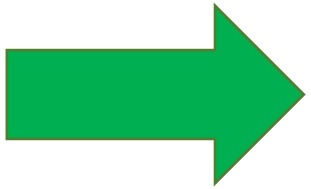
A brief introduction of escape behavior of *Drosophila* larvae

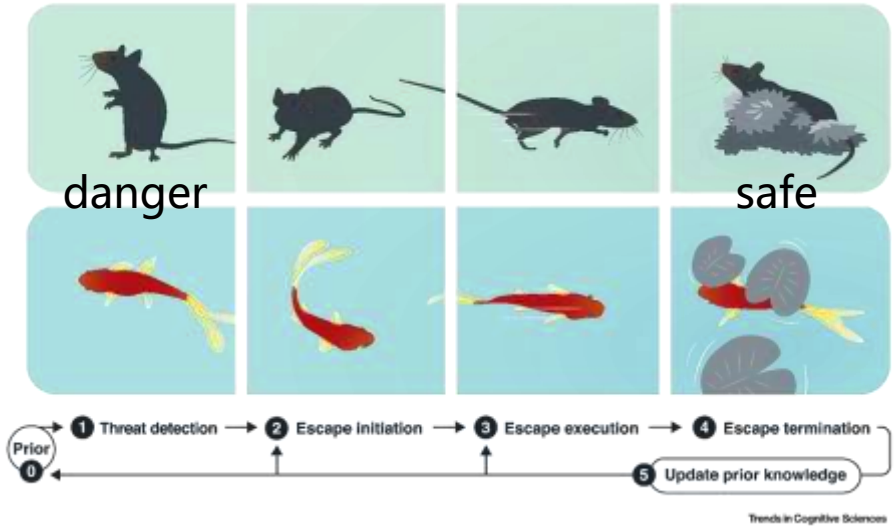
20221027

MMZ JXX CJ

What do you do when you are in dangerous/boring things?



Multiple manifestations of escape behavior



Stimuli { Non-noxious stimuli
Nociceptive/Noxious stimuli

→ Avoidance/Escape

When does *Drosophila* escape?
How do they escape?

The peripheral sensory neurons and escape behavior of *Drosophila* larvae

——Ma Mingze

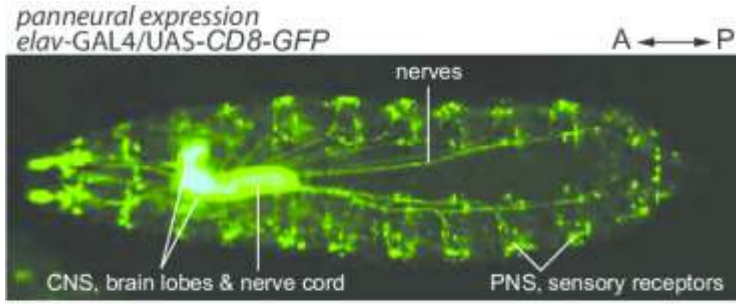
Escape behavior induced by noxious heat and mechanical stimuli in *Drosophila* larvae

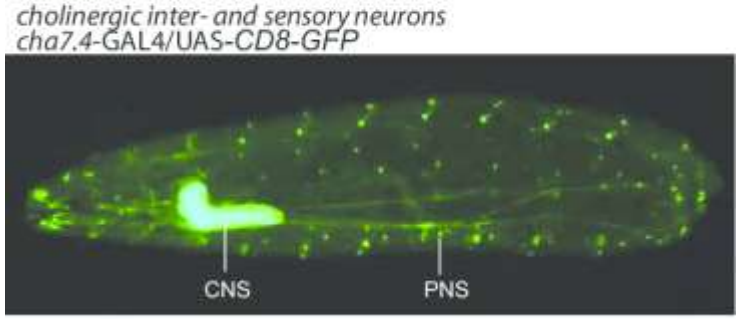
——Ji Xiaoxiao

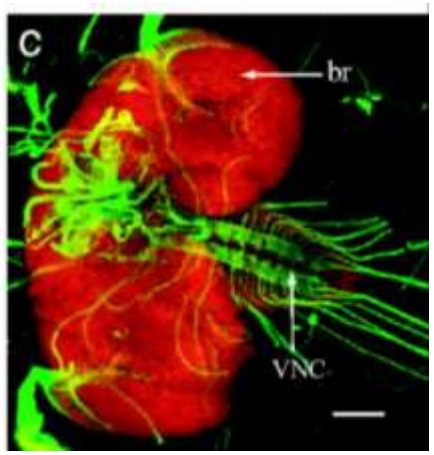
Integrated output of multiple sensory stimuli—taking avoidance from predators as an example

——Chen Jie

PNS of *Drosophila* larvae





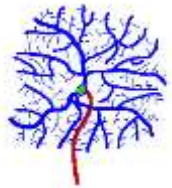


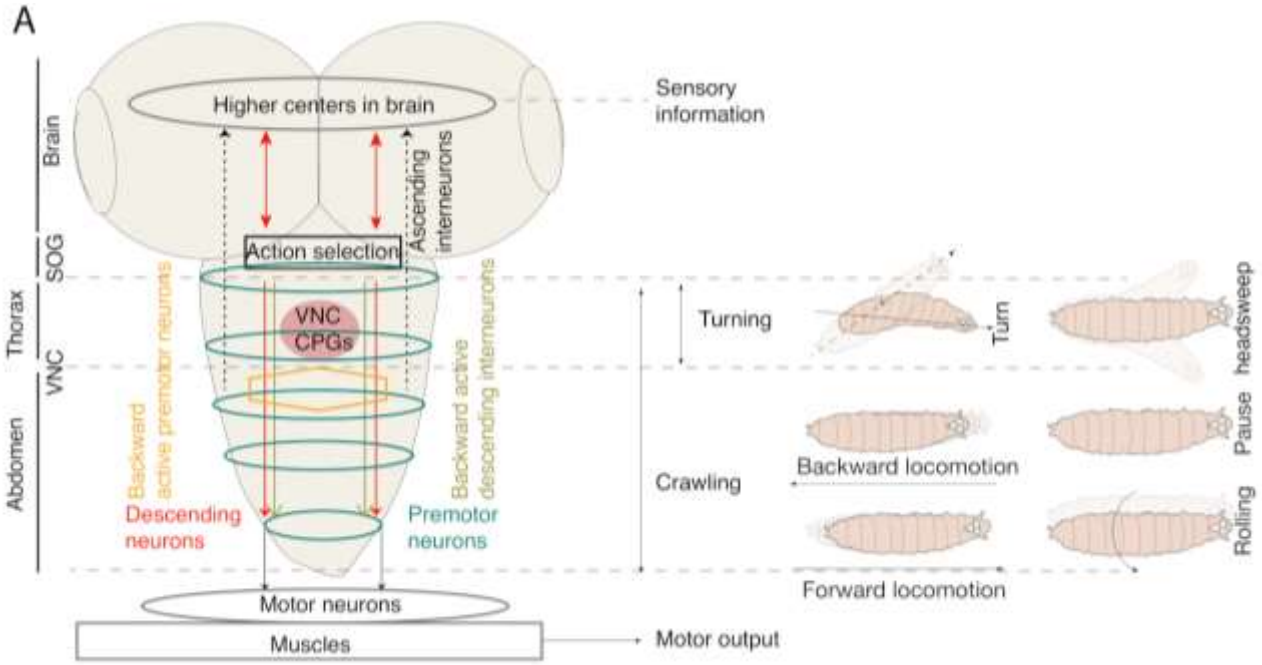
Berni J, et al., *Undergrad Neurosci Educ*, 2010

peripheral sensory neurons
(below the barrier epidermis)

- type I

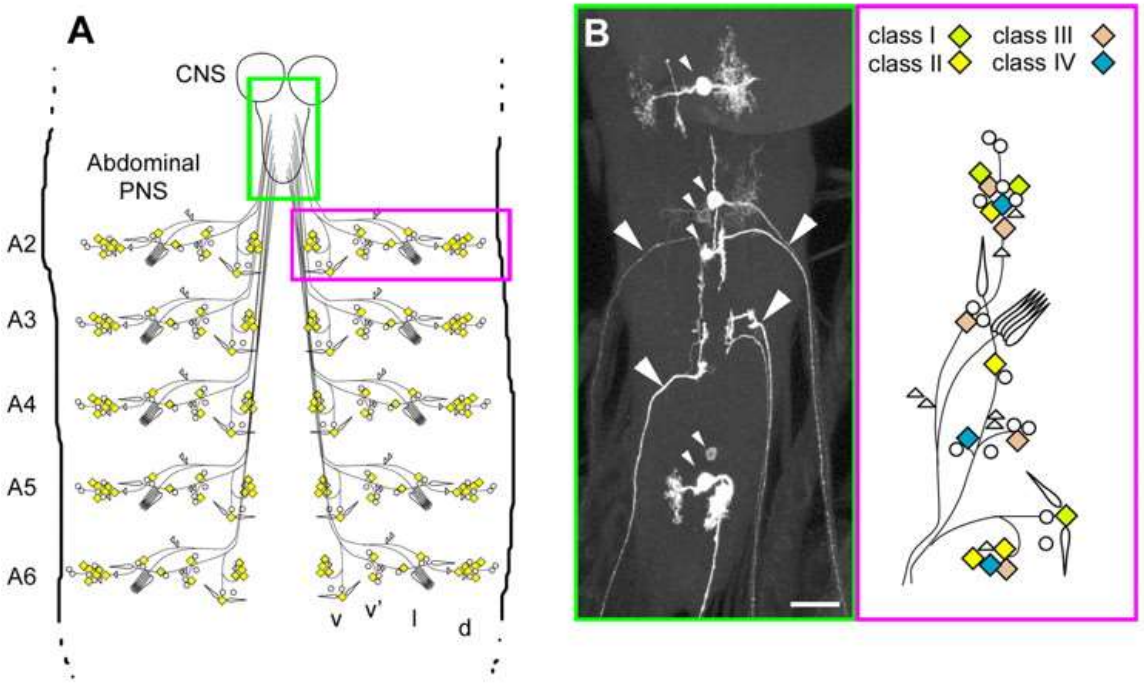
- type II: multidendritic (md) neurons

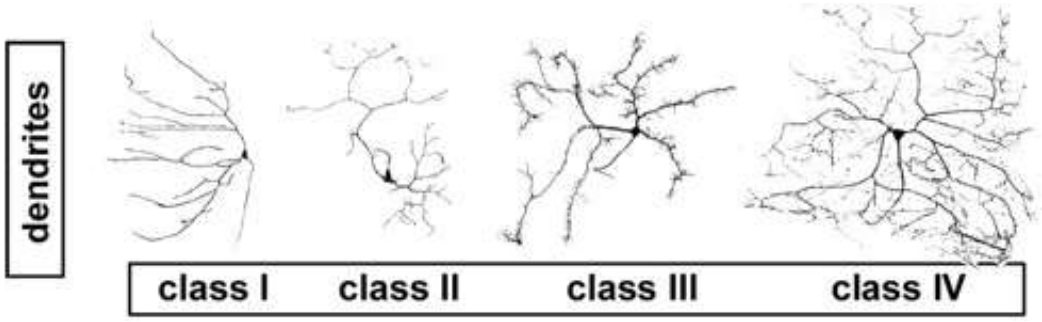




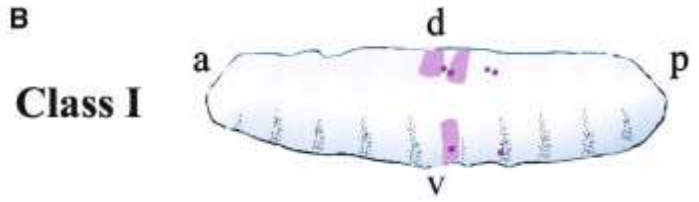
Gowda SBM, et al., *Biology (Basel)*, 2021

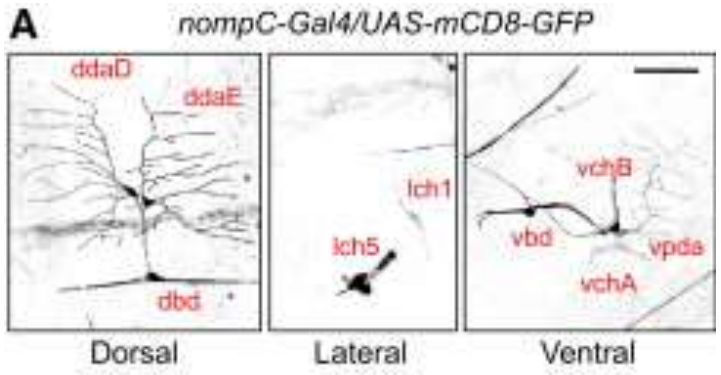
Multidendritic (md) neurons

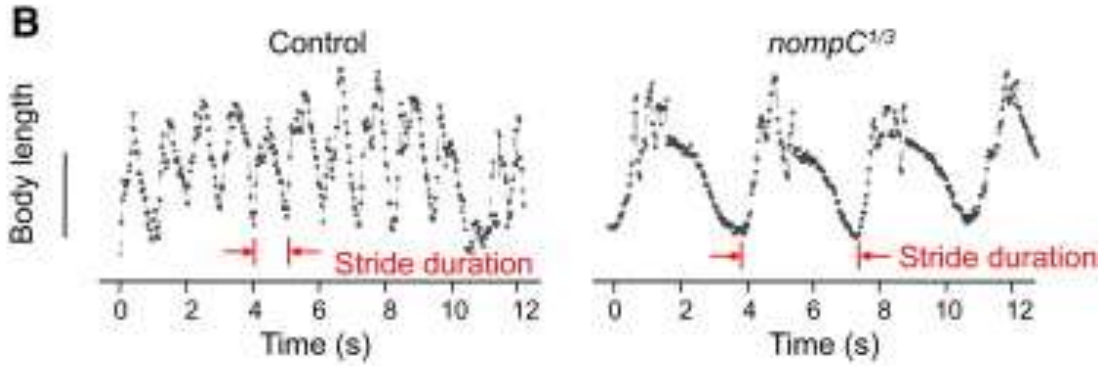


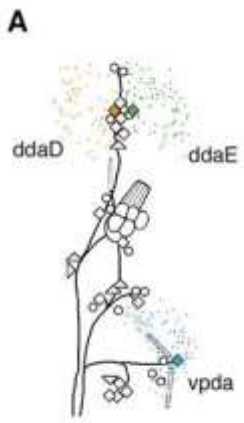


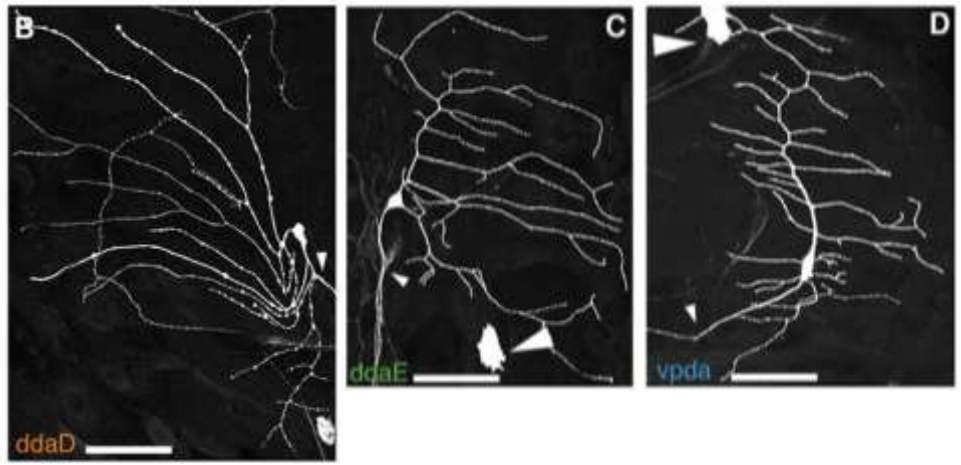
Class I md are related to motor coordination

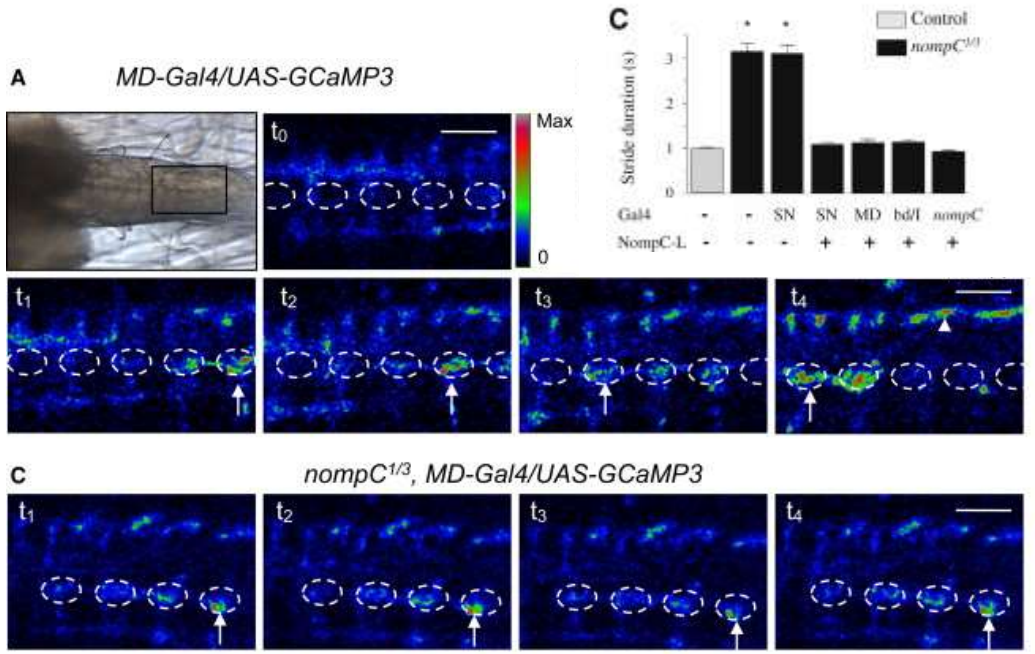






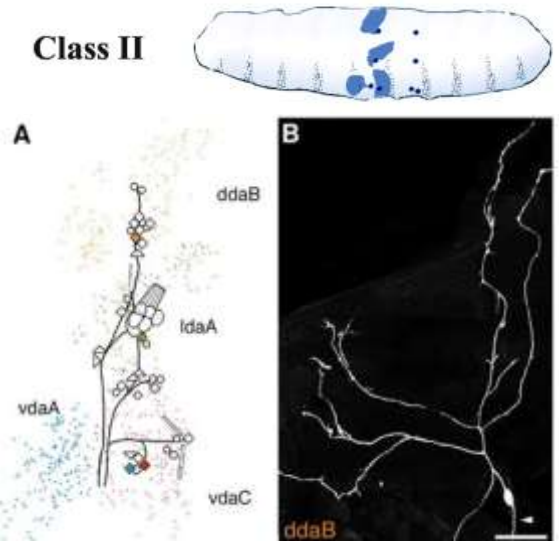


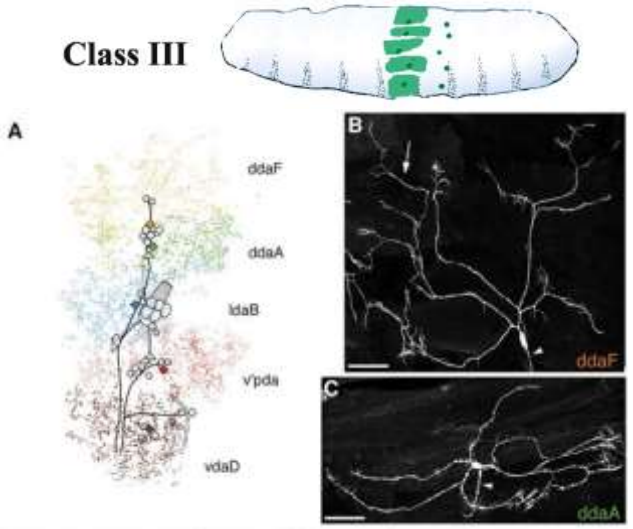


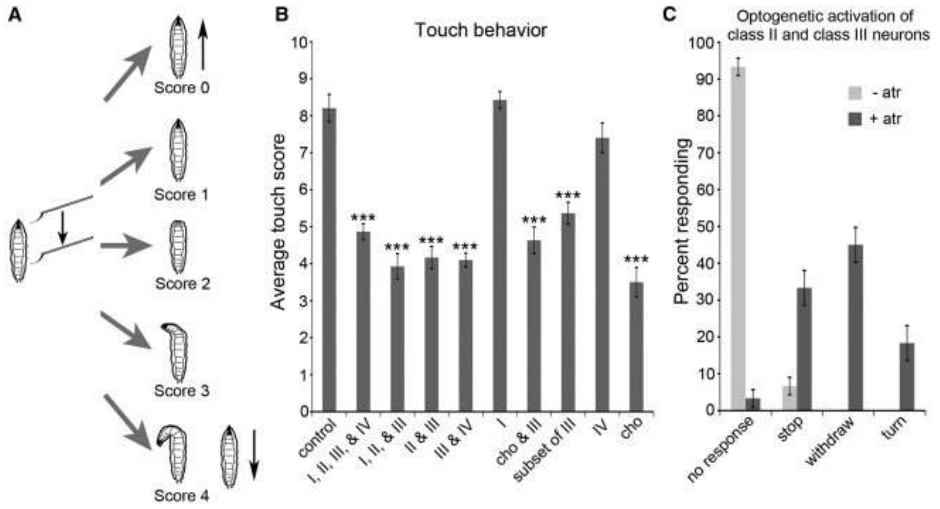


Li E.Cheng, et al., *Neuron,* 2010

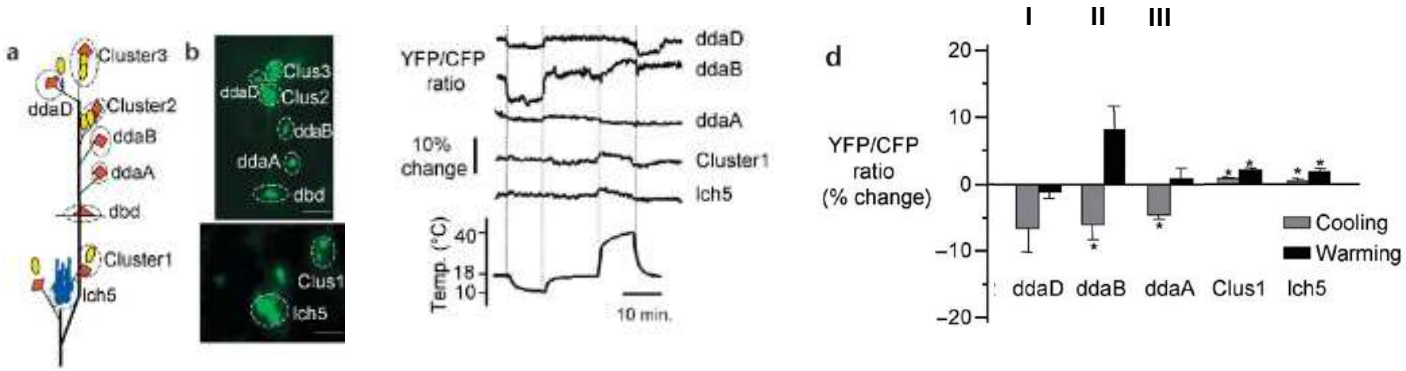
Class II and Class III md perceive mild stimuli







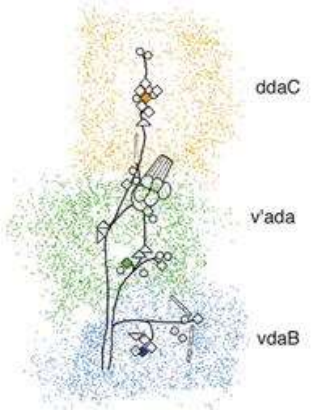
Asako Tsubouchi, et al., *Current Biology,* 2012

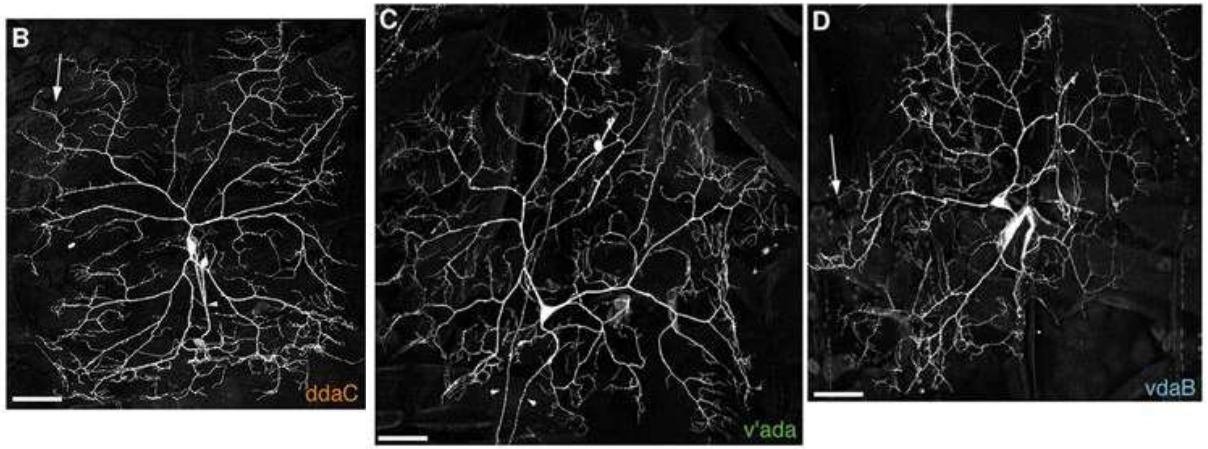


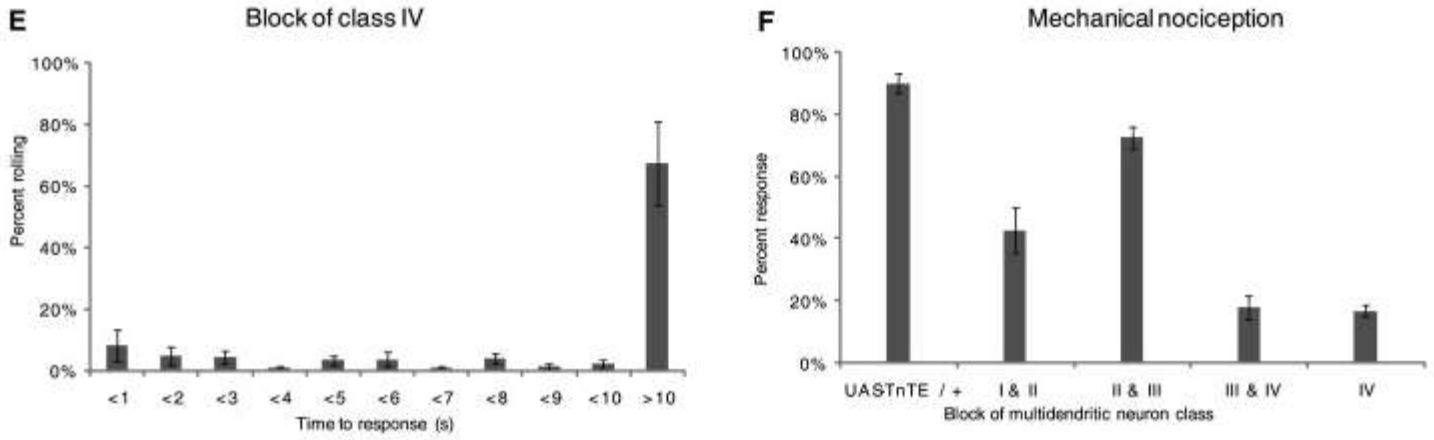
Lei Liu, et al., *Nat Neurosci,* 2003

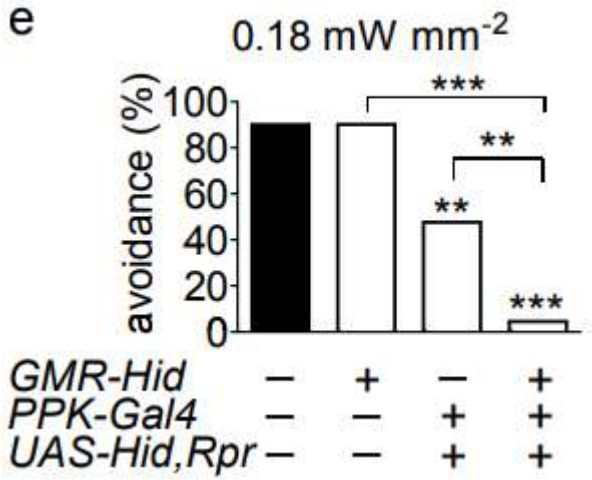
Multimodal sensor——C4 da

(C4 da)
Class IV









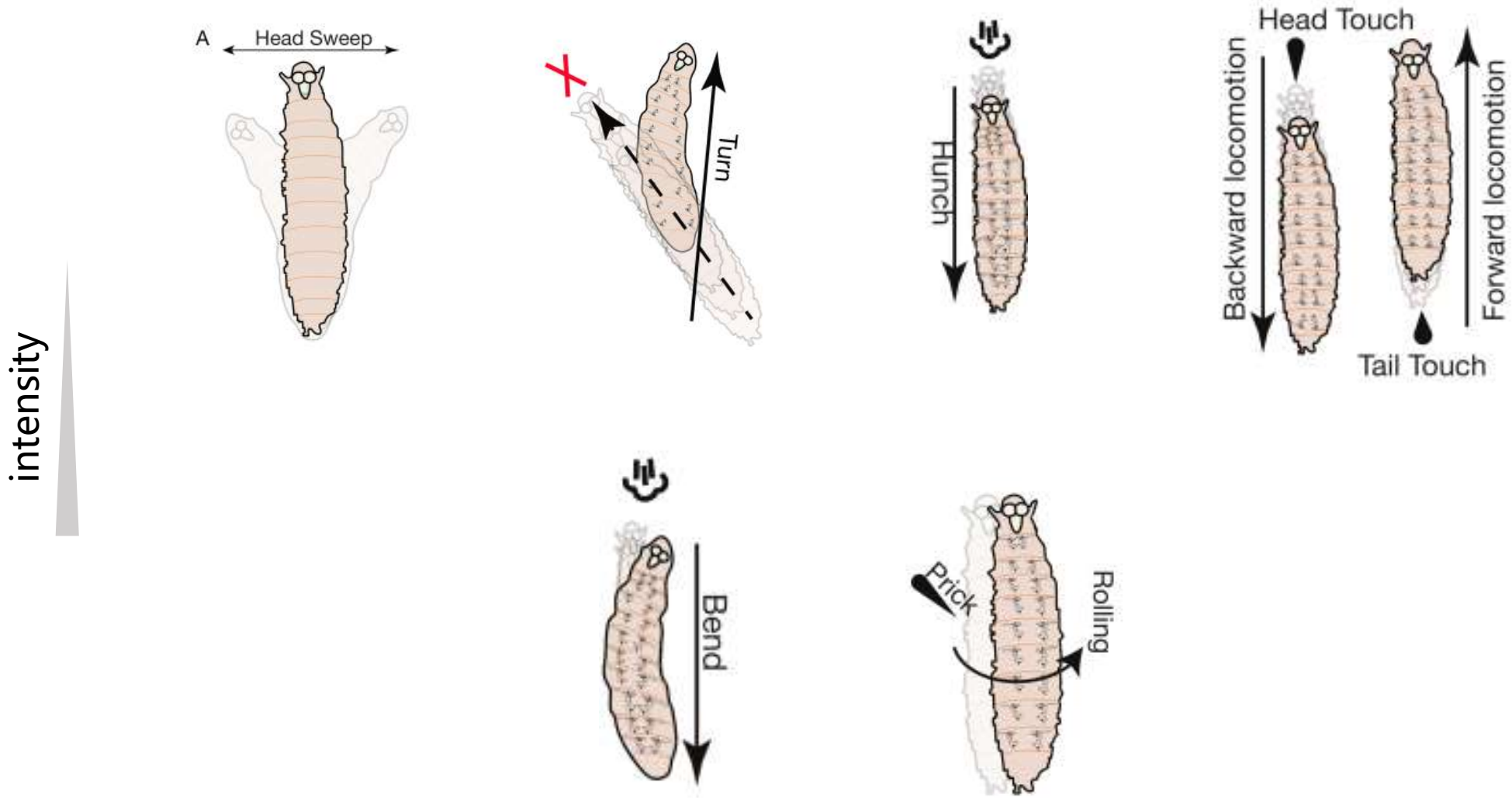
Richard Y. et al., *Current Biology*, 2007

Xiang, Y., et al., *Nature*, 2010

The function of md neurons

Class I	Class II
Proprioception/Somatosensory(*nompC*) (Li E.Cheng, et al., *Neuron*, 2010)	Light-touch(Asako Tsubouchi, et al., *Current Biology*, 2012) Cooling (Lei Liu, et al., *Nat Neurosci*, 2003) Warming(Lei Liu, et al., *Nat Neurosci*, 2003)
Class III	**Class IV**
Light-touch(*nompC*)(Yan, Z., et al., Nature, 2013) Cooling (Lei Liu, et al., *Nat Neurosci*, 2003) Warming (Lei Liu, et al., *Nat Neurosci*, 2003) **Cold nociception**	**Heat nociception(*TrpA1*、*painless*、*pyrexia*、*Subdued*)** (Zhong et al., Cell Reports, 2012 ; Jang et al., J Biol Chem, 2015) **Low wavelength light(*TrpA1*、*GR28b*)** (Xiang, Y., et al., Nature, 2010) **Harsh mechanical stimuli(*ppk*、*ppk26*、*painless*、 *piezo*)** (Kim, S. E., et al., *Nature*, 2012)

Escape behavior of *Drosophila* larvae



W. Dan Tracey

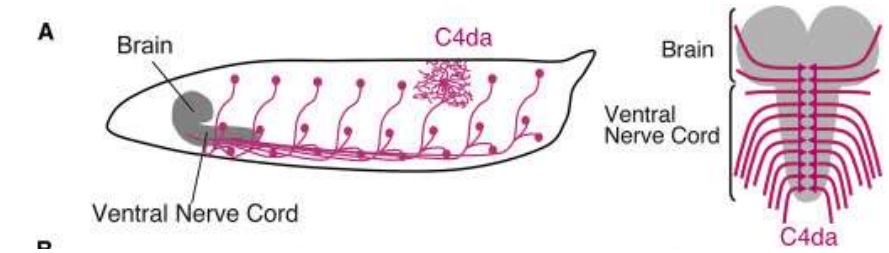
Gill Chair of Biology

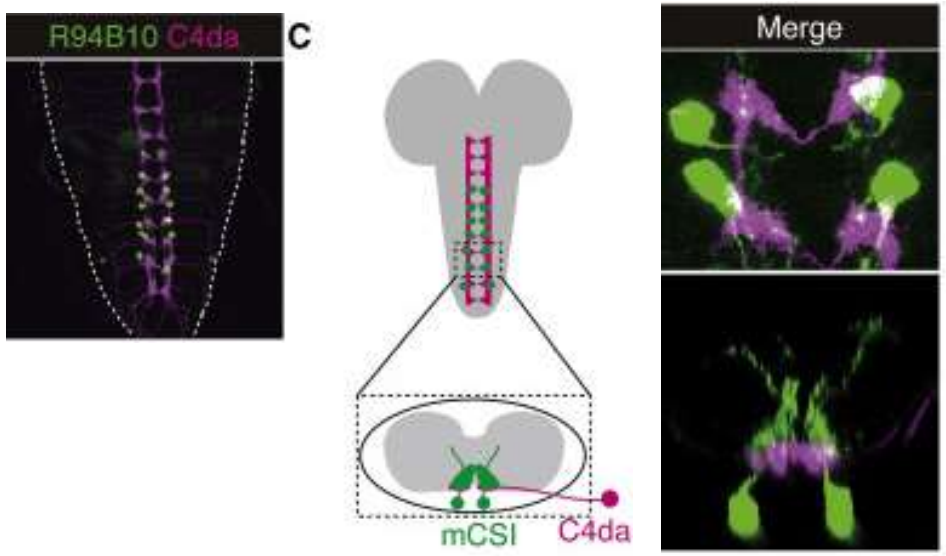
Tracey's primary focus is to use the fly model to identify circuits and genes that function in **nociception**. These studies lead to a greater understanding of pain signaling. In addition, they are attempting to identify the molecules that are used in neurosensory **mechanotransduction**, which underlies the human sense of touch.

