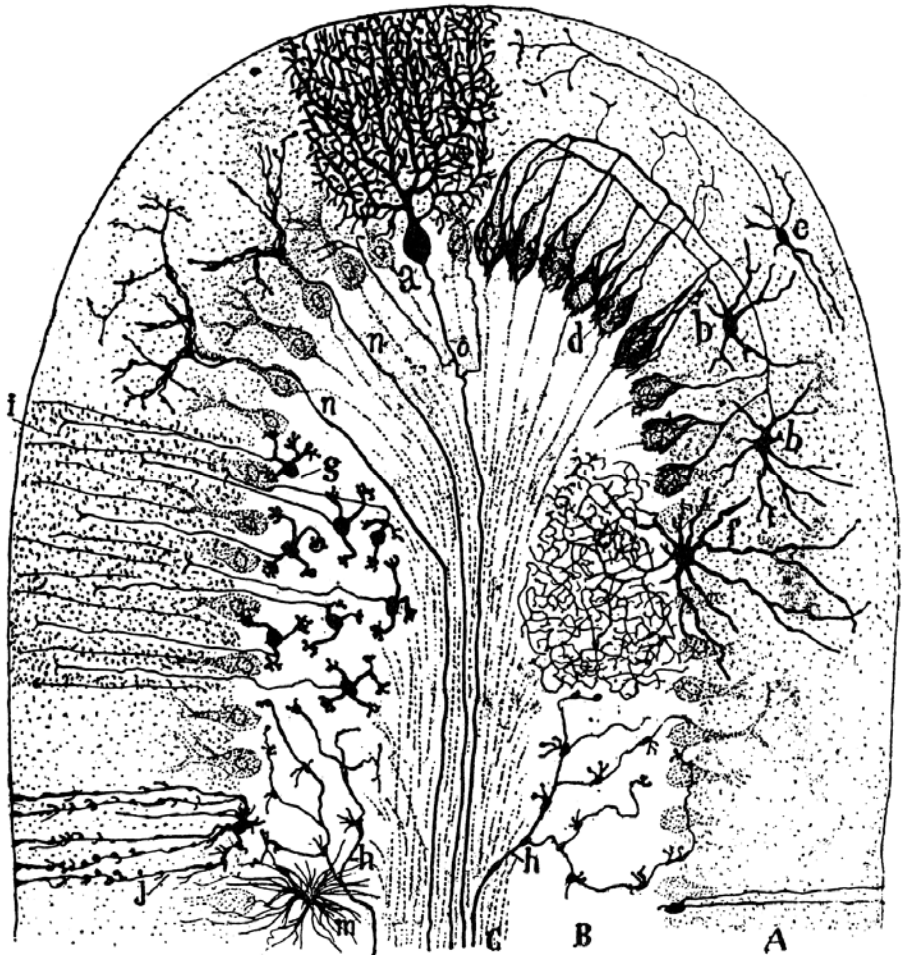
Dendrites---NS 201 B

Yuh-Nung Jan

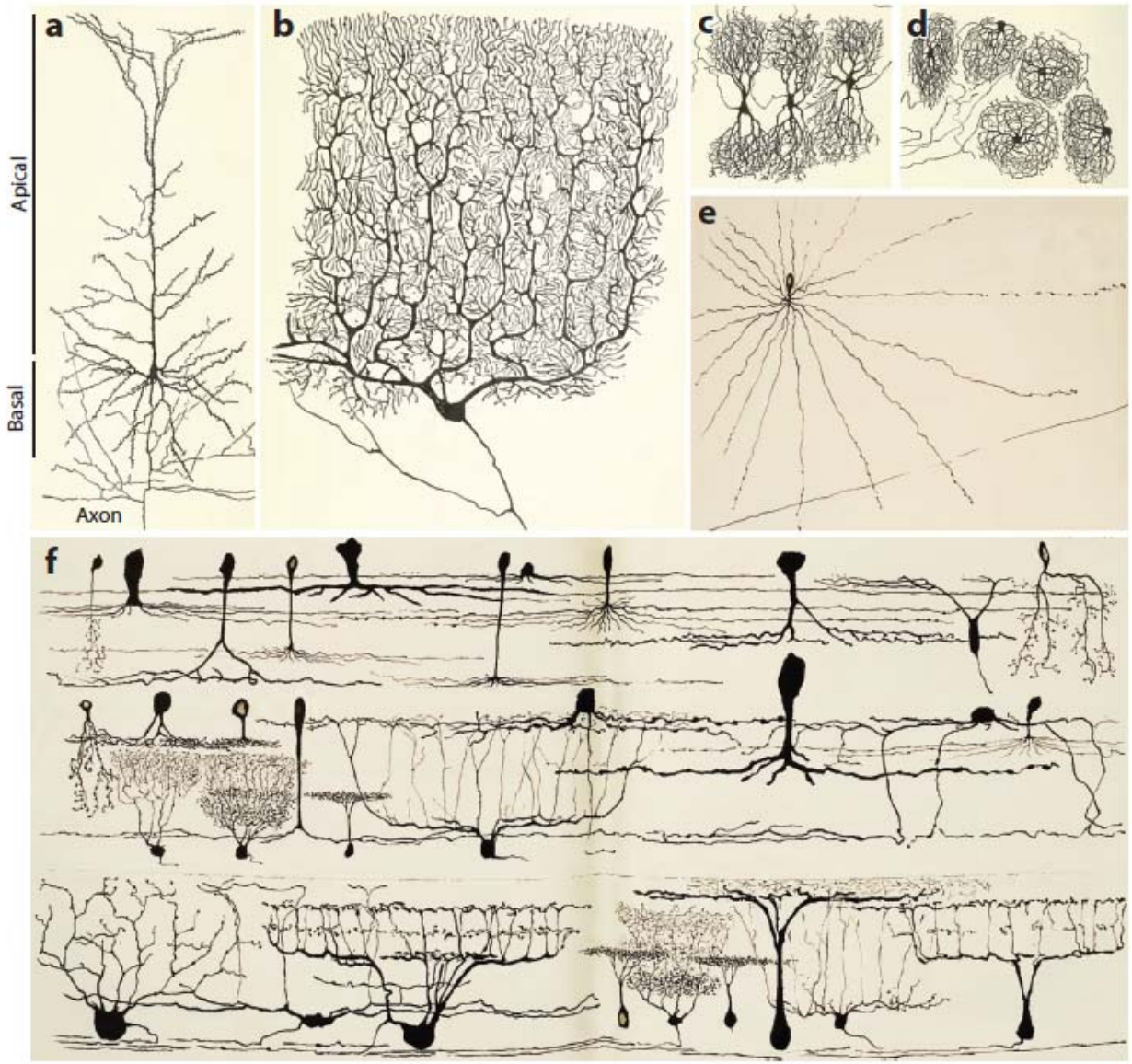
December, 5, 2016

Dendrite morphogenesis



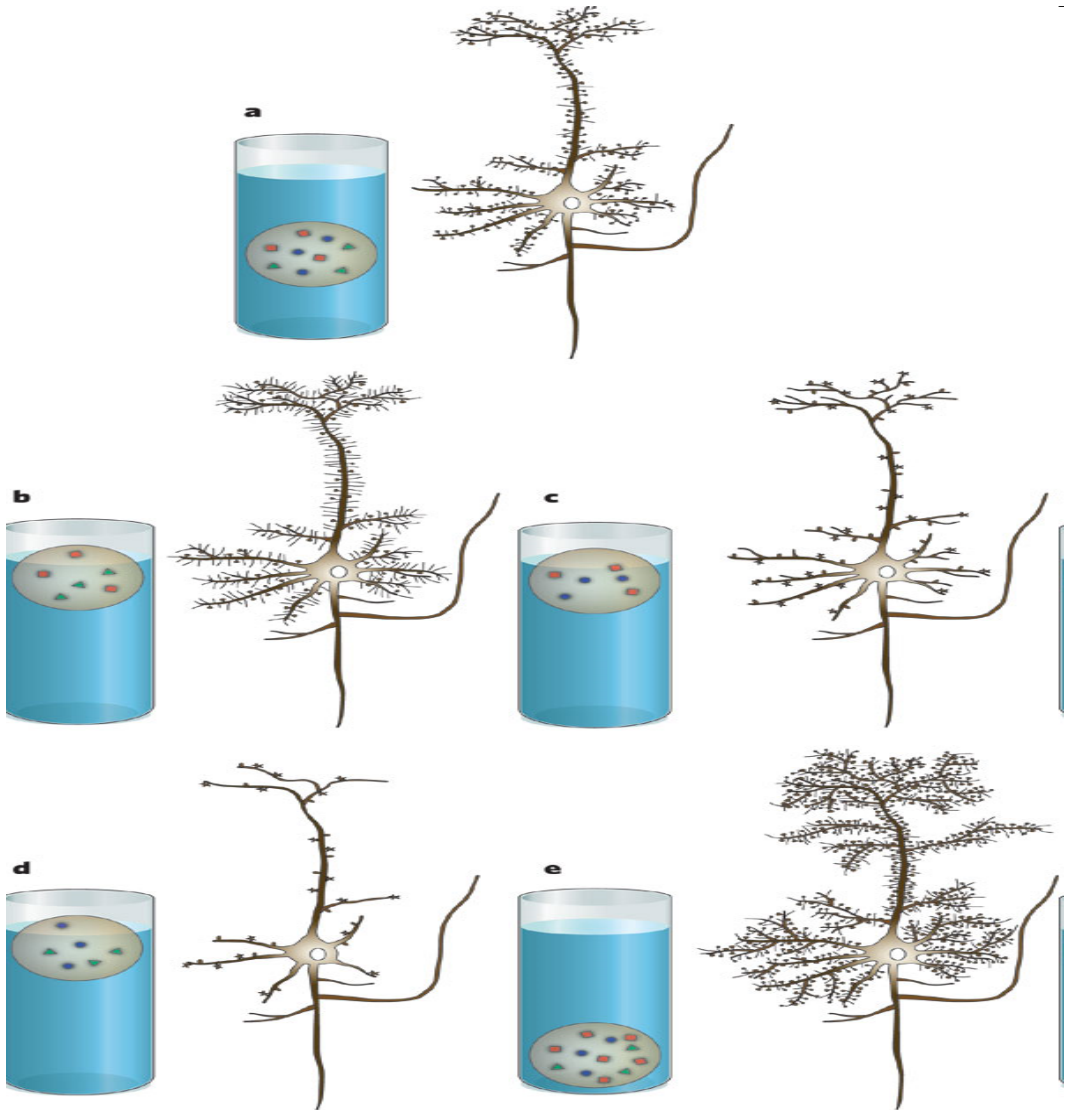
Ramón y Cajal, *Histology of the Nervous System*

Diversity of dendrite morphology



Ramón y Cajal

Dendrite defects are often found to be associated with mental disorders



Fragile X

Angelman syndrome

Rett's syndrome

Mecp2 duplication

Ramocki& Zoghbi, Nature, 2008

Axon and dendrites differ in many aspects

TABLE 4.1 Functional and Morphological Hallmarks of Axons and Dendrites

Axons	Dendrites
With rare exceptions, each neuron has a single axon.	Most neurons have multiple dendrites arising from their cell bodies.
Axons appear first during neuronal differentiation.	Dendrites begin to differentiate only after the axon has formed.
Axon initial segments are distinguished by a specialized plasma membrane containing a high density of ion channels and distinctive cytoskeletal organization.	Dendrites are continuous with the perikaryal cytoplasm, and the transition point cannot be readily distinguished.
Axons typically are cylindrical in form with a round or elliptical cross section.	Dendrites usually have a significant taper and small spinous processes that give them an irregular cross section.
Large axons are myelinated in vertebrates, and the thickness of the myelin sheath is proportional to the axonal caliber.	Dendrites are not myelinated, although a few wraps of myelin may occur rarely.
Axon caliber is a function of neurofilament and microtubule numbers with neurofilaments predominating in large axons.	The dendritic cytoskeleton may appear less organized, and microtubules dominate even in large dendrites.
Microtubules in axons have a uniform polarity with plus ends distal from the cell body.	Microtubules in proximal dendrites have mixed polarity, with both plus and minus ends oriented distal to the cell body.
Axonal microtubules are enriched in tau protein with a characteristic phosphorylation pattern.	Dendritic microtubules may contain some tau protein, but MAP2 is not present in axonal compartments and is highly enriched in dendrites.
Ribosomes are excluded from mature axons, although a few may be detectable in initial segments.	Both rough endoplasmic reticulum and cytoplasmic polysomes are present in dendrites, with specific mRNAs being enriched in dendrites.
Axonal branches tend to be distal from the cell body.	Dendrites begin to branch extensively near the perikaryon and form extensive arbors in the vicinity of the perikaryon.
Axonal branches form obtuse angles and have diameters similar to the parent stem.	Dendritic branches form acute angles and are smaller than the parent stem.
Most axons have presynaptic specializations that may be *en passant* or at the ends of axonal branches.	Dendrites are rich in postsynaptic specializations, particularly on the spinous processes that project from the dendritic shaft.
Action potentials are usually generated at the axon hillock and conducted away from the cell body.	Some dendrites can generate action potentials, but more commonly they modulate the electrical state of the perikaryon and initial segment.
Traditionally, axons are specialized for conduction and synaptic transmission, i.e., neuronal output.	Dendritic architecture is most suitable for integrating synaptic responses from a variety of inputs, i.e., neuronal input.

Note. Neurons typically have two classes of cytoplasmic extensions that may be distinguished using electrophysiological, morphological and biochemical criteria. Although some neuronal processes may lack one or more of these features, enough parameters can generally be defined to allow unambiguous identification.

