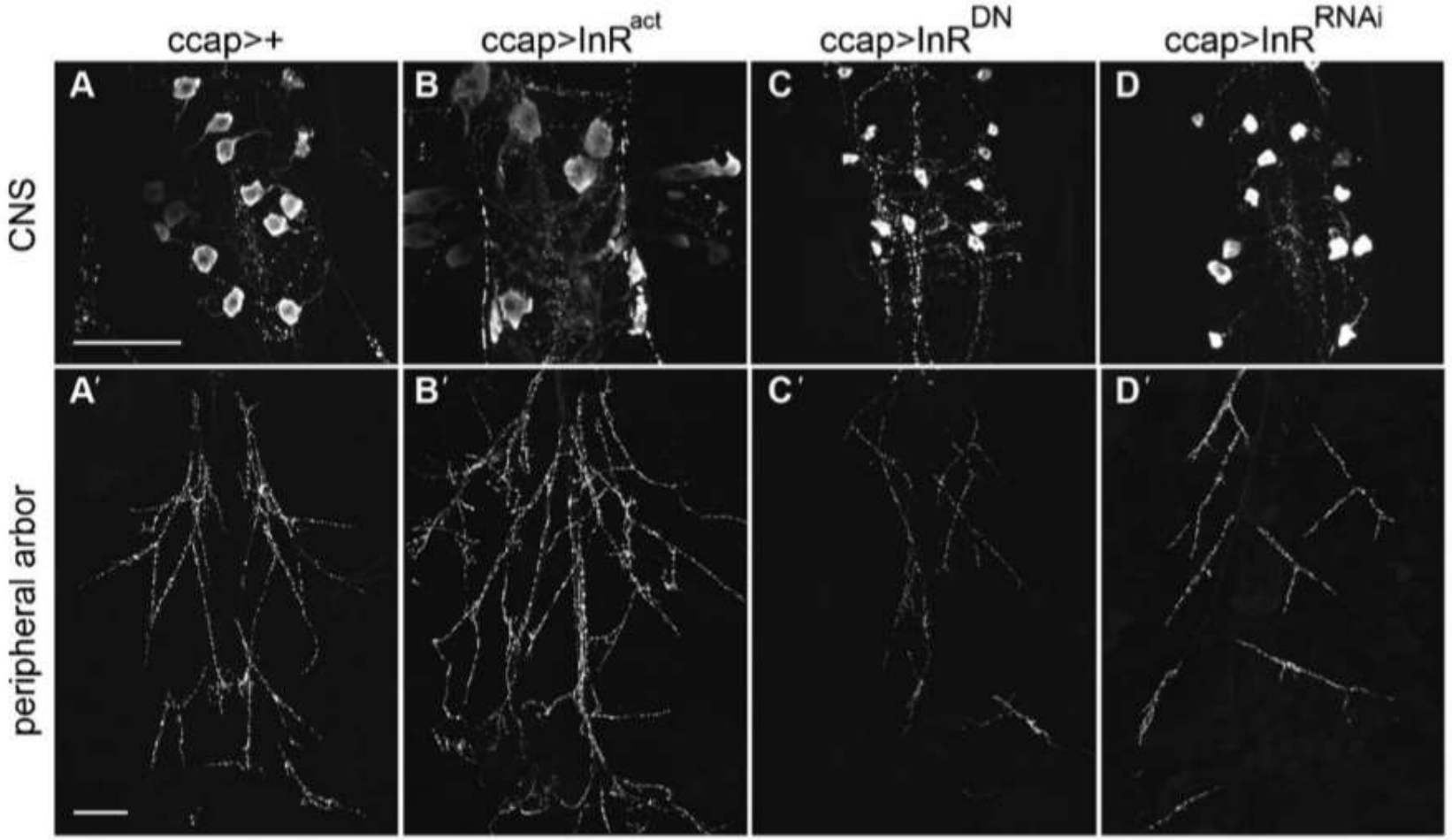


Overexpression of foxo disrupted pharate adult CCAP/bursicon neuron morphology



Tingting Gu, Tao Zhao and Randall S. Hewes. Biol Open. 2014

InR regulated metamorphic growth of the CCAP/bursicon neurons



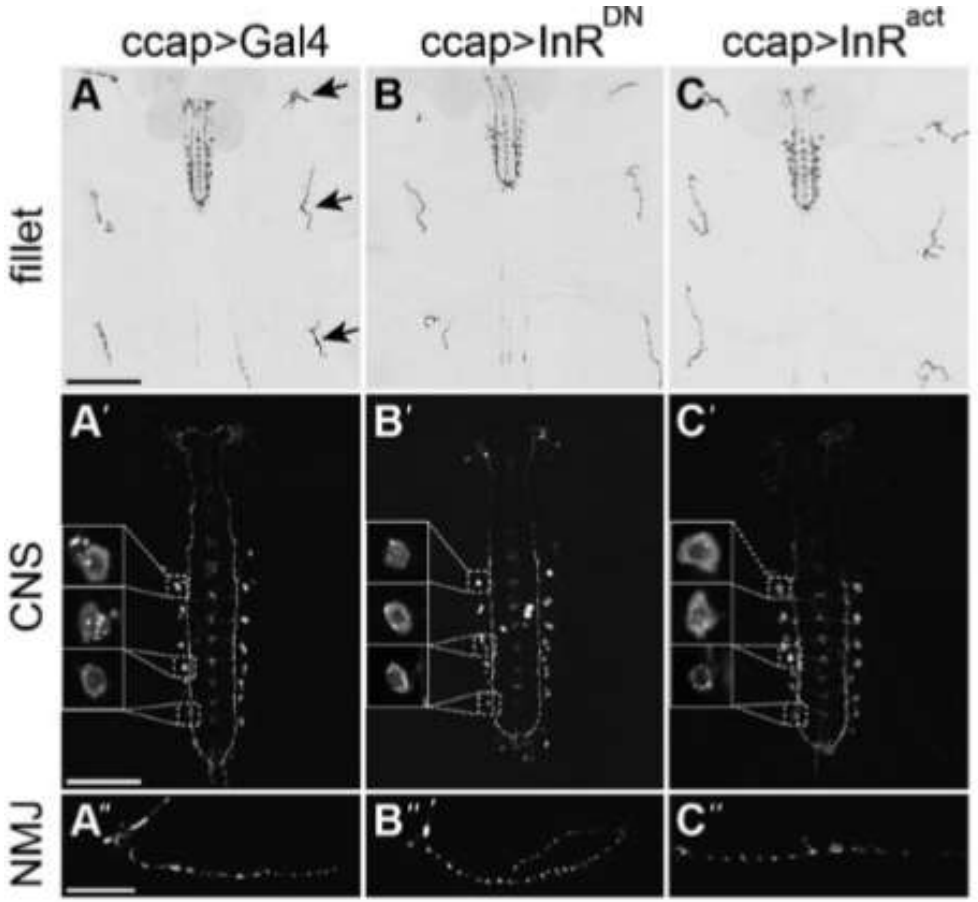
Tingting Gu, Tao Zhao and Randall S. Hewes. Biol Open. 2014