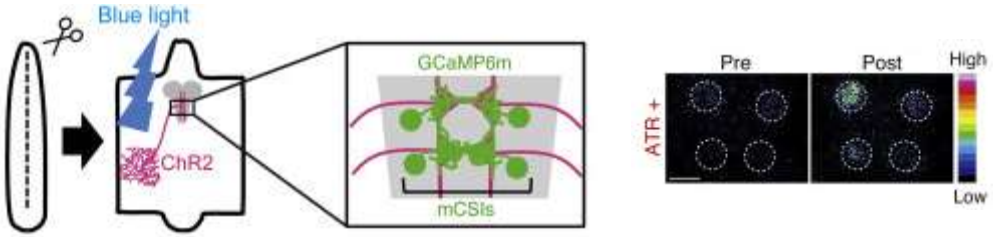
- 研究决定果蝇幼虫的各种本能偏好的神经回路，并以此为基础揭示感觉信息在神经回路中的加工模式以及抉择行为的核心神经机制
- 果蝇光偏好行为的发育形成及后期变化的神经基础
- 以果蝇幼虫为模型，研究视觉感觉信息和运动动作的神经元表征方式及其相互关系。

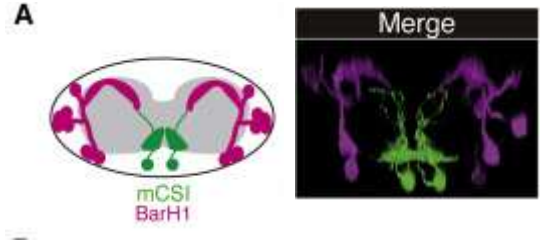
姓名:	龚哲峰
职务:	教授
职称:	教授
学历:	博士
专业:	神经生物学
所属院系:	基础医学系
研究方向:	行为的神经回路基础
电话:	0571-88208850
信箱:	zfgong@zju.edu.cn
个人主页:	http://mypage.zju.edu.cn/gonglab

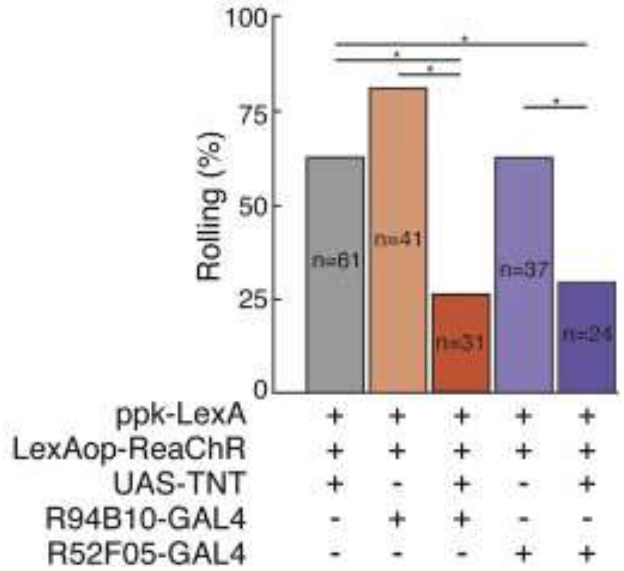
A simple circuit of escape behavior

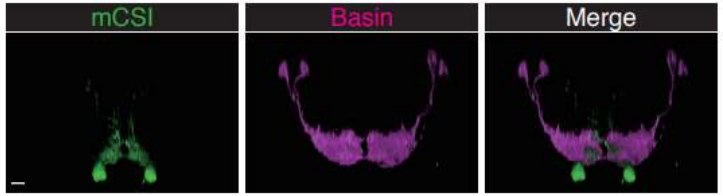






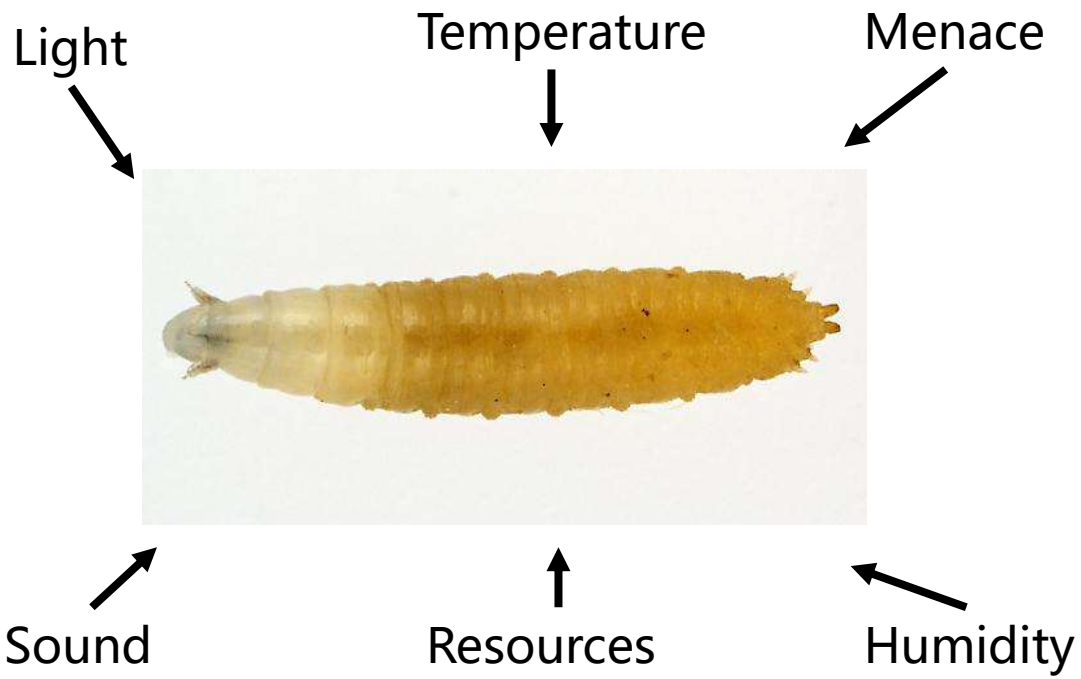


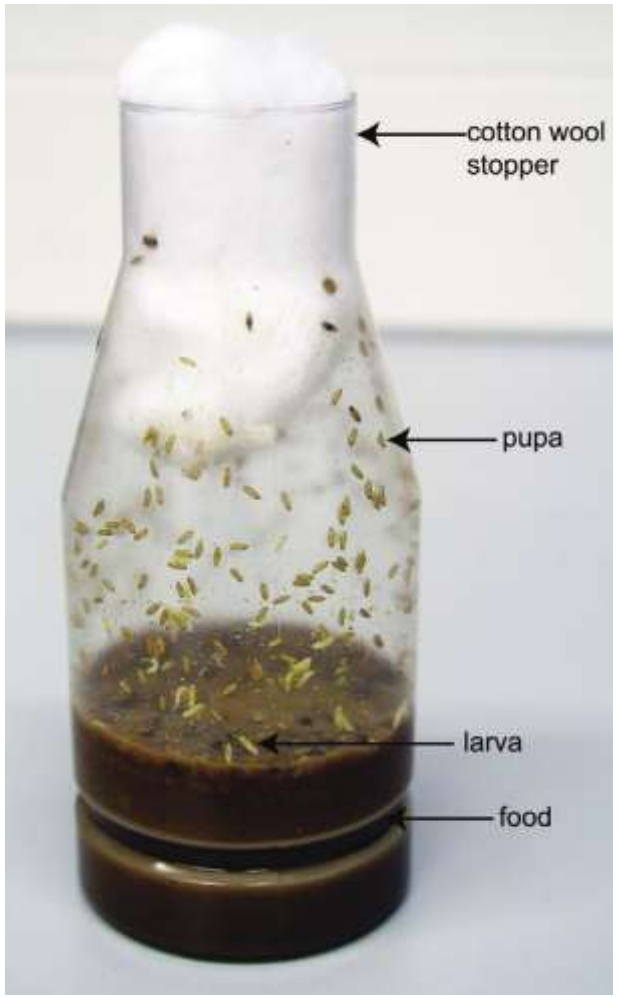




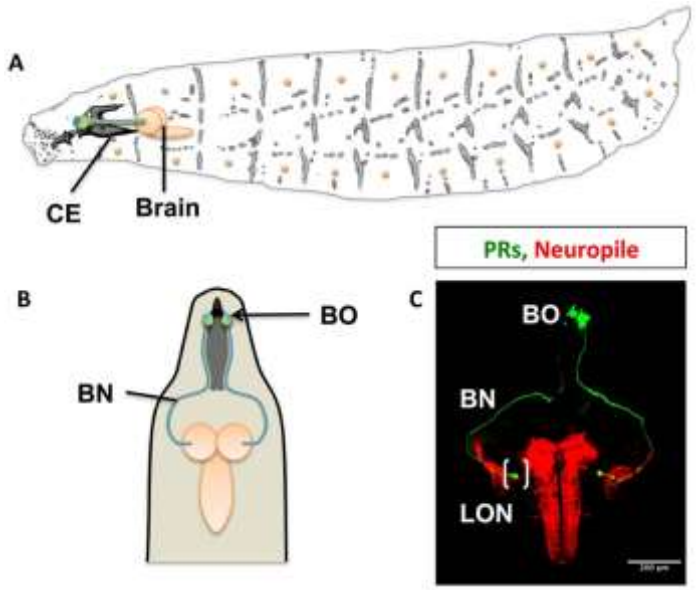
Yoshino J, et al., *Curr Biol.*, 2017

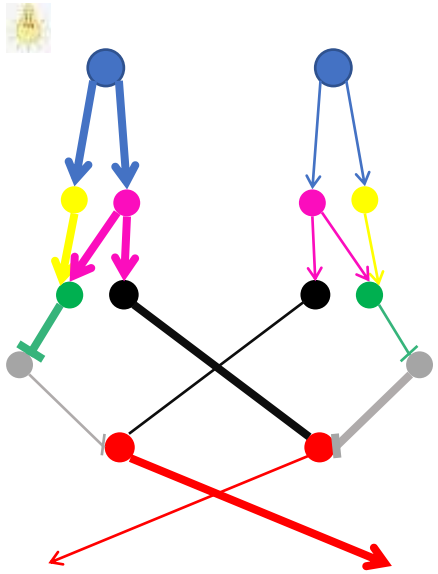
Darkening in *Drosophila* larvae

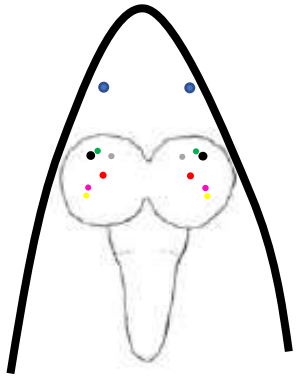




Bolwig’s organ mediated tropotactic respond

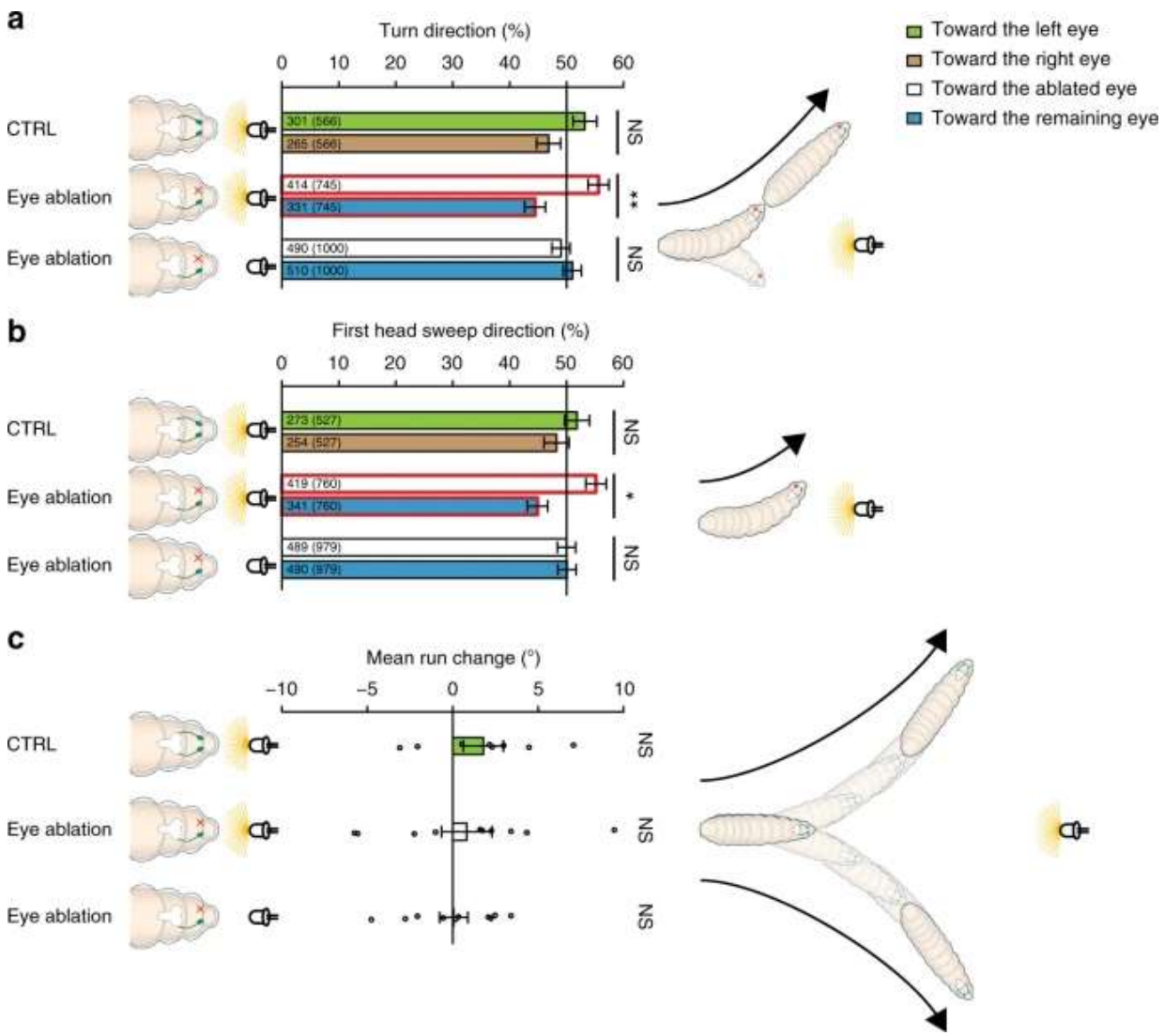


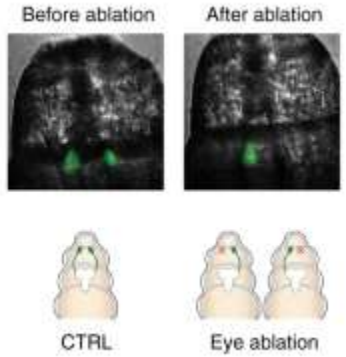


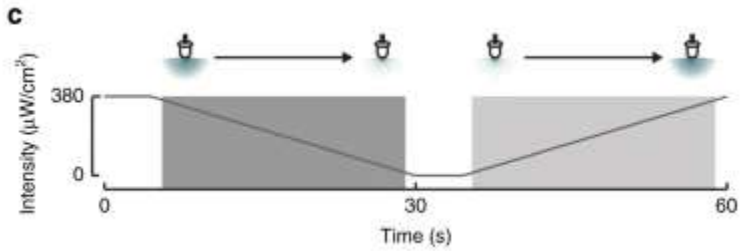


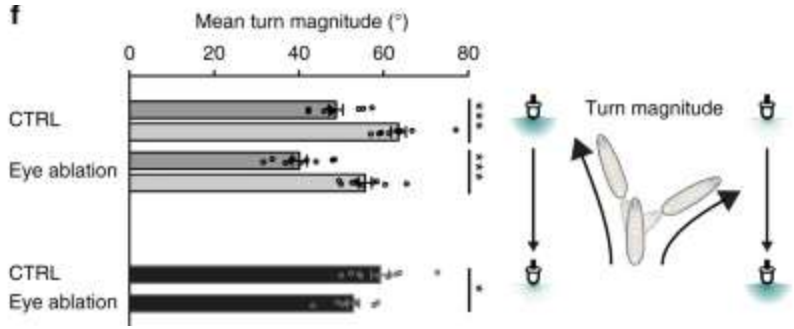
rh5
5th LN
pdf
DN1
ACLP
IN
CCLP

Bolwig’ s organ mediated klinotactic respond



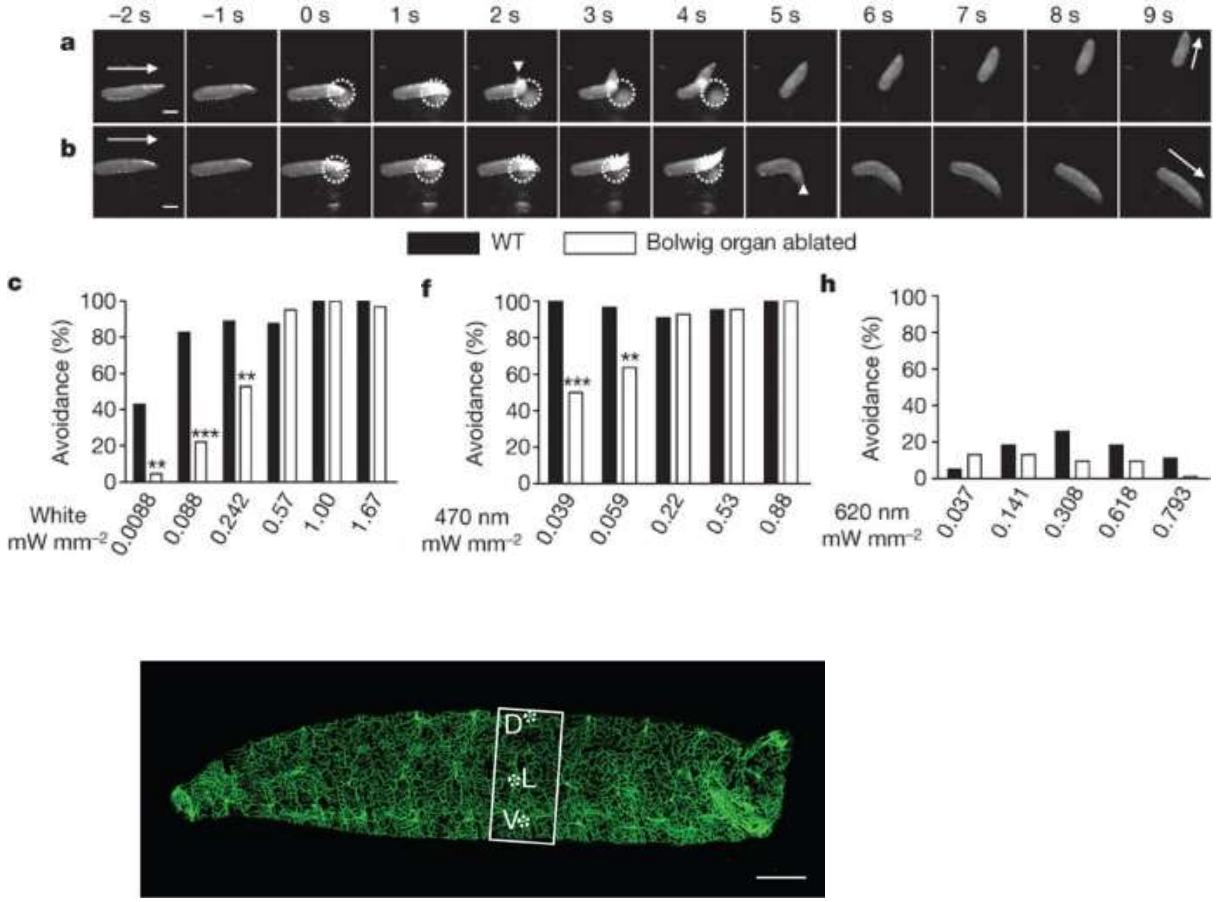


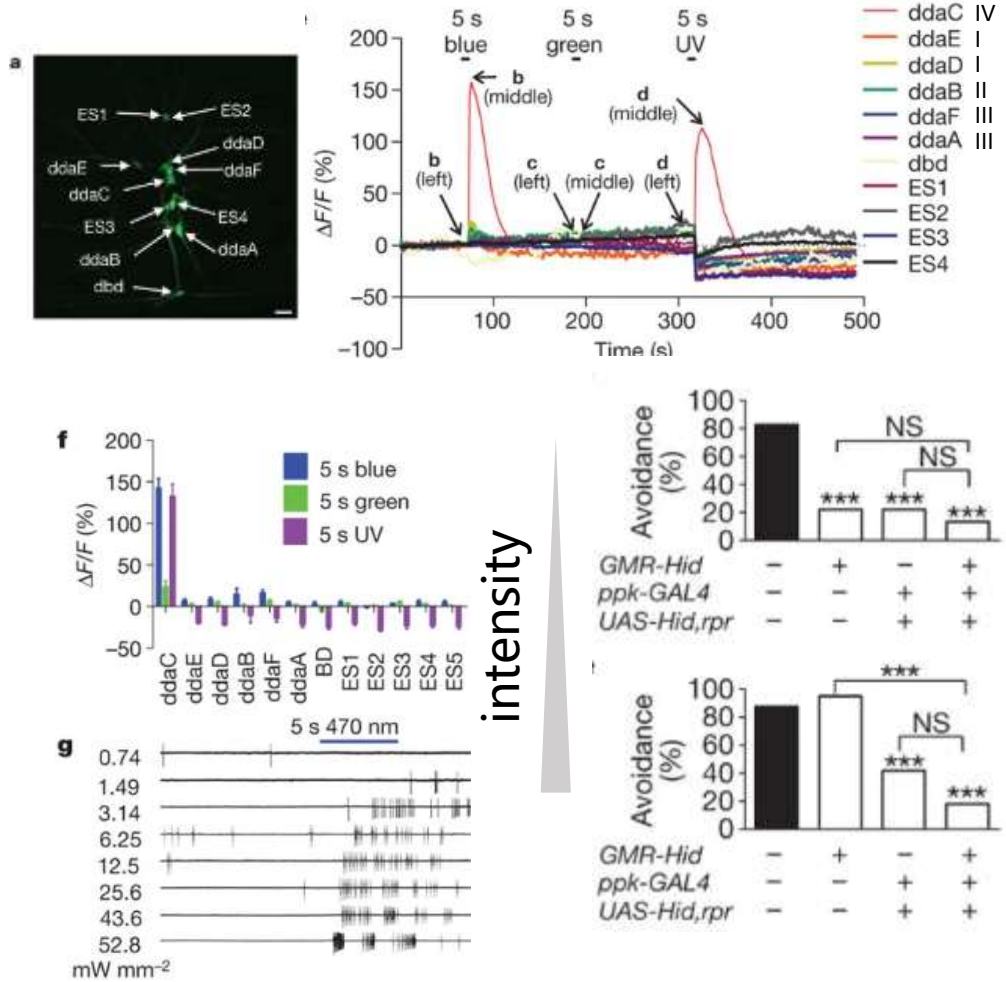




Humberg, TH., et al., *Nat Commun.*, 2018

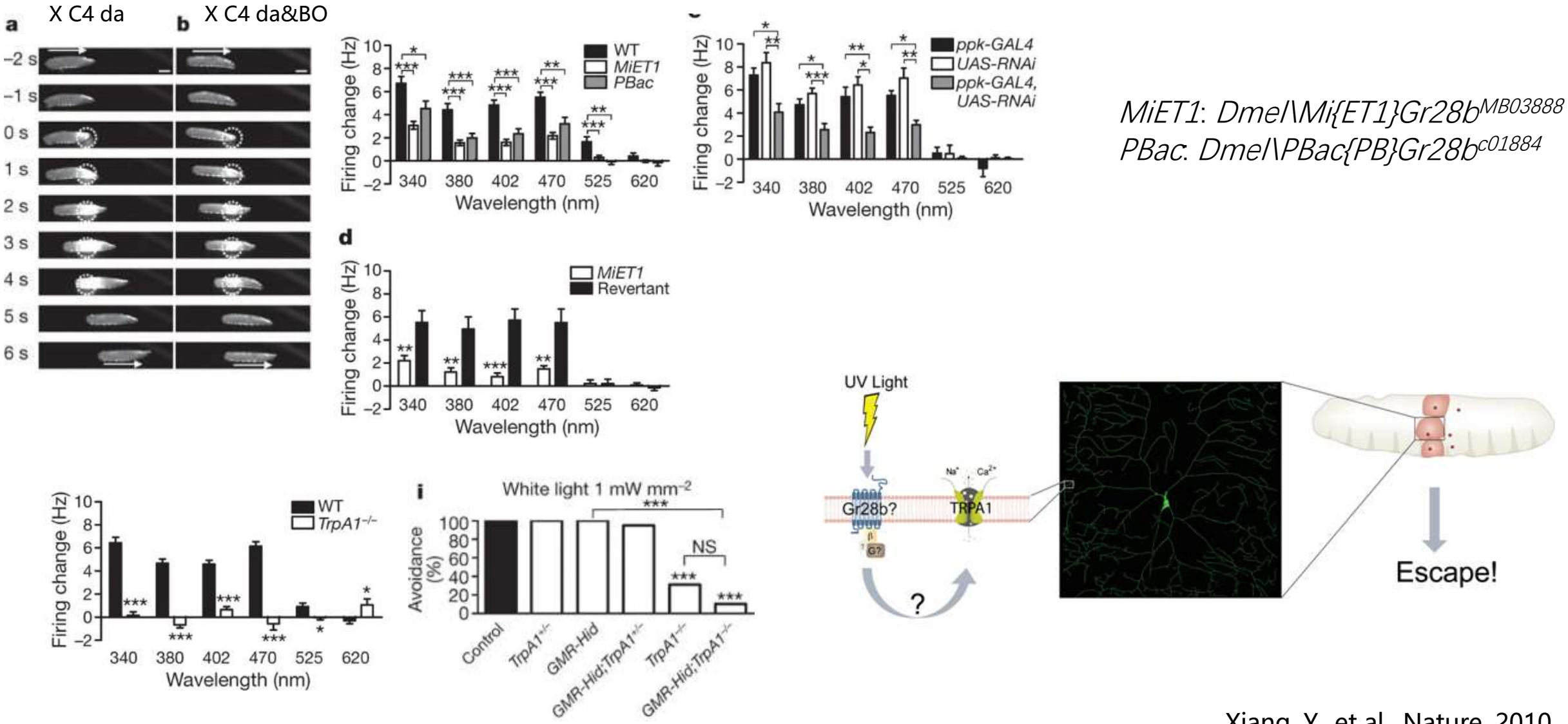
Class IV md in addition to Bolwig’ s organs contribute to photoavoidance





Xiang, Y., et al., *Nature*, 2010

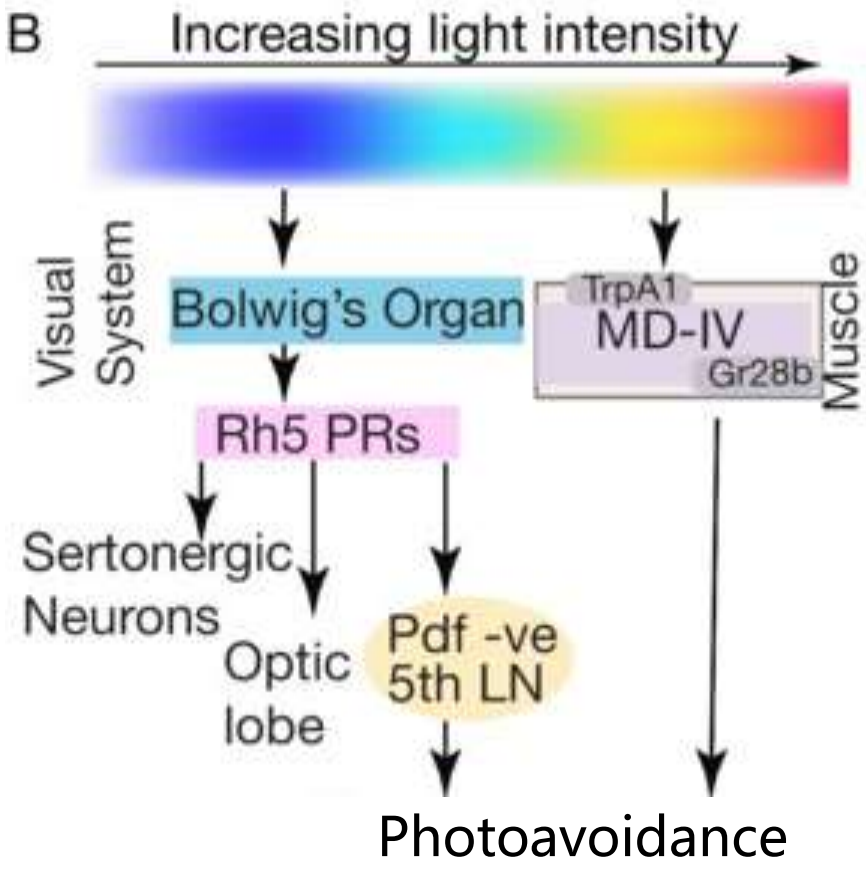
Gr28b and *TrpA1* are required in light transduction in class IV neurons

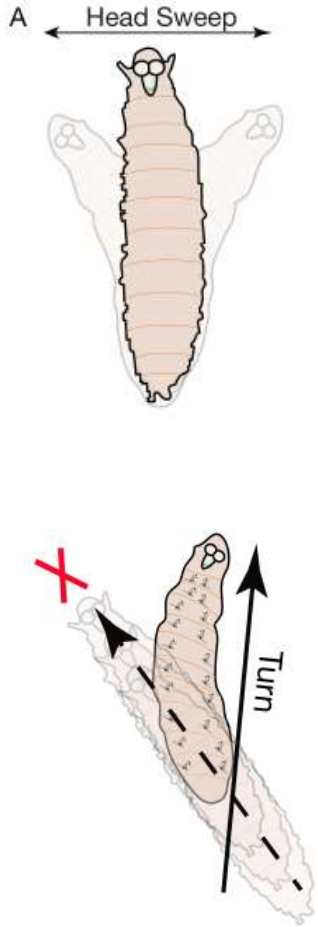


MiET1: *Dmel\Mi{ET1}Gr28b*^{MB03888}
PBac: *Dmel\PBac{PB}Gr28b*^{c01884}

Xiang, Y., et al., Nature, 2010

Mechanism of *Drosophila* larvae escape induced by light





Summary I

- C4 da is the sensory of noxious stimuli.
- *Drosophila* larvae exhibit multiple escape behaviors
- How *Drosophila* larva judges the brightness of the environment?