Choosing a suitable model system to study dendrite morphogenesis

- Choosing a simple experimental system that is capable of providing straightforward answers to a scientific question---Stephen Kuffler

- You can study just about any biological problem by using *Drosophila* ---Seymour Benzer

Neurobiology---Harvard Medical School 1978

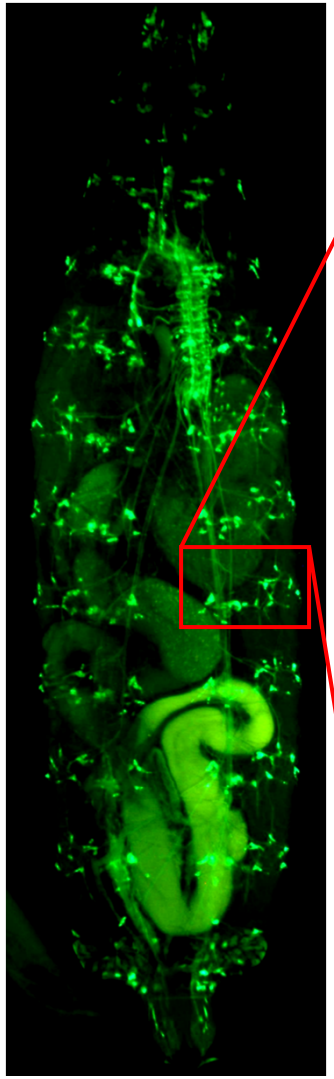
D Potter D Hubel YN D Eddington T Wiesel

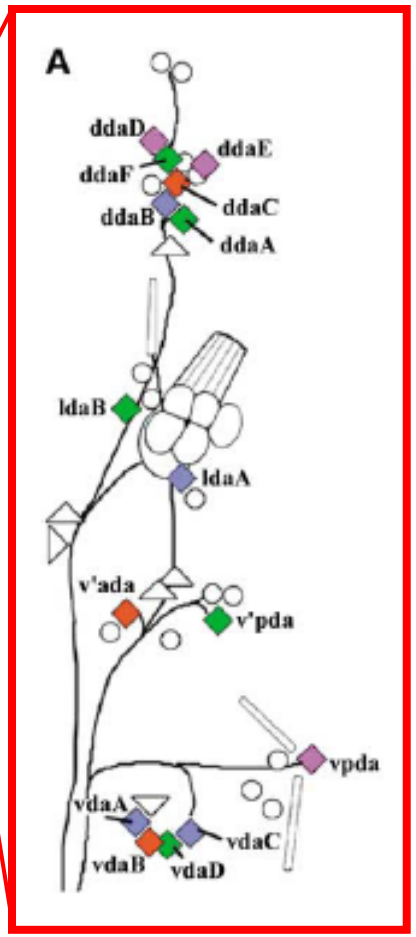
S kuffler E Kravitz E Furshpan B Bosler Lily

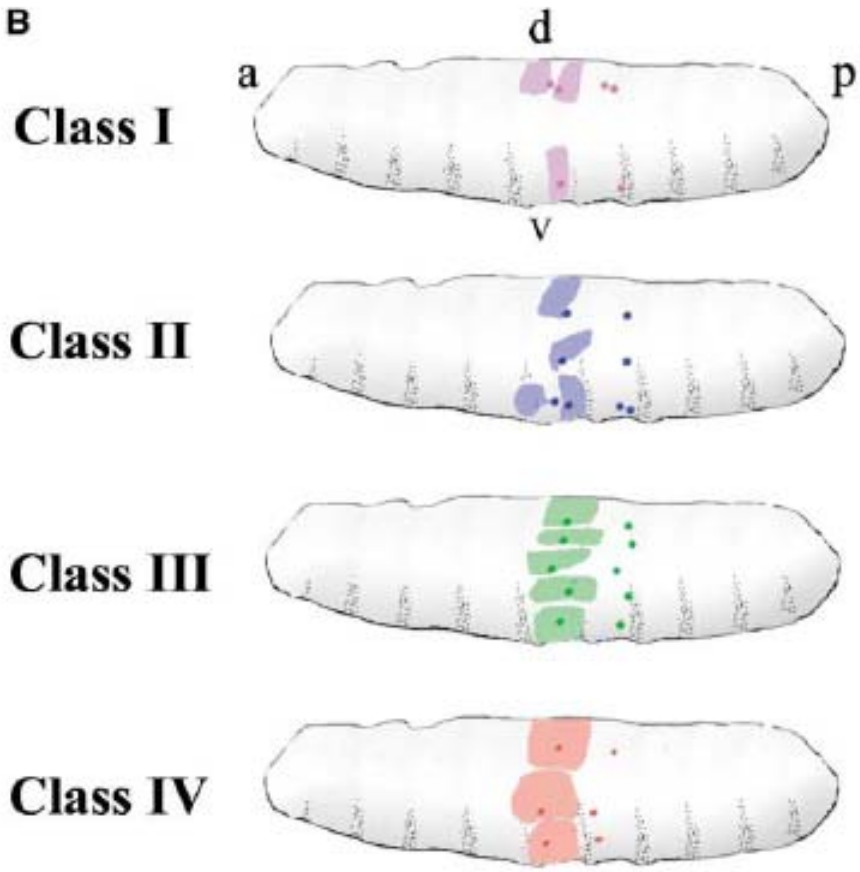
Seymour Benzer 70th birthday Symposium (Caltech, 1991)

Lewis Levi-Montalcini Brenner Crick Benzer

Dendritic arborization (da) neurons: sensory multidendritic neurons of the larval peripheral nervous system

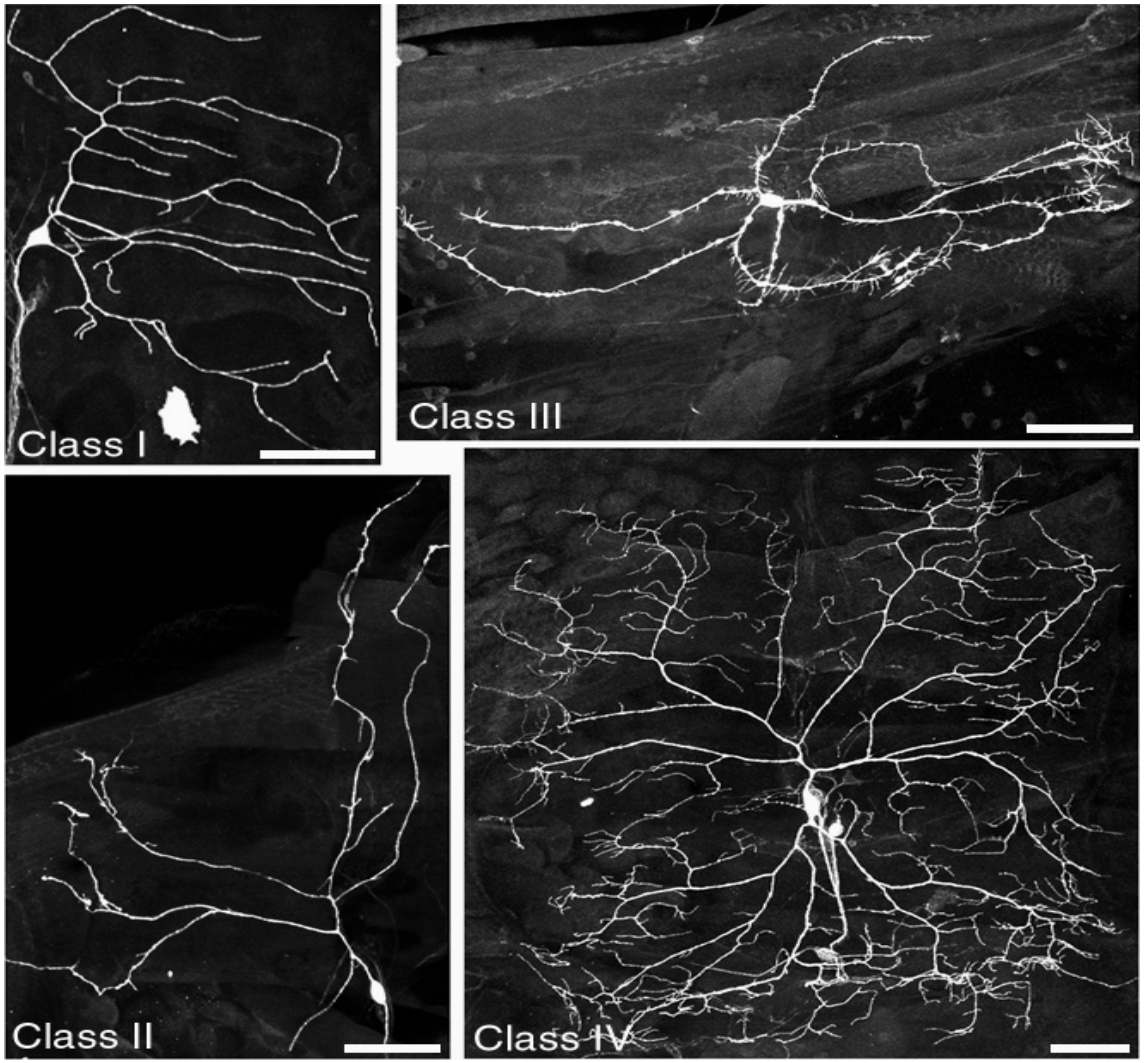






(Grueber, Ye, Moore, Jan & Jan, Curr. Biol. 2003)

Our assay system: four classes of da neurons with distinctive dendritic morphology



(Grueber, Jan & Jan., Dev., 2002)

Mechanisms that control dendrite development
(Jan and Jan, Nature Rev Neuroscience, 2010)

- What differentiates axon and dendrite? (*dar* genes (Ye et al., Cell, 2007), *dlic2* (Zheng et al., Nat Cell Biol, 2008))
- How does a neuron acquire its neuronal-type-specific dendritic arbor? (Hamlet (Moore et al., Science, 2002), Cut (Grueber et al., Cell, 2003), Spineless (Kim et al., G&D, 2006))
- How are dendrites of different neurons organized relative to one another? (self-avoidance, Dscam (Soba et al., Neuron, 2007)) (tiling, Trc, Fry (Emoto et al., Cell, 2004; Han et al., Neuron, 2012), Sema2b (Meltzer et al., Neuron, 2016))
- How is the size of a dendritic arbor controlled? (Hpo, Wts (Emoto et al., Nature, 2006), PcG (Parrish et al., G&D, 2007), *bantam* (Parrish et al., Neuron, 2009))
- What regulates the pruning, remodeling and regeneration of a dendritic arbor? pruning (UPS, Caspases (Kuo et al., Neuron 2006), Ik2, Katanin-60-like (Lee et al., PNAS, 2009), VCP (Rumpf et al., Dev, 2011), regeneration (Song et al., G&D, 2012; Nat Neurosci, 2015; Thompson-Peer et al., G&D, 2016)

How do different neurons develop their type-specific dendritic arbors?

- Influence of intrinsic factors
- Influence of extrinsic factors

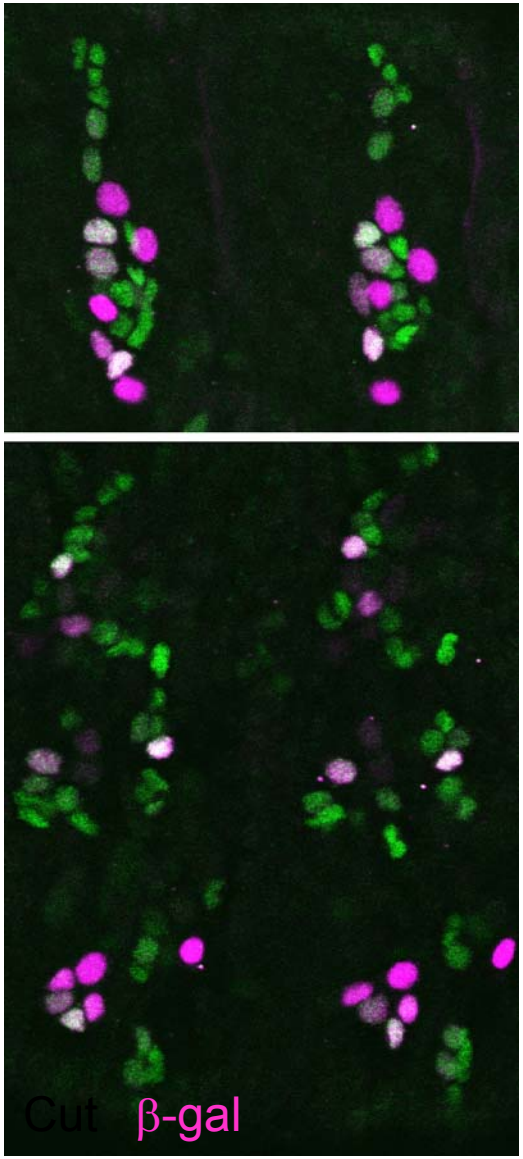
Transcription factors can affect dendritic morphology in very specific ways

- Hamlet functions as a binary switch controlling to branch or not to branch (Moore et al., Science, 2002)

- Abrupt is a regulator specific for class I da neuron dendritic branching and patterning (Li et al., and Sugimura et al., Neuron 2004)

- Cut is a multi-level regulator of neuronal-type-specific dendritic morphology (Grueber et al., Cell, 2003)