Larval growth of the CCAP/bursicon neurons was insensitive to loss of InR

larval peripheral arbor →

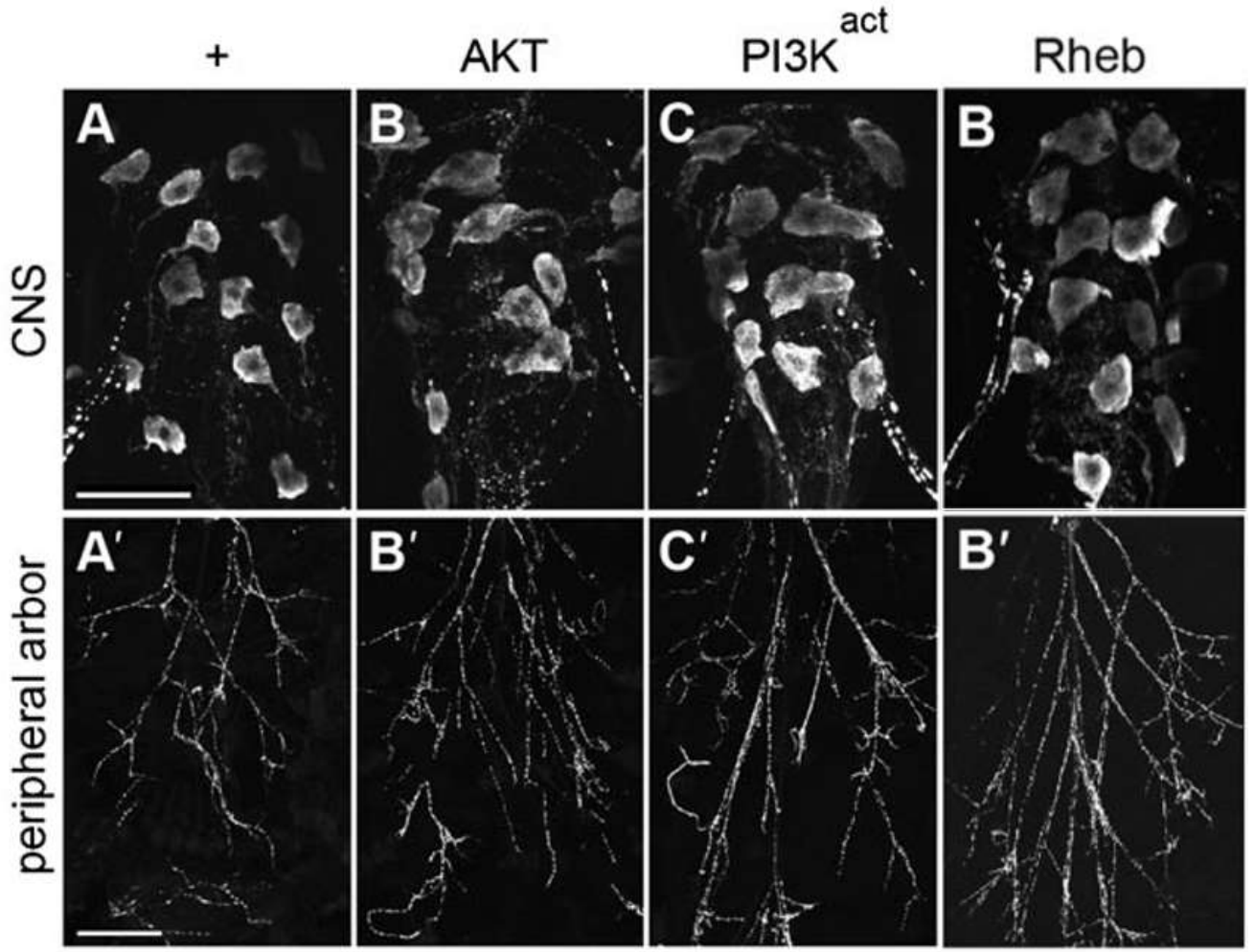
central projection pattern →

neuromuscular junctions (NMJ) →



Tingting Gu, Tao Zhao and Randall S. Hewes. Biol Open. 2014

Akt, PI3K, and Rheb regulated metamorphic growth of CCAP/bursicon neurons



Tingting Gu, Tao Zhao and Randall S. Hewes. Biol Open. 2014

ELSEVIER

Developmental Biology

Volume 431, Issue 2, 15 November 2017, Pages 226-238

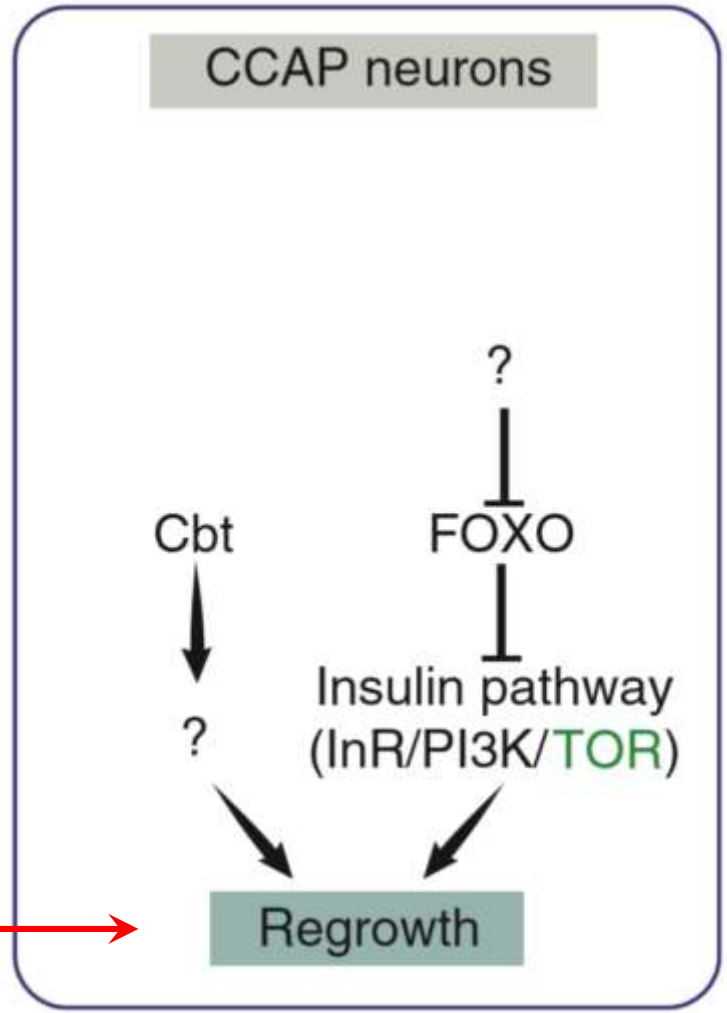
The large and small SPEN family proteins stimulate axon outgrowth during neurosecretory cell remodeling in *Drosophila*