  Tropotactic& Klinotactic

  BO&C4 da

References

Grueber WB, Ye B, Moore AW, Jan LY, Jan YN. Dendrites of distinct classes of Drosophila sensory neurons show different capacities for homotypic repulsion. *Curr Biol*. 2003 Apr 15;13(8):618-26.

Yoshino J, Morikawa RK, Hasegawa E, Emoto K. Neural Circuitry that Evokes Escape Behavior upon Activation of Nociceptive Sensory Neurons in Drosophila Larvae. *Curr Biol*. 2017 Aug 21;27(16):2499-2504.e3.

Xiang, Y., Yuan, Q., Vogt, N. *et al.* Light-avoidance-mediating photoreceptors tile the *Drosophila* larval body wall. *Nature* 468, 921–926 (2010).

Humberg, TH., Bruegger, P., Afonso, B. *et al.* Dedicated photoreceptor pathways in *Drosophila* larvae mediate navigation by processing either spatial or temporal cues. *Nat Commun* 9, 1260 (2018).

Hwang RY, Zhong L, Xu Y, Johnson T, Zhang F, Deisseroth K, Tracey WD. Nociceptive neurons protect Drosophila larvae from parasitoid wasps. *Curr Biol*. 2007 Dec 18;17(24):2105-2116.

Bodmer R, Jan YN. Morphological differentiation of the embryonic peripheral neurons in Drosophila. *Rouxs Arch Dev Biol*. 1987 Feb;196(2):69-77.

Ohyama T, Schneider-Mizell CM, Fetter RD, Aleman JV, Franconville R, Rivera-Alba M, Mensh BD, Branson KM, Simpson JH, Truman JW, Cardona A, Zlatic M. A multilevel multimodal circuit enhances action selection in Drosophila. *Nature*. 2015 Apr 30;520(7549):633-9.

Escape behavior induced by noxious heat and mechanical stimuli in *Drosophila* larvae

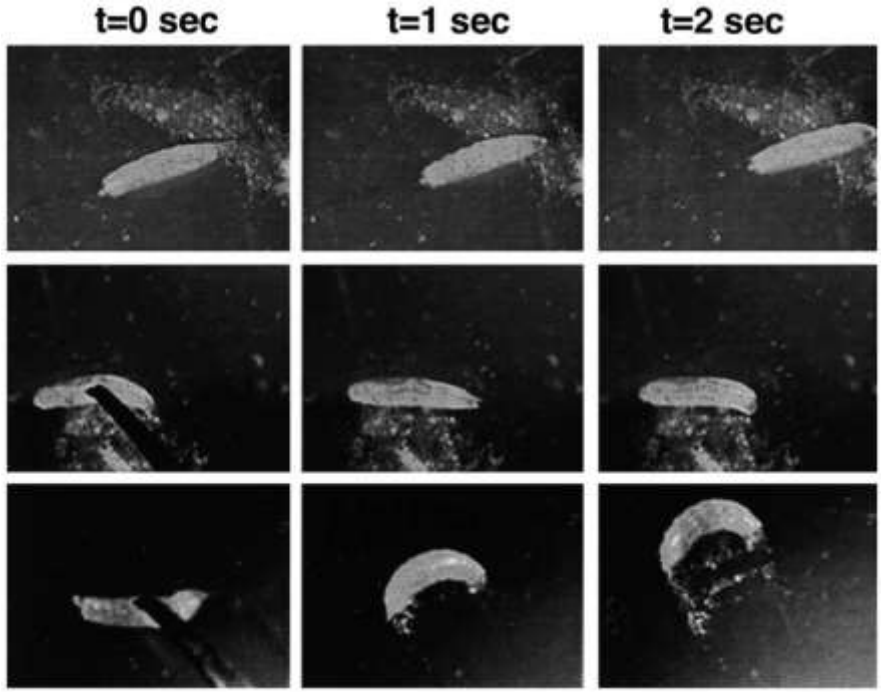
JXX

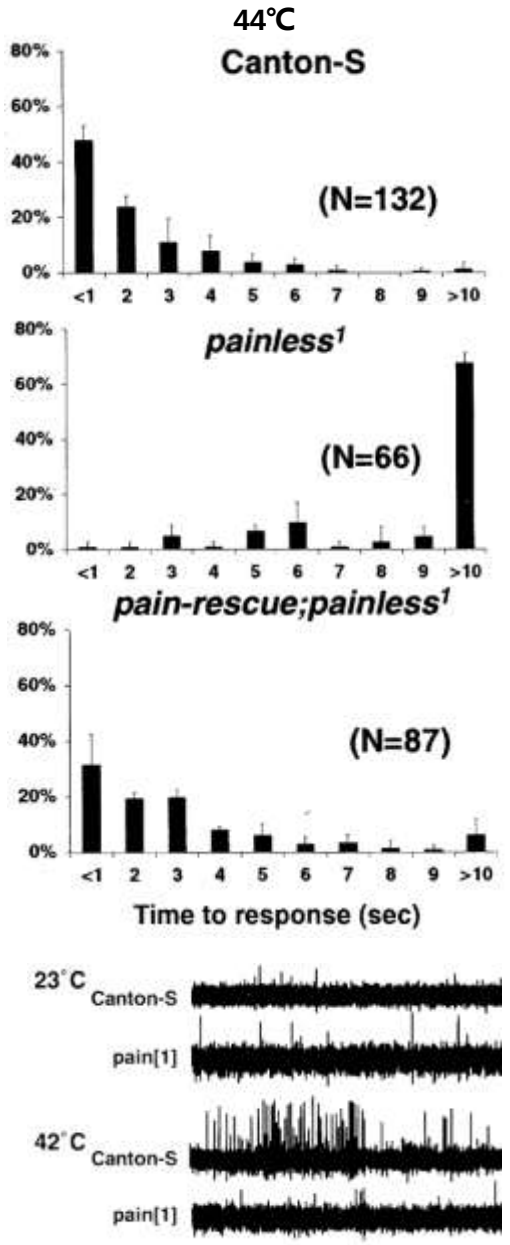
- Molecular basis
- Neural circuit basis

Cell, Vol. 113, 261–273, April 18, 2003, Copyright ©2003 by Cell Press

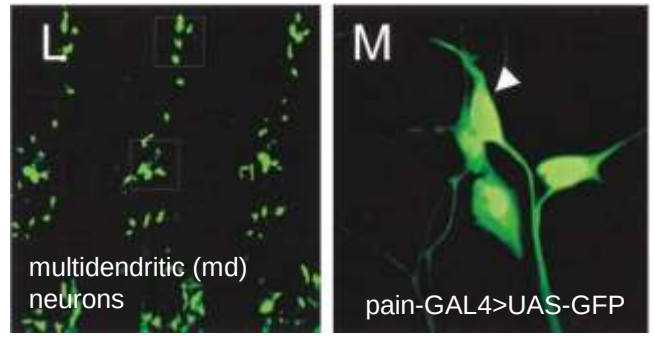
painless, a *Drosophila* Gene Essential for Nociception

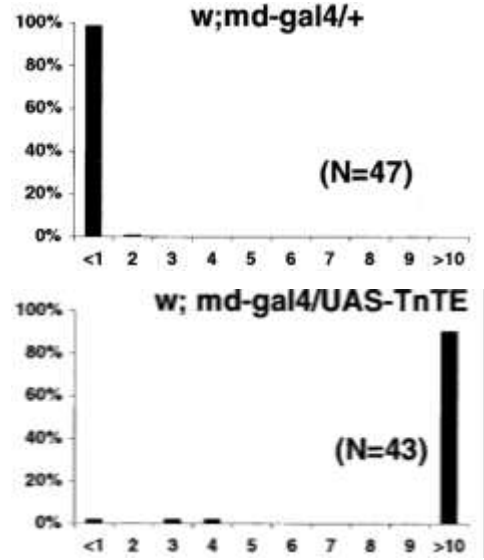
W. Daniel Tracey, Jr.,[1,*] Rachel I. Wilson,[2]
Gilles Laurent,[2] and Seymour Benzer[1,*]





Painless encodes a non-selective cation channel in the TRPA family.

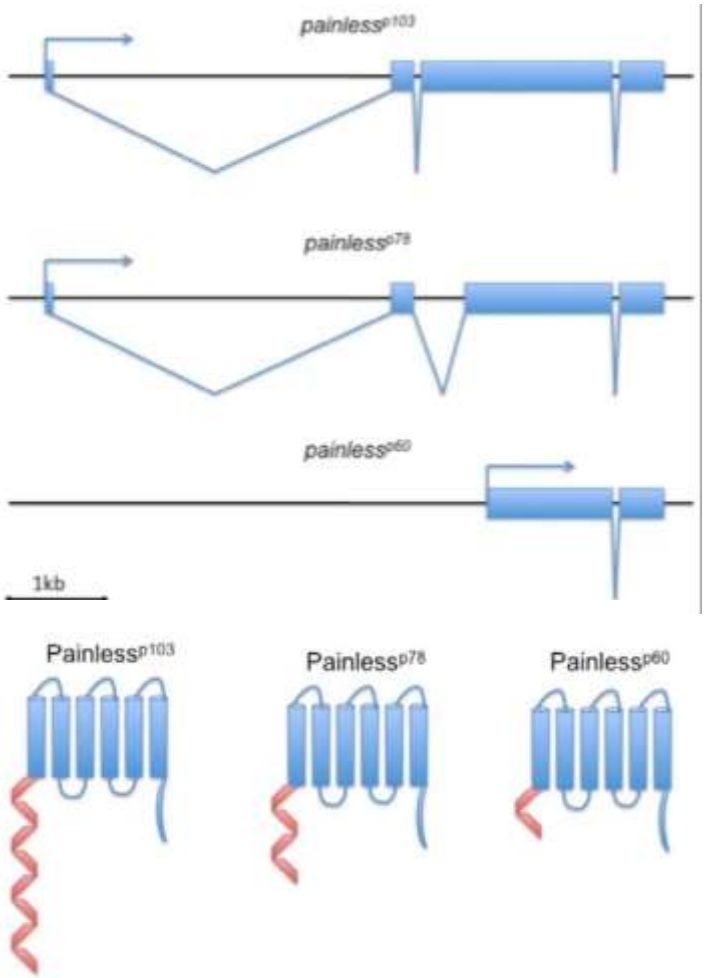




Painless mutant
Light touch(10 mN):not effected
Harsh touch (45 mN): decreased

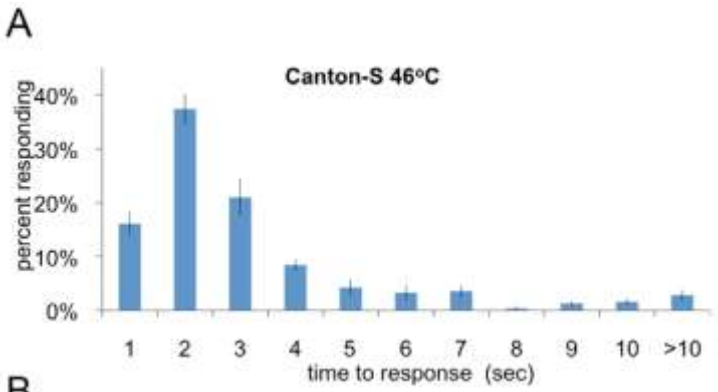
***Painless* is required for the detection of noxious heat and mechanical stimuli**

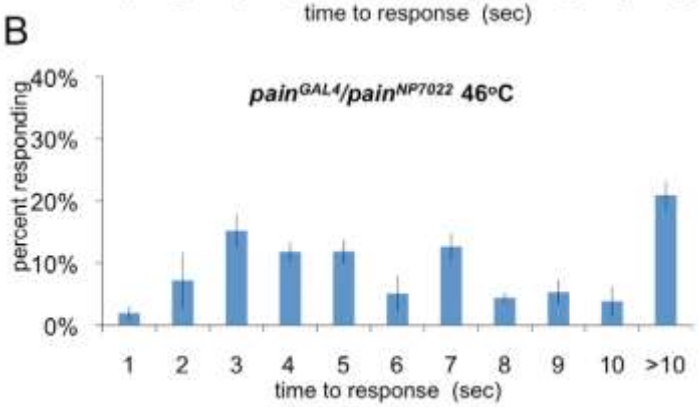
Different *painless* isoforms for thermal and mechanical nociception

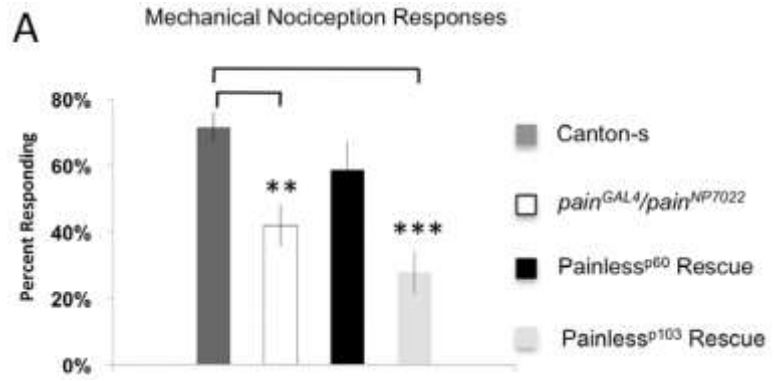


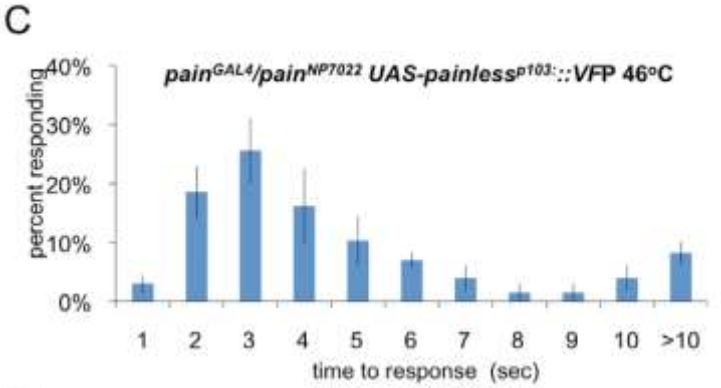
Thermal nociception

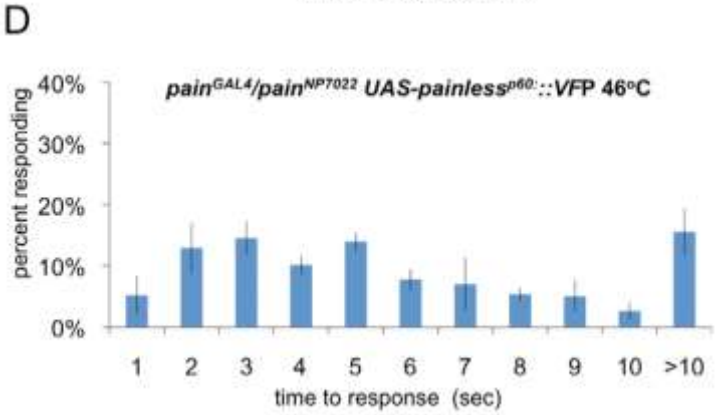
Mechanical nociception









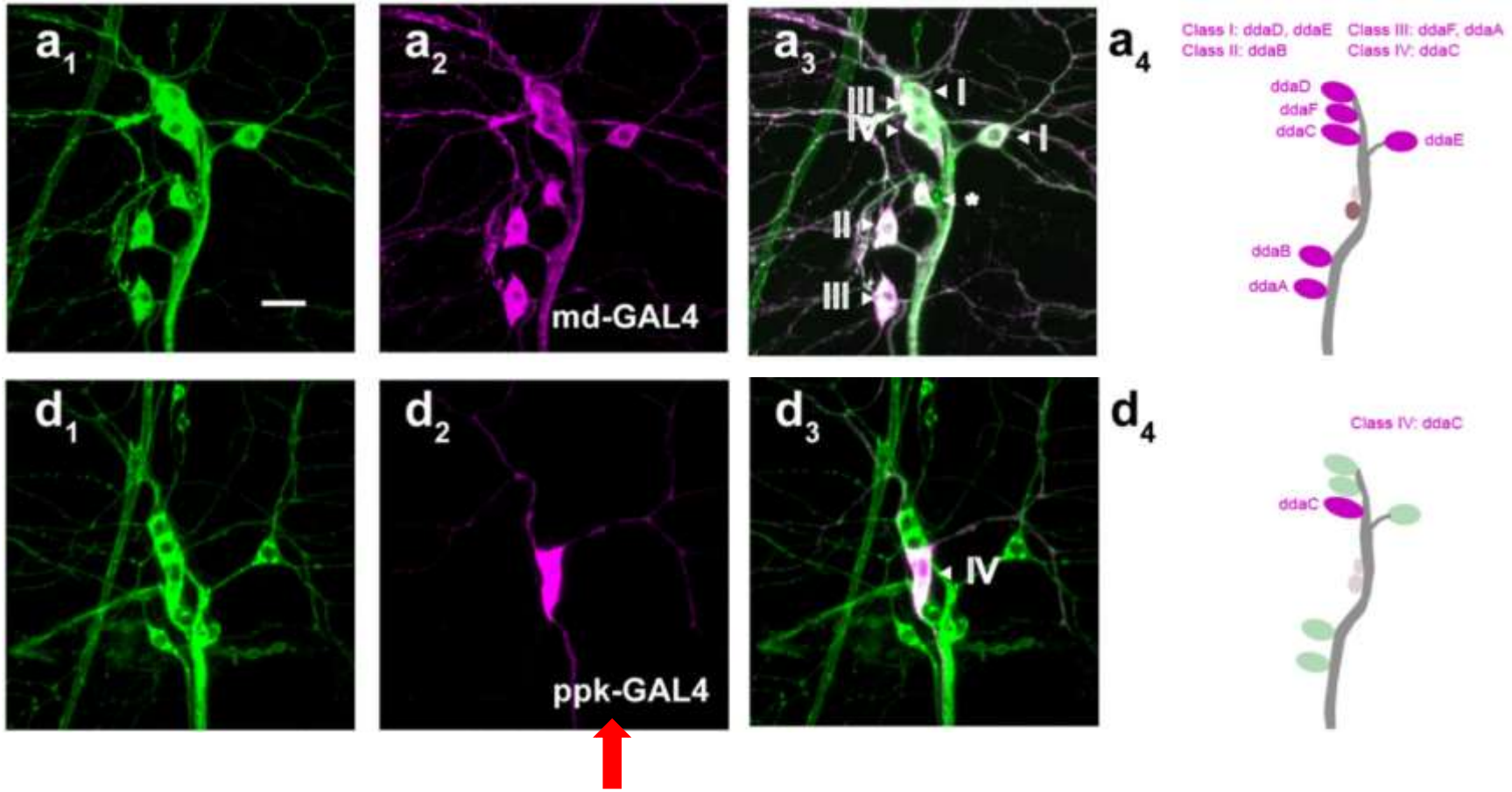


Hwang et al.,Plos one, 2012

Class IV multidendritic neurons are necessary for nocifensive behavior

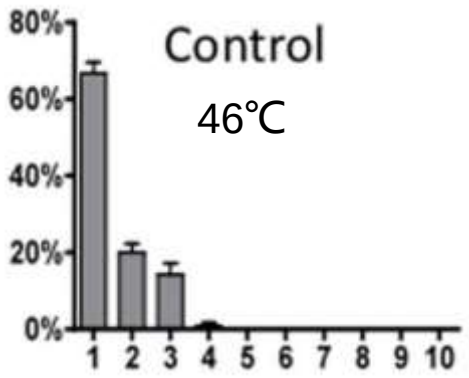
md neurons

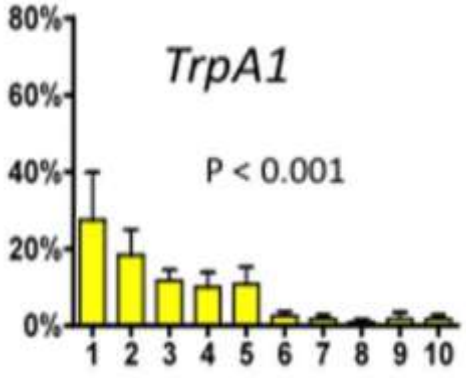
Tracey et al., Cell, 2003



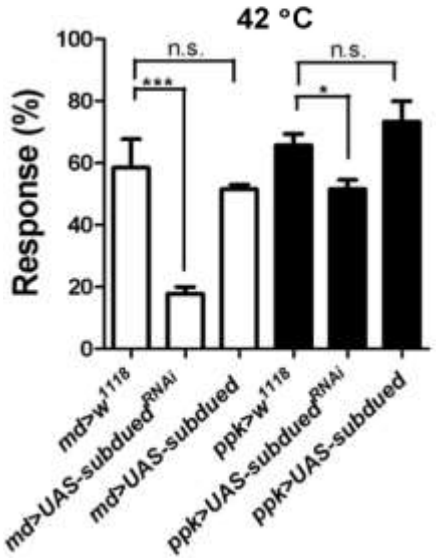
Hwang et al., Curr Biol, 2007

dTrpA1 and *subdued* are required for thermal nociception

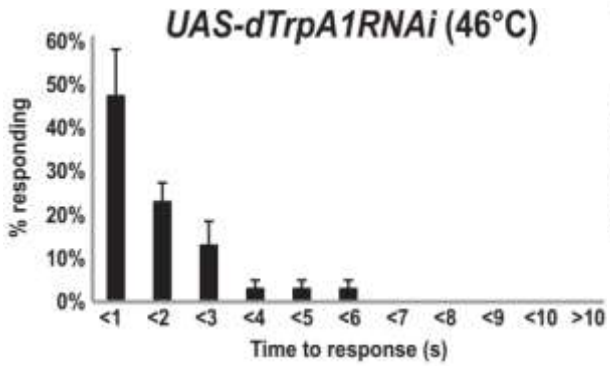


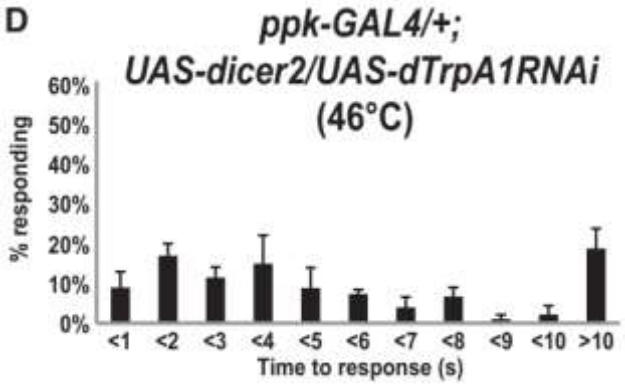


Neely et al., Plos one, 2011



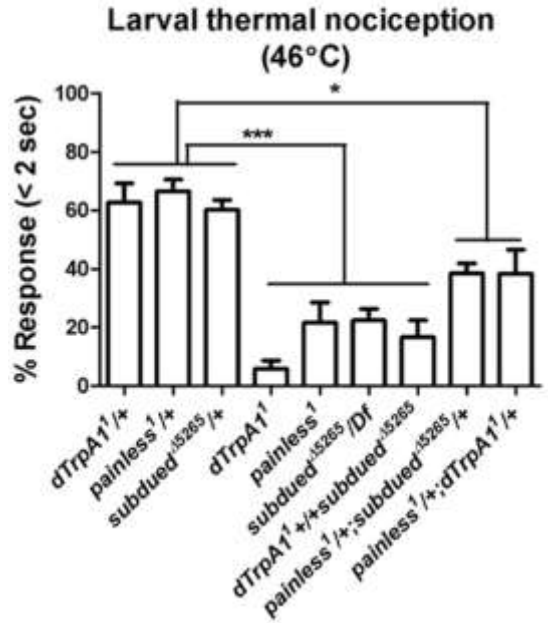
subdued encodes a chloride ion channel belonging to the TMEM16 family.





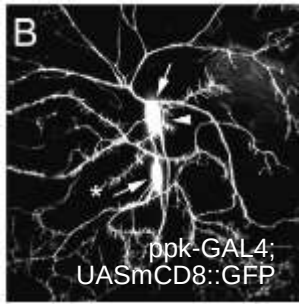
Transient receptor potential cation channel A1 (TrpA1) encodes a cation channel activated by warming.

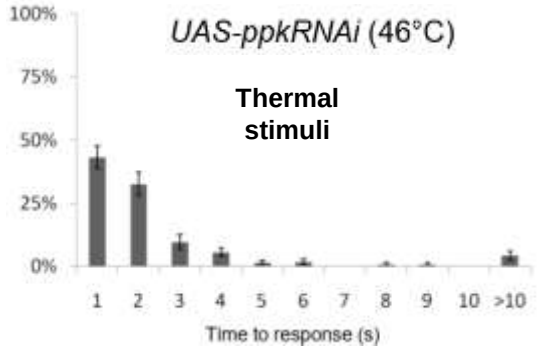
Zhong et al., Cell Reports, 2012

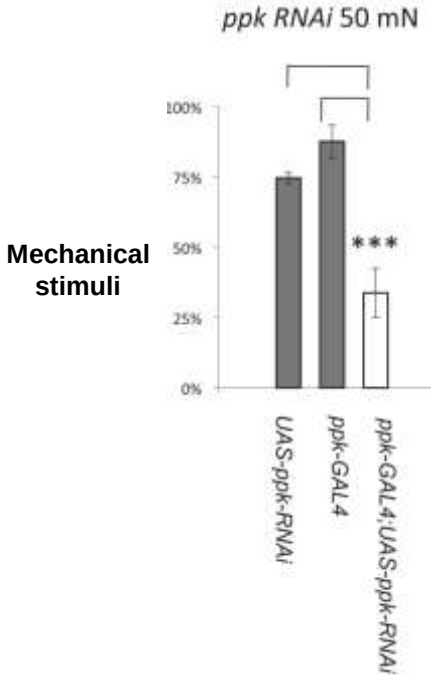


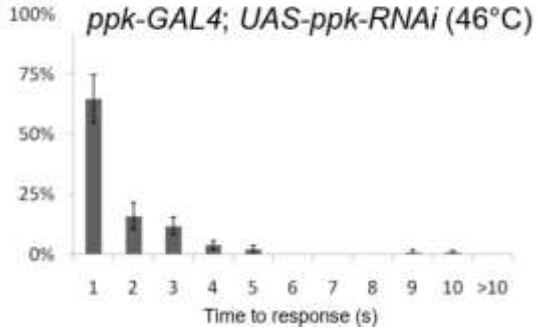
Jang et al., J Biol Chem, 2015

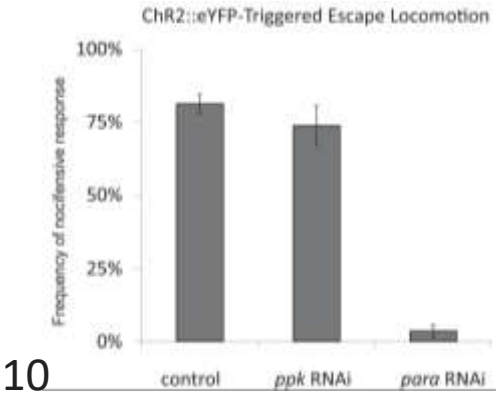
Pickpocket (*ppk*) and *balboa* (*bba/ppk26*) are required for mechanical nociception responses

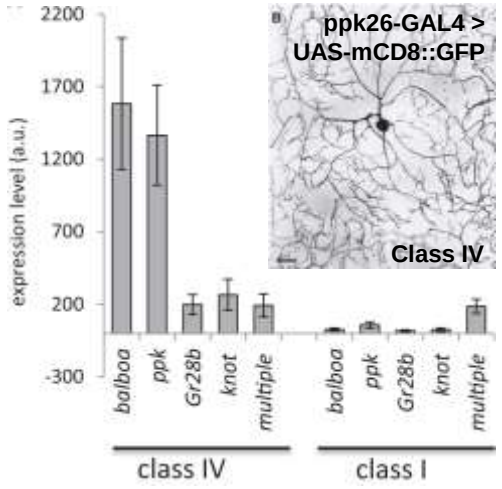


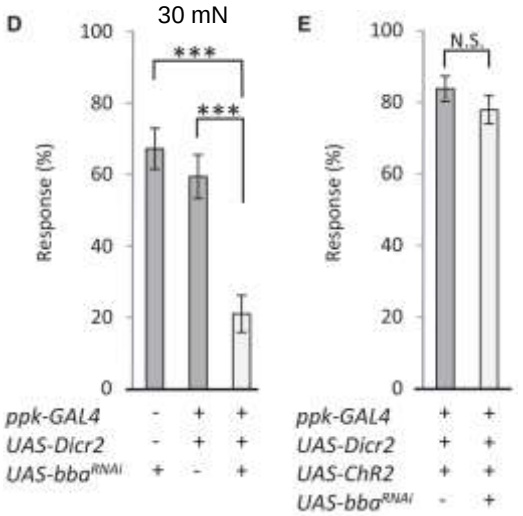


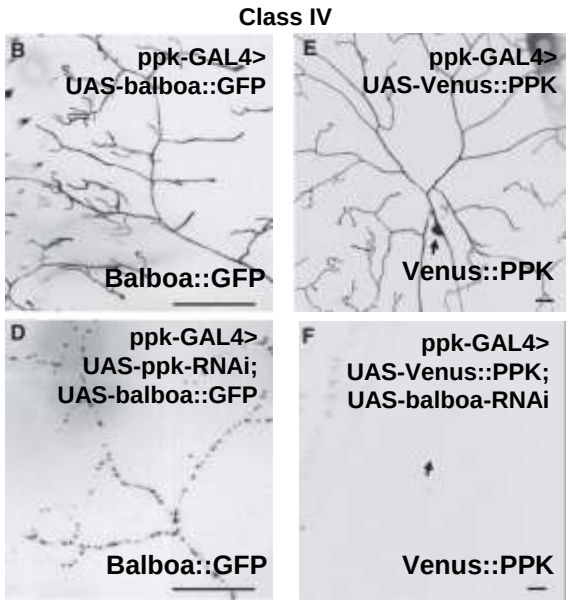










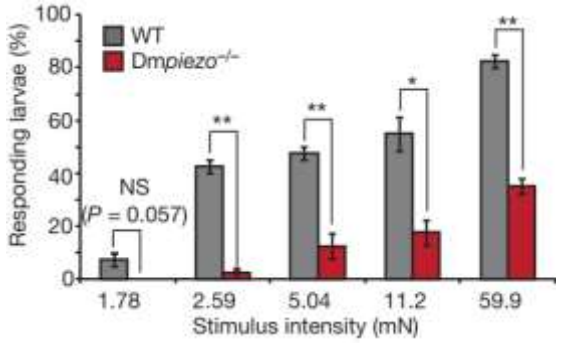


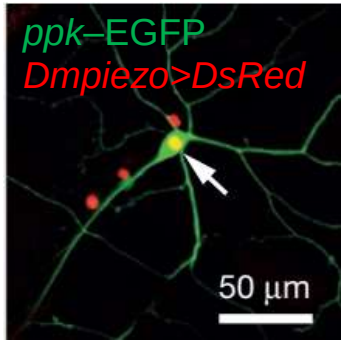
ppk and ppk26 belong to the degenerin/epithelial sodium channel (DEG/ENaC) family.