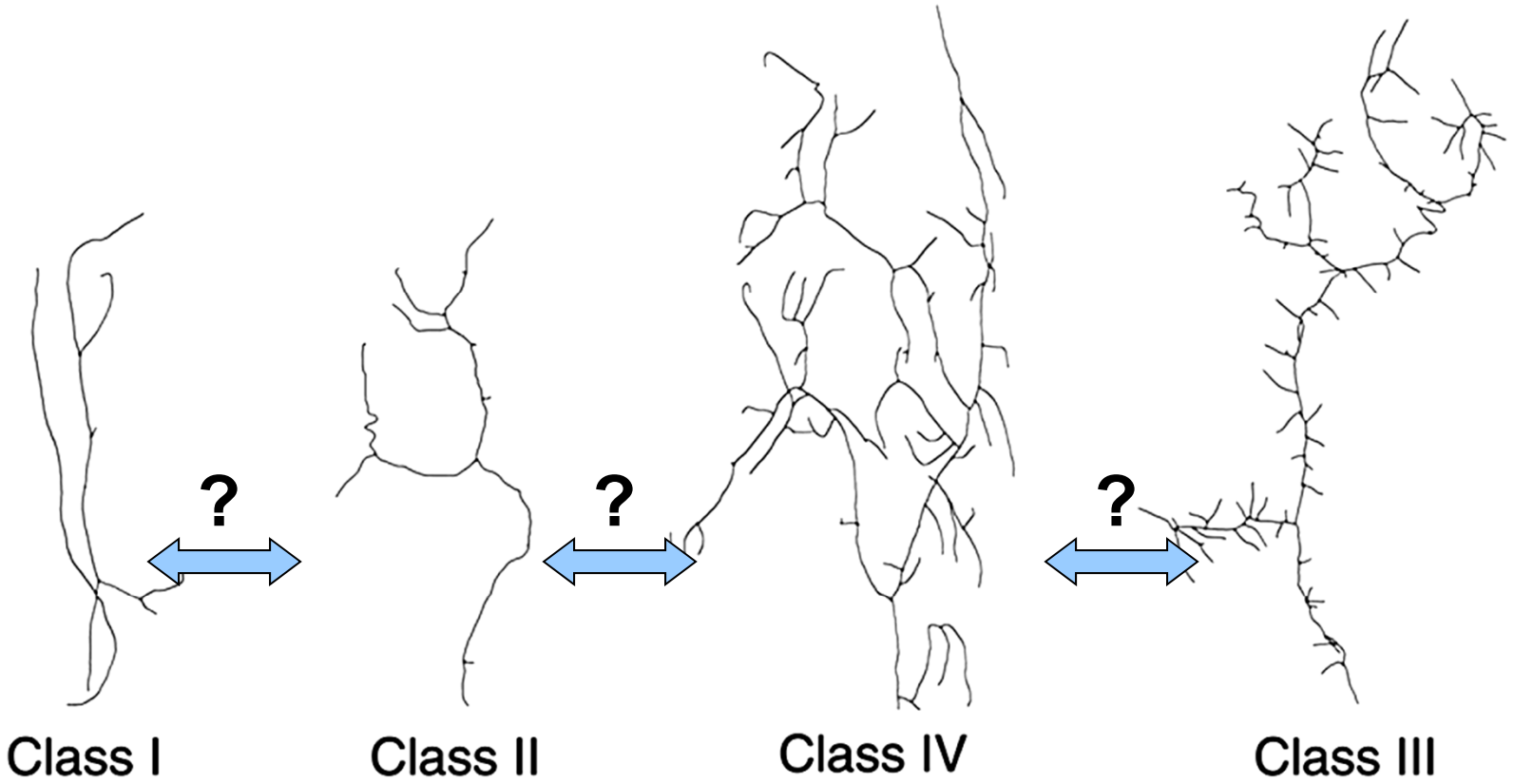
Cut expression levels in da neurons are strictly class-correlated



Class	Cut level	Dendrite morphology
I	n.d.	simple
II	low	simple
III	high	spiny
IV	intermediate	complex

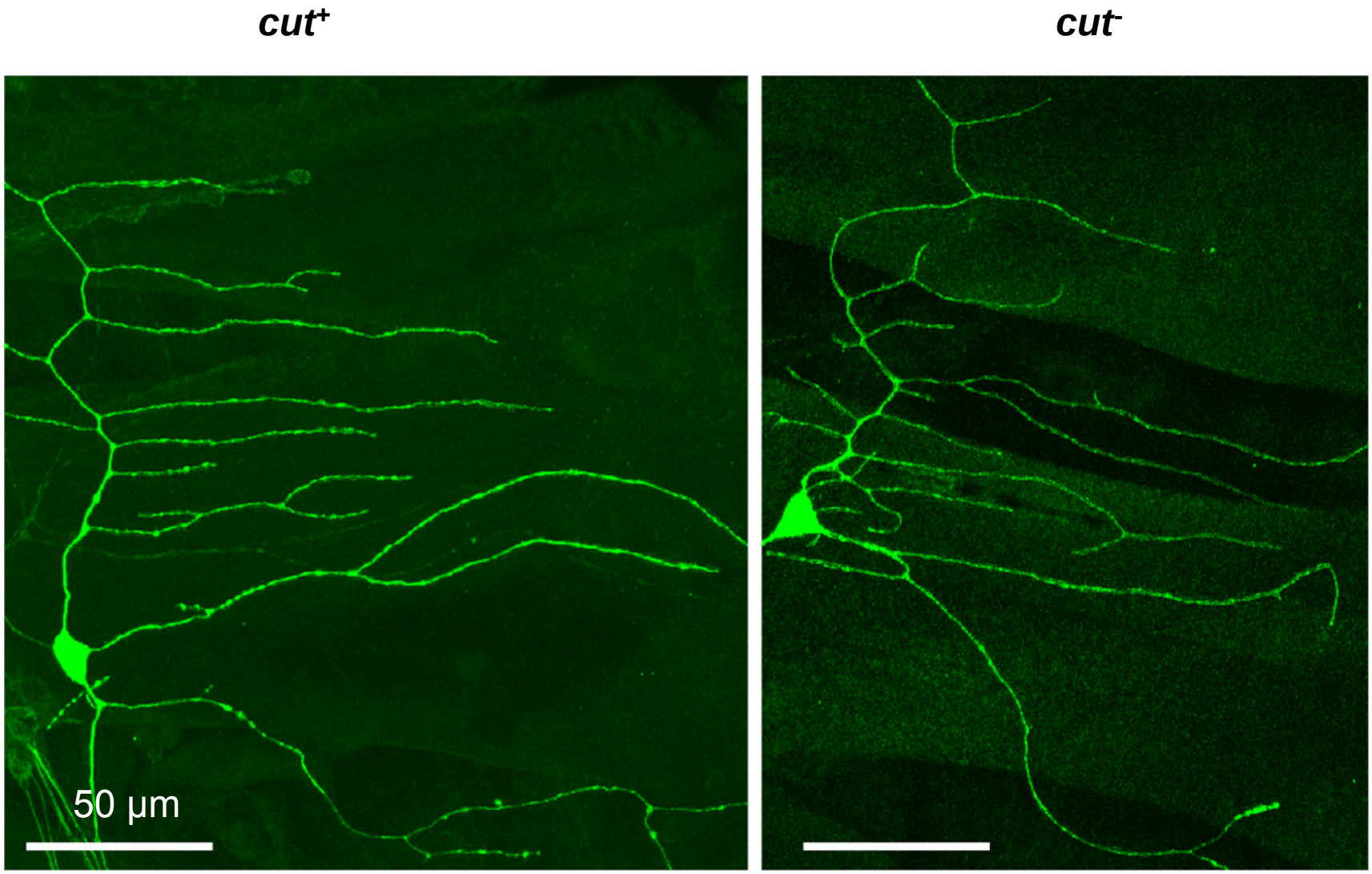
→ Cut levels are maintained throughout development

Do class-specific patterns of *cut* expression contribute to dendrite morphogenesis?

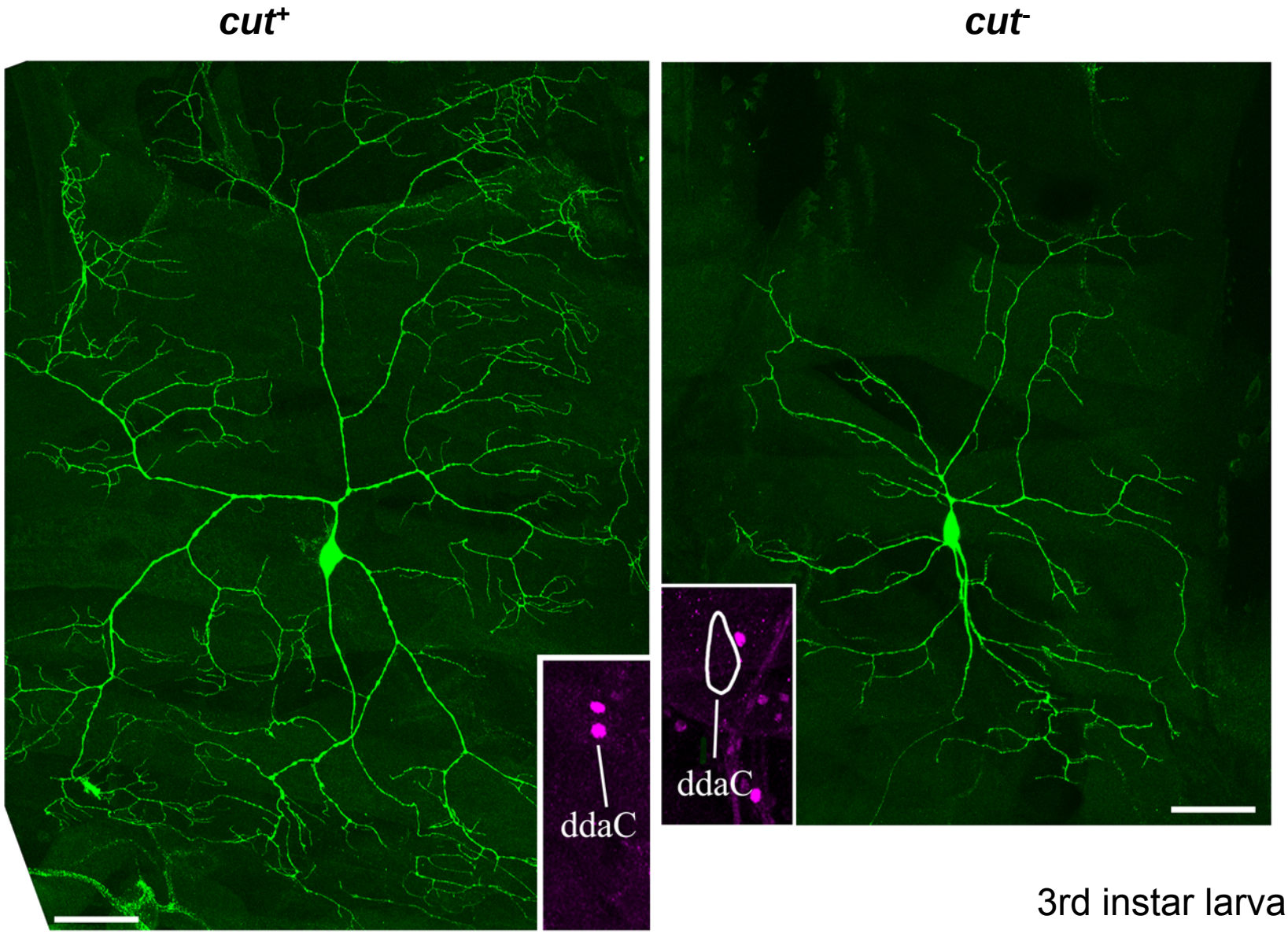


Grueber, Jan & Jan., Cell, 2003

cut mutant class I neurons show normal dendritic patterning



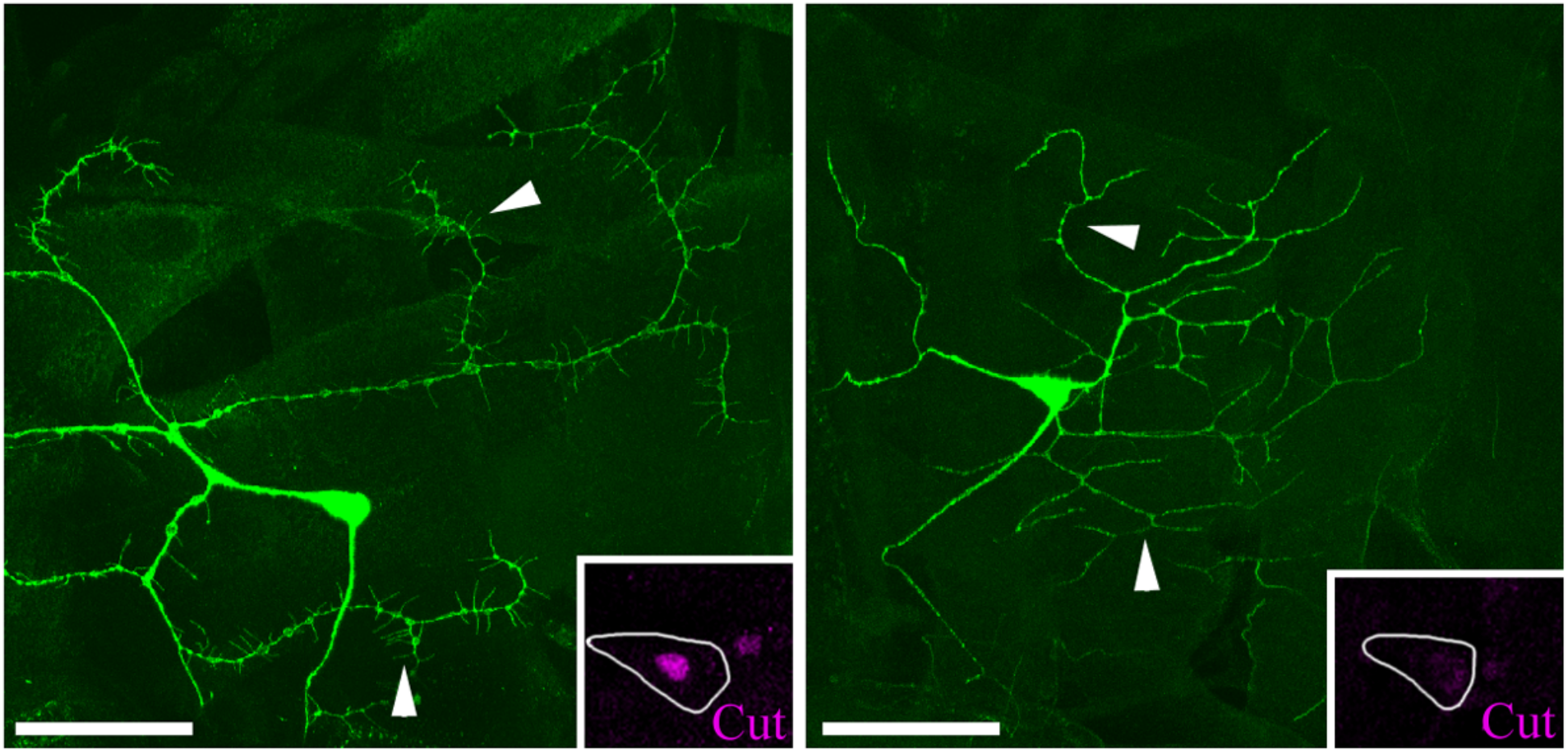
cut mutant class IV neurons lose their "space-filling" arbor