Tingting Gu [1], Tao Zhao [1], Uday Kohli, Randall S. Hewes

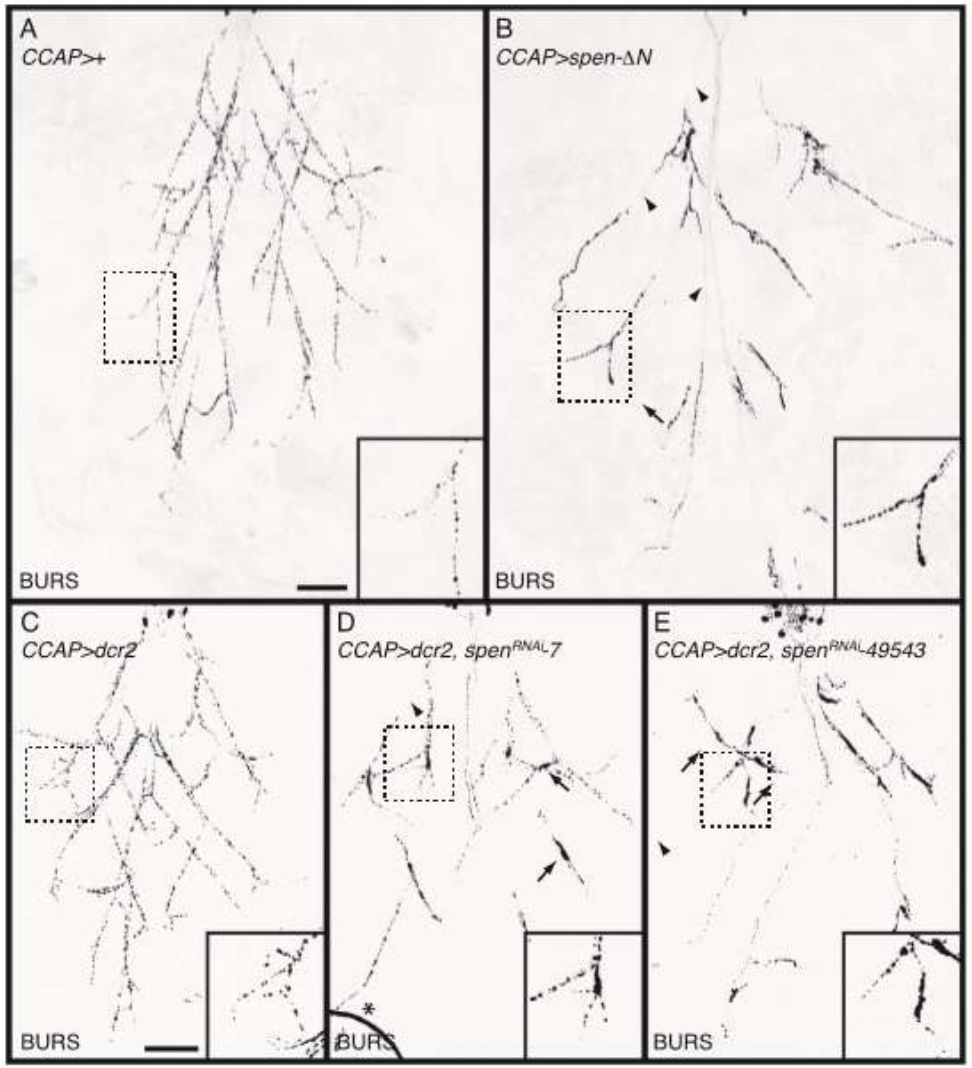
Show more

https://doi.org/10.1016/j.ydbio.2017.09.013

SPEN →

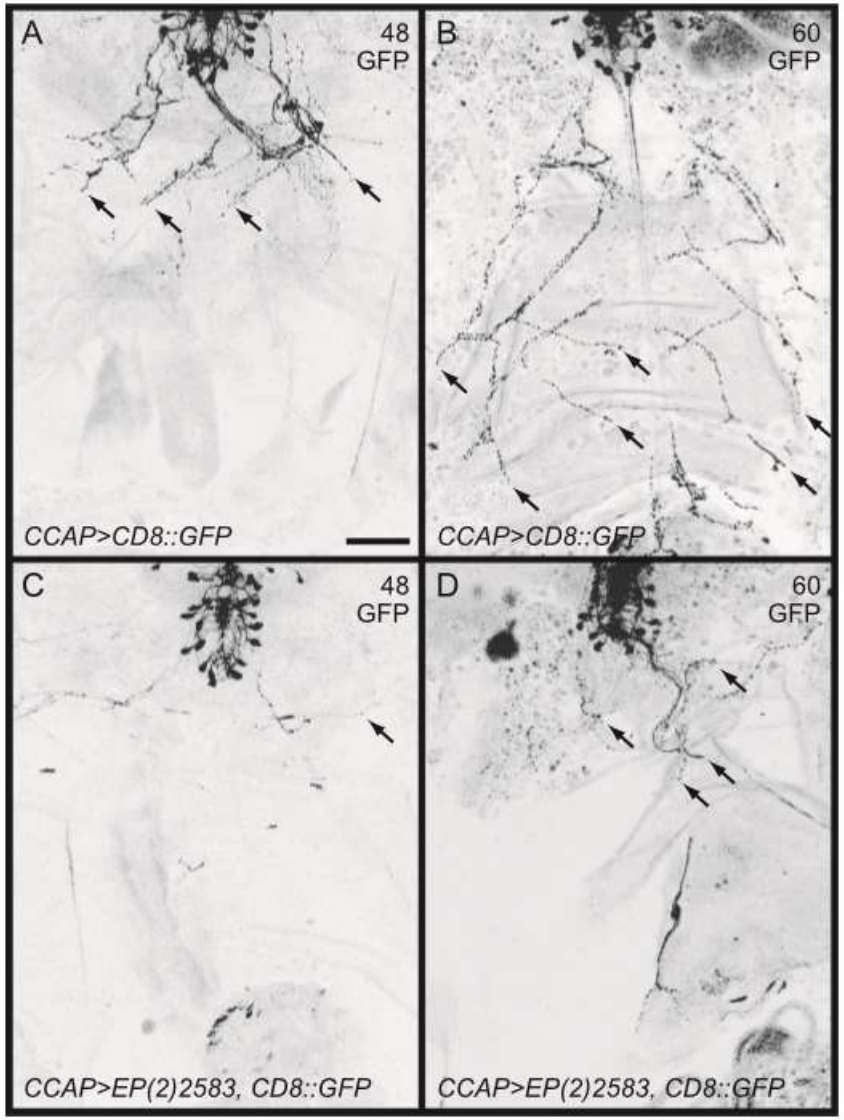