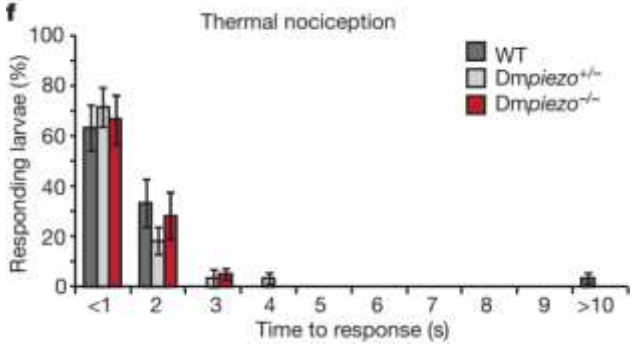
Zhong et al., Curr Biol, 2010

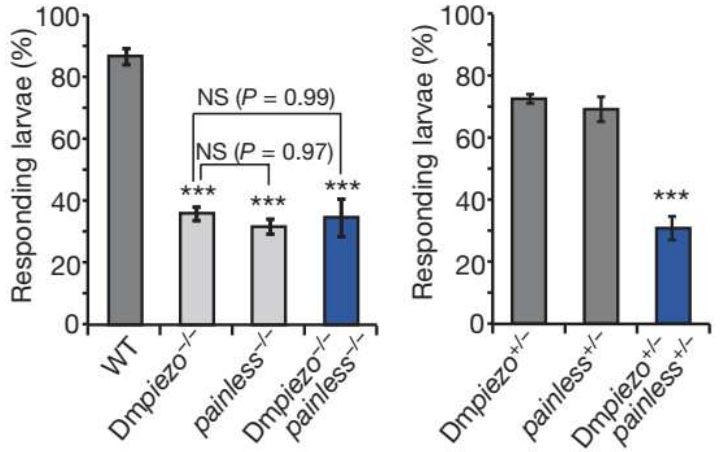
Mauthner et al., Curr Biol, 2014

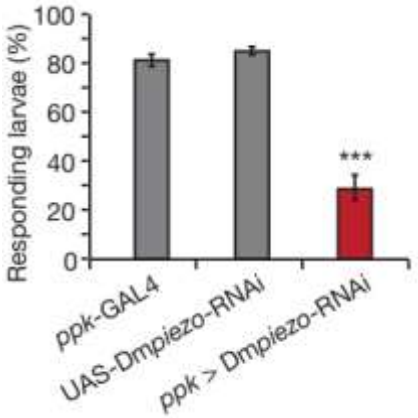
piezo and *ppk* function in parallel pathways in mechanical nociception

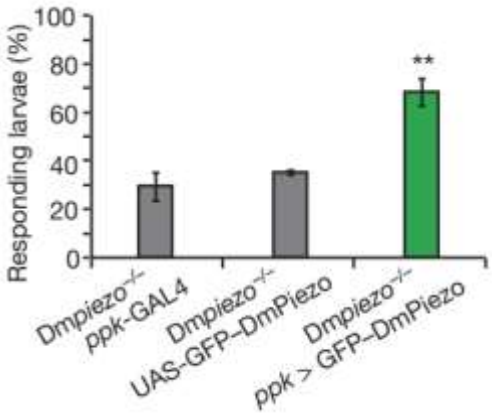




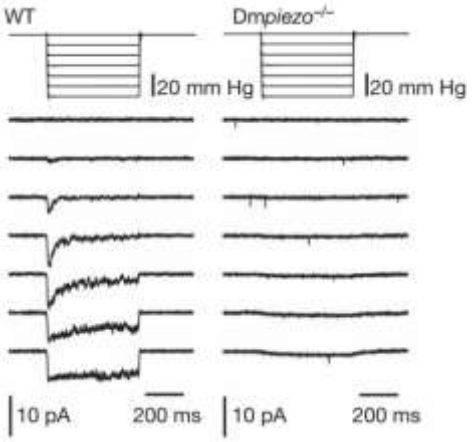


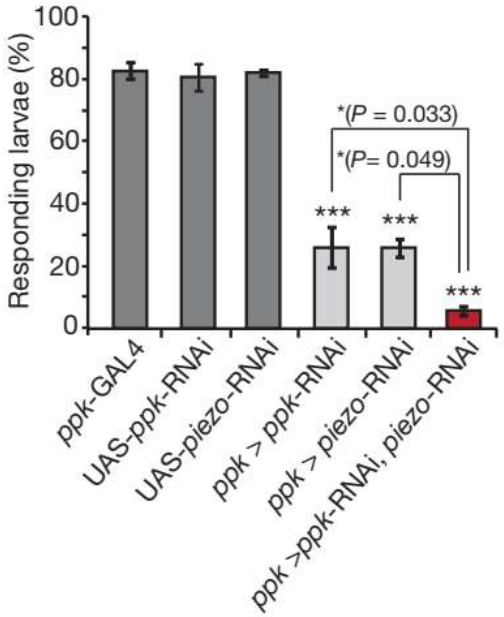






Patch-clamp recordings of isolated *ppk* neurons





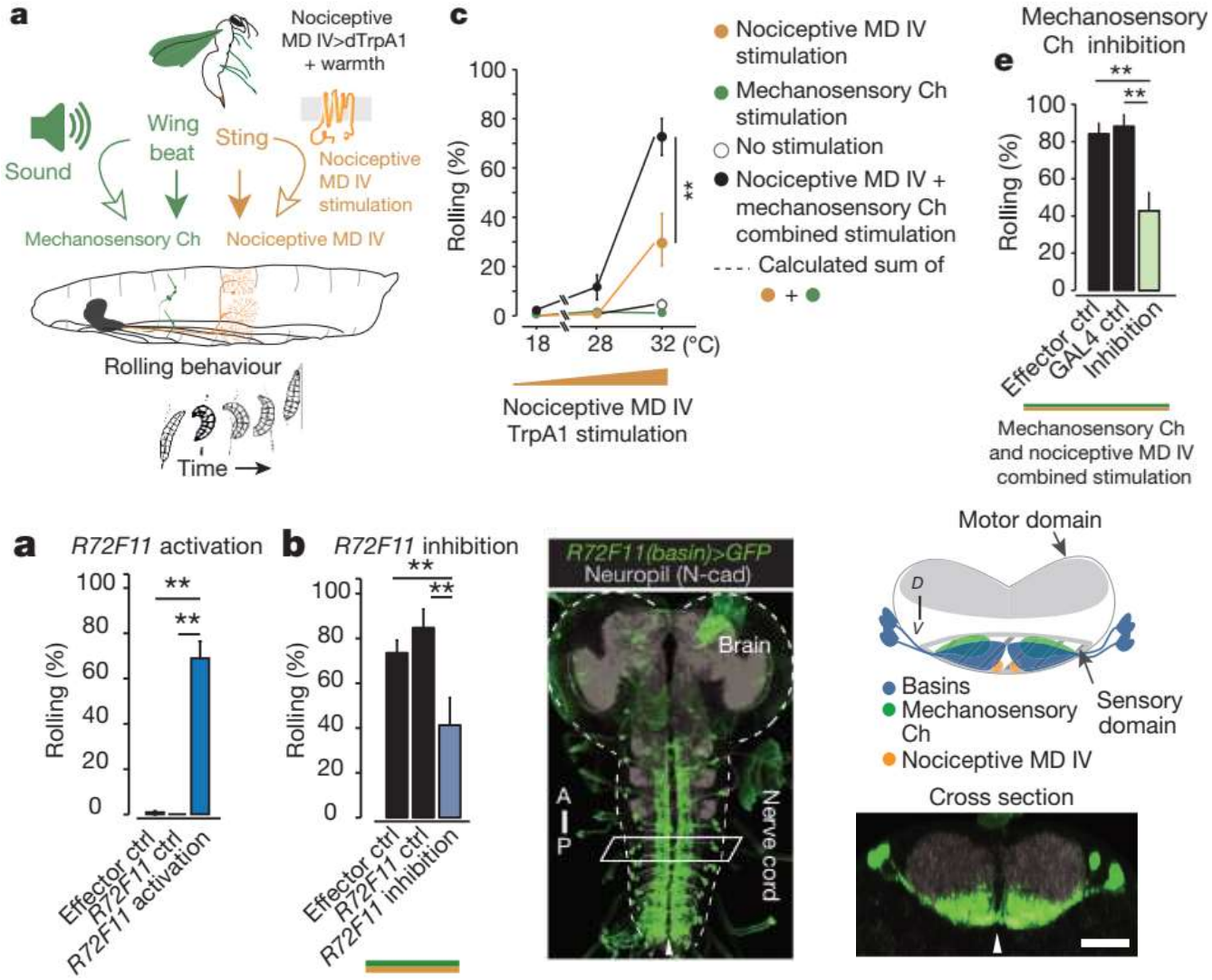
Piezo proteins are an evolutionarily conserved ion channel family involved in mechanotransduction.

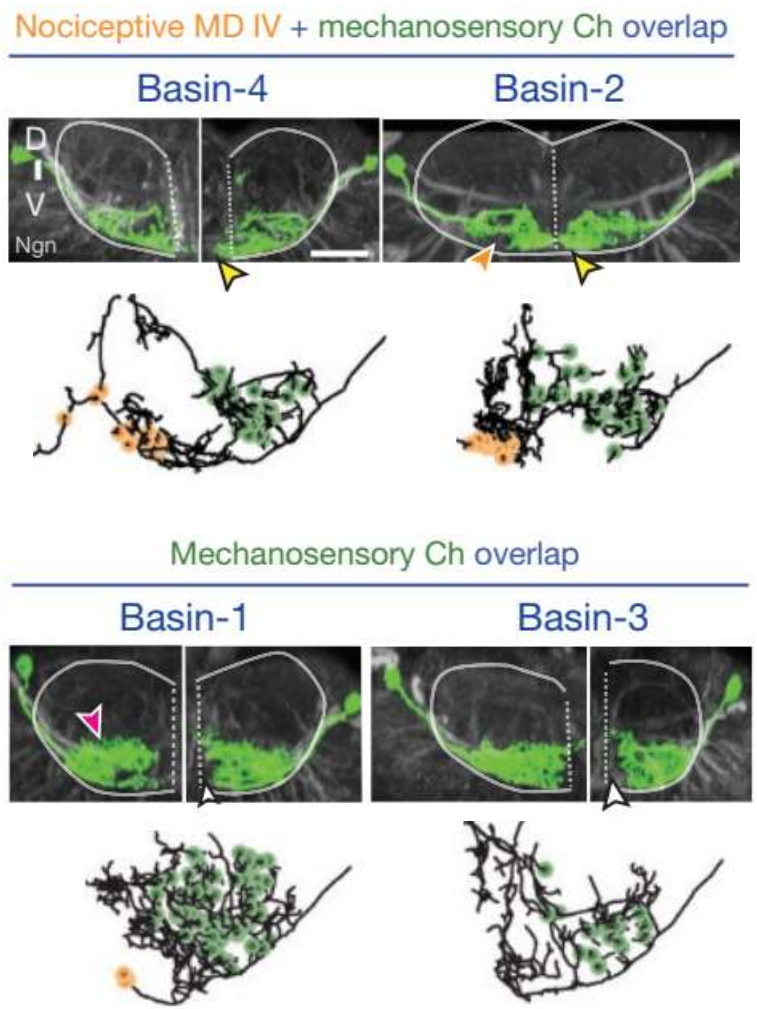
Kim et al., Nature, 2012

Molecular basis of thermal and mechanical nociception in *Drosophila* larvae

Nociception modality	Genes
Noxious heat stimuli	***painless, dTrpA1, subdued***
Noxious mechanical stimuli	***painless, ppk, bba/ppk26, piezo***

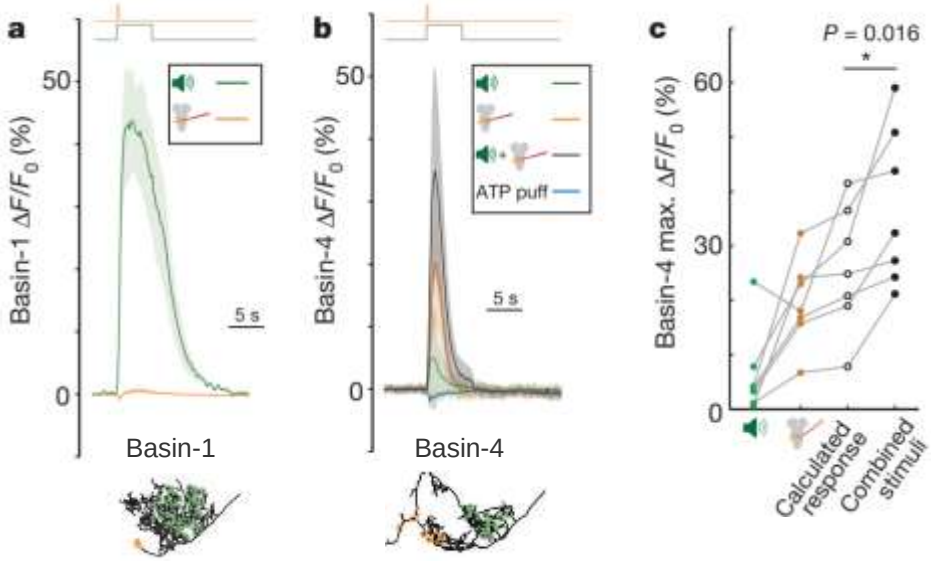
Basin neurons are downstream neurons of ClassIV MD and Ch neurons

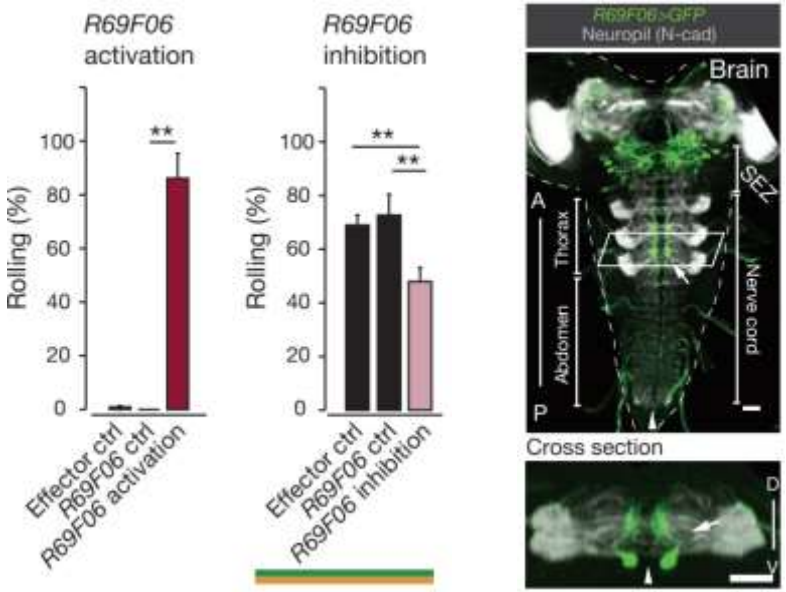




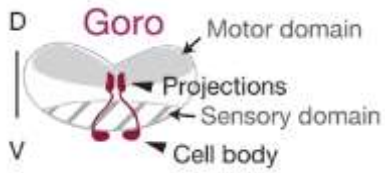
Ohyama et al., Nature, 2015

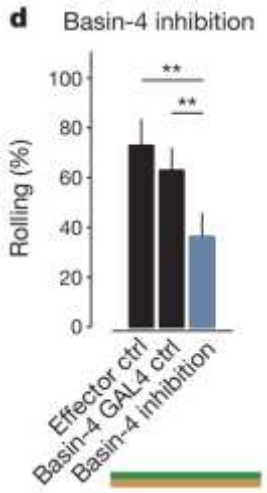
Basins are functionally connected to command-like Goro neurons

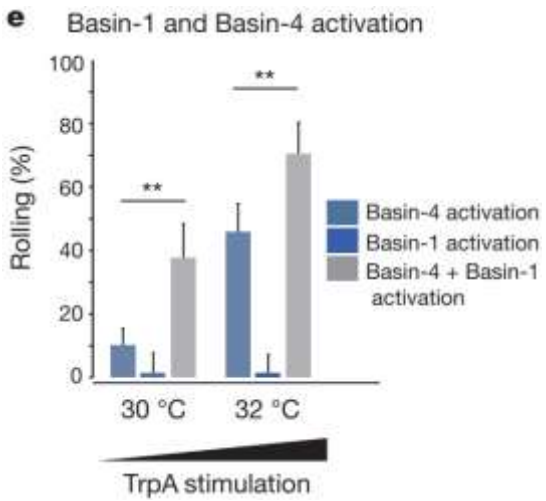


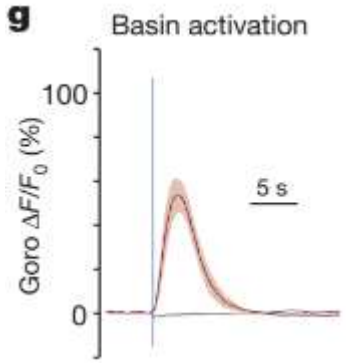


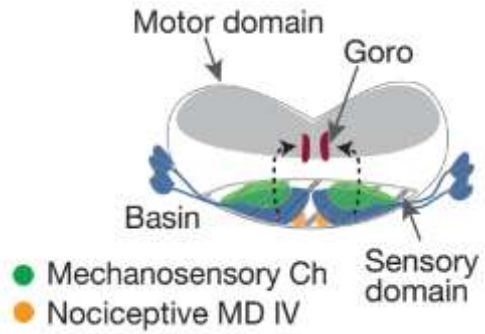
a pair of thoracic neurons





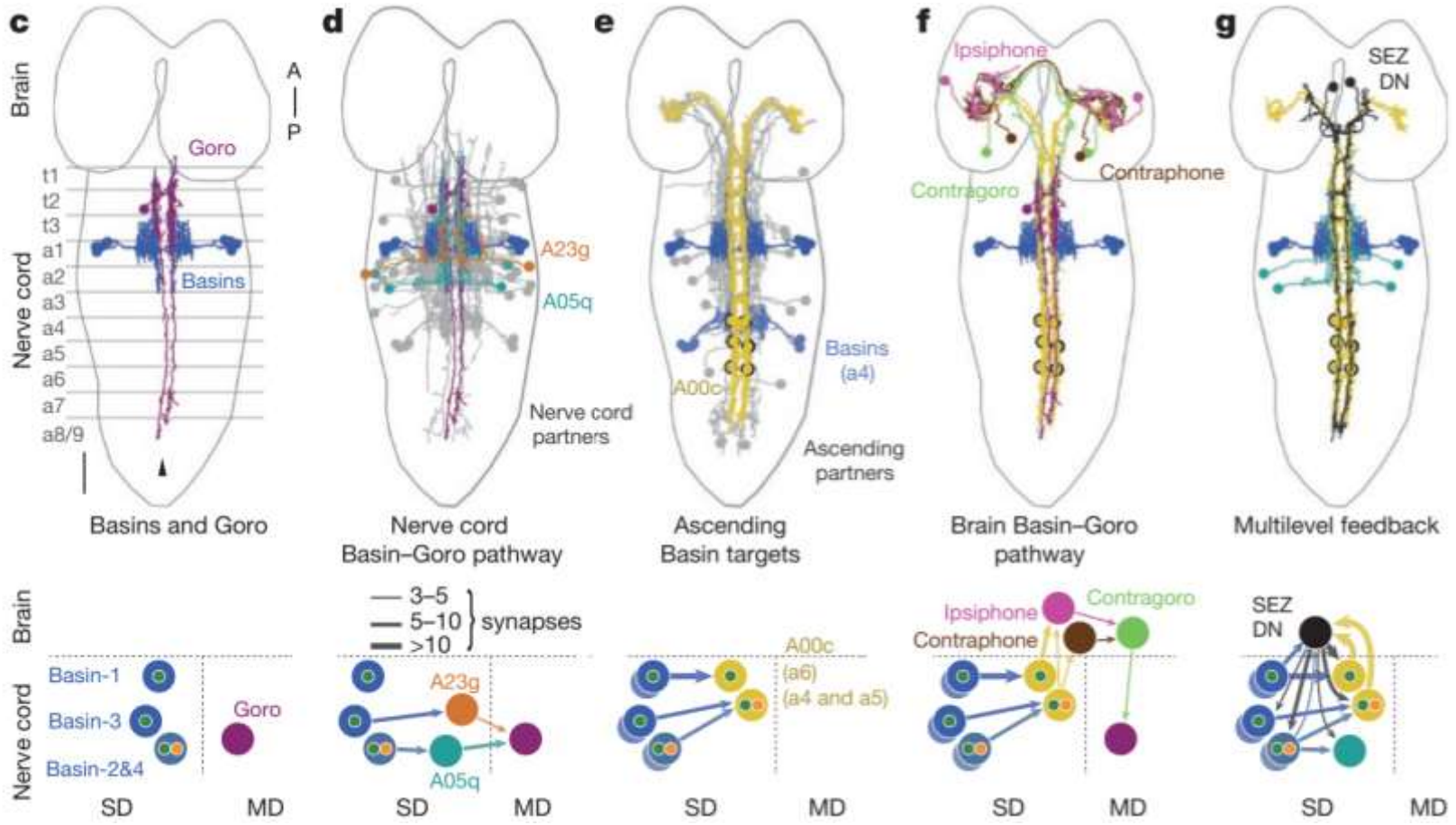


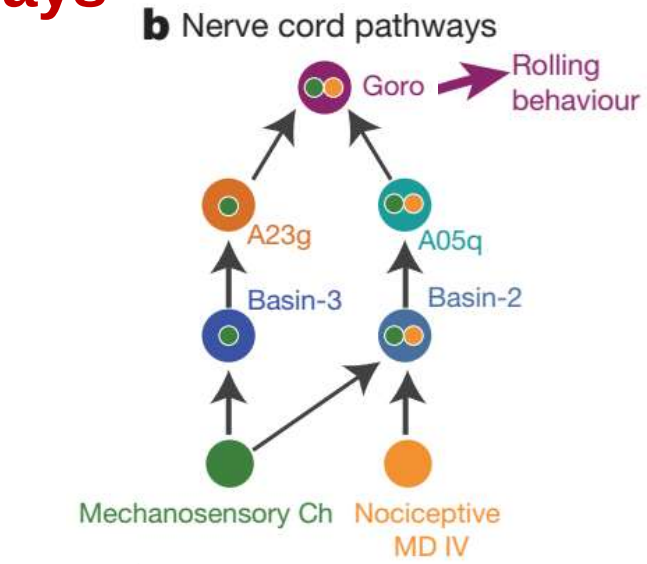


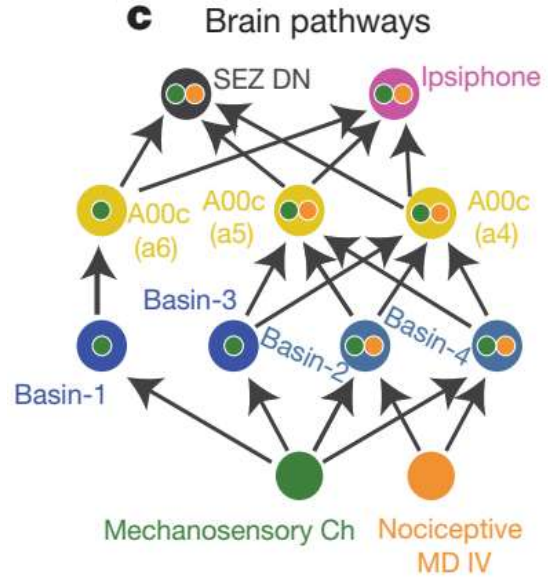


Ohyama et al., Nature, 2015

Electron microscopy reconstruction reveals multiple levels of multimodal convergence within Basins-to-Goro pathways

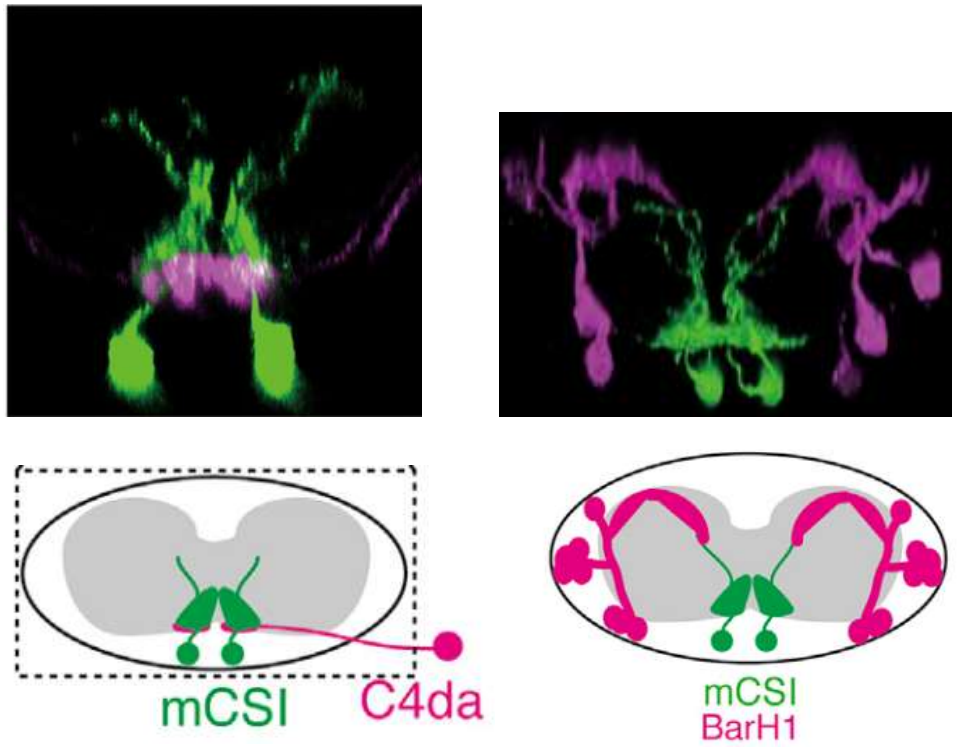






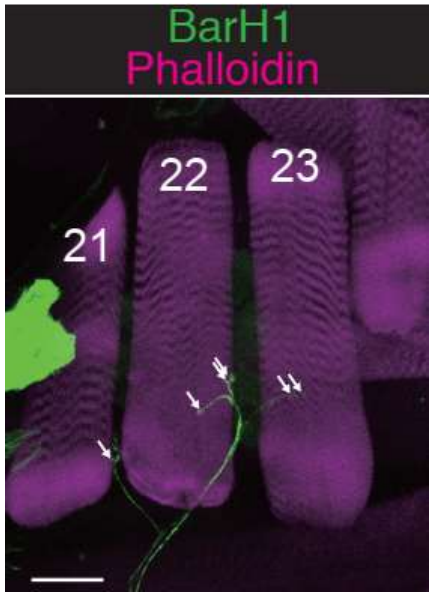
Ohyama et al., Nature, 2015

C4da-mCSI-SNa pathway
is parallel to the Basin-Goro pathway in the rolling behavior control

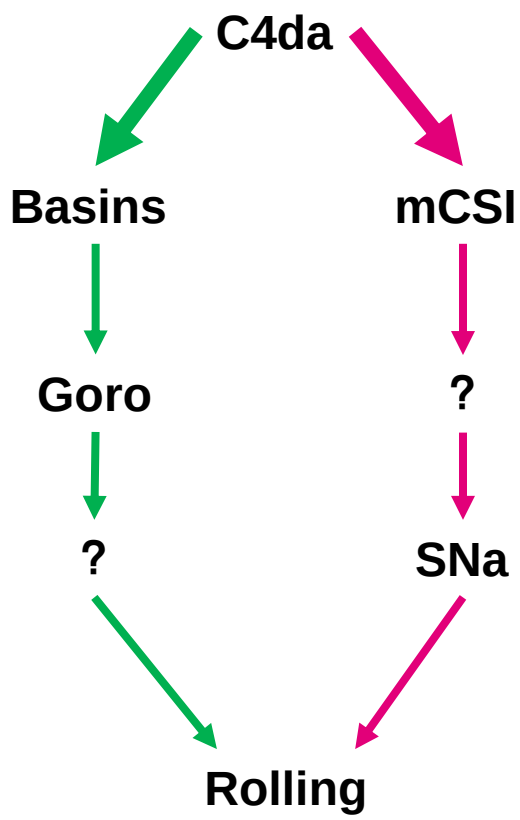


class IV dendrite arborization (C4da)

C4 da second-order interneurons (mCSIs)

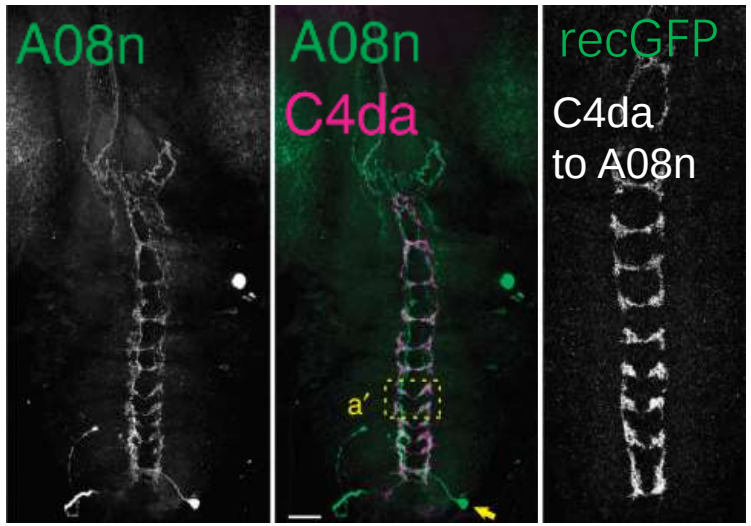


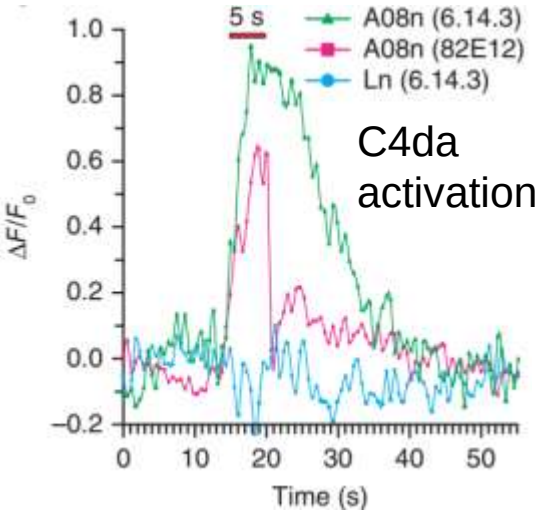
SNa motor neurons
in the abdominal segments are essential for self-righting rolling behavior

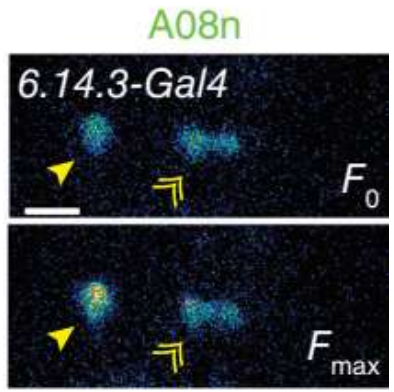


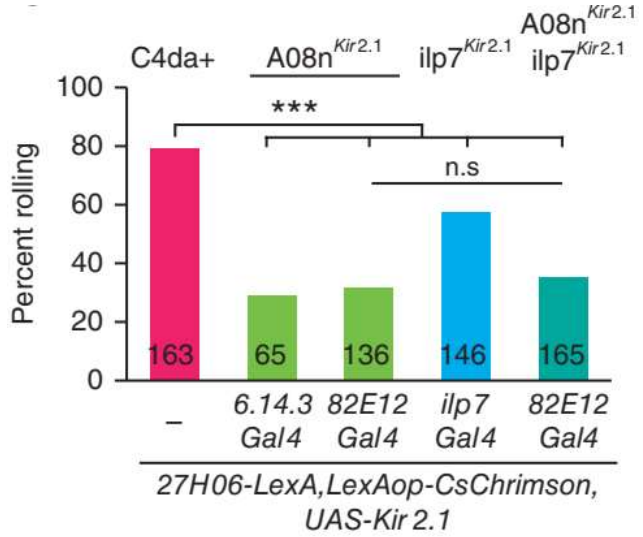
Yoshino et al., Curr Biol, 2017

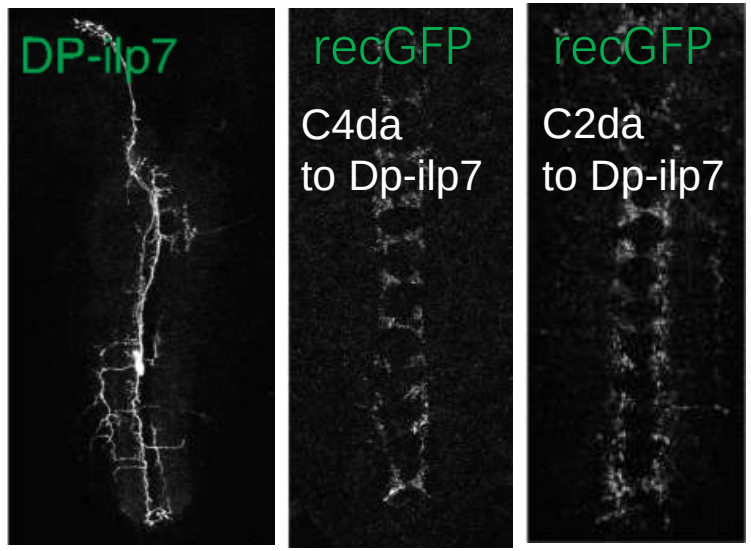
A08n neurons are necessary and sufficient for nociceptive responses downstream of C4da neurons