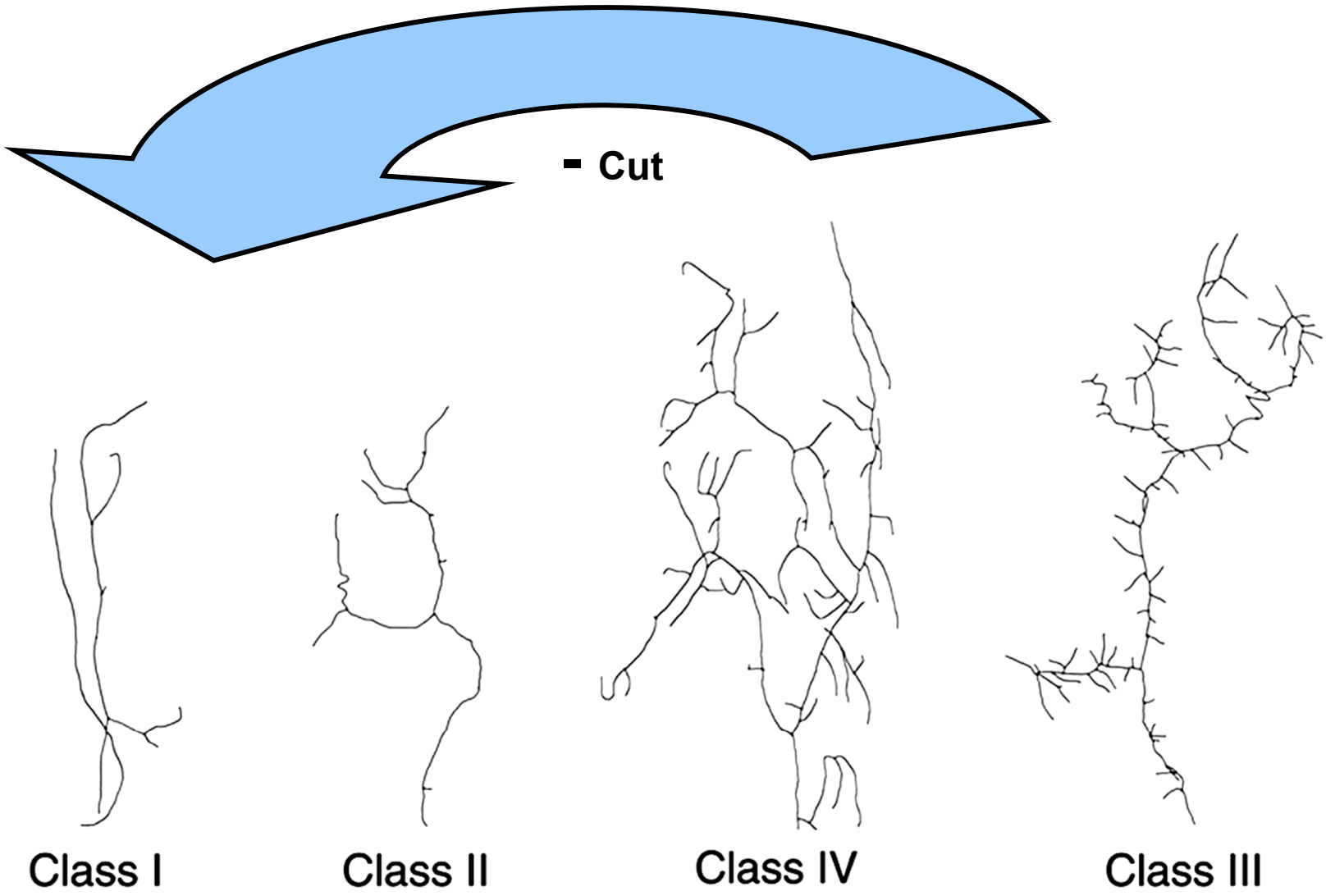
3rd instar larva

cut mutant class III neurons lose their characteristic protrusions

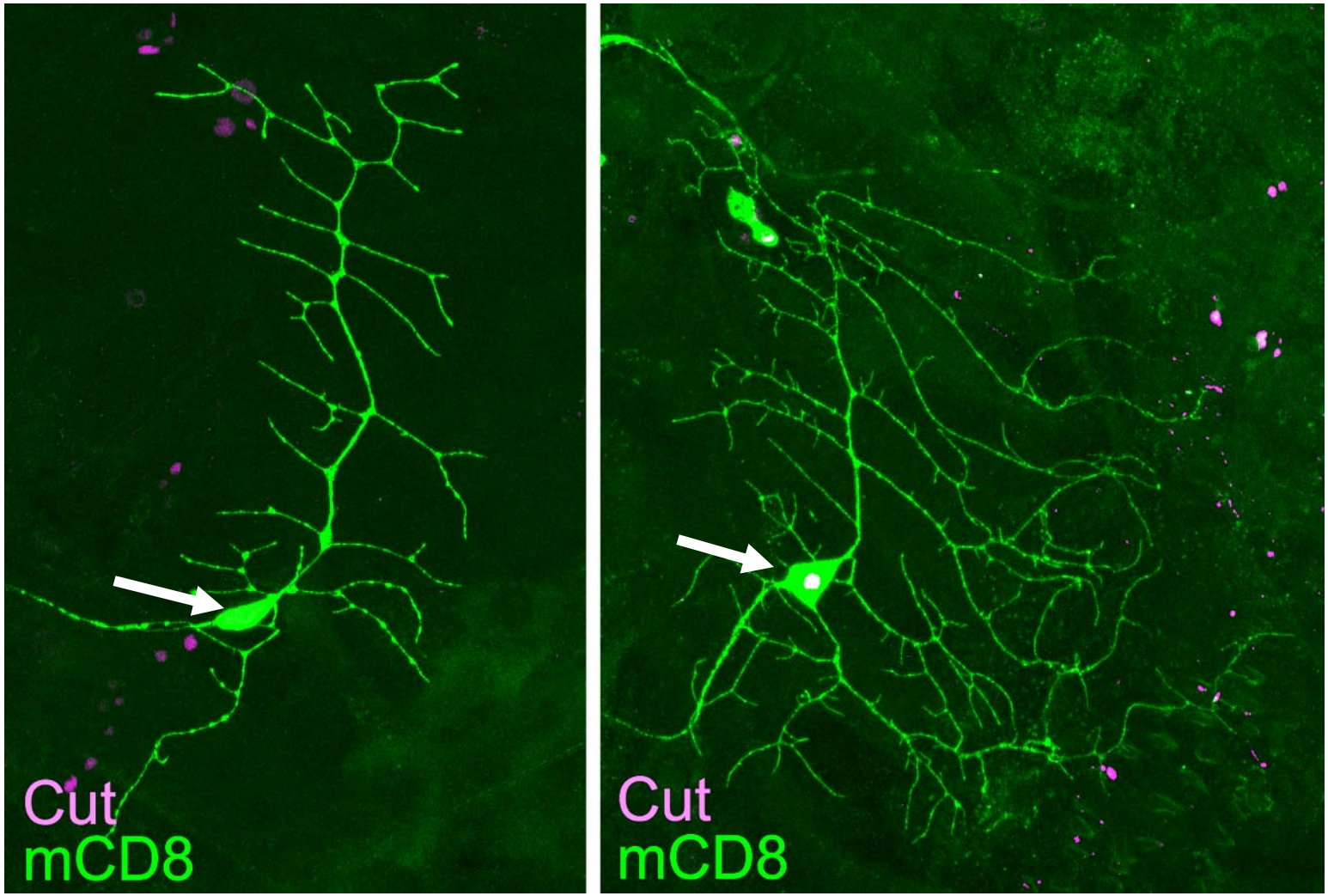
***cut*$^{+}$** ***cut*$^{-}$**



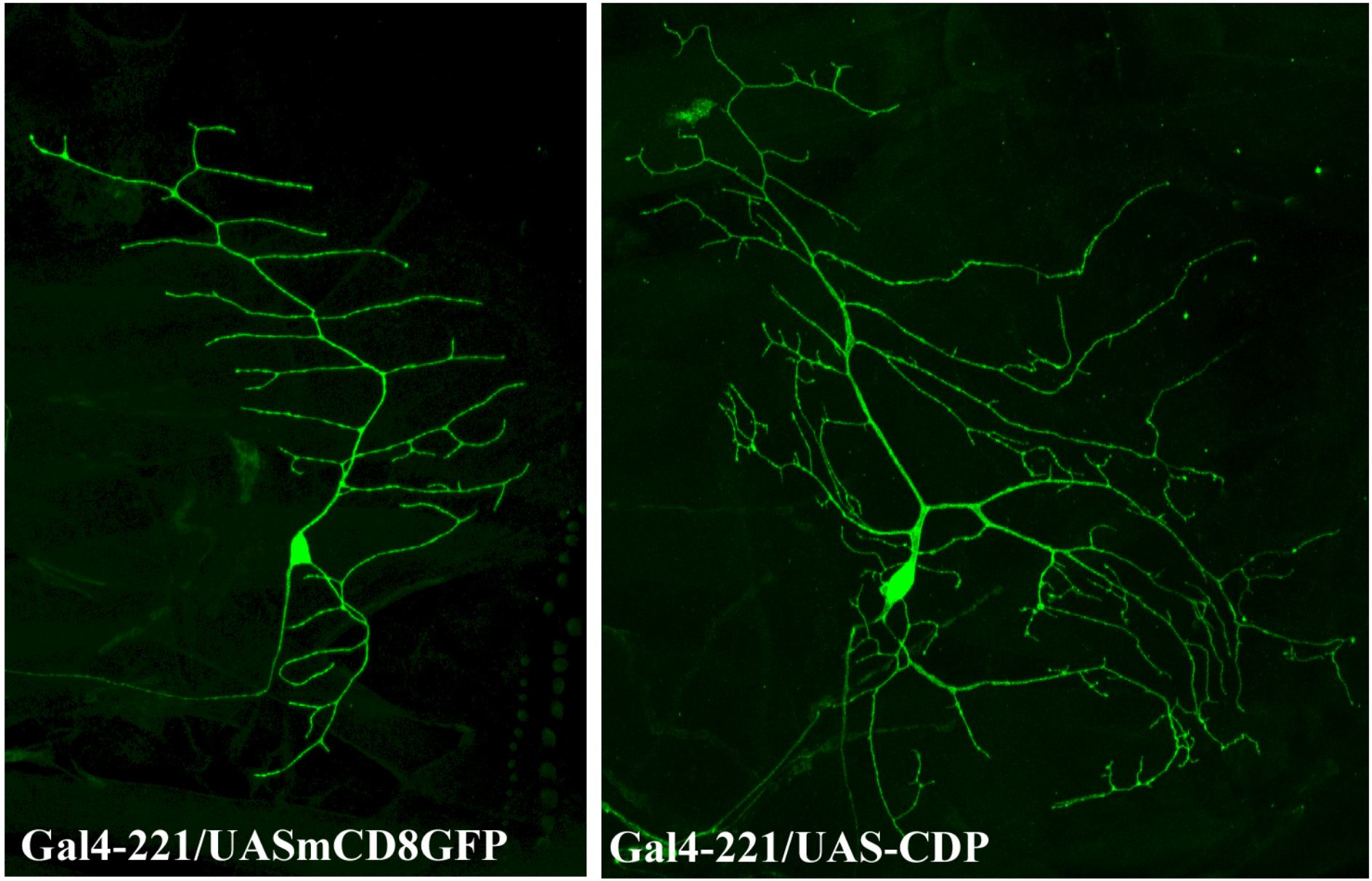
3rd instar larva 3rd instar larva

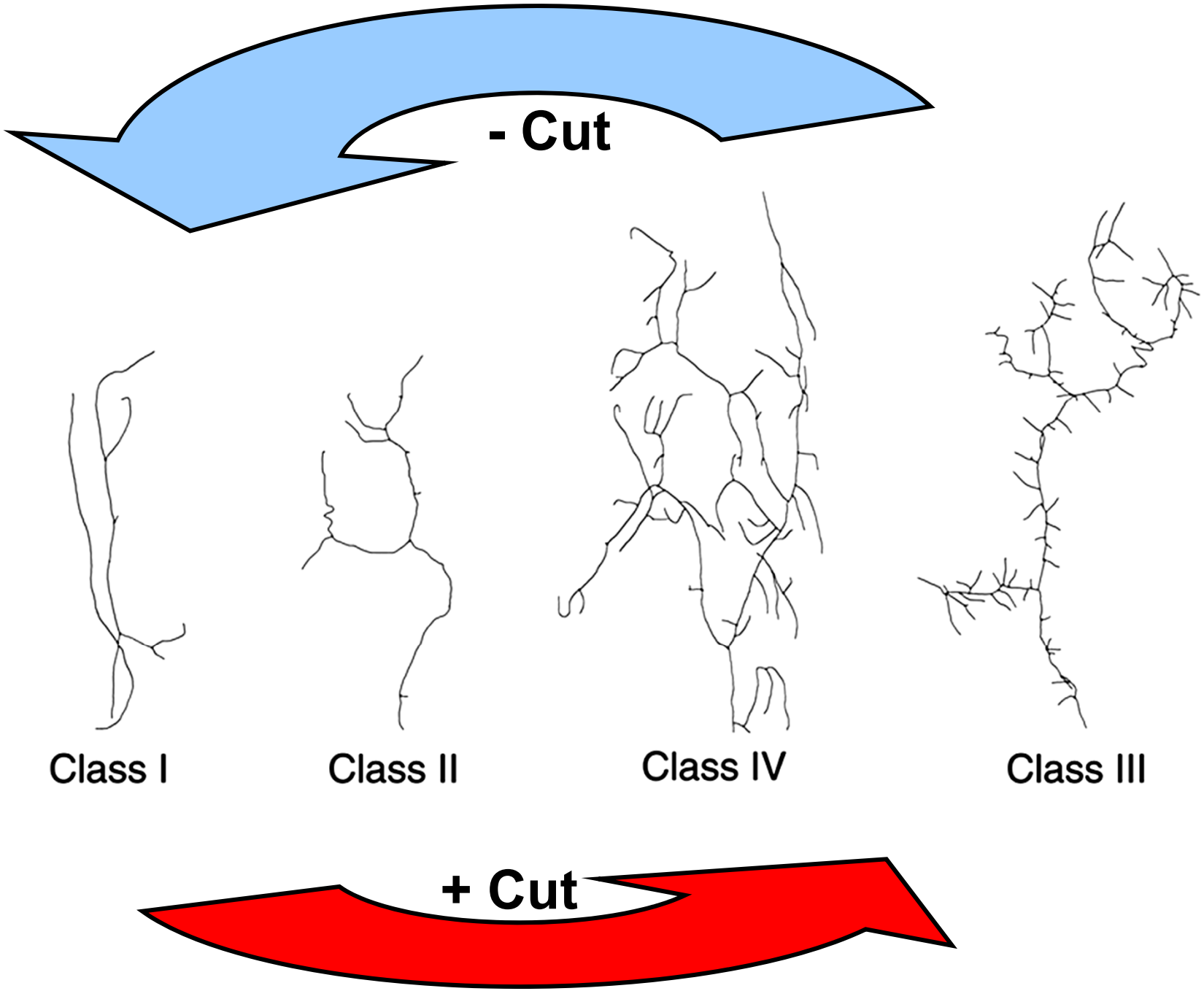

Cut
Class I
Class II
Class IV
Class III

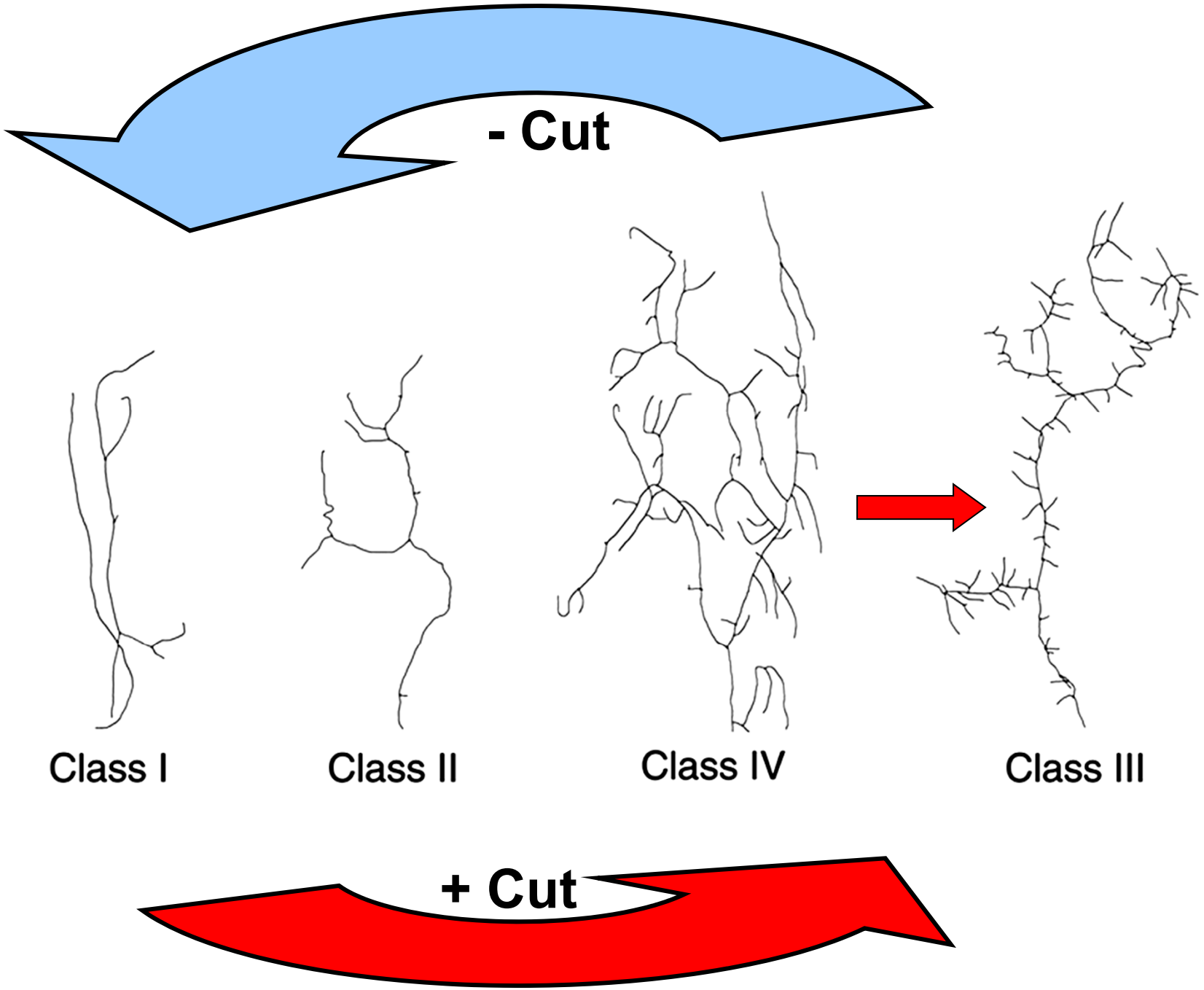
Post-mitotic ectopic *cut* expression in class I neurons leads to class III dendritic morphology



Human Cut can substitute for fly Cut in promoting Class III type of dendrite growth