SPEN activity is required for normal axon outgrowth during metamorphic remodeling of the CCAP/bursicon neurons



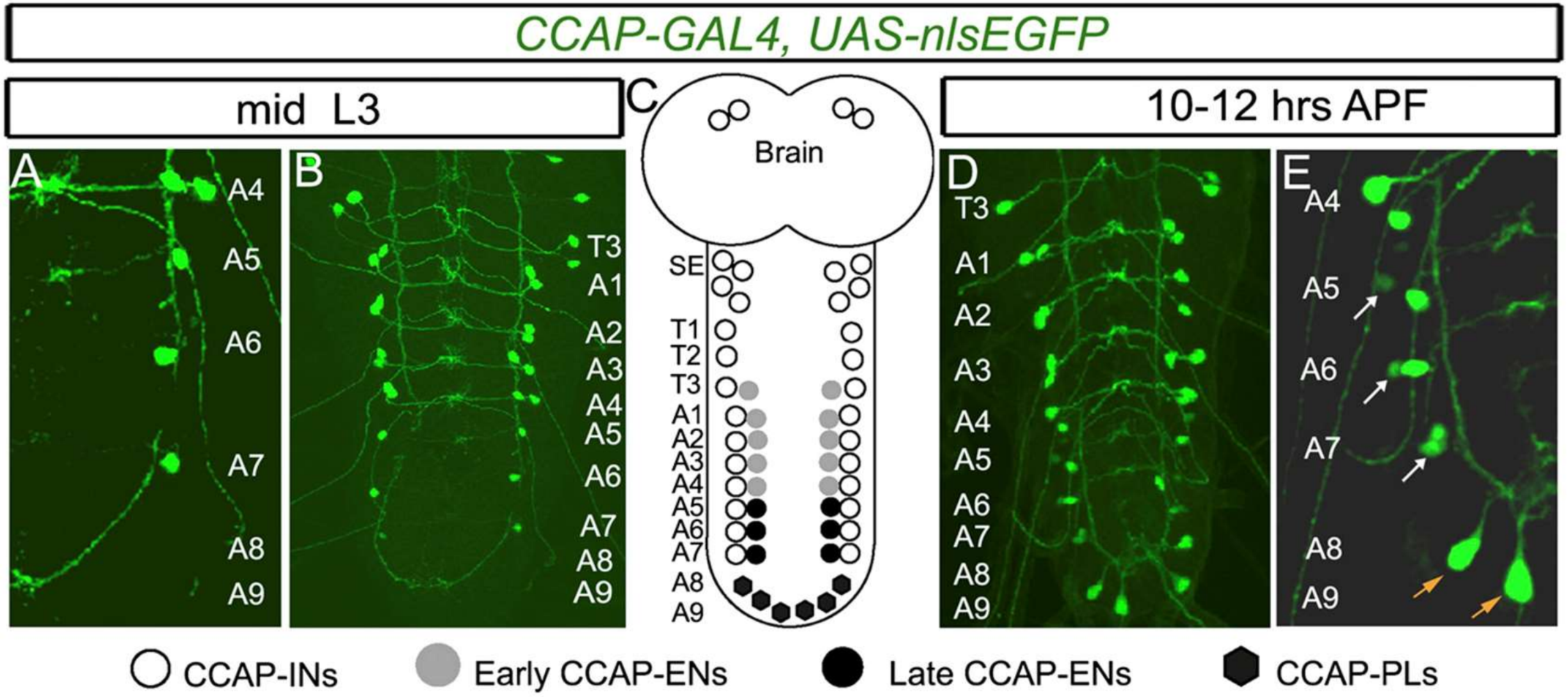
Tingting Gu, et al. Developmental Biology. 2017