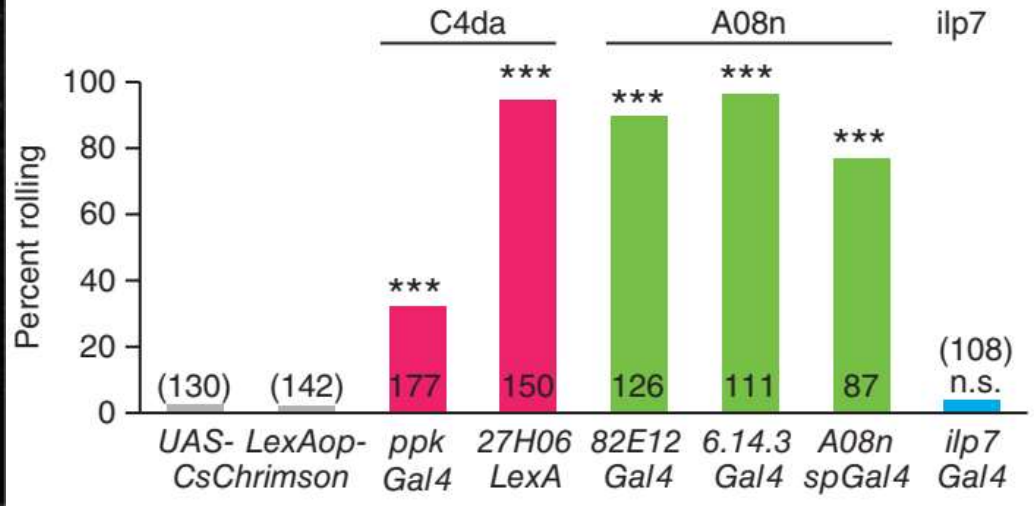


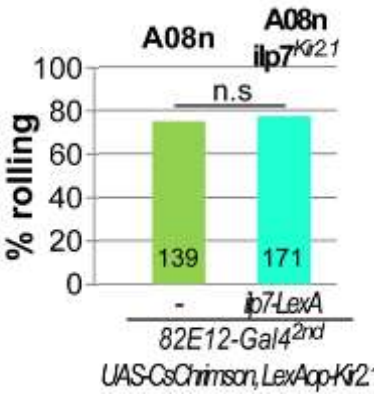








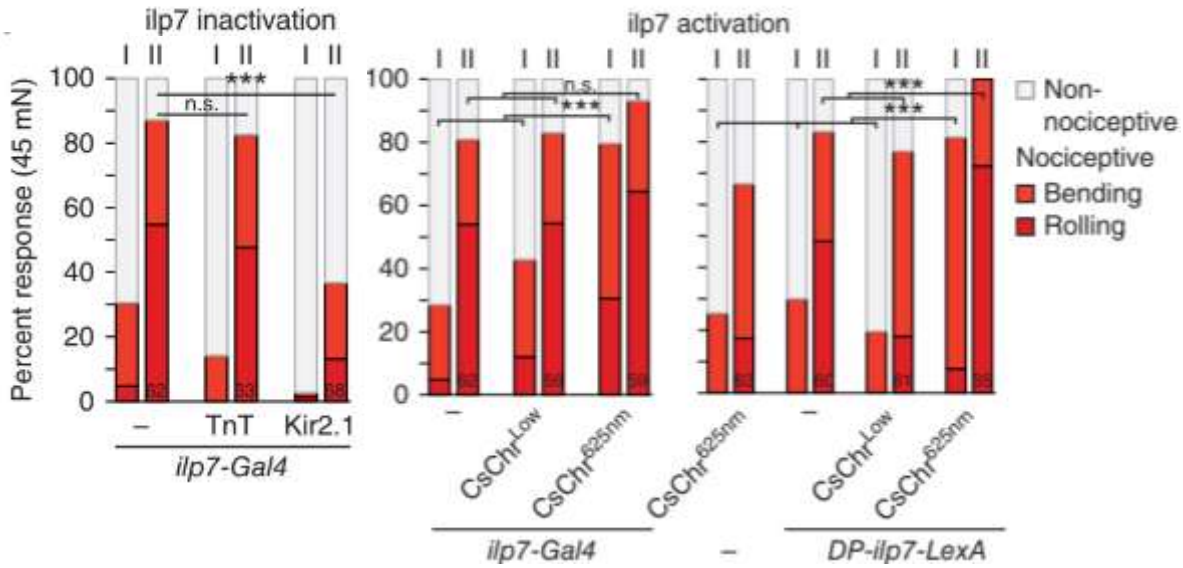


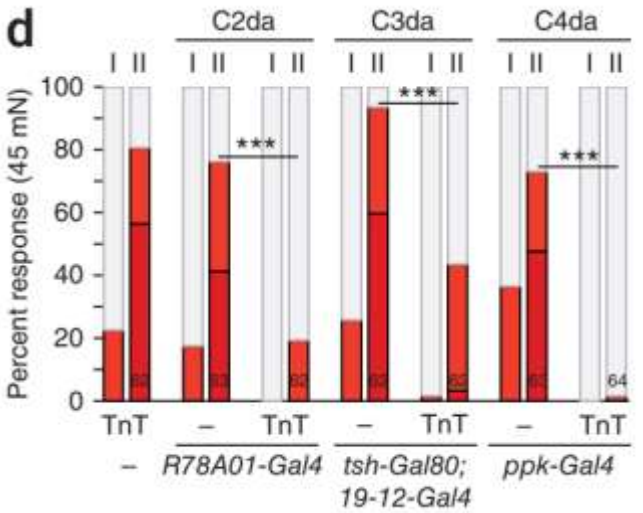


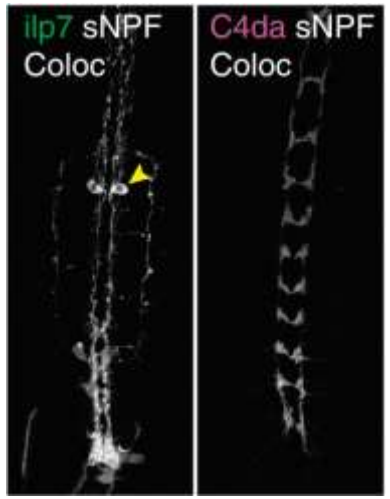
C4da and ilp7 neurons both act upstream of A08n neurons

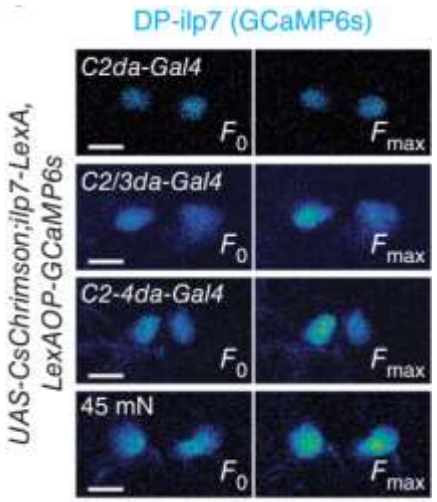
Hu et al., Nat Neurosci, 2017

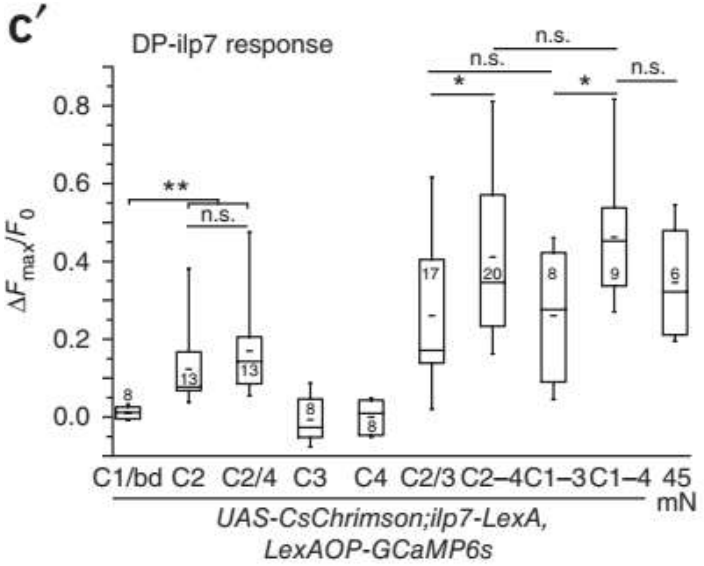
DP-ilp7 neurons integrate multi-mechanosensory input and facilitate nociceptive behavior through sNPF

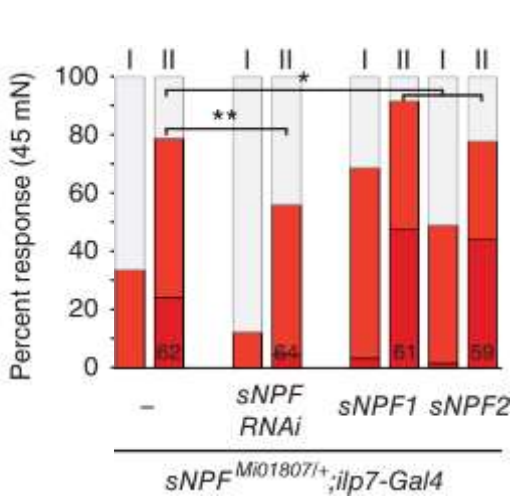


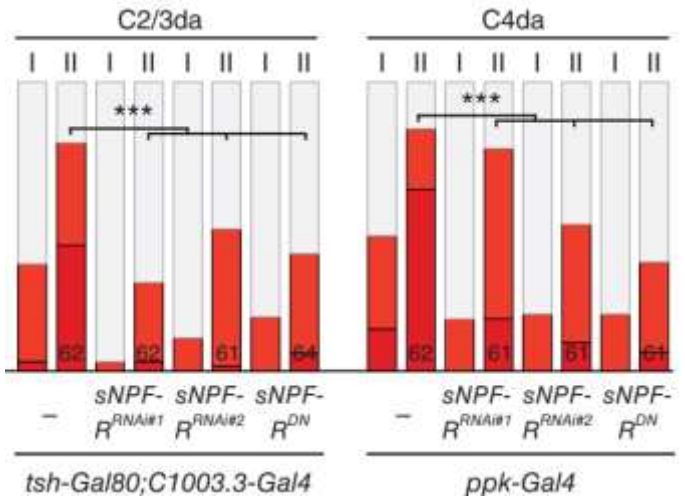






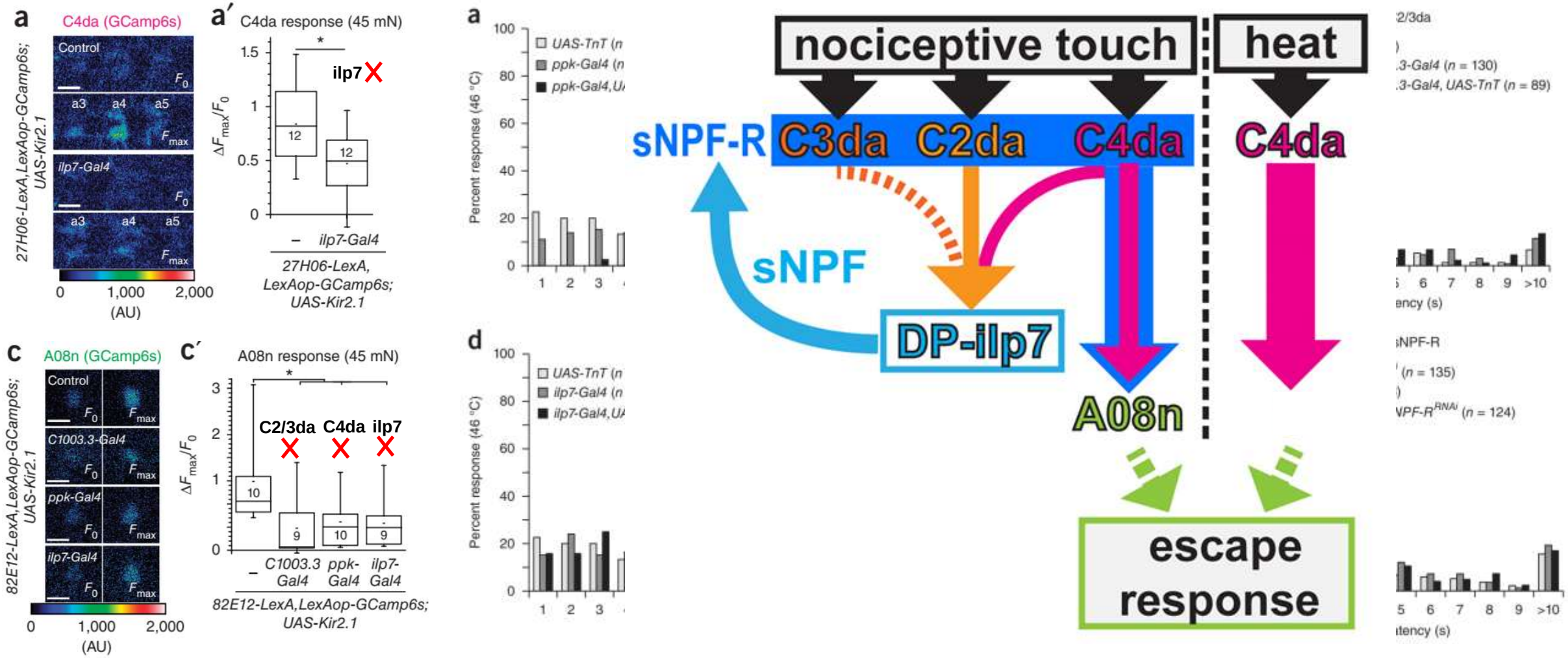






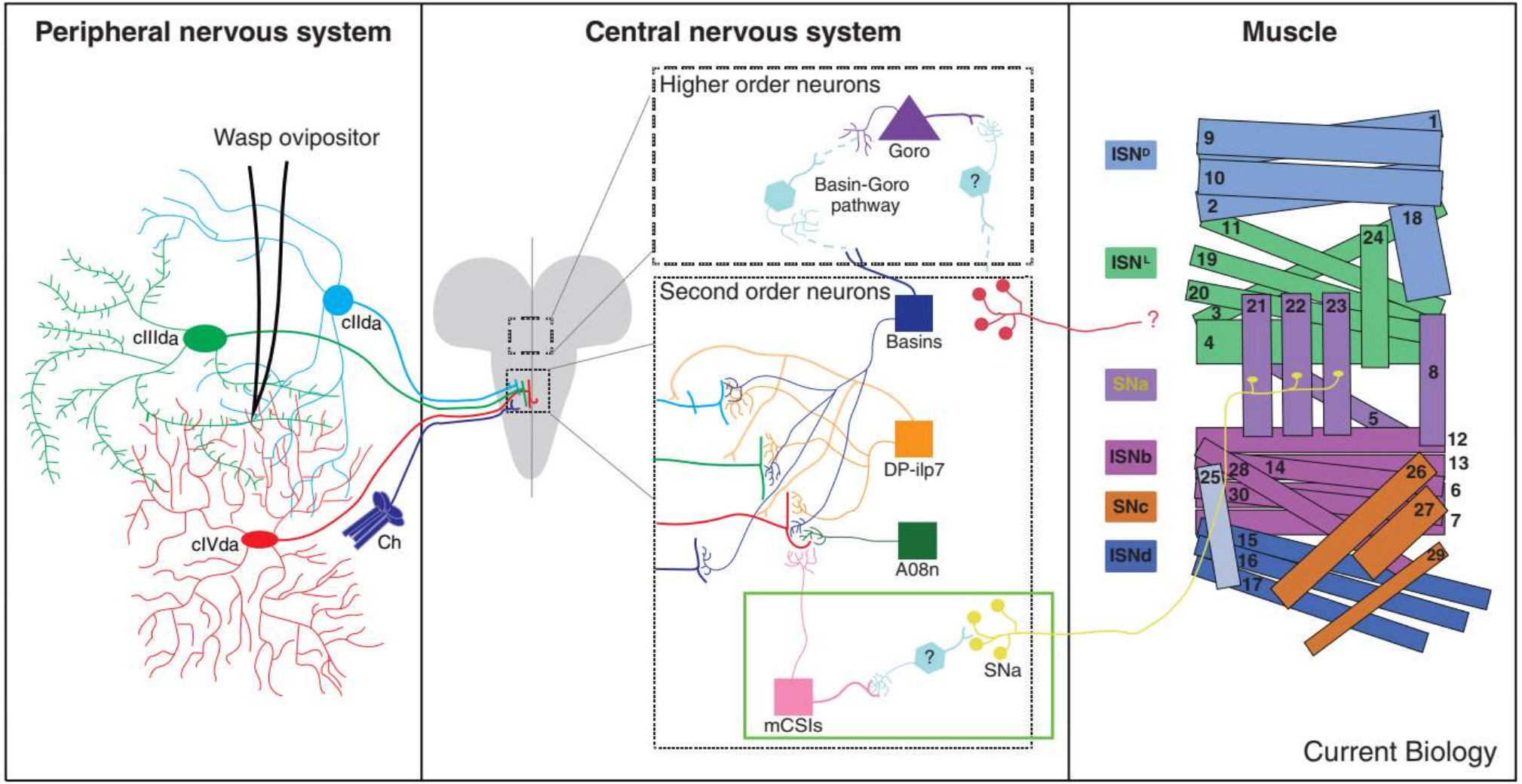
Hu et al., Nat Neurosci, 2017

Mechanonociceptive circuit elements and sNPF-R function are not required for C4da neuron-dependent thermonociception



Hu et al., Nat Neurosci, 2017

Schematic of neurons involved in generating nociceptive behavior in *Drosophila* larvae



Chin and Tracey, Curr Biol, 2017

Summary

Nociceptive behavior in *Drosophila* larvae

- Molecular basis

painless, dTrpA1, subdued are required for thermal nociceptive behavior.

painless, ppk, bba/ppk26, piezo are required for mechanical nociceptive behavior.

- Neural circuit basis

Class IV multidendritic neurons (cIVMD/C4da) are critical sensory neurons for thermal and mechanical nociceptive behavior.

C4da-Basins-to-Goro pathways and C4da-mCSI-SNa pathway are parallel in the nociceptive rolling behavior control.

C4da-A08n (DP-ilp7) pathway is required for mechanical not thermal nociceptive behavior.

DP-ilp7-dependent sNPF signaling facilitates C4da neuron synaptic output.

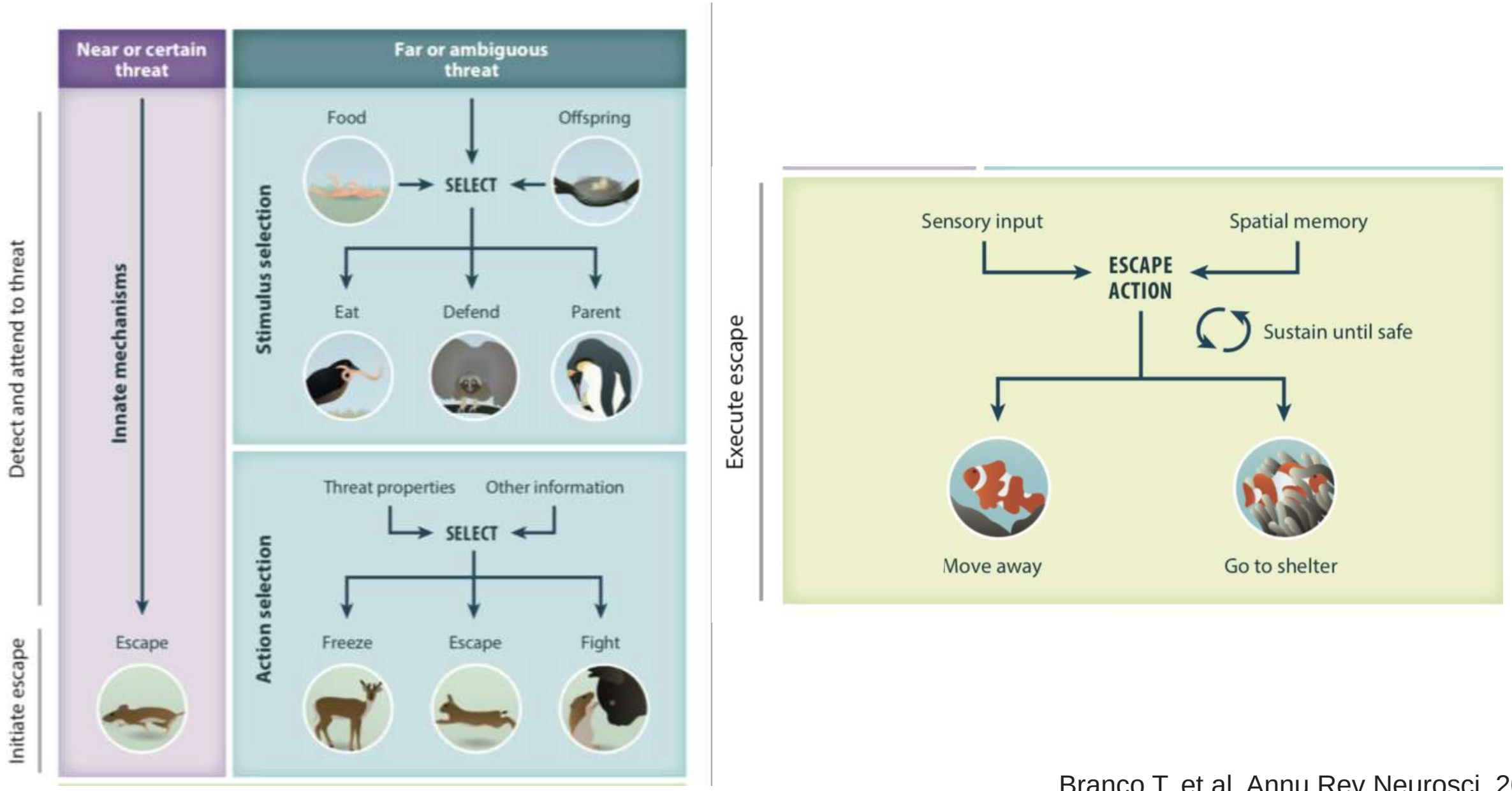
Integrated output of multiple sensory stimuli

—taking avoidance from predators as an example

Chen

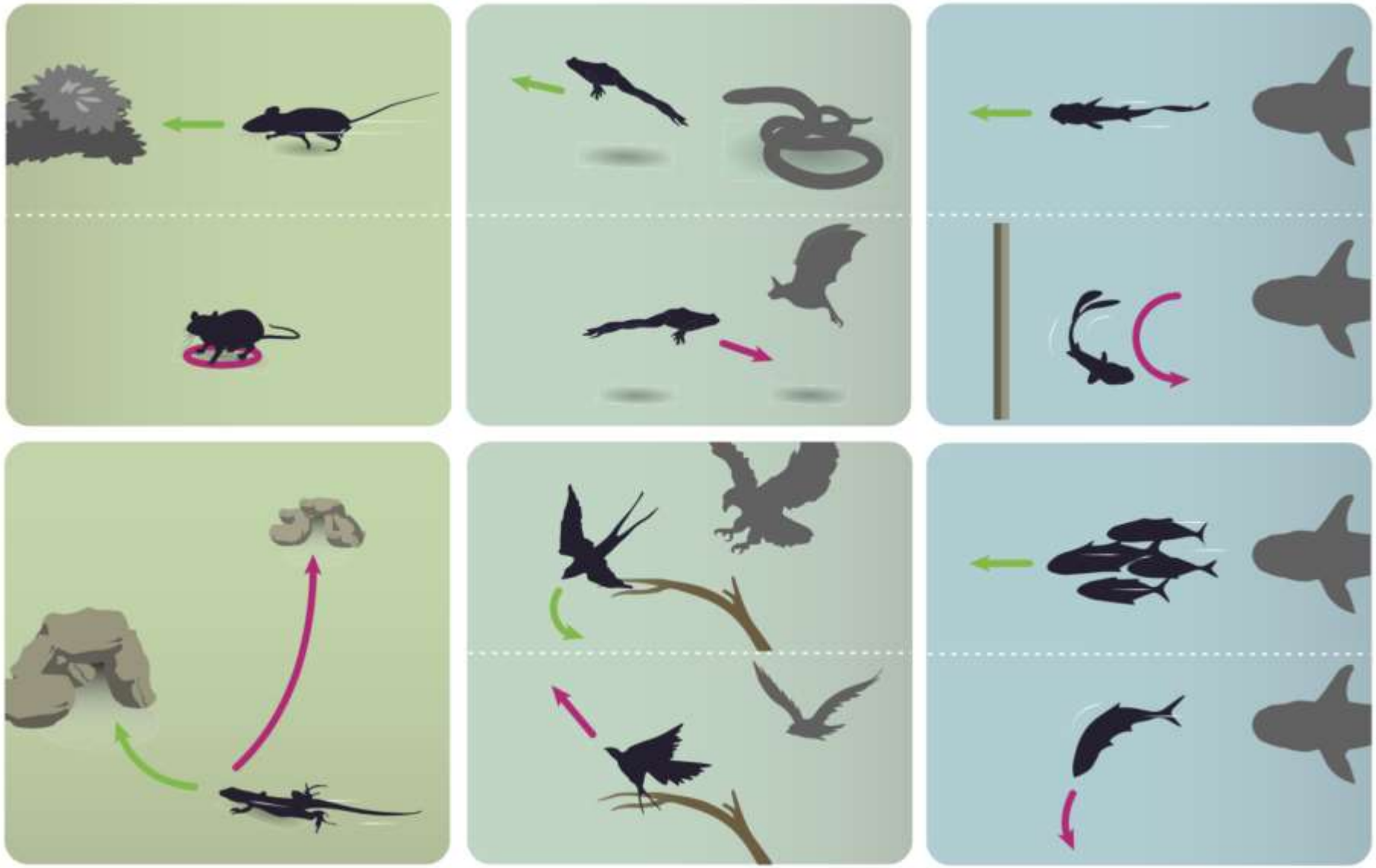
2022.10.27

Basic algorithmic steps for escaping from threat



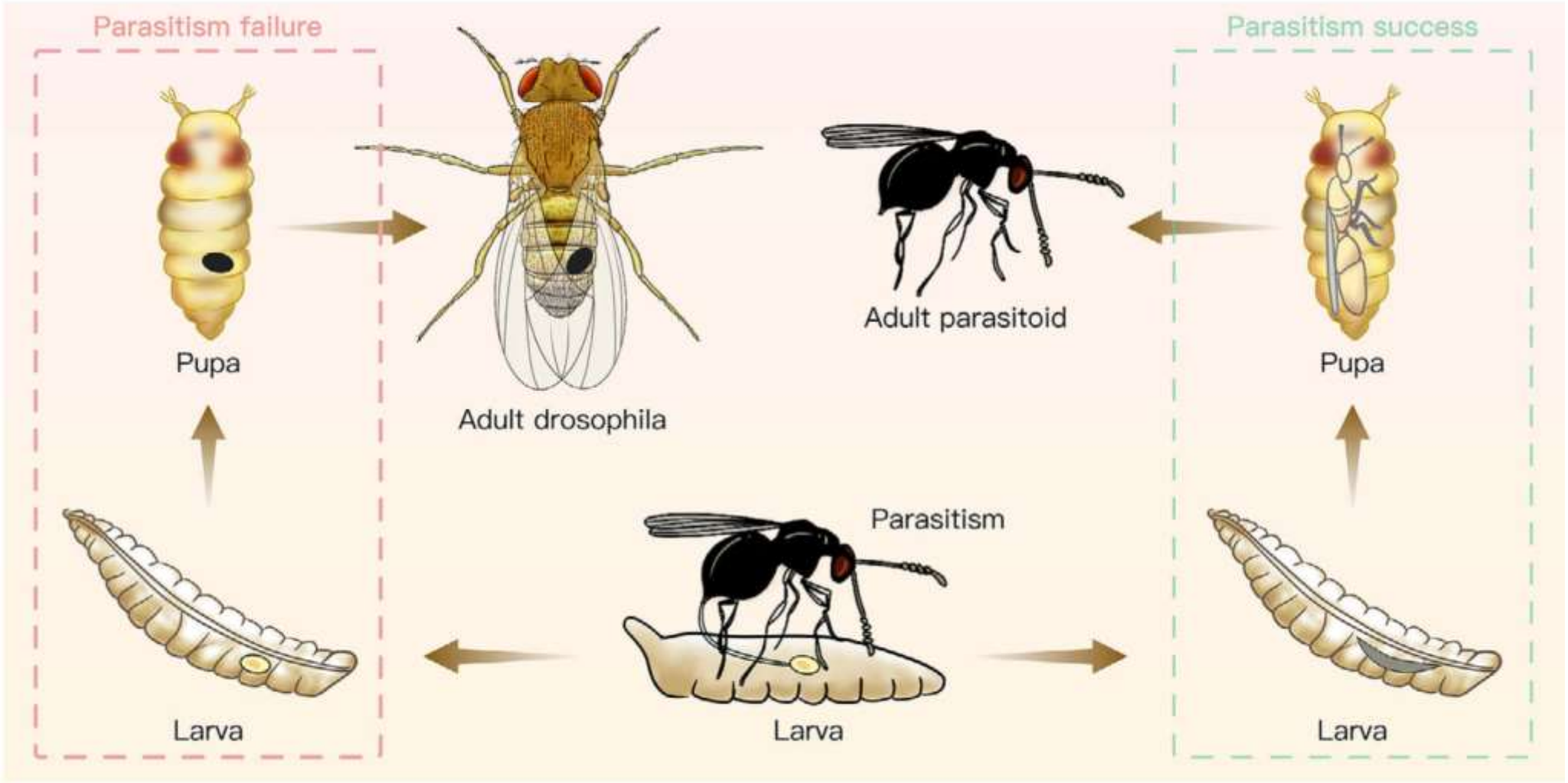
Branco T, et al. Annu Rev Neurosci. 2020.

Flexibility of Escape Execution in Different Species



Evans DA, et al. *Trends Cogn Sci*. 2019.

Drosophila and its larval parasitoids



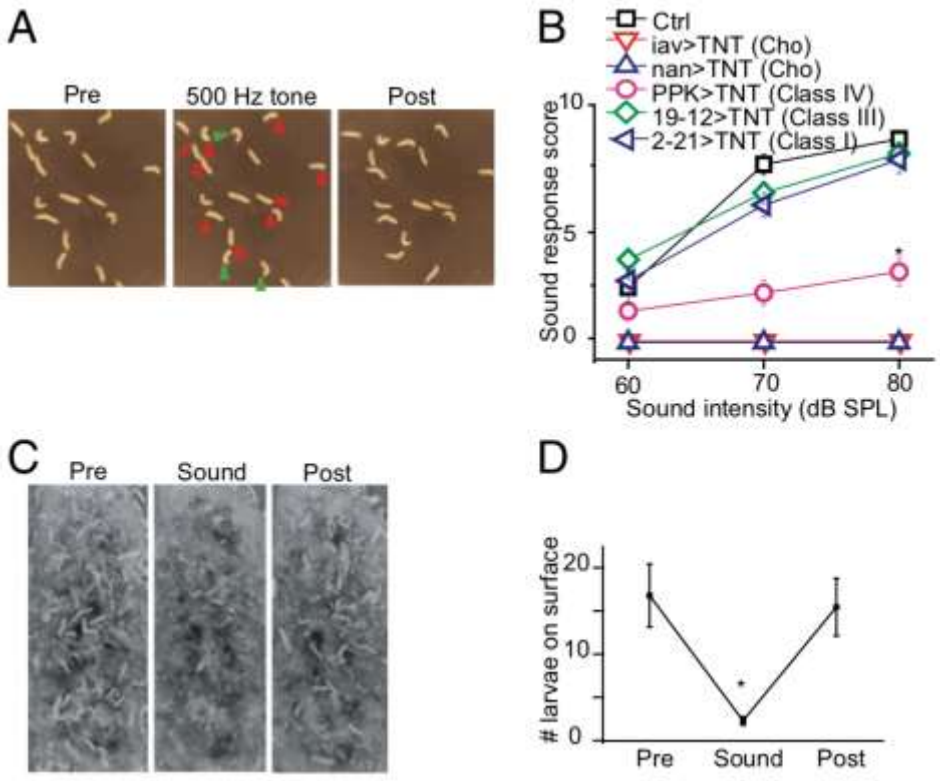
Yang L, et al. Insect Sci. 2021.