- Cut
Class I
Class II
Class IV
Class III
+ Cut


- Cut
Class I
Class II
Class IV
Class III
+ Cut

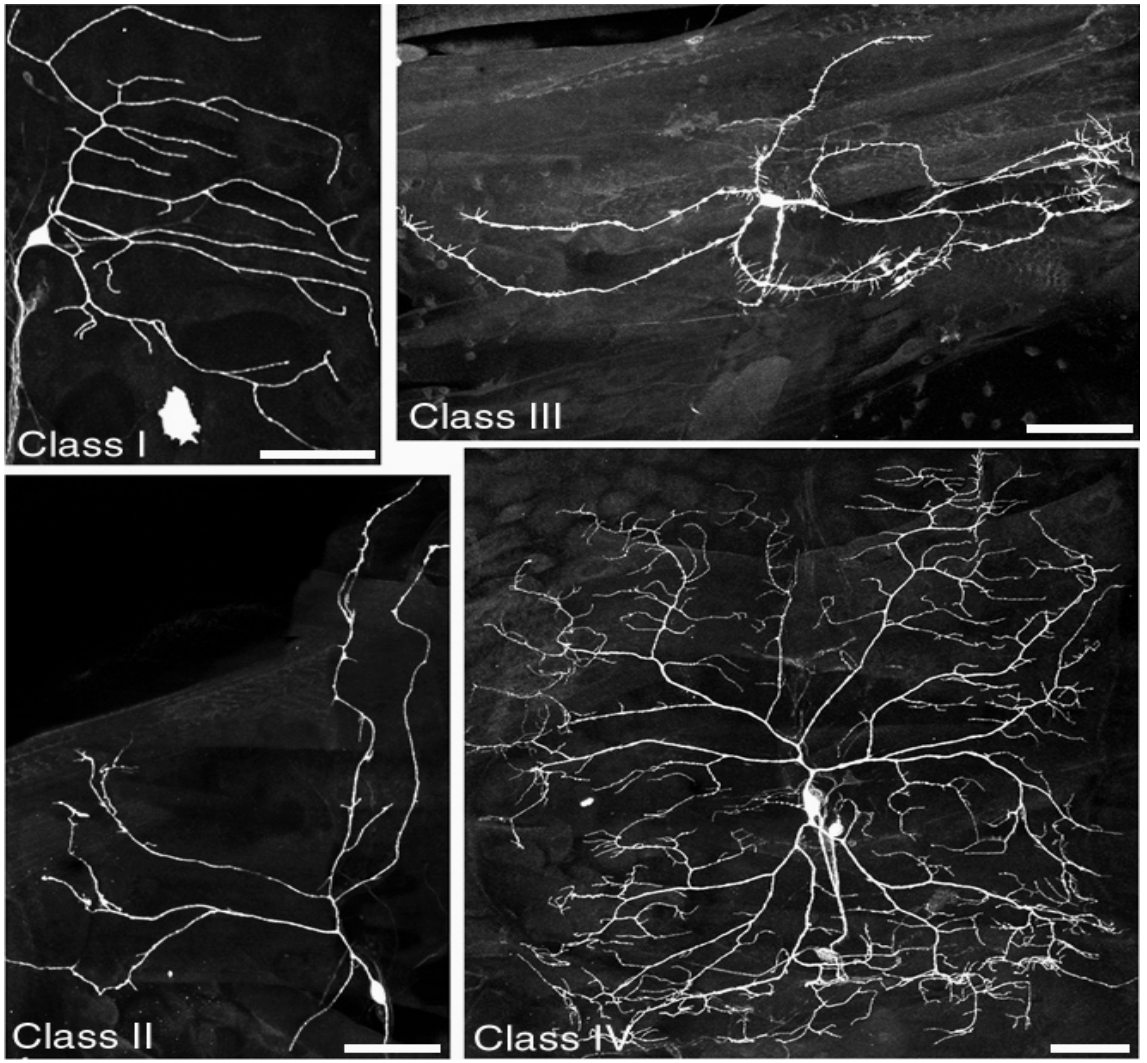
Cut functions as a multi-level regulator of class-specific dendrite morphogenesis

- Cut is expressed at different levels in da neurons in a persistent and class-correlated pattern

- Loss of function and gain of function manipulations cause reciprocal switches in dendrite branching patterns

Grueber, Jan & Jan., Cell, 2003

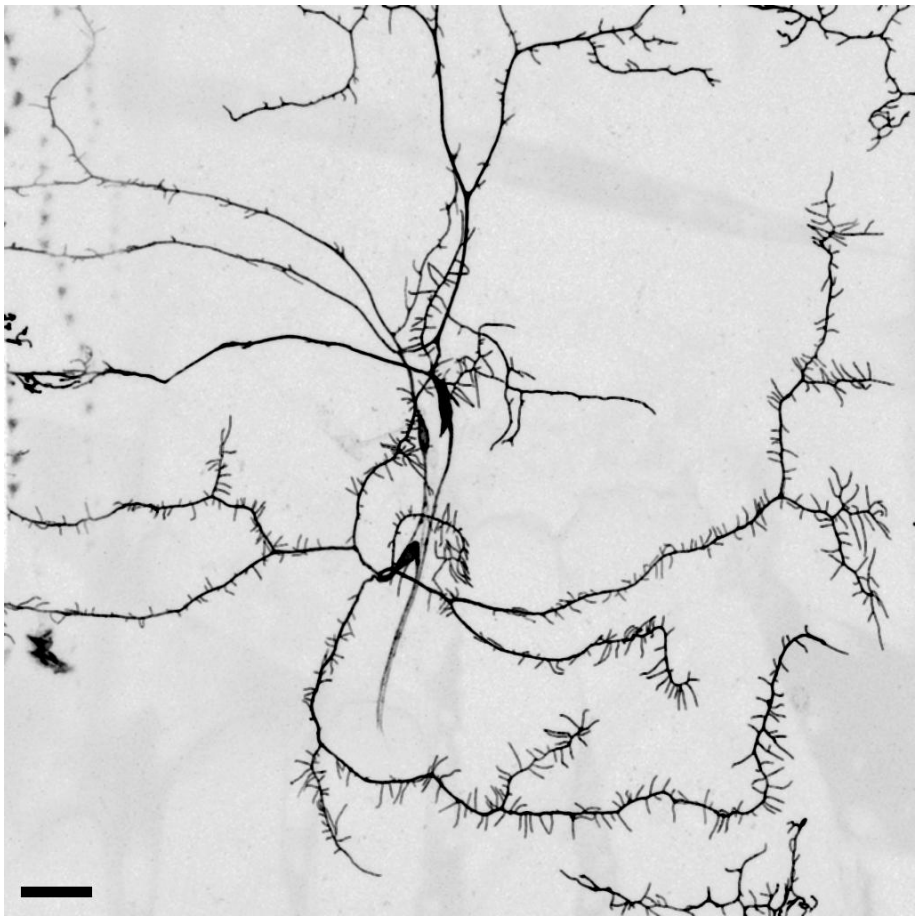
Four classes of da neurons with distinctive dendritic morphology and function