SPEN overexpression inhibited outgrowth of the peripheral CCAP/bursicon axons



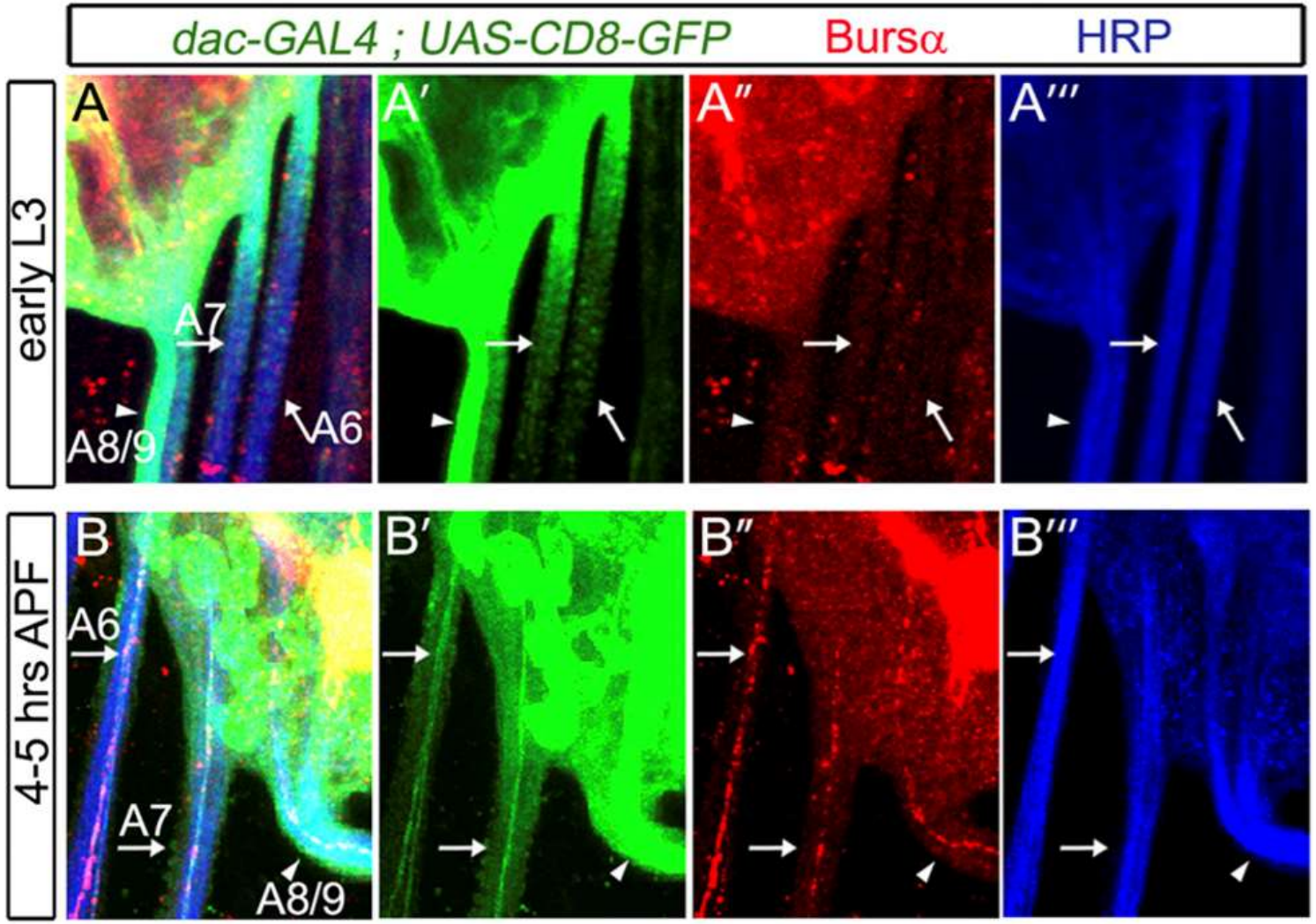
Tingting Gu, et al. Developmental Biology. 2017