Respond to sound of predators

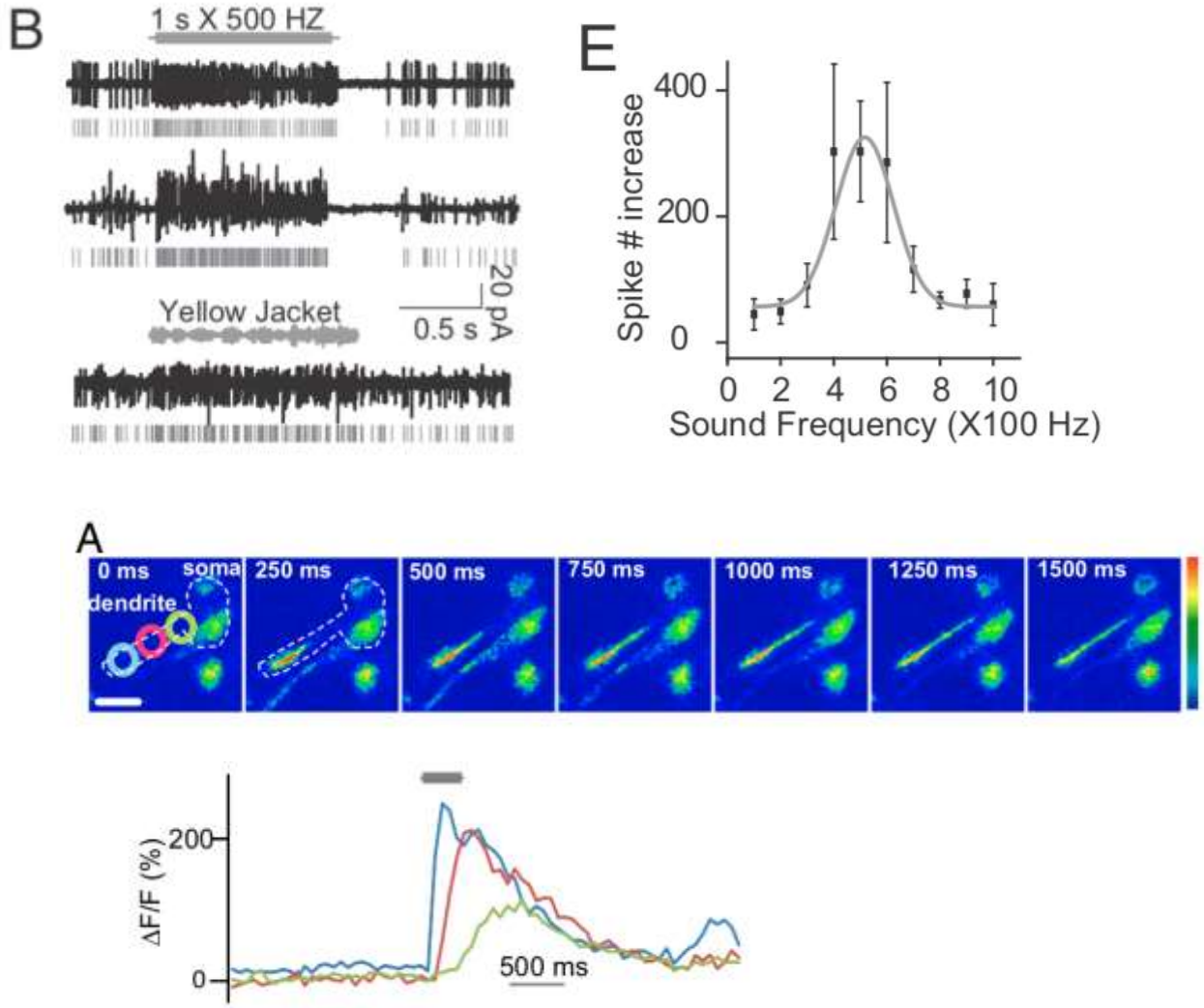
> Proc Natl Acad Sci U S A. 2013 Aug 13;110(33):13612-7. doi: 10.1073/pnas.1312477110. Epub 2013 Jul 29.

Sound response mediated by the TRP channels NOMPC, NANCHUNG, and INACTIVE in chordotonal organs of Drosophila larvae

Wei Zhang [1], Zhiqiang Yan, Lily Yeh Jan, Yuh Nung Jan



Drosophila Larvae Are Capable of Sensing Sound



Cho neurons respond to sound

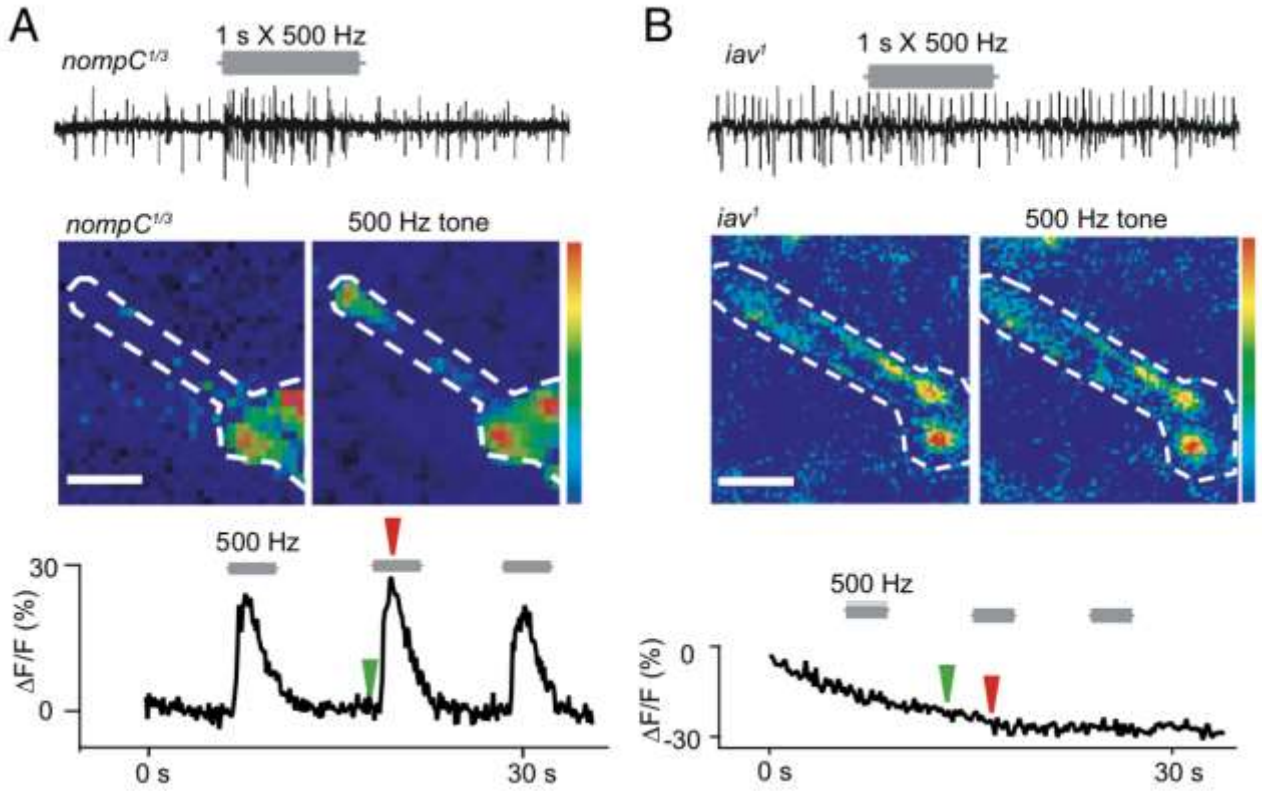
Zhang W,et al. *Proc Natl Acad Sci U S A*. 2013

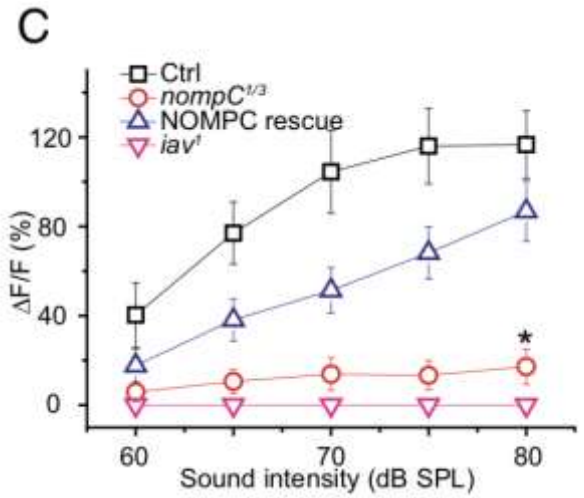
Respond to sound of predators

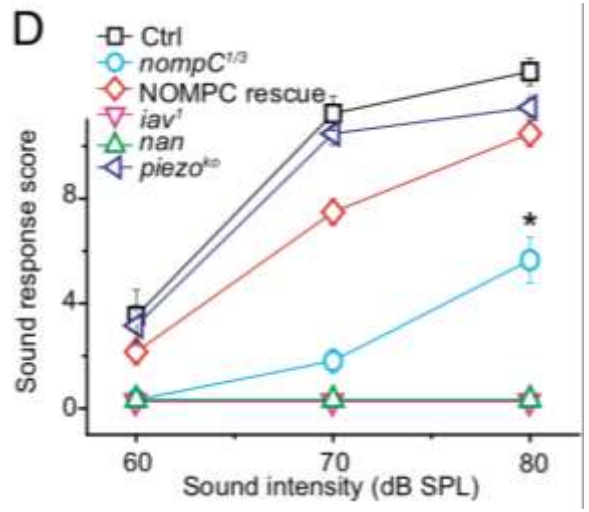
> Proc Natl Acad Sci U S A. 2013 Aug 13;110(33):13612-7. doi: 10.1073/pnas.1312477110.
Epub 2013 Jul 29.

Sound response mediated by the TRP channels NOMPC, NANCHUNG, and INACTIVE in chordotonal organs of Drosophila larvae

Wei Zhang [1], Zhiqiang Yan, Lily Yeh Jan, Yuh Nung Jan







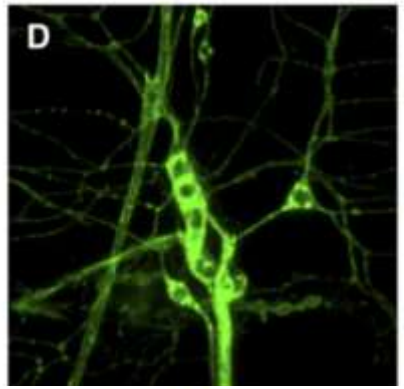
Sound response mediated by the TRP channels NOMPC, NANCHUNG, and INACTIVE in chordotonal organs

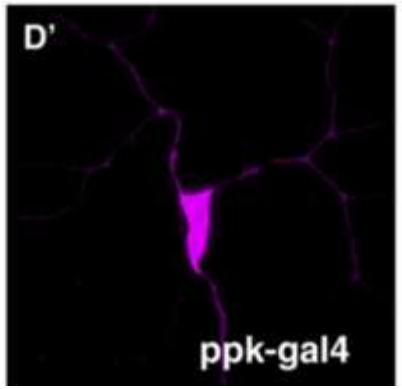
Respond to attack of predators

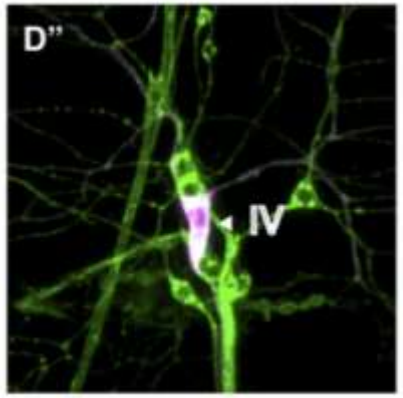
> Curr Biol. 2007 Dec 18;17(24):2105-2116. doi: 10.1016/j.cub.2007.11.029. Epub 2007 Nov 29.

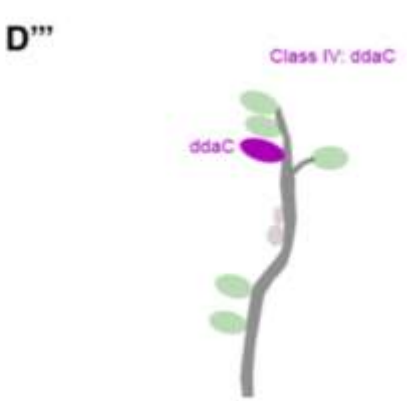
Nociceptive neurons protect Drosophila larvae from parasitoid wasps

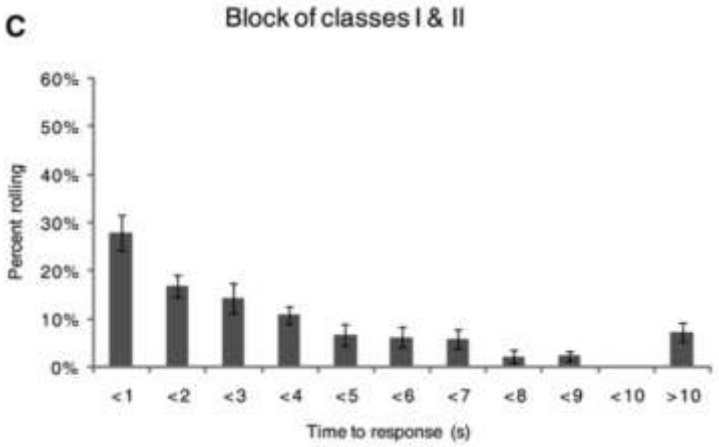
Richard Y Hwang [# 1], Lixian Zhong [# 2], Yifan Xu [3], Trevor Johnson [1], Feng Zhang [4 5], Karl Deisseroth [4 5], W Daniel Tracey [3 1 6]

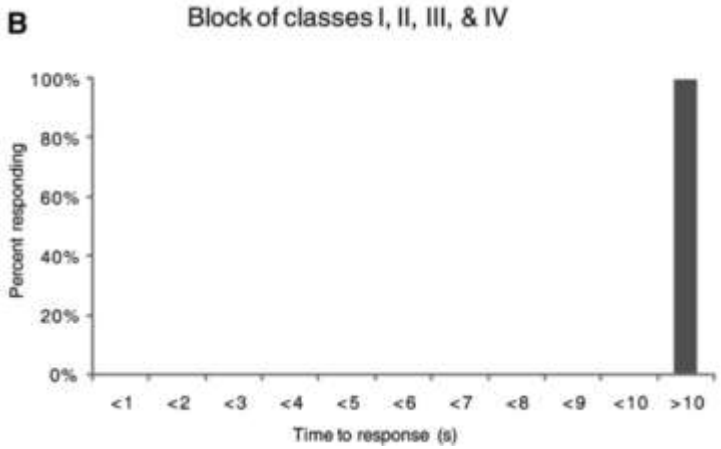


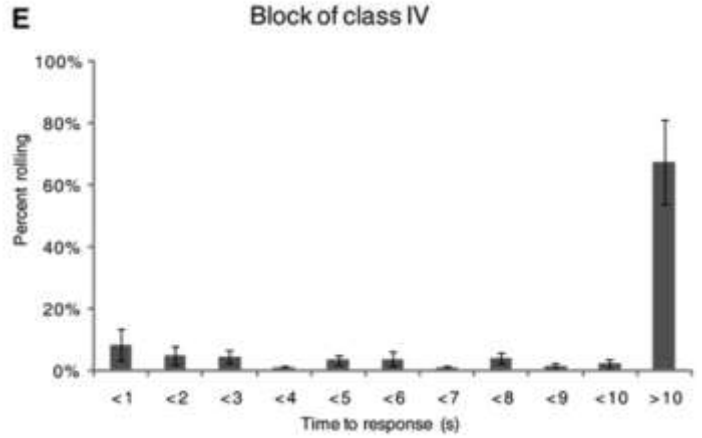






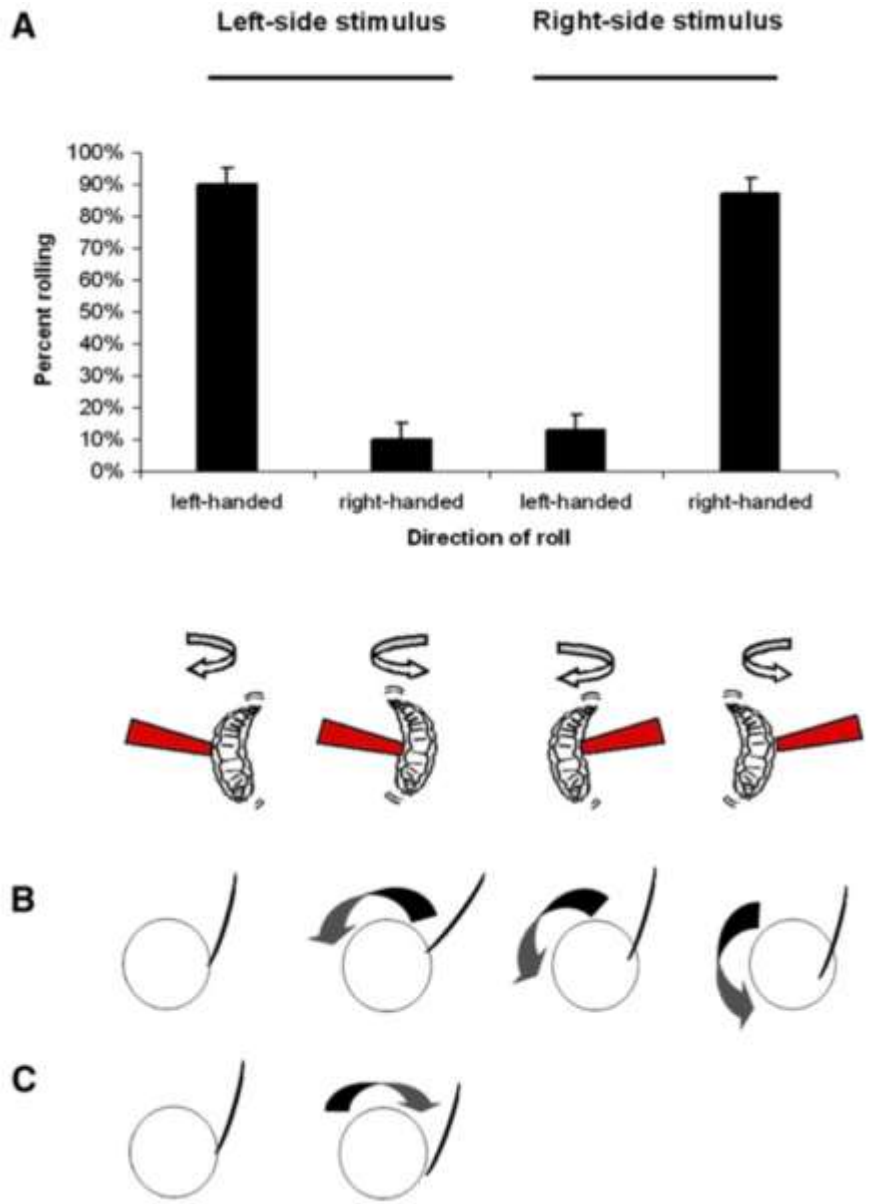


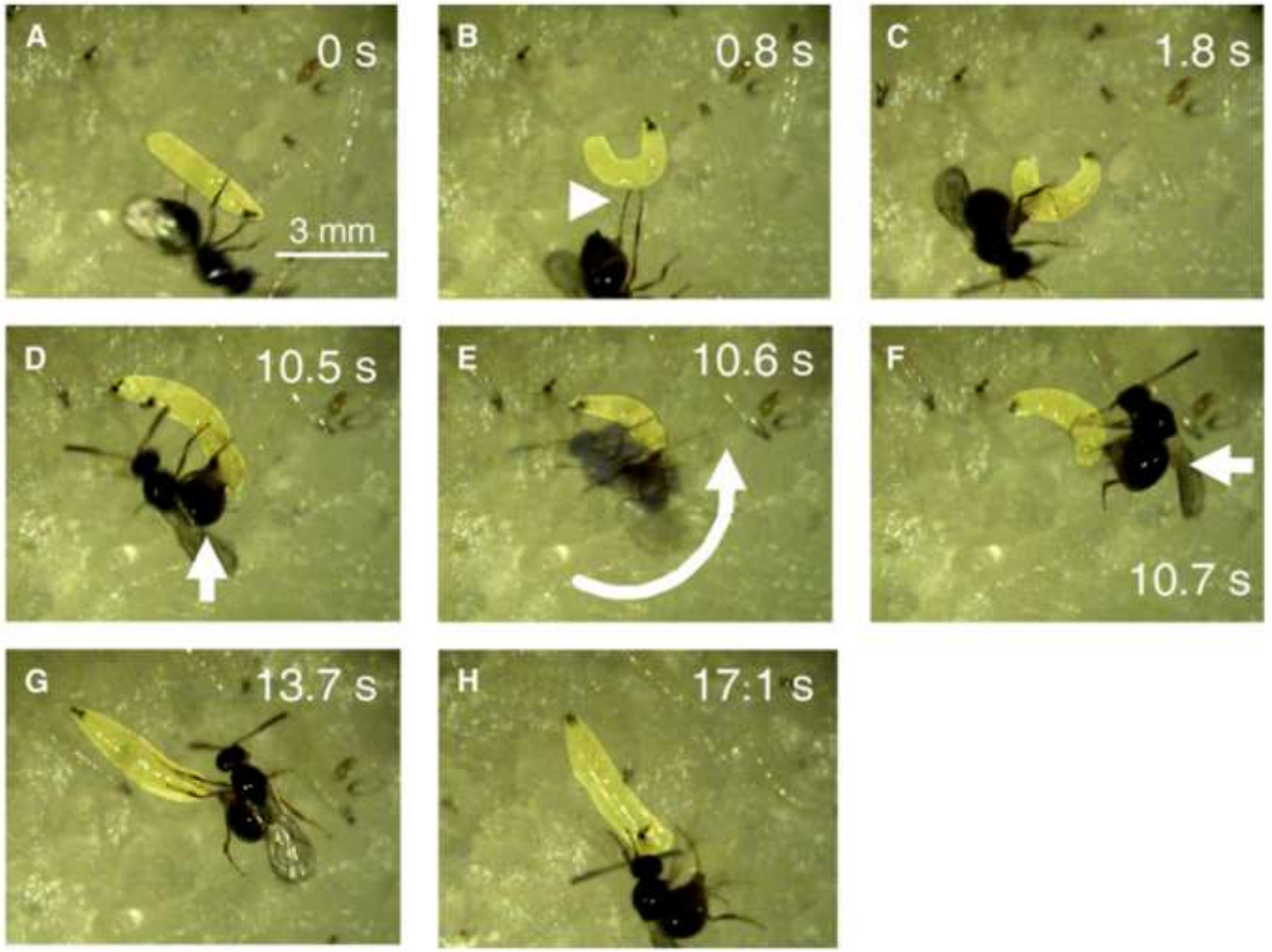




Hwang RY, et al. Curr Biol. 2007.

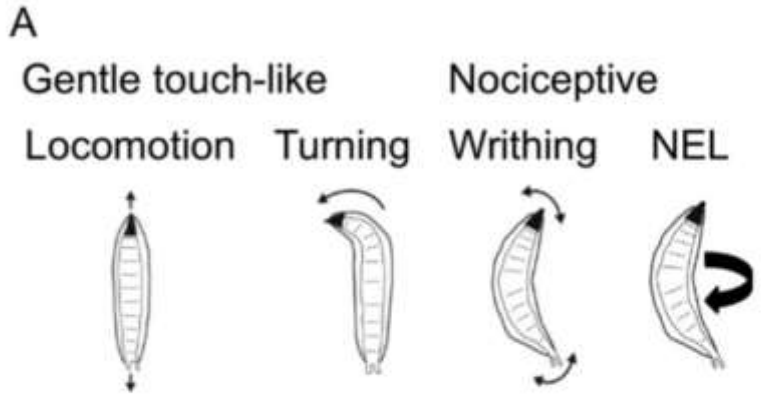
Respond to attack of predators

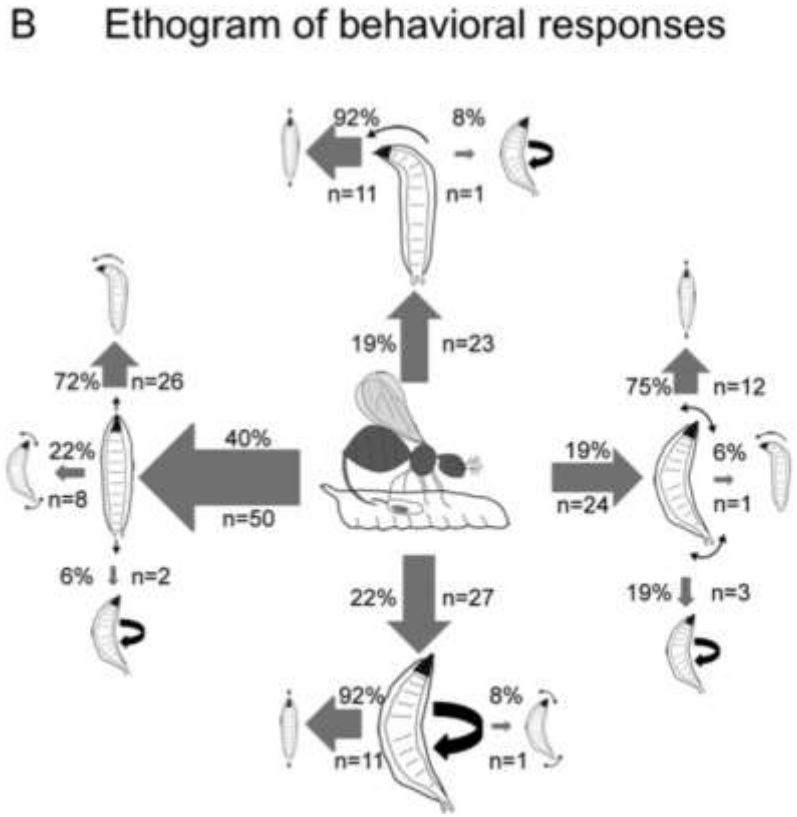


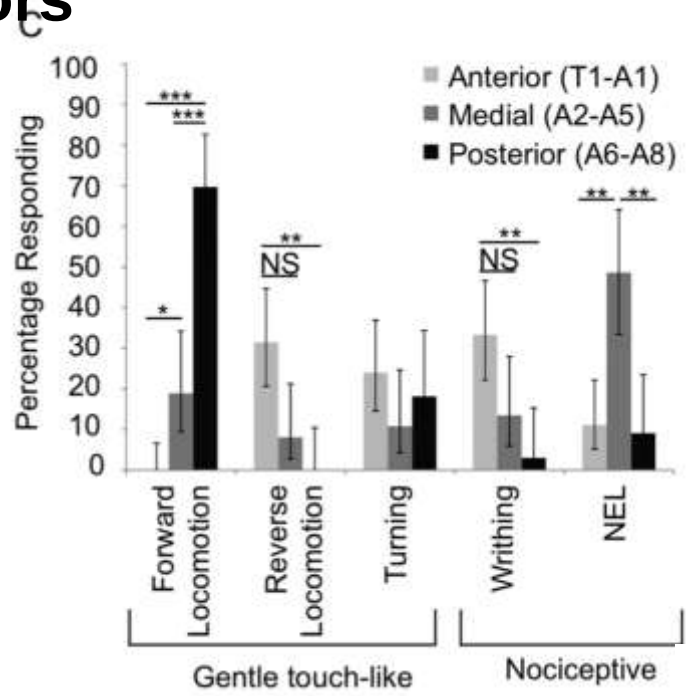


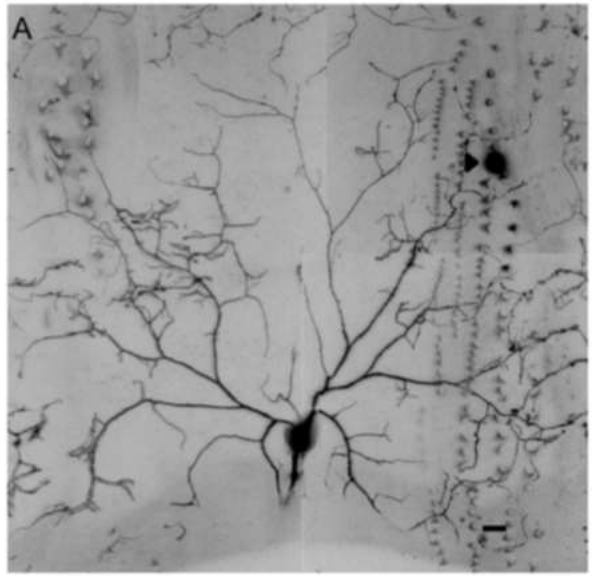
Hwang RY, et al. Curr Biol. 2007.

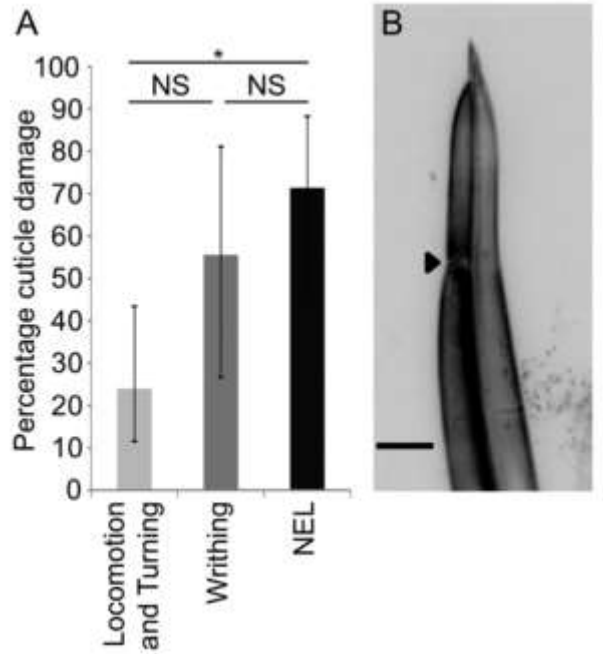
Respond to attack of predators

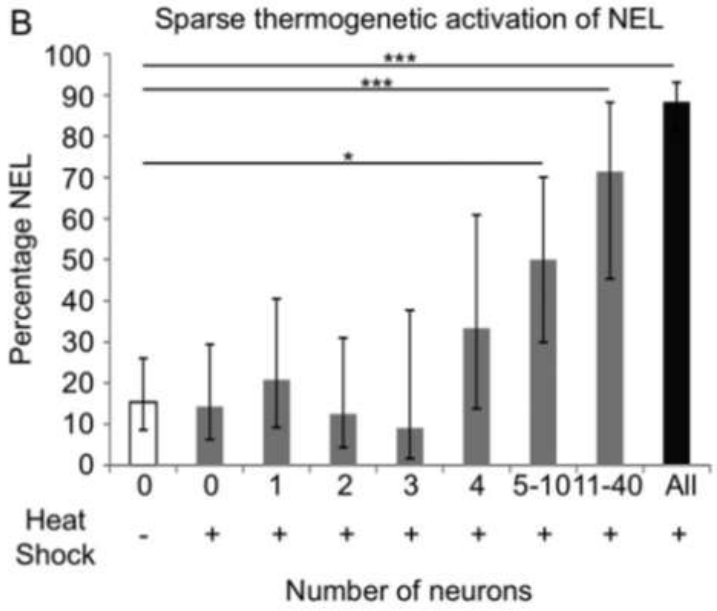






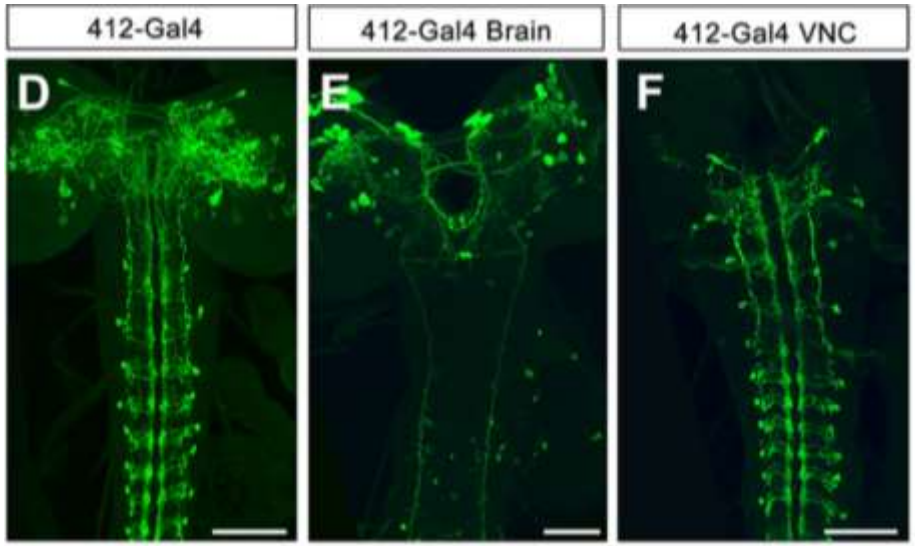


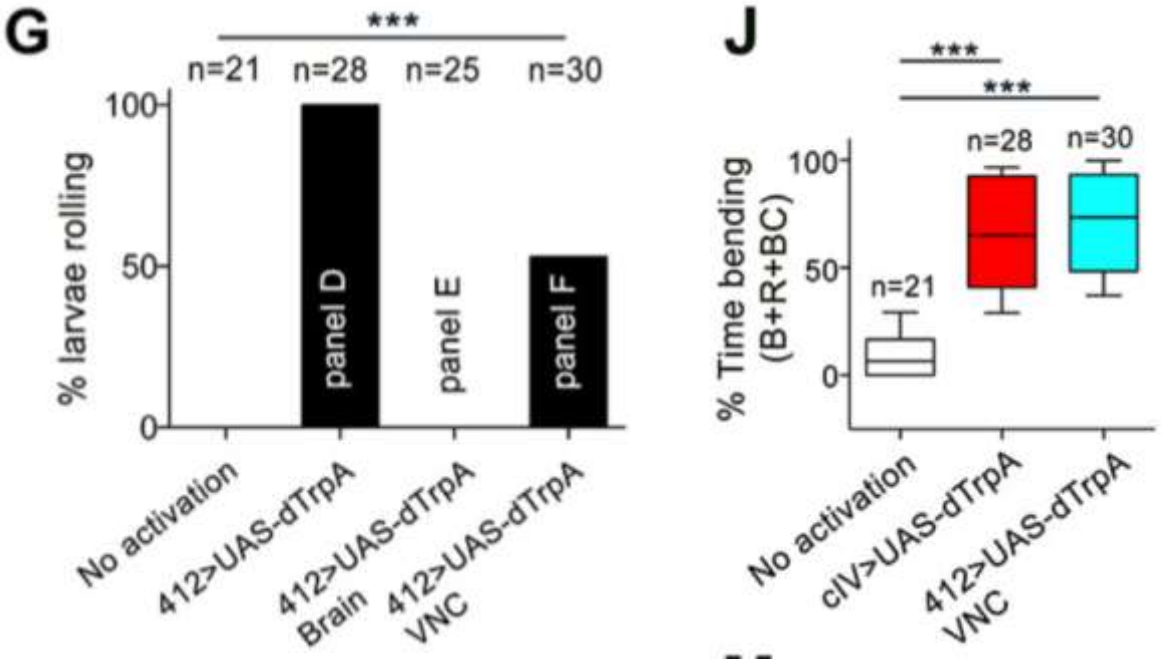


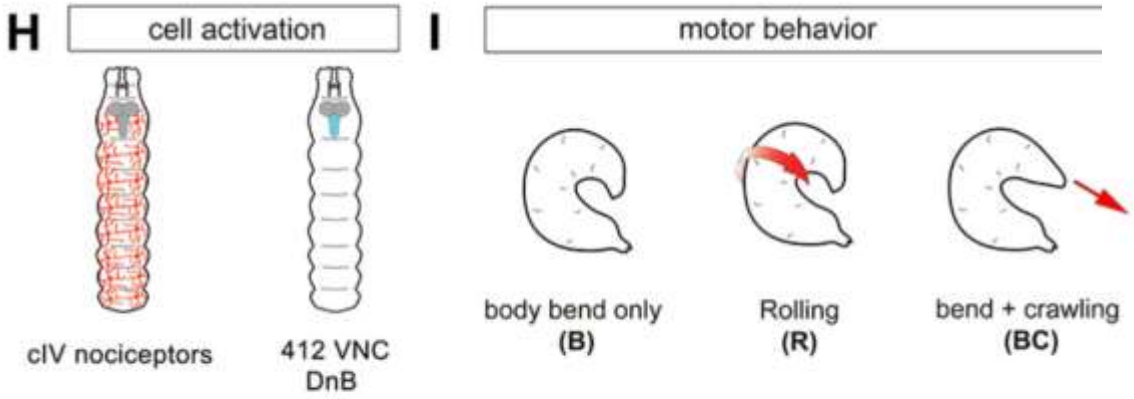


Robertson JL, et al. PLoS One. 2013

Nociceptive interneurons control modular motor pathways to promote escape behavior in *Drosophila*