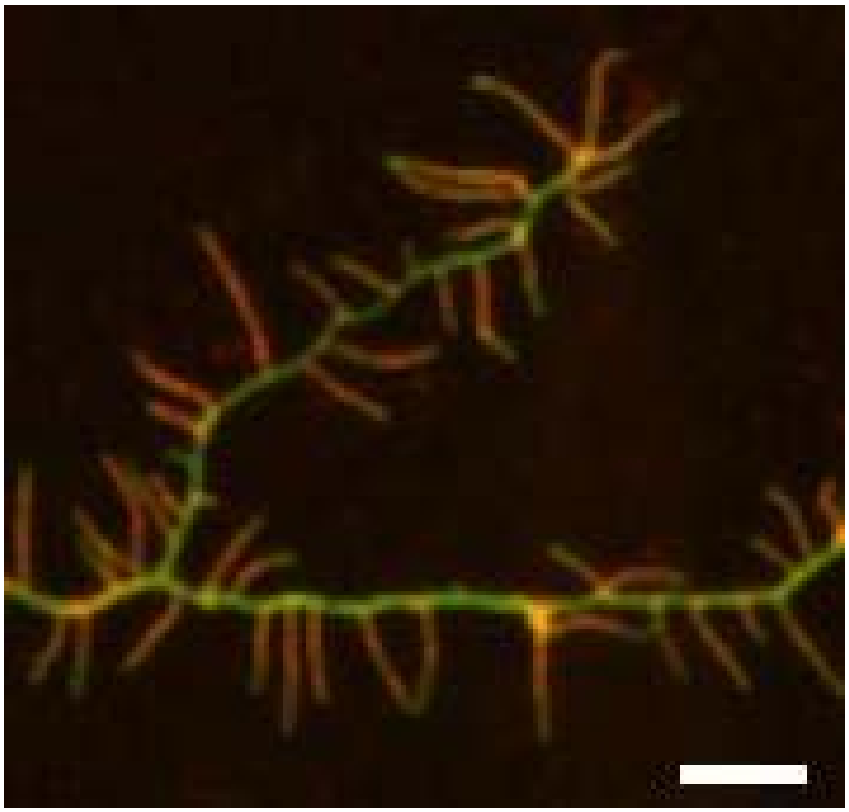


Gentle touch, mediated by NompC (Yan et al., Nature, 2013)

Nociception, mediated by DmPiezo (Kim et al., Nature, 2012)

The touch sensitive class III da neurons contain short, actin-rich terminal branches (the dendritic spikes)

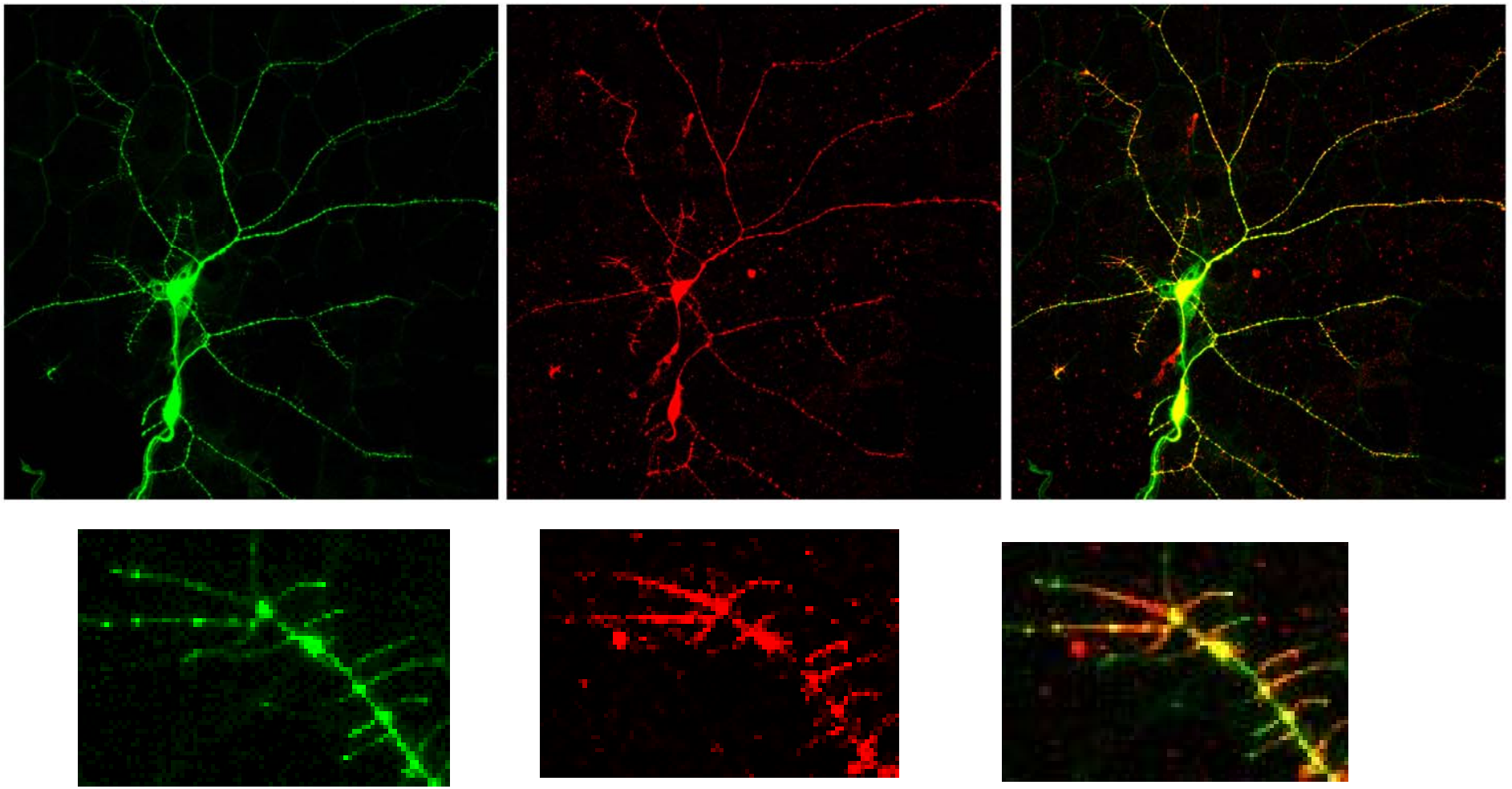




CD4-tdGFP
LifeActin-tdTOM

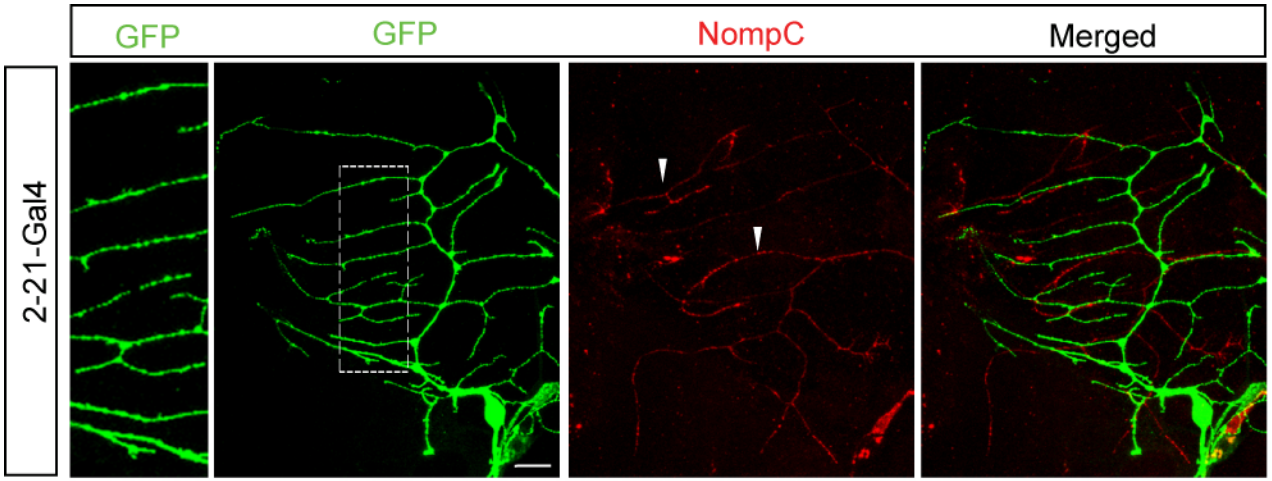
NompC is expressed in class III da neuron

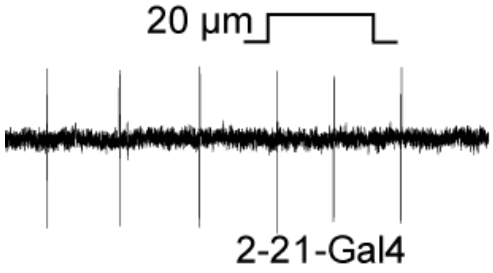
19-12 Gal4, UAS-CD4 td GFP/ NompC

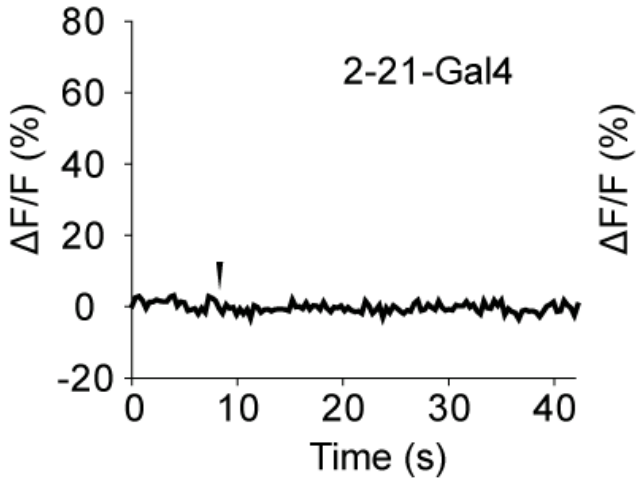


Yan et al., Nature, 2013

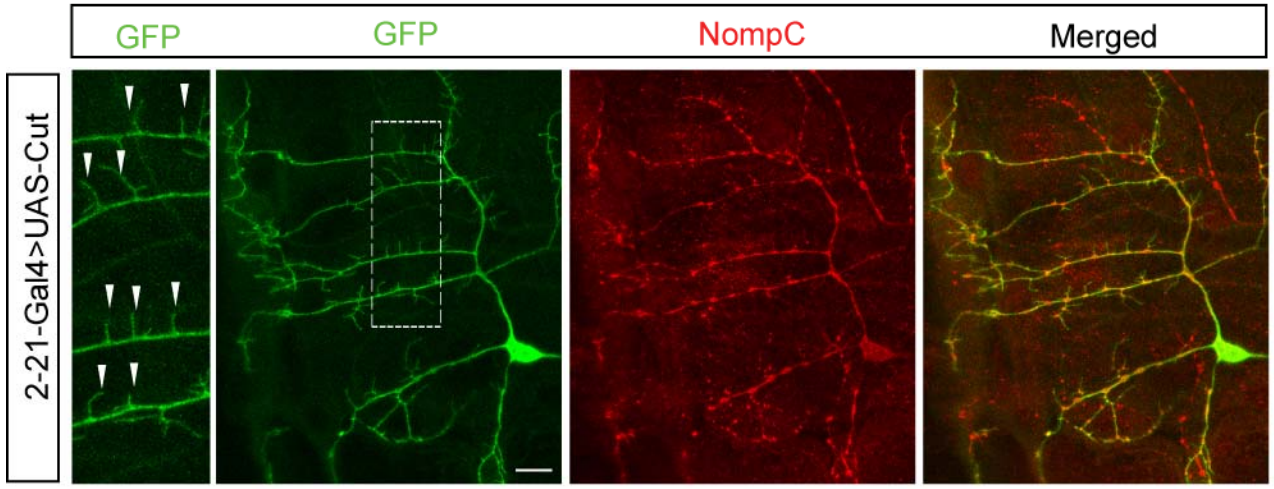
Class I da neurons do not express high level of NompC and are not sensitive to gentle touch

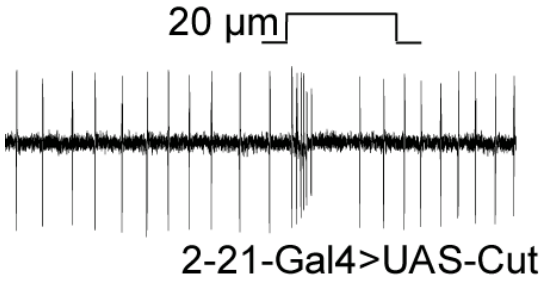


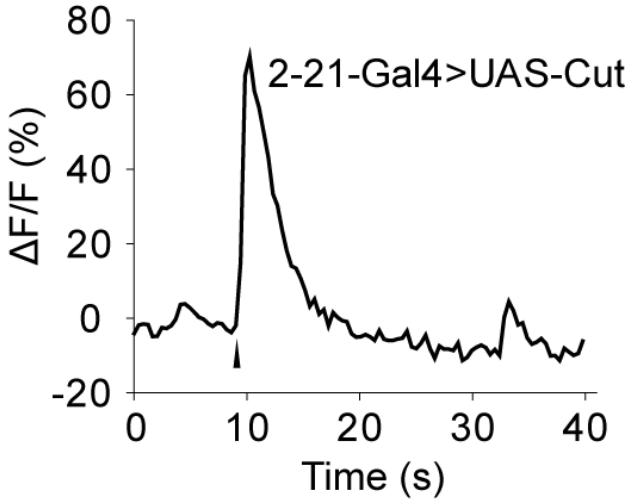




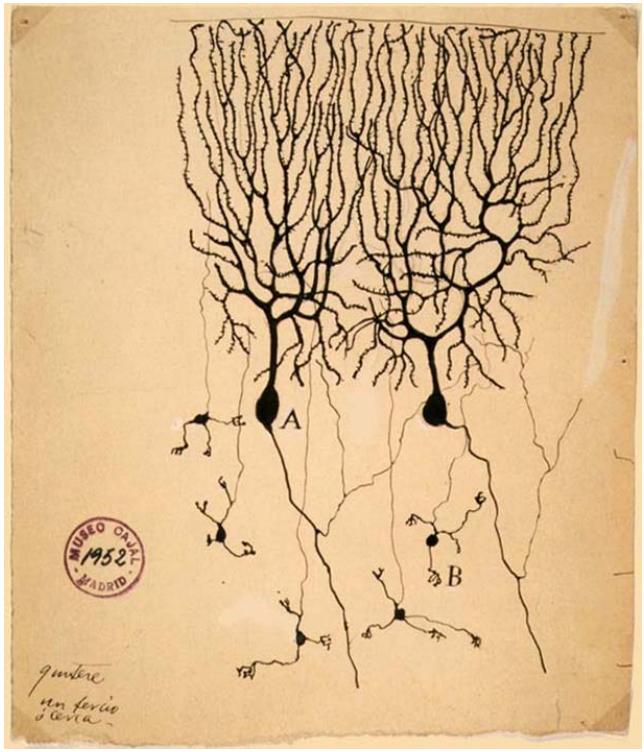
Over-expression of Cut in class I da neurons induces spike formation, NompC expression and touch sensitivity