Emergence of late CCAP neurons in the A5-A9 abdominal VNC at pupariation



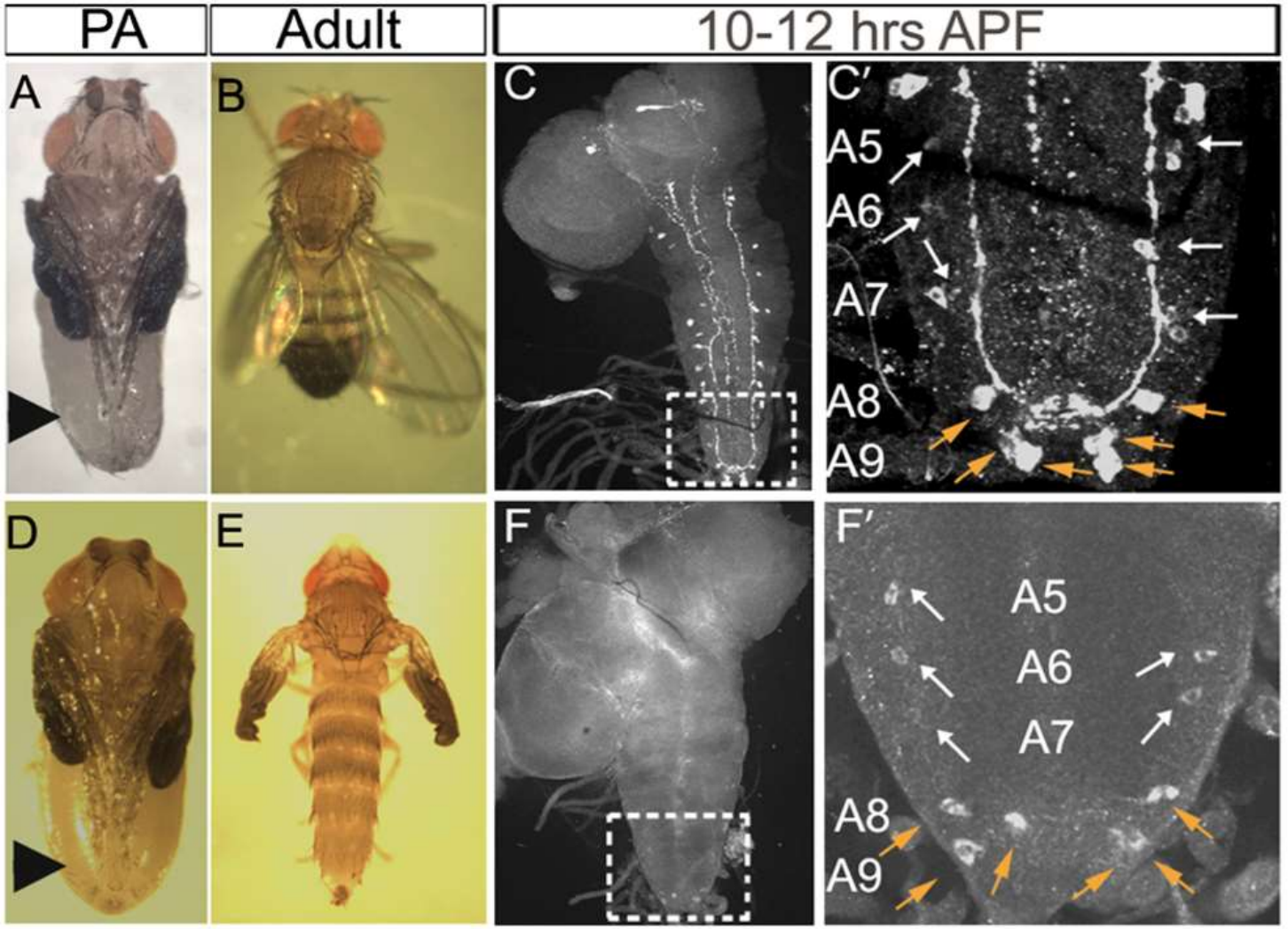
Lyubov Veverytsa and Douglas W. Allan. PNAS. 2012

Late CCAP neurons exit the VNC during pupariation



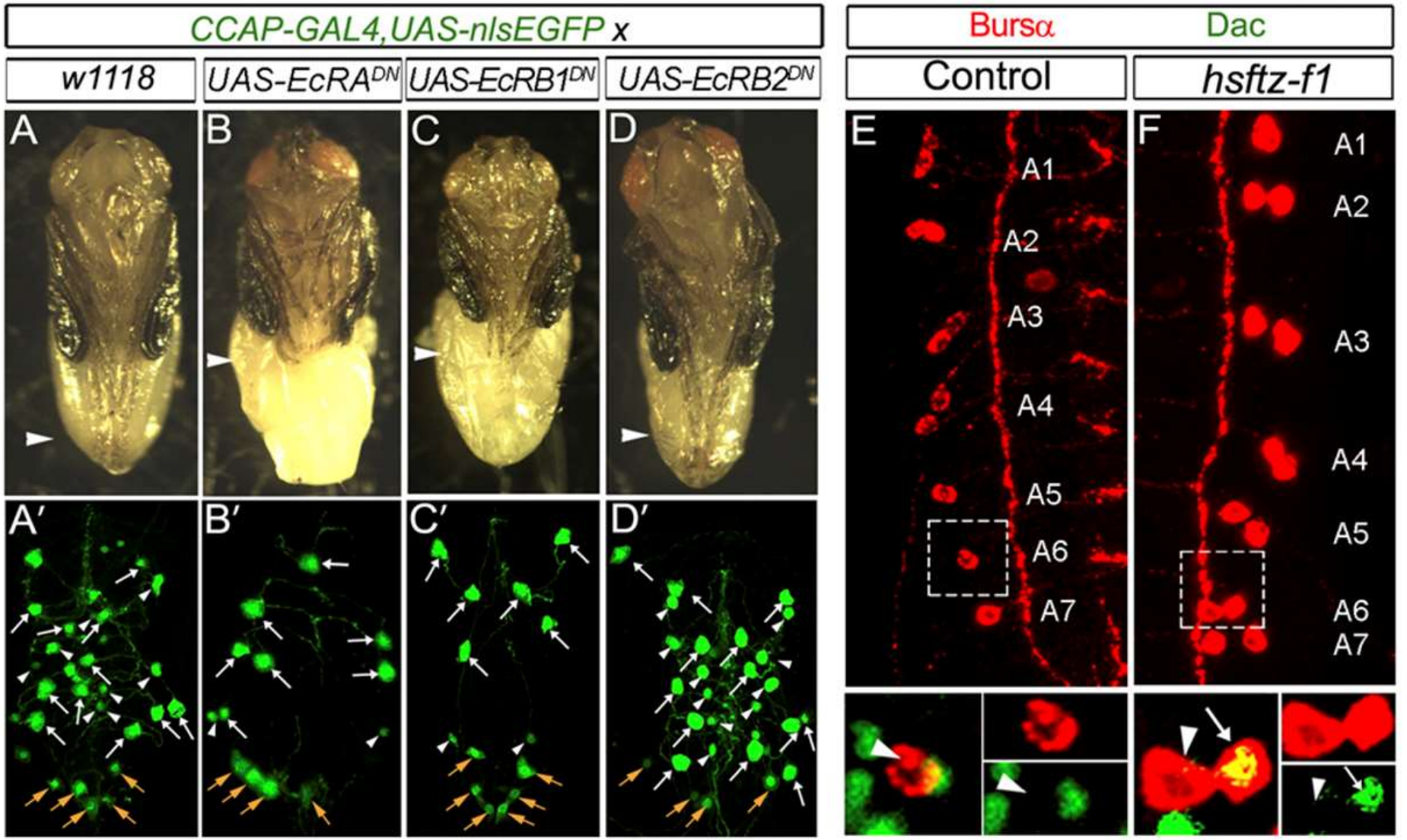
Lyubov Veverytsa and Douglas W. Allan. PNAS. 2012