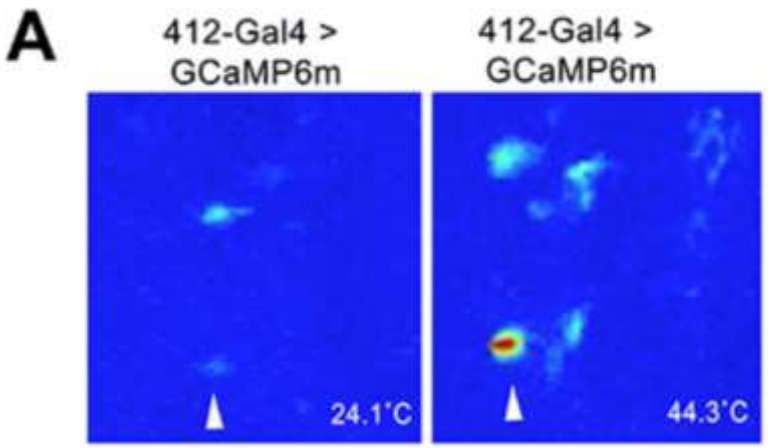


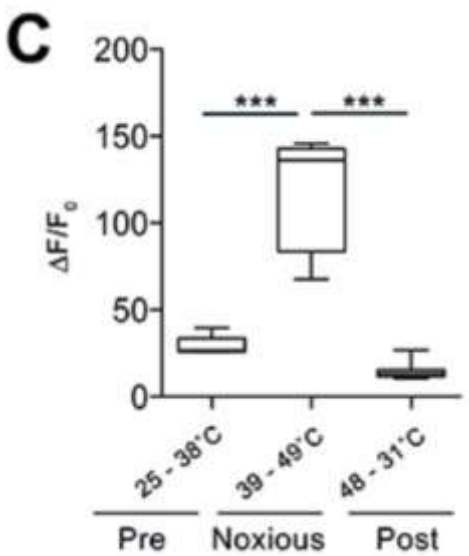
Identification of interneurons that promote nociceptive behavior

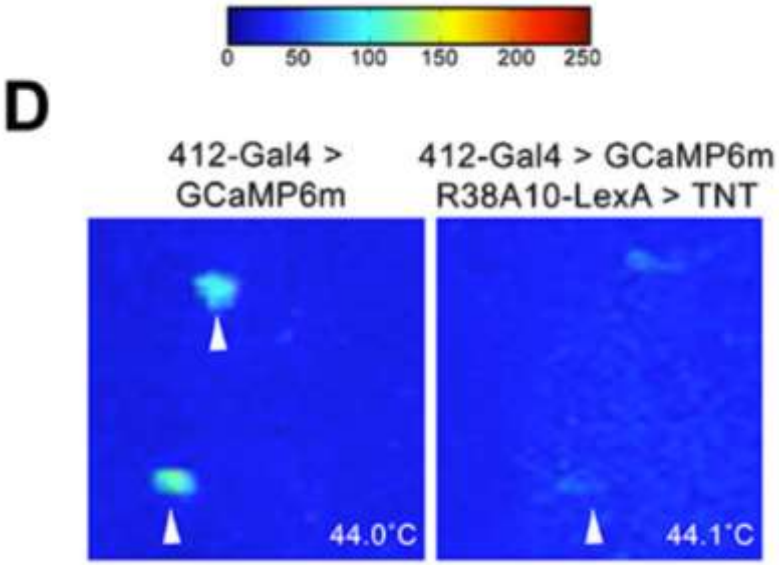
Burgos A,et al. *Elife*. 2018.

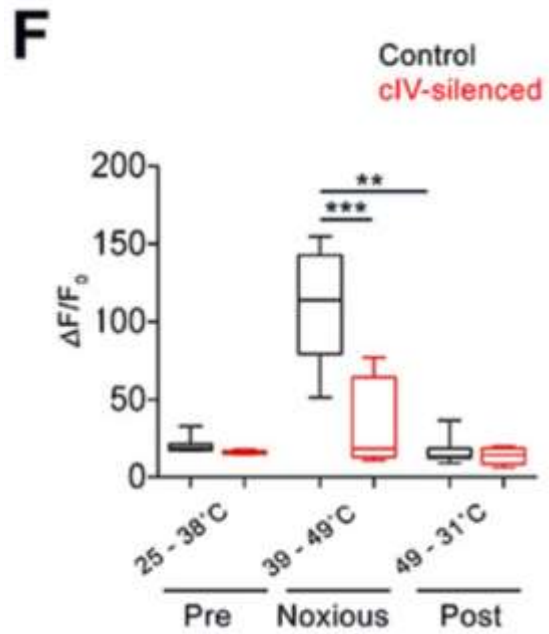
eLIFE
elifesciences.org

Nociceptive interneurons control modular motor pathways to promote escape behavior in *Drosophila*





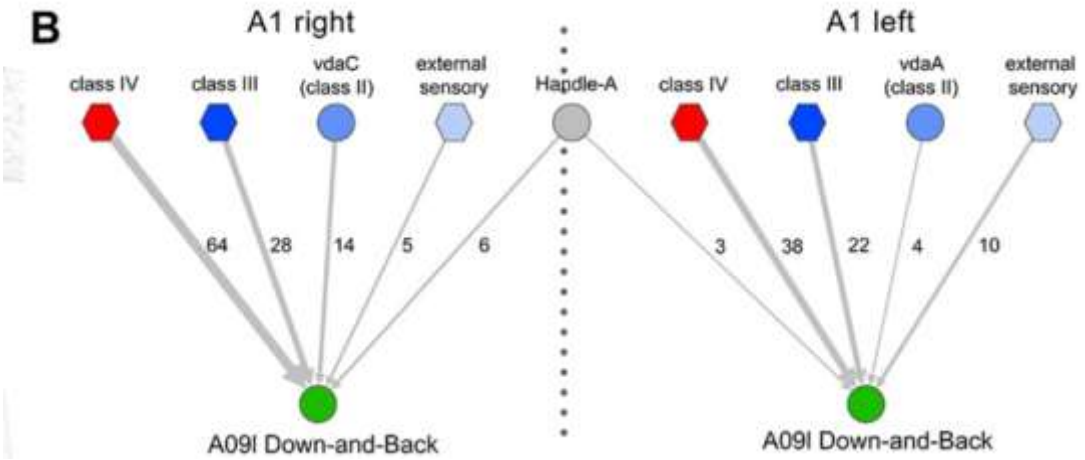


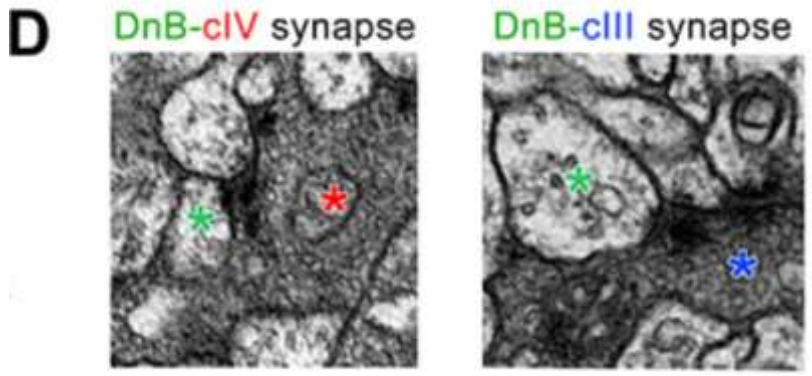


DnB neurons function downstream of cIV neurons

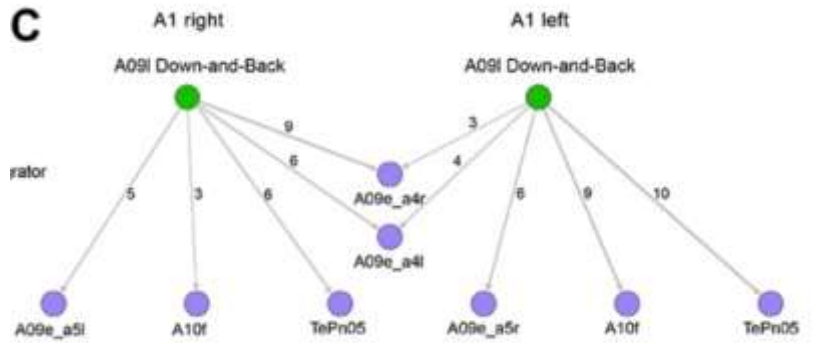
eLIFE
elifesciences.org

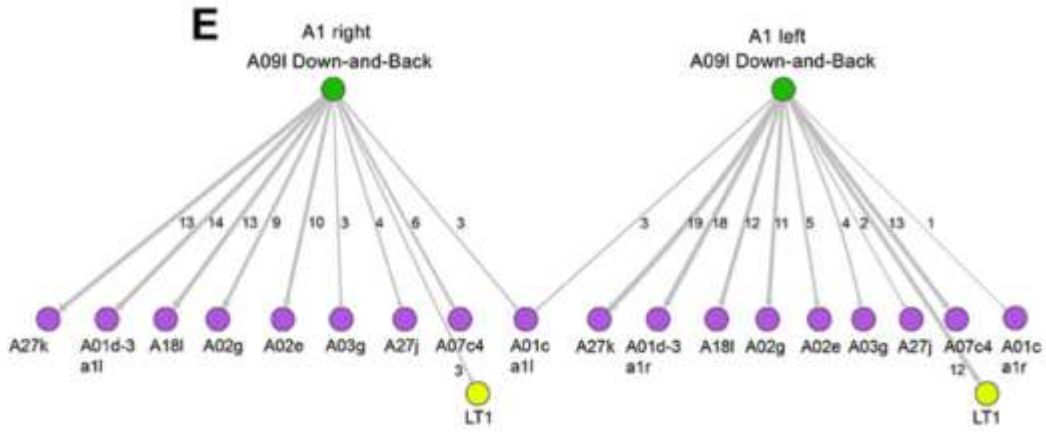
Nociceptive interneurons control modular motor pathways to promote escape behavior in *Drosophila*



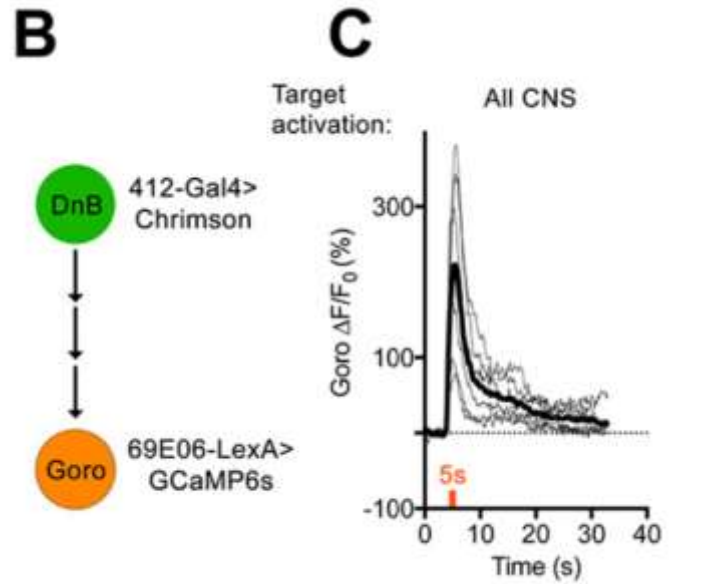


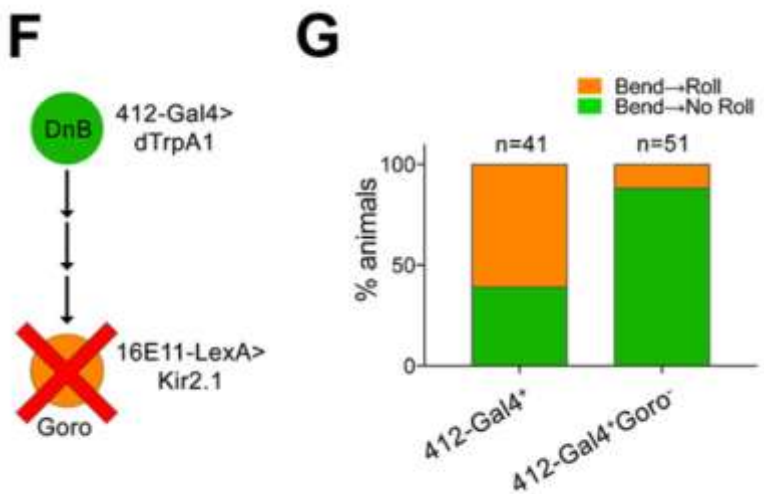
Connectome of sensory and interneuron inputs to DnB neurons.

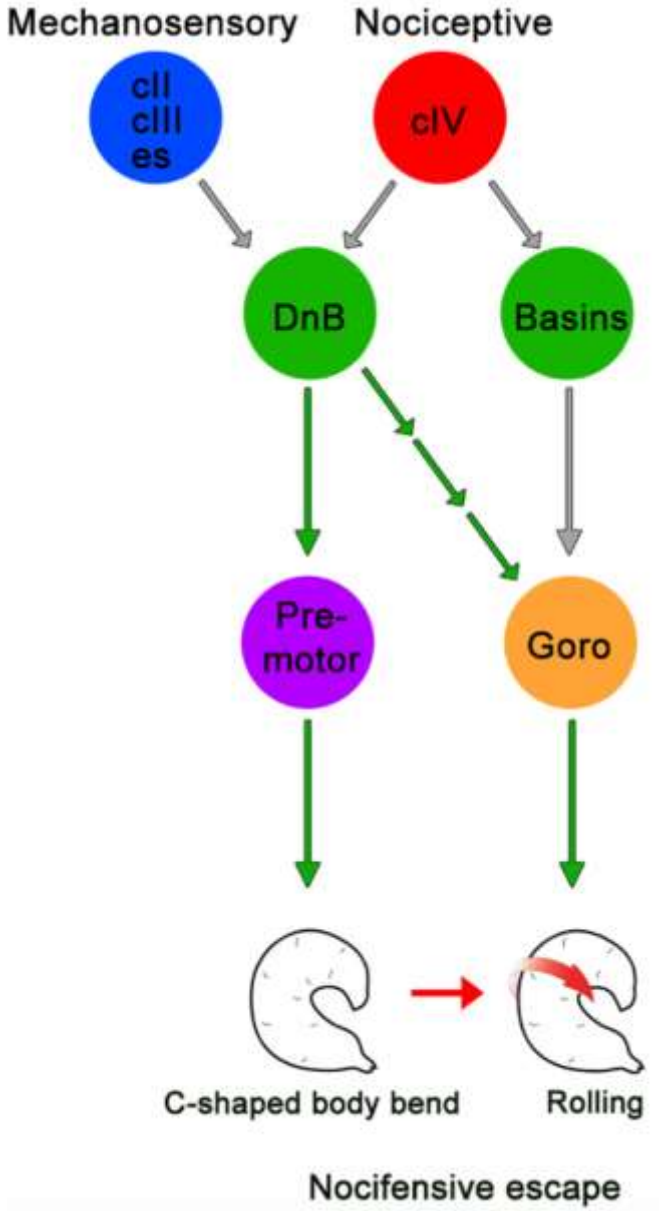




Connectome of DnB to premotor and nociceptive interneuron outputs.


B
C
DnB
412-Gal4>
Chrimson
Goro
69E06-LexA>
GCaMP6s
Target
activation:
All CNS
Goro ΔF/F0 (%)
300
100
-100
5s
0
10
20
30
40
Time (s)


F
G
DnB
412-Gal4>
dTrpA1
16E11-LexA>
Kir2.1
Goro
Bend→Roll
Bend→No Roll
n=41
n=51
% animals
100
50
0
412-Gal4+
412-Gal4+Goro-


Mechanosensory
Nociceptive
cII
cIII
es
cIV
DnB
Basins
Pre-
motor
Goro
C-shaped body bend
Rolling
Nocifensive escape

Neuropeptide and escape behavior

> Nat Neurosci. 2017 Aug;20(8):1085-1095. doi: 10.1038/nn.4580. Epub 2017 Jun 12.

Sensory integration and neuromodulatory feedback facilitate Drosophila mechanonociceptive behavior

Chun Hu [1], Meike Petersen [1], Nina Hoyer [1], Bettina Spitzweck [1], Federico Tenedini [1], Denan Wang [1], Alisa Gruschka [1], Lara S Burchardt [1], Emanuela Szpotowicz [1], Michaela Schweizer [1], Ananya R Guntur [2], Chung-Hui Yang [2], Peter Soba [1]

Soba, Prof. Dr. rer. nat.

Peter

Neuronal Patterning and Connectivity

Head of the Department

Room No. I-111

Phone: 73 - 6 27 41

Fax: 73 - 6 26 41

psoba@uni-bonn.de

> Curr Biol. 2022 Jan 10;32(1):149-163.e8. doi: 10.1016/j.cub.2021.10.069. Epub 2021 Nov 18.

A neuropeptidergic circuit gates selective escape behavior of Drosophila larvae

Bibi Nusreen Imambocus [1], Fangmin Zhou [1], Andrey Formozov [2], Annika Wittich [2], Federico M Tenedini [2], Chun Hu [2], Kathrin Sauter [2], Ednilson Macarenhas Varela [3], Fabiana Herédia [3], Andreia P Casimiro [3], André Macedo [3], Philipp Schlegel [4], Chung-Hui Yang [5], Irene Miguel-Aliaga [6], J Simon Wiegert [2], Michael J Pankratz [4], Alisson M Gontijo [7], Albert Cardona [8], Peter Soba [9]

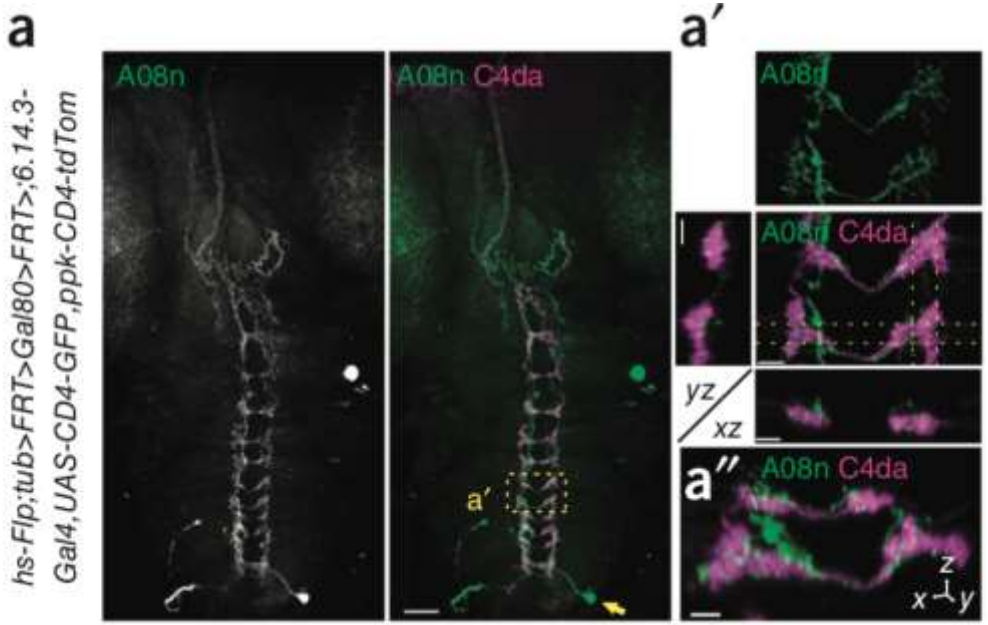
Research Interests:

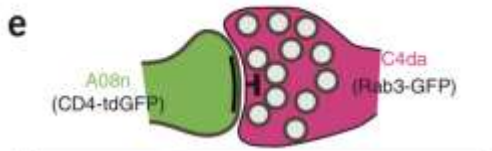
- Molecular mechanisms of dendrite patterning
- Maintenance of circuit integrity and synaptic specificity
- Neuromodulatory control of behavior

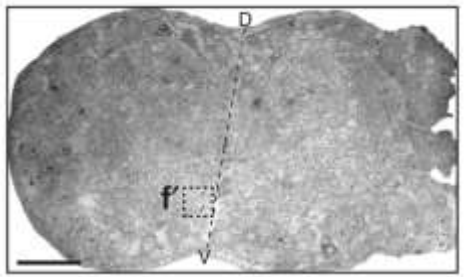
Neuropeptide and escape behavior

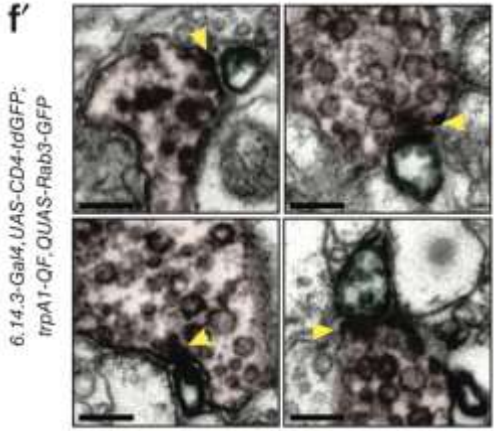
Nat Neurosci. 2017 August ; 20(8): 1085–1095. doi:10.1038/nn.4580.

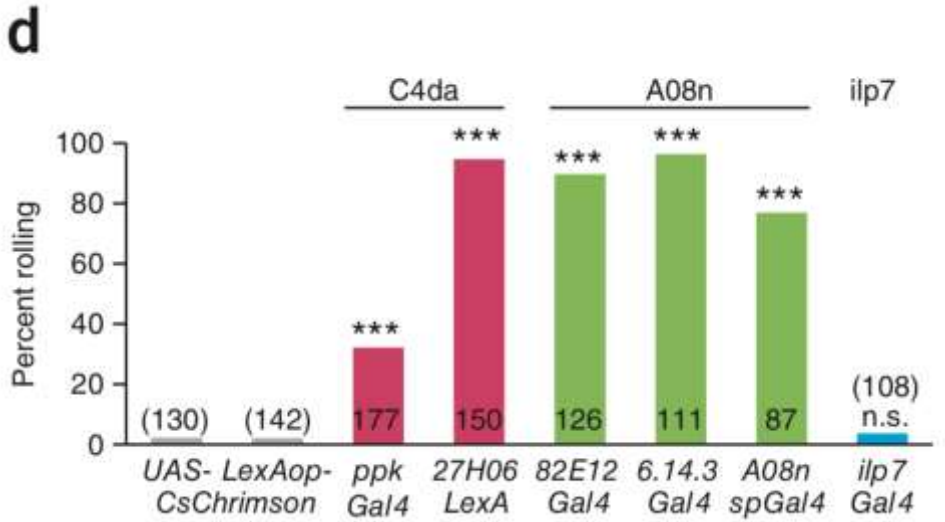
Modality-specific sensory integration and neuropeptide-mediated feedback facilitate mechano-nociceptive behavior in *Drosophila*

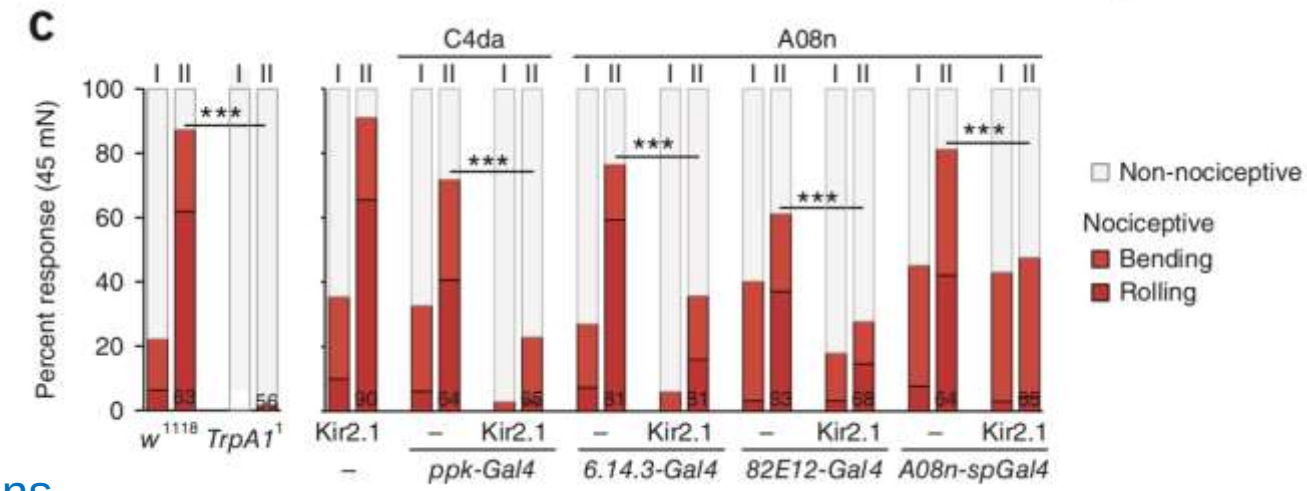










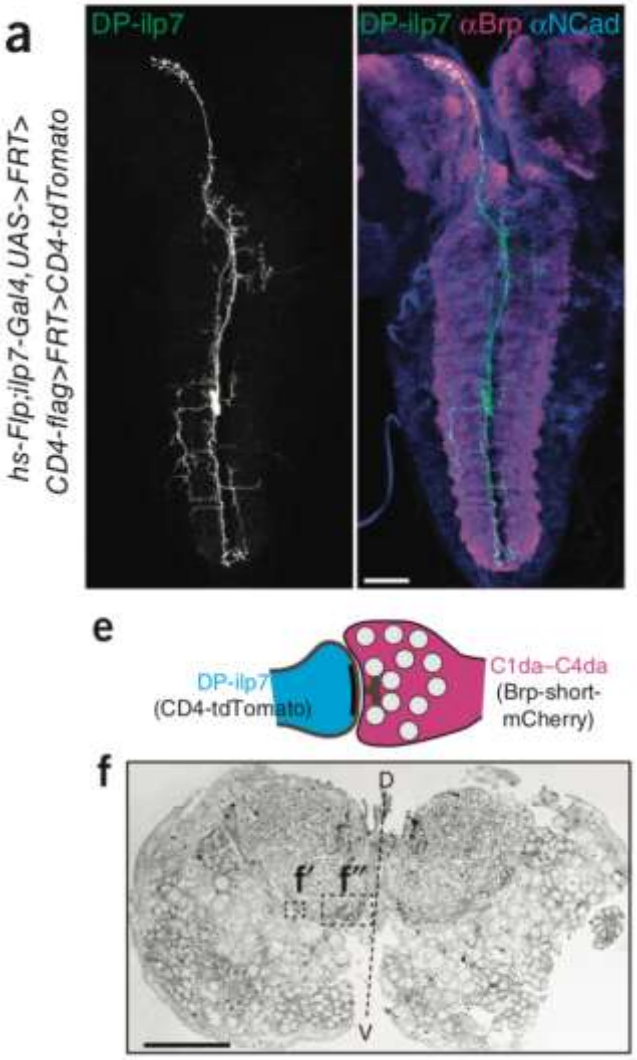


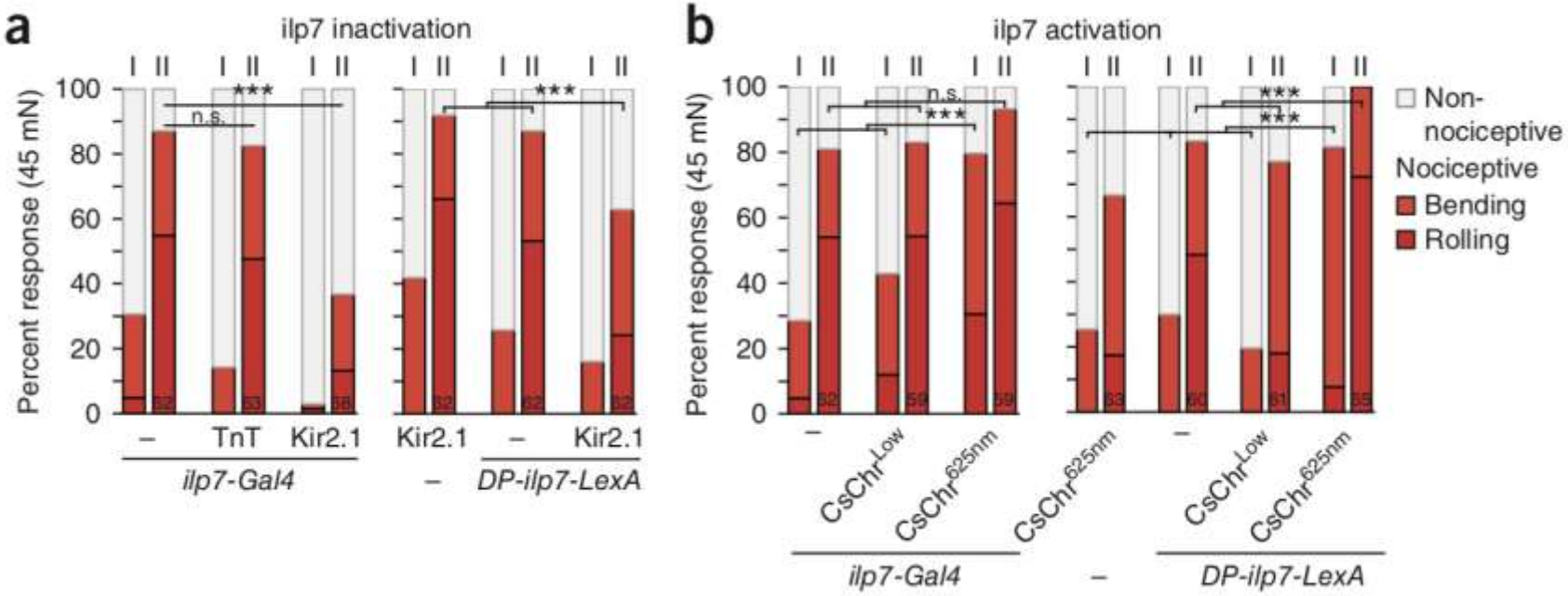
A08n neurons receive synaptic input from C4da neurons

Neuropeptide and escape behavior

Nat Neurosci. 2017 August ; 20(8): 1085–1095. doi:10.1038/nn.4580.