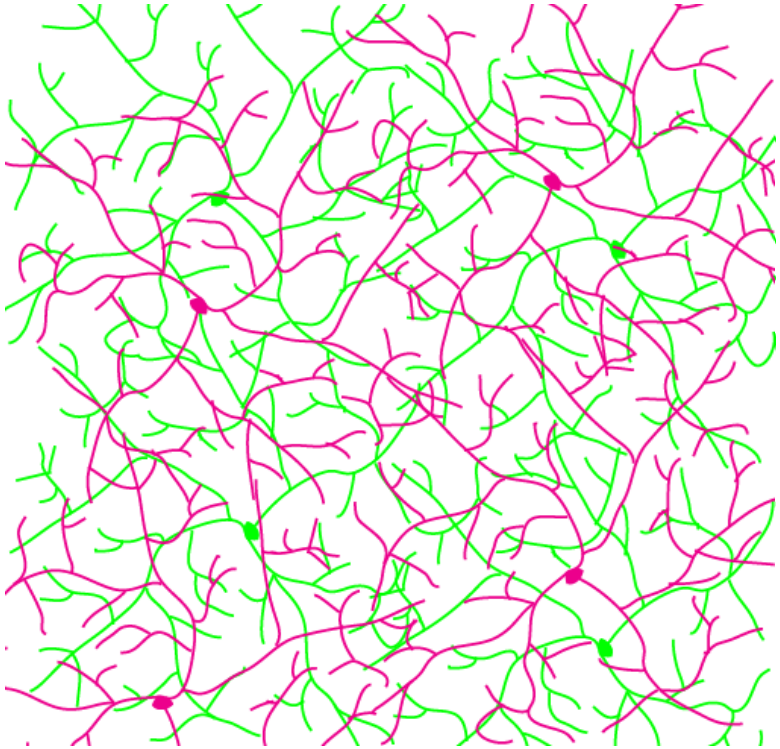




Organization principles of the dendritic fields



Santiago Ramón y Cajal, 1899.

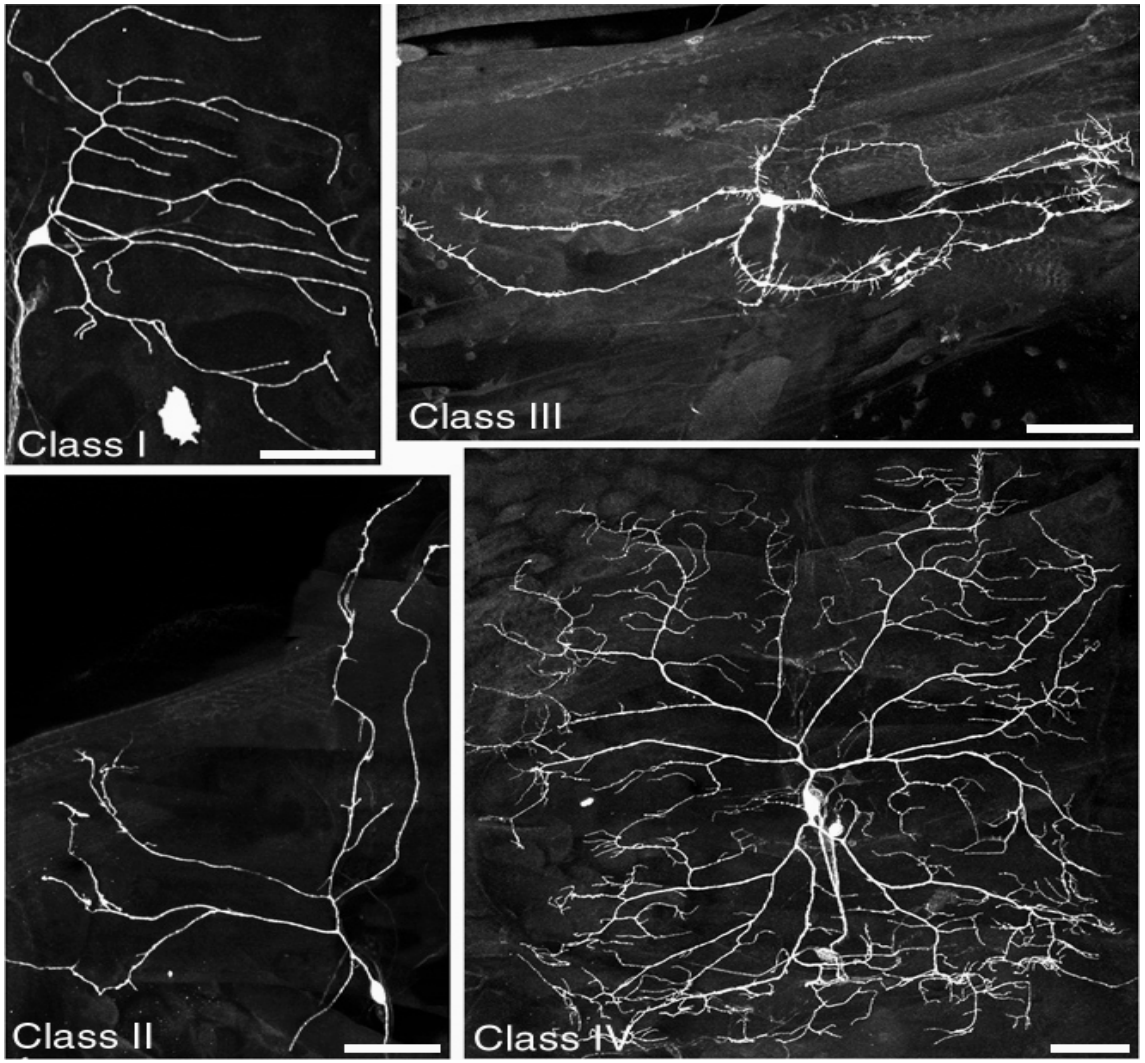


- **Self-avoidance:** spatial separation of isoneuronal dendrites
- **Tiling:** dendrites of neurons of the same class cover a field completely but without redundancy
- **Co-existence:** different classes have highly overlapping dendritic fields

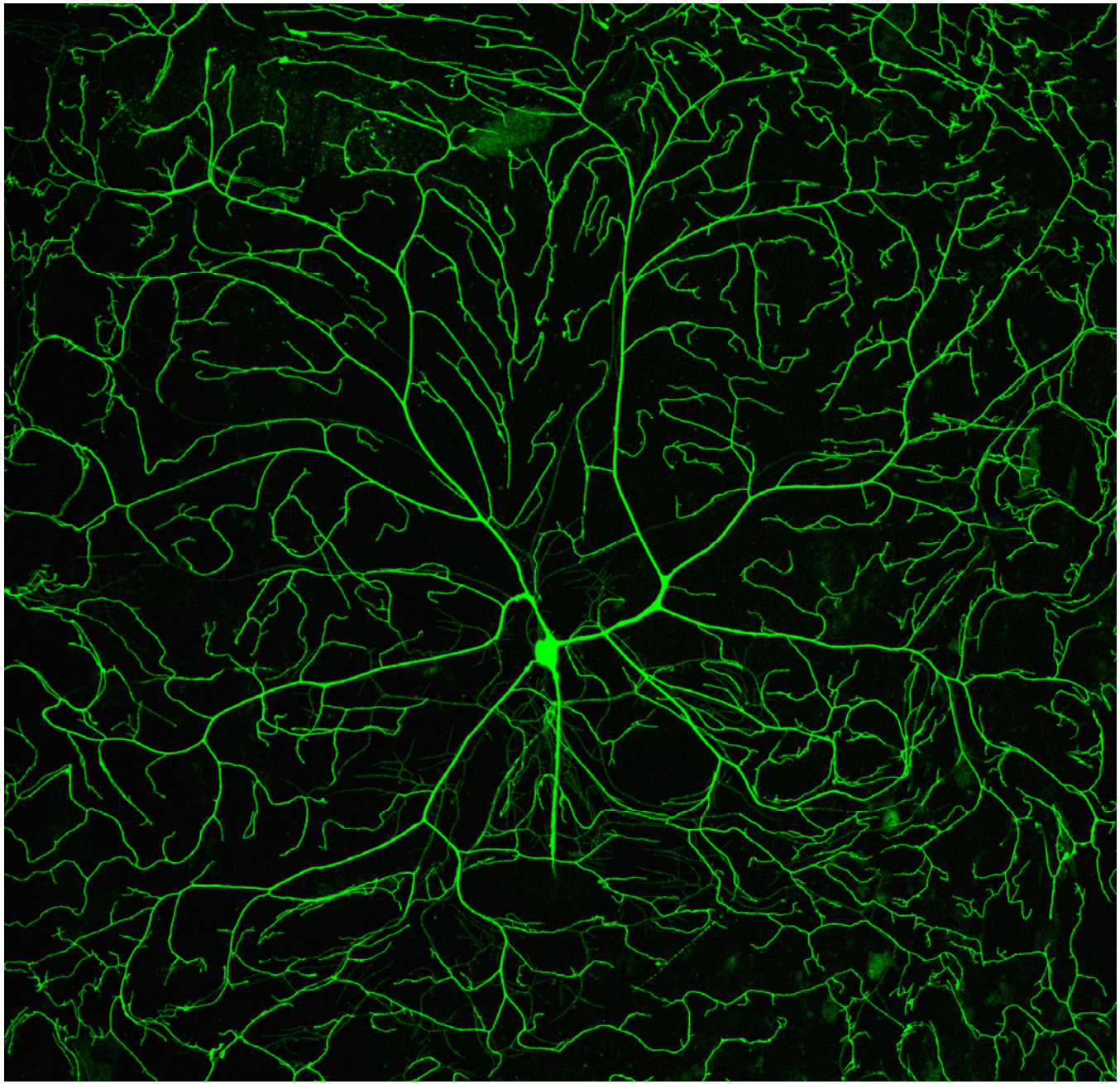
Interactions that pattern dendritic arbors

(1) Repulsions between sister dendrites of a neuron---self avoidance

Dendrites of da neurons exhibit self-avoidance



(Grueber, Jan & Jan., Dev, 2002)

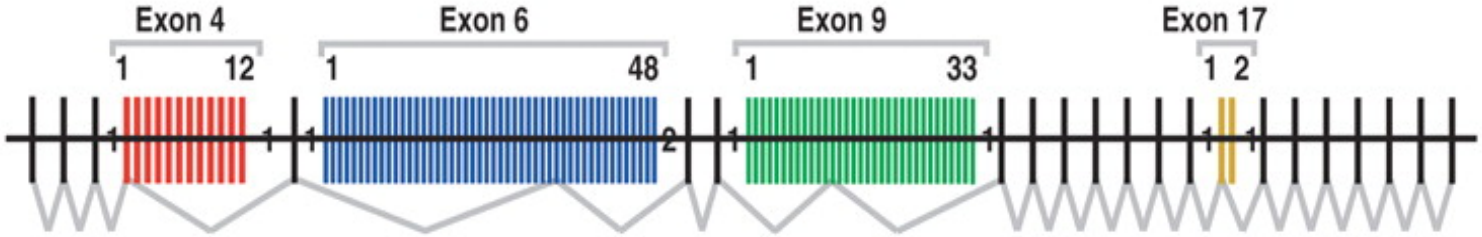


Down syndrome cell adhesion molecule (Dscam) is required for Self-avoidance of dendrites and Co-existence of dendritic fields of the da neurons

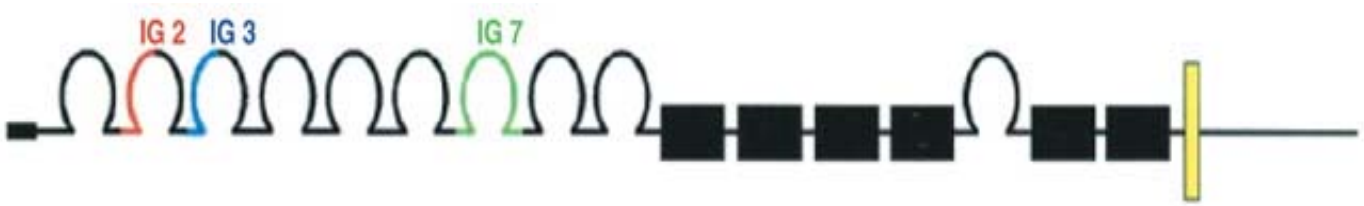
(Peter Soba & Sijun Zhu)

Soba et al., Neuron, 2007
Mathews et al., Cell, 2007 (Grueber, Zipursky labs)
Hughes et al., Neuron, 2007 (Schmucker lab)