Late CCAP neurons are sufficient for pupal ecdysis



Lyubov Veverytsa and Douglas W. Allan. PNAS. 2012

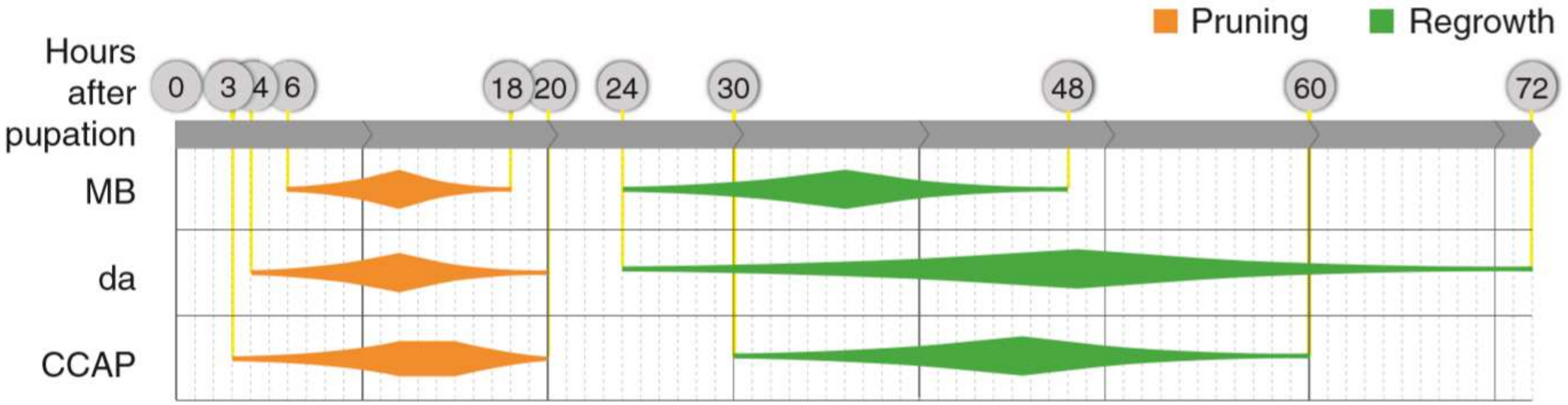
Ecdysone signaling is required for late CCAP-EN differentiation



Lyubov Veverytsa and Douglas W. Allan. PNAS. 2012

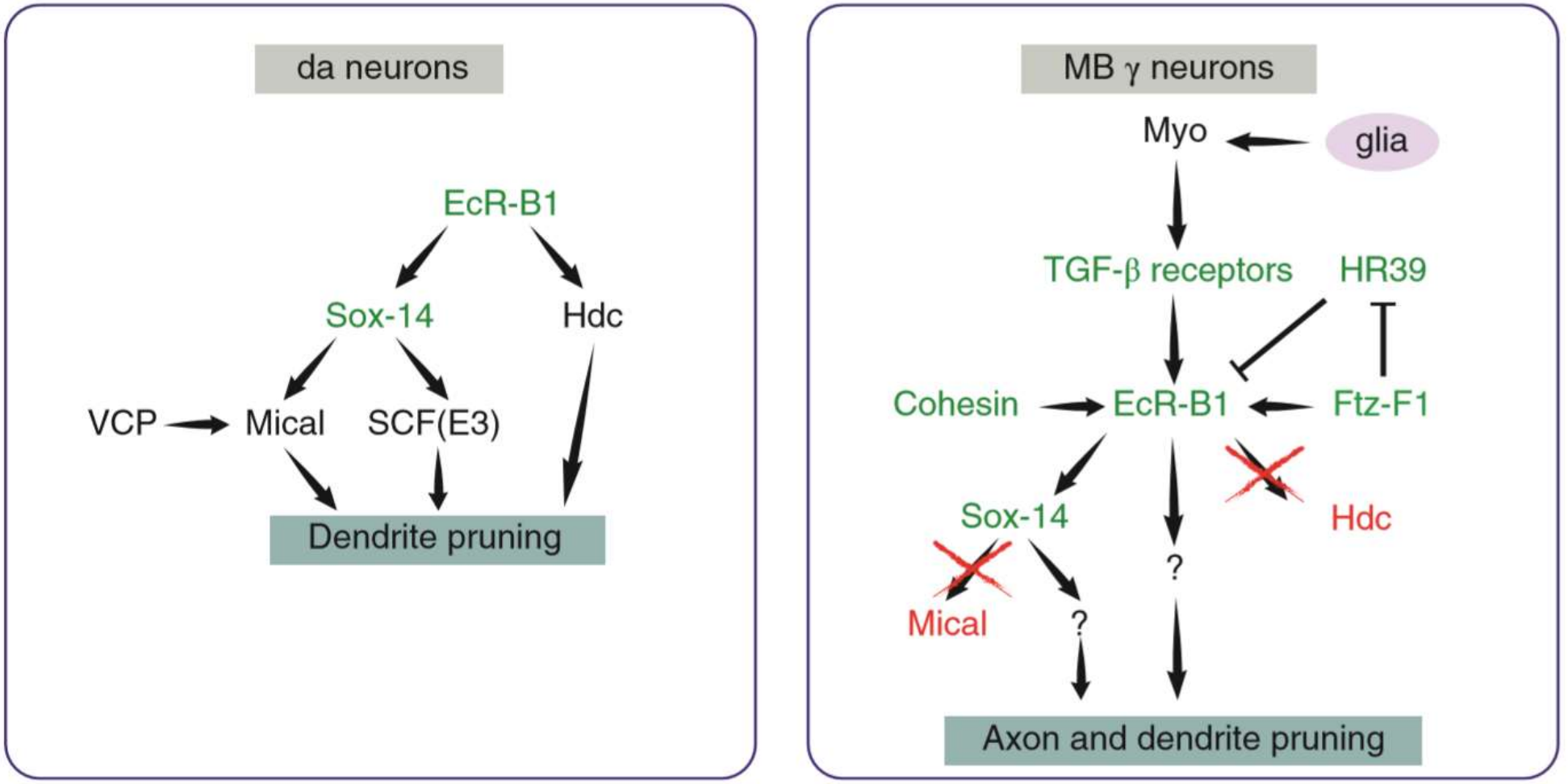
PART 4 Comparing the traits involved in remodeling of those three neuronal types