Modality-specific sensory integration and neuropeptide-mediated feedback facilitate mechano-nociceptive behavior in *Drosophila*



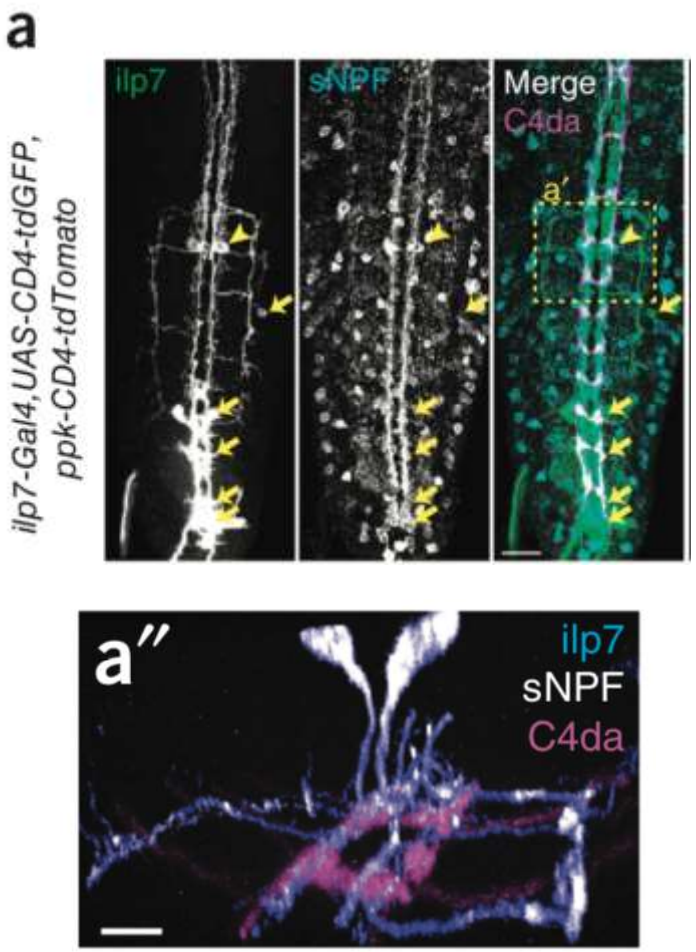


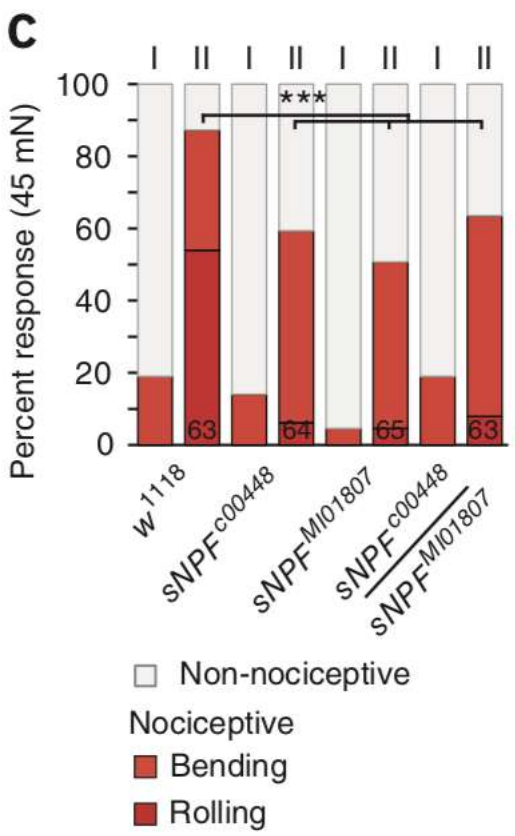
DP-ilp7 neurons receive direct sensory input from C2da and C4da neurons (at least).

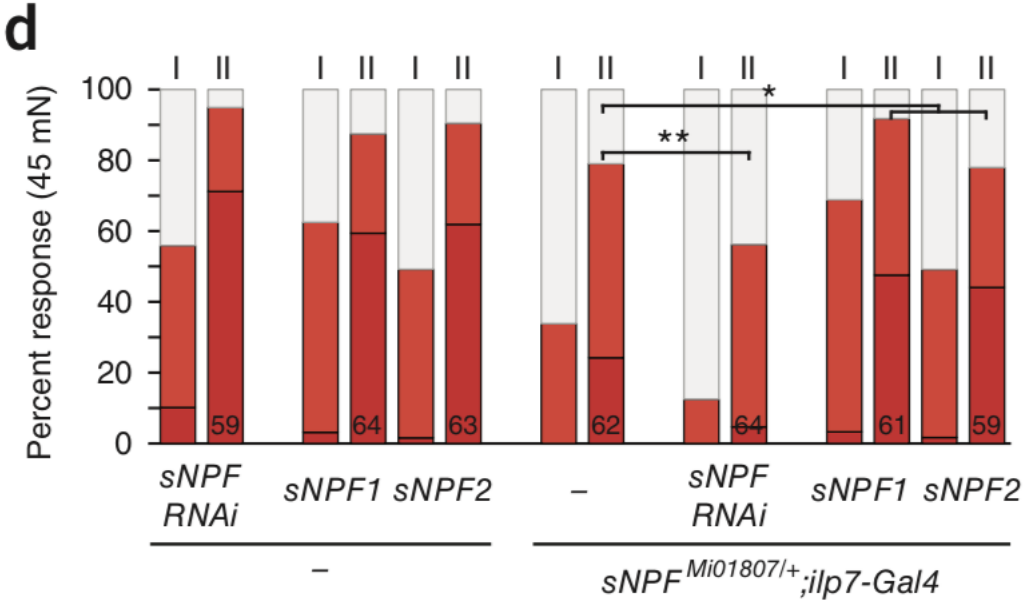
Neuropeptide and escape behavior

Nat Neurosci. 2017 August ; 20(8): 1085–1095. doi:10.1038/nn.4580.

Modality-specific sensory integration and neuropeptide-mediated feedback facilitate mechano-nociceptive behavior in *Drosophila*





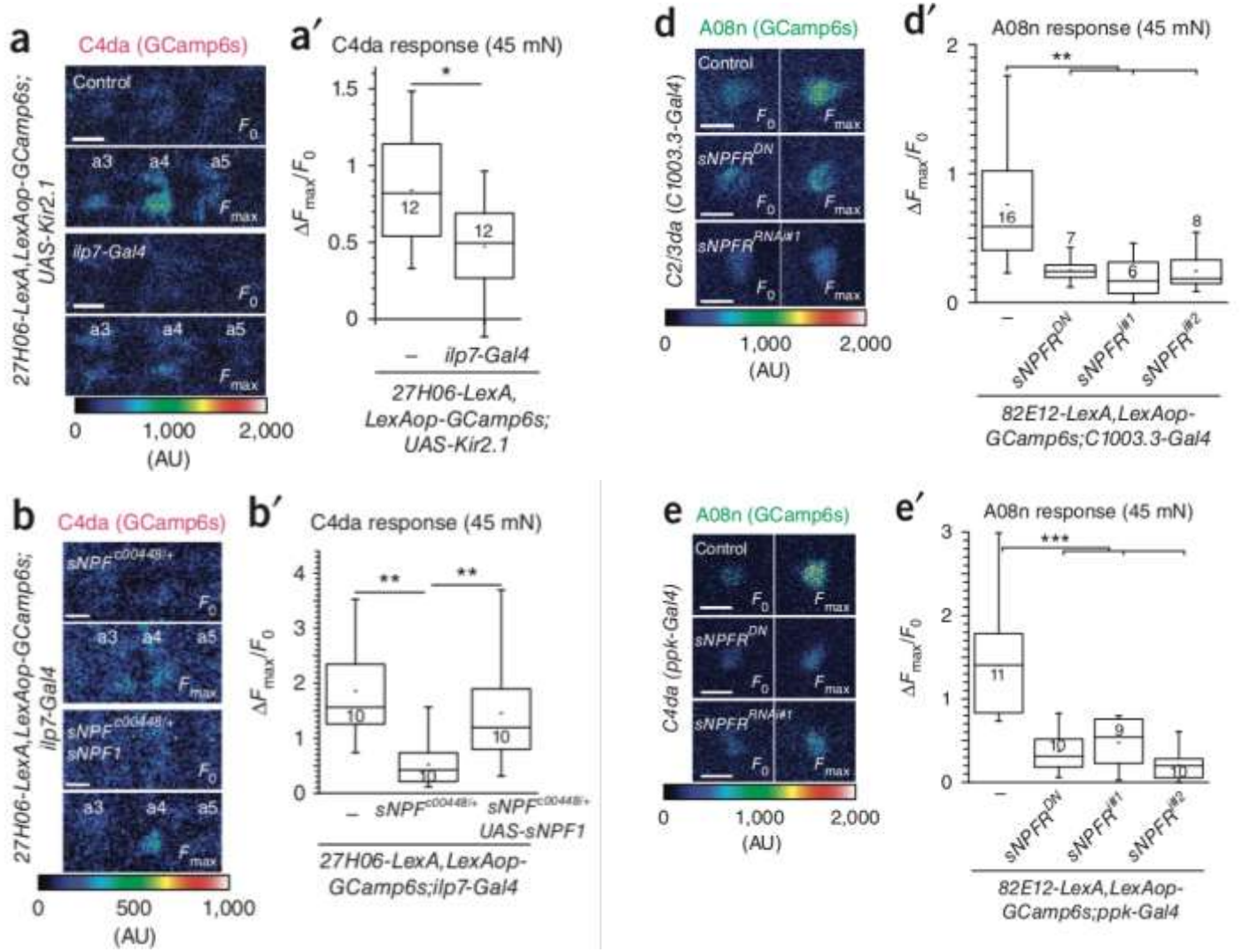


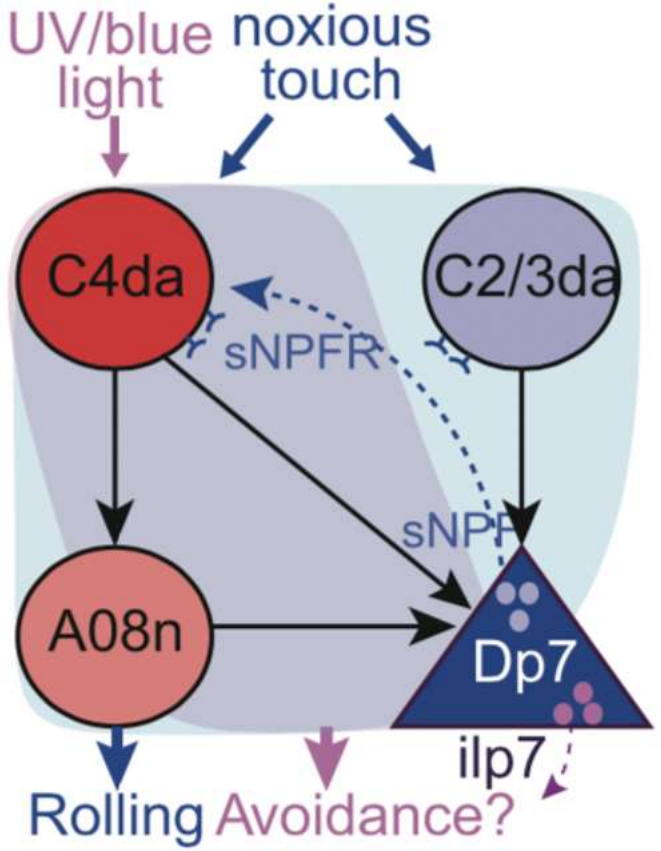
sNPF localizes to DP-ilp7 dendrites and is required for nociceptive behavior

Neuropeptide and escape behavior

Nat Neurosci. 2017 August ; 20(8): 1085–1095. doi:10.1038/nn.4580.

Modality-specific sensory integration and neuropeptide-mediated feedback facilitate mechano-nociceptive behavior in *Drosophila*



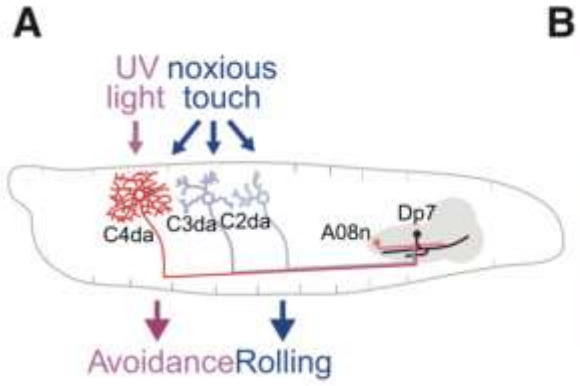


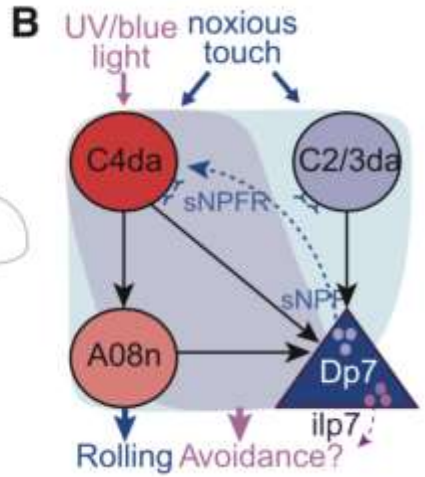
Neuropeptide and escape behavior

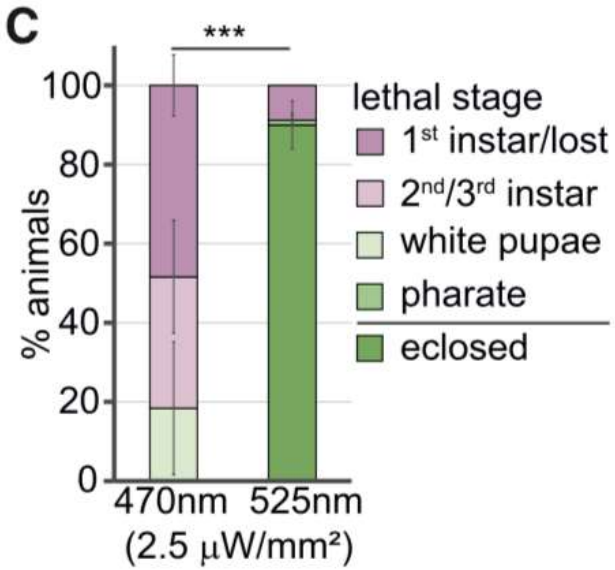
› Curr Biol. 2022 Jan 10;32(1):149-163.e8. doi: 10.1016/j.cub.2021.10.069. Epub 2021 Nov 18.

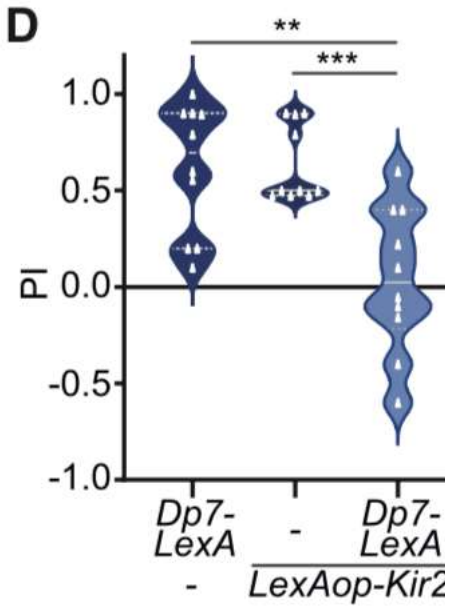
A neuropeptidergic circuit gates selective escape behavior of Drosophila larvae

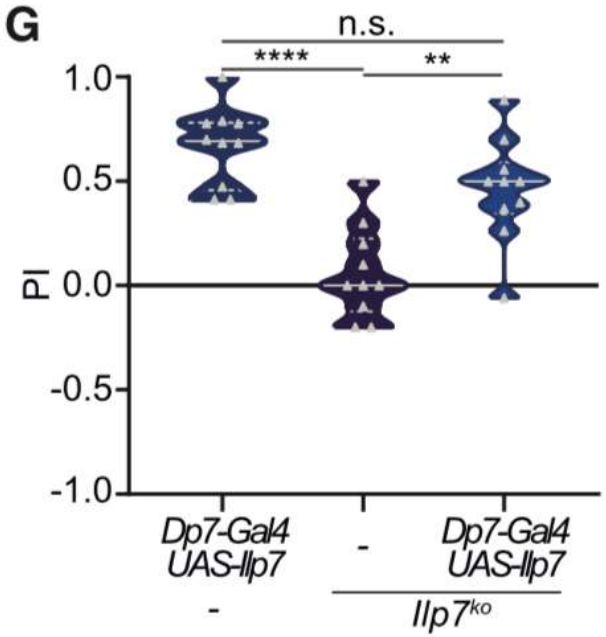
Bibi Nusreen Imambocus [1], Fangmin Zhou [1], Andrey Formozov [2], Annika Wittich [2], Federico M Tenedini [2], Chun Hu [2], Kathrin Sauter [2], Ednilson Macarenhas Varela [3], Fabiana Herédia [3], Andreia P Casimiro [3], André Macedo [3], Philipp Schlegel [4], Chung-Hui Yang [5], Irene Miguel-Aliaga [6], J Simon Wiegert [2], Michael J Pankratz [4], Alisson M Gontijo [7], Albert Cardona [8], Peter Soba [9]

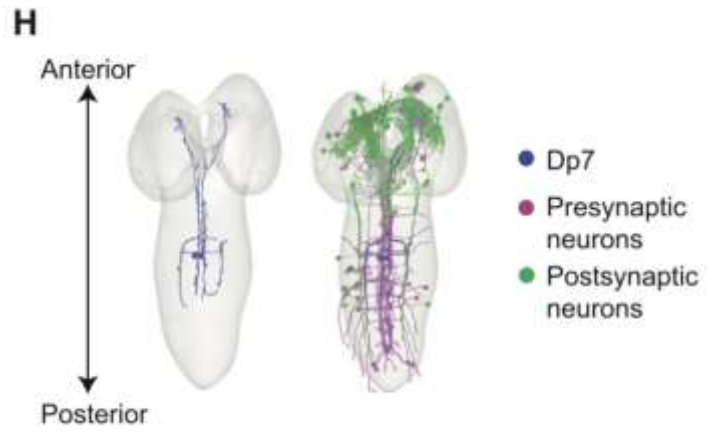






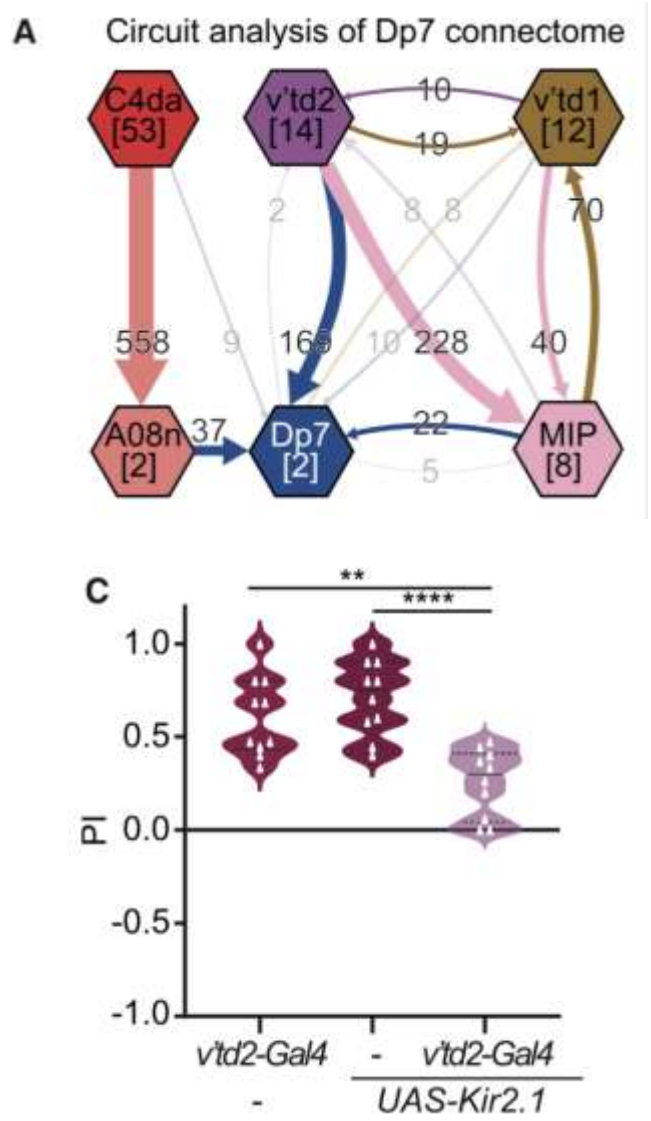


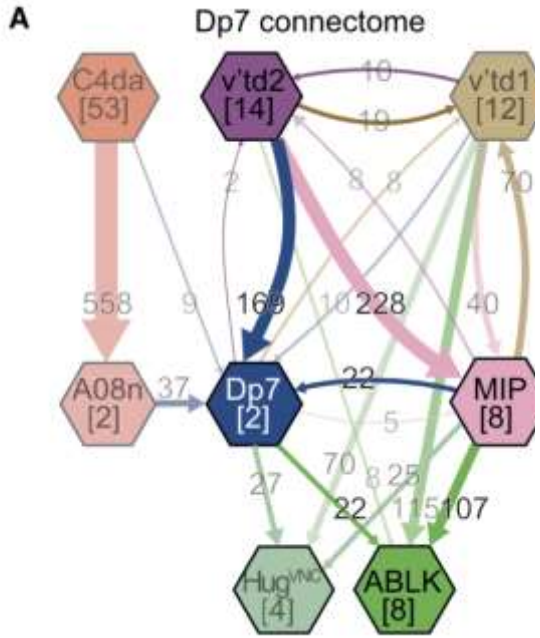


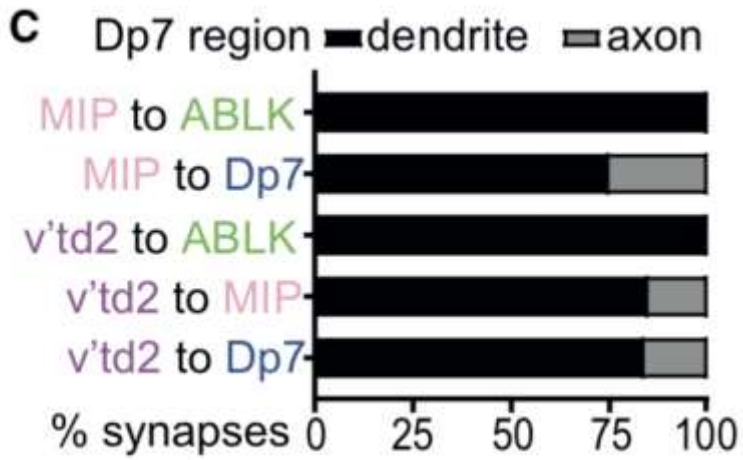


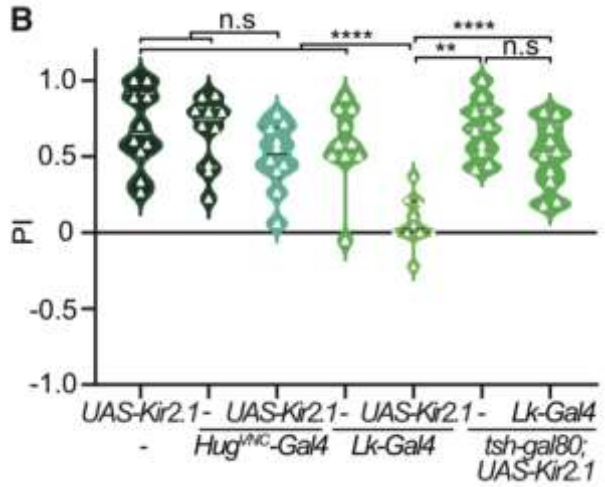
Imambocus BN, et al. *Curr Biol*. 2022.

Neuropeptide and escape behavior



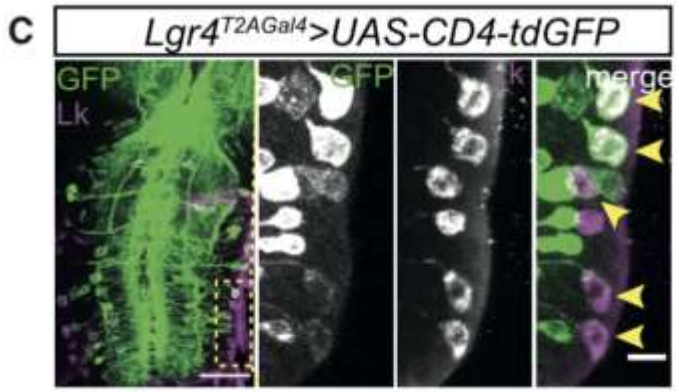


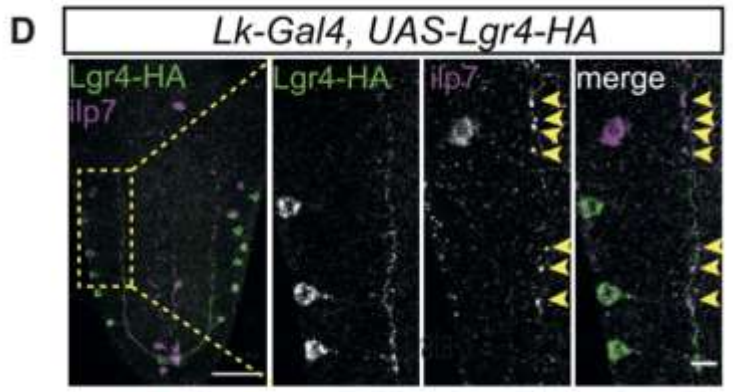


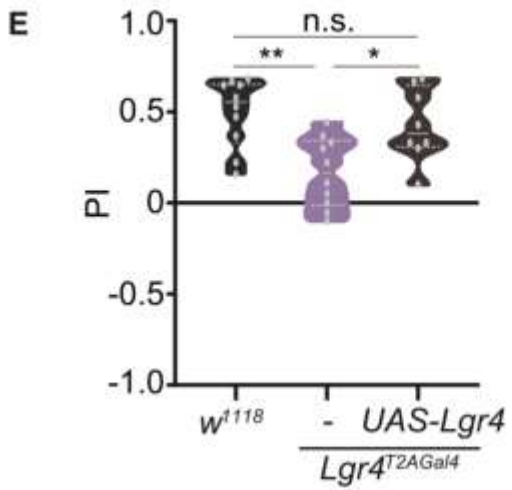


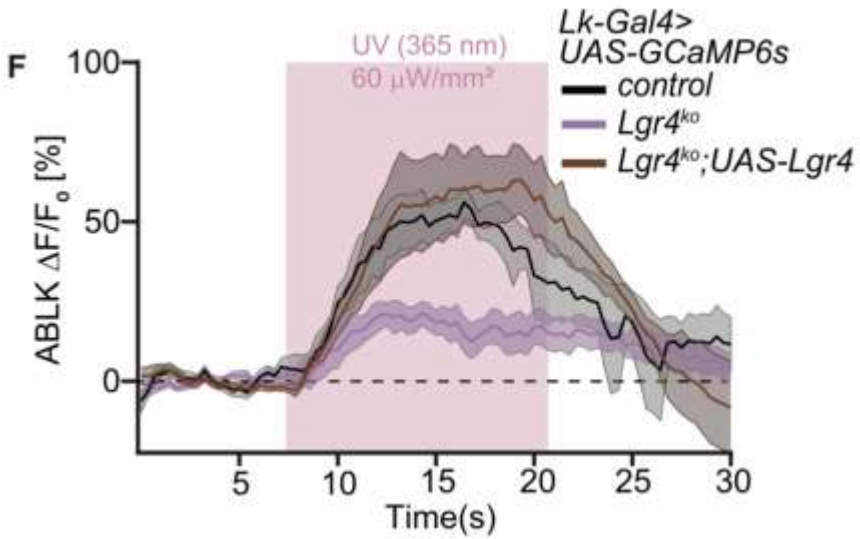
v'td2 neurons → Dp7 neurons

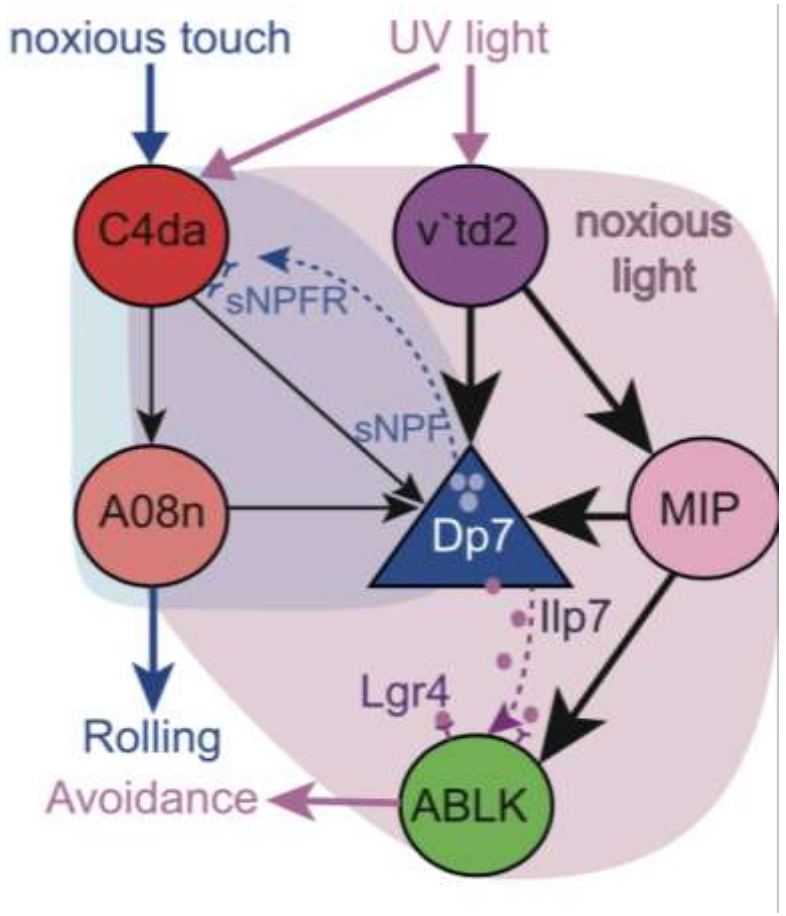
Neuropeptide and escape behavior











Lgr4 : the relaxin family receptor of Ilp7

Summary

1. The larval Cho neurons use TRP channels (NOMPC, NANCHUNG, and INACTIVE) to detect sound waves and respond to the appearance of predators or other environmental cues at a distance.

2. The class IV neurons allow for a nociceptive behavioral response to a naturally occurring predator of *Drosophila*.

3. Nociceptive interneurons (DnB neurons) control modular motor pathways to promote escape behavior in *Drosophila*

4. Neuropeptide sNPF is required for noxious touch induced escape behavior.

5. Ilp7 involved in the avoidance of noxious light.

Take home messages

- Factors Causing *Drosophila* Larvae Escape
- The basis of C4 da mediated escape behavior
- Decision making of *Drosophila* larvae at facing complex stimuli

References:

1. Hwang RY, Zhong L, Xu Y, et al. Nociceptive neurons protect Drosophila larvae from parasitoid wasps. *Curr Biol*. 2007;17(24):2105-2116.
2. Robertson JL, Tsubouchi A, Tracey WD. Larval defense against attack from parasitoid wasps requires nociceptive neurons. *PLoS One*. 2013;8(10):e78704.
3. Zhang W, Yan Z, Jan LY, Jan YN. Sound response mediated by the TRP channels NOMPC, NANCHUNG, and INACTIVE in chordotonal organs of Drosophila larvae. *Proc Natl Acad Sci U S A*. 2013;110(33):13612-13617.
4. Ohyama T, Schneider-Mizell CM, Fetter RD, et al. A multilevel multimodal circuit enhances action selection in Drosophila. *Nature*. 2015;520(7549):633-639.
5. Burgos A, Honjo K, Ohyama T, et al. Nociceptive interneurons control modular motor pathways to promote escape behavior in *Drosophila*. *Elife*. 2018;7:e26016. Published 2018 Mar 12.
6. Imambocus BN, Zhou F, Formozov A, et al. A neuropeptidergic circuit gates selective escape behavior of Drosophila larvae. *Curr Biol*. 2022;32(1):149-163.e8.
7. Hu C, Petersen M, Hoyer N, et al. Sensory integration and neuromodulatory feedback facilitate Drosophila mechanonociceptive behavior. *Nat Neurosci*. 2017;20(8):1085-1095.