Remodeling of MB γ neurons, da dendrites and CCAP neurons occur on similar time scales



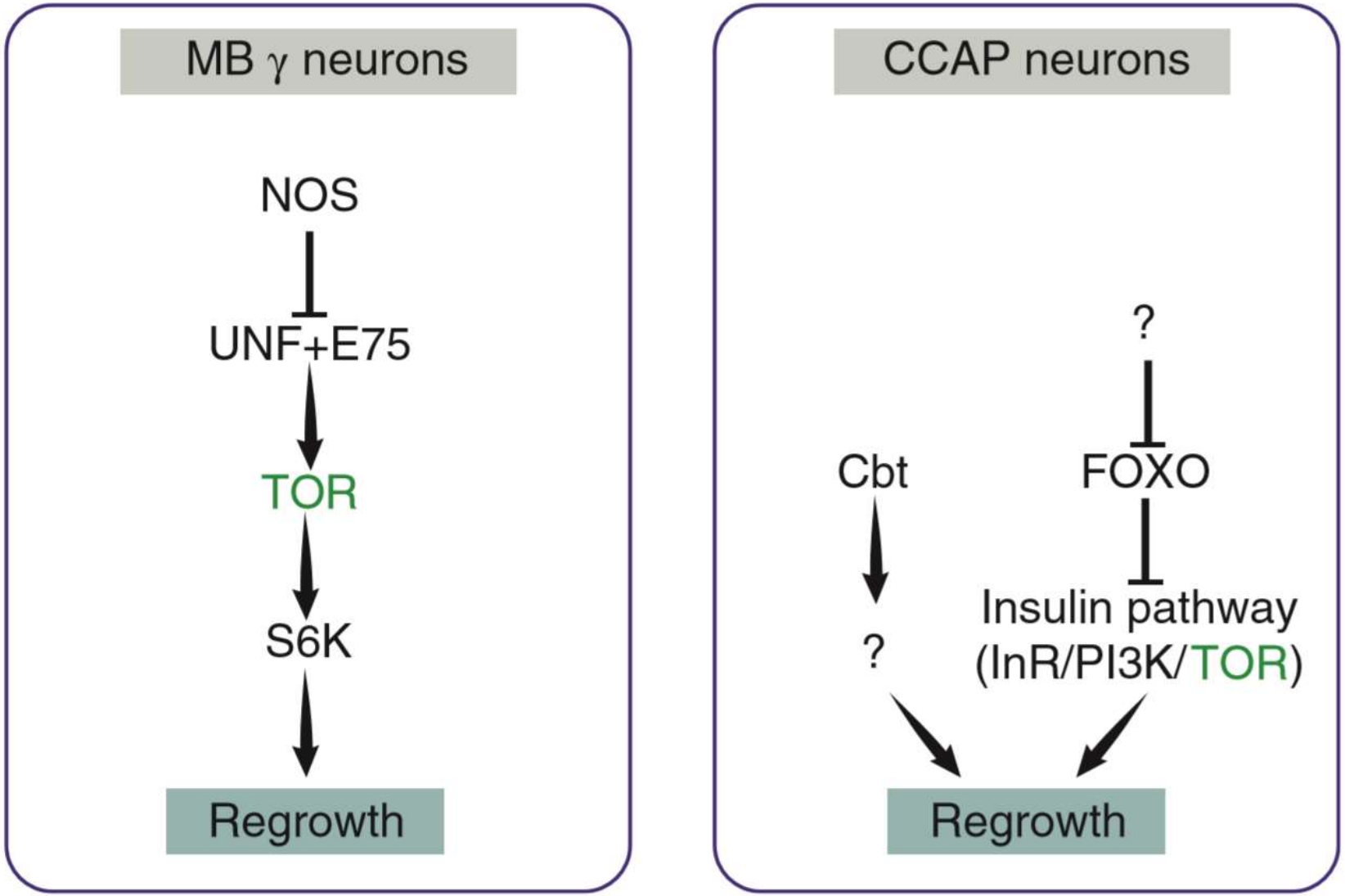
Shiri P. Yaniv and Oren Schuldiner. 2016

Mechanisms of ecdysone receptor B1 (EcR-B1) signaling to trigger pruning in MB γ and da neurons



Shiri P. Yaniv and Oren Schuldiner. 2016

Regrowth in MB γ and CCAP neurons requires TOR signaling



Shiri P. Yaniv and Oren Schuldiner. 2016

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[6] Tingting Gu. et al. Insulin signaling regulates neurite growth during metamorphic neuronal remodeling. Biol Open. 2014 Jan 15;3(1):81-93. doi: 10.1242/bio.20136437.

[7] Tingting Gu, et al. The large and small SPEN family proteins stimulate axon outgrowth during neurosecretory cell remodeling in Drosophila . Developmental Biology. 431 (2017) 226 − 238