Domain structures of Dscam



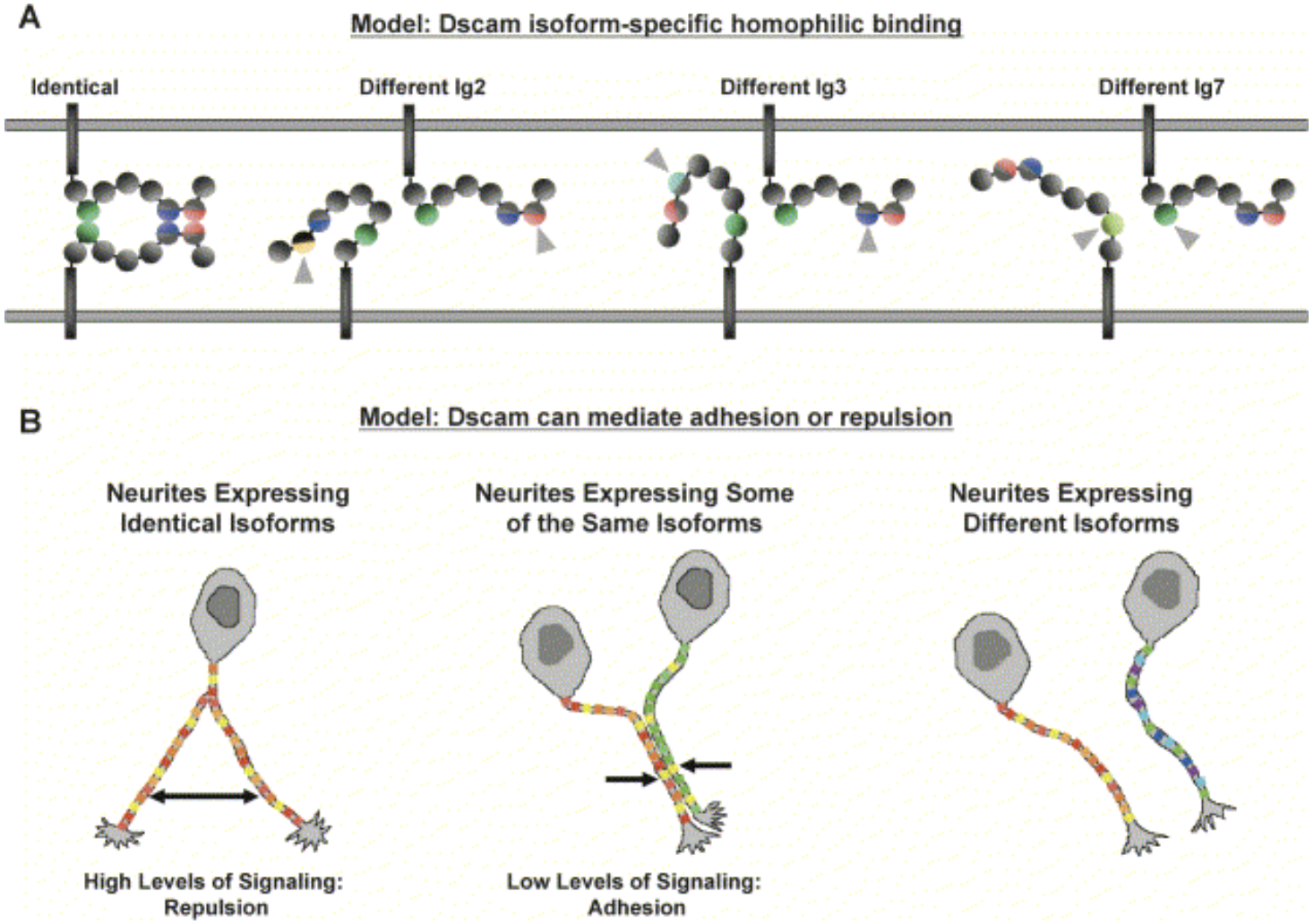
(38,016 isoforms)



Ig domain Fibronectin domain TM domain

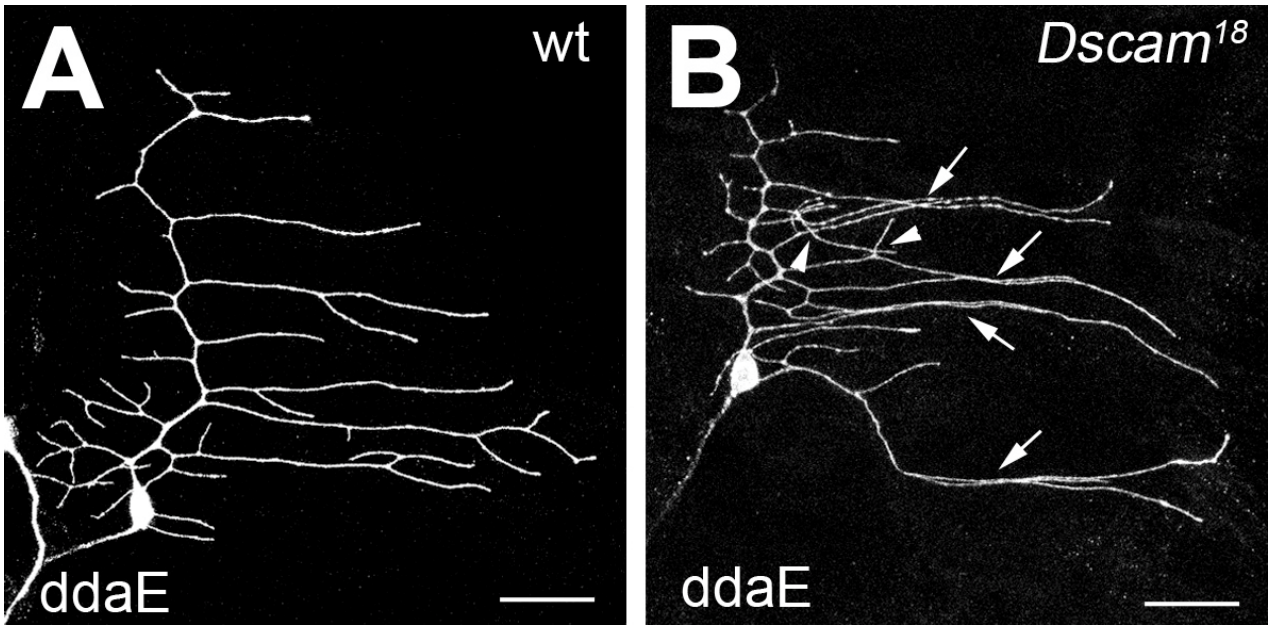
(Schmucker et al., Cell 2000)---Zipursky Lab

A Model for Dscam-Mediated Interactions



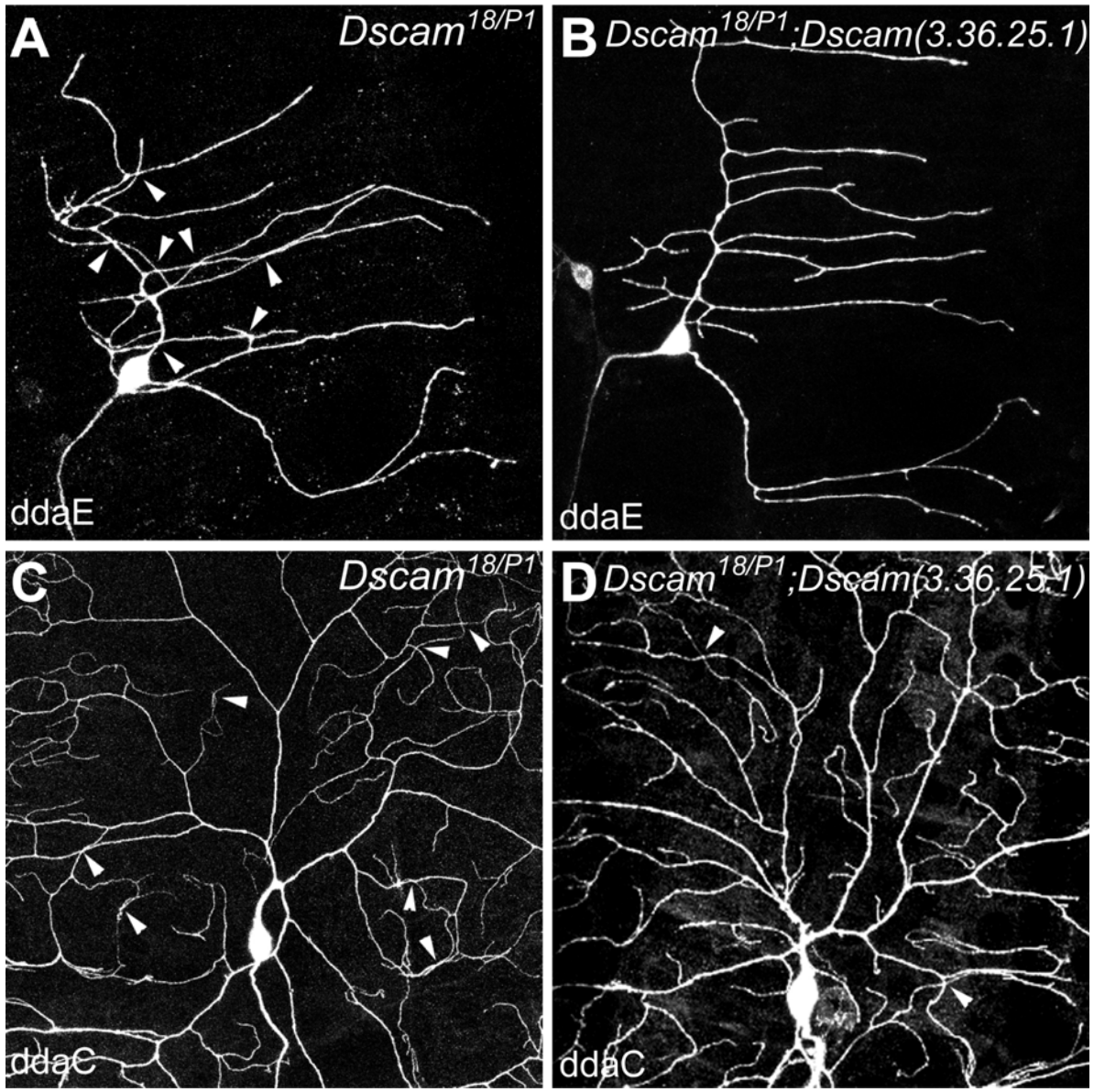
(Wojtowicz et al., Cell, 2004)

Dscam loss of function causes branch segregation and self-avoidance defects



(Soba et al., Neuron, 2007)

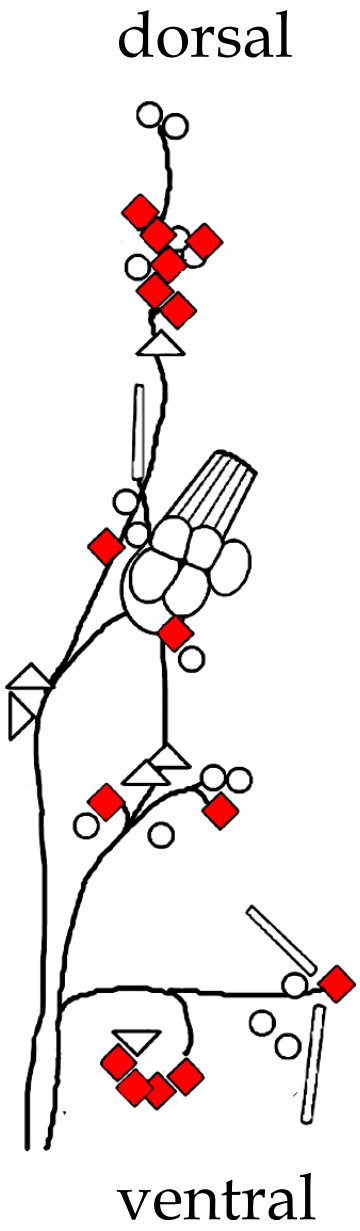
A single arbitrary Dscam isoform can rescue self-avoidance defects in da neurons

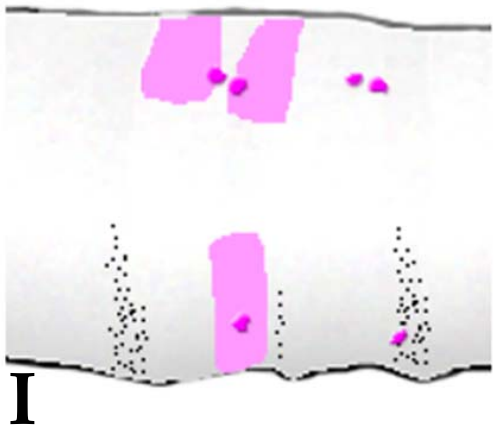


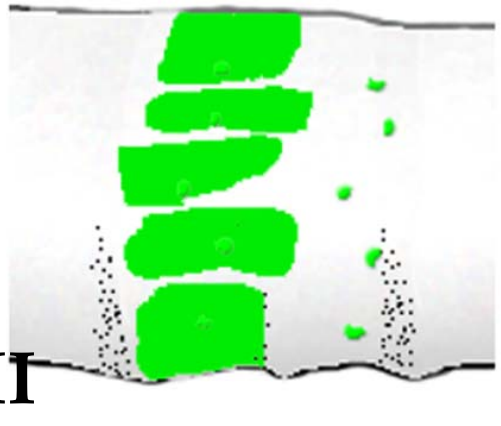
Interactions that pattern dendritic arbors

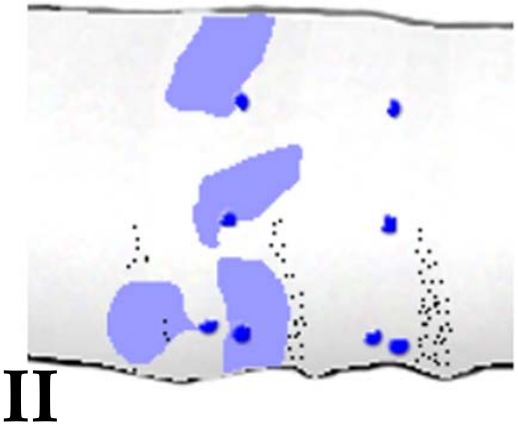
(2) Repulsions between dendrites of neighboring neurons of the same type---tiling

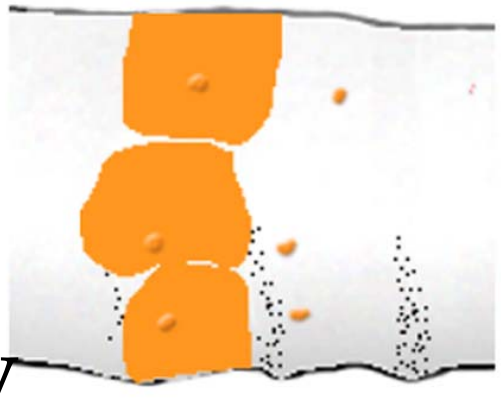
Class III and IV da neurons exhibit “tiling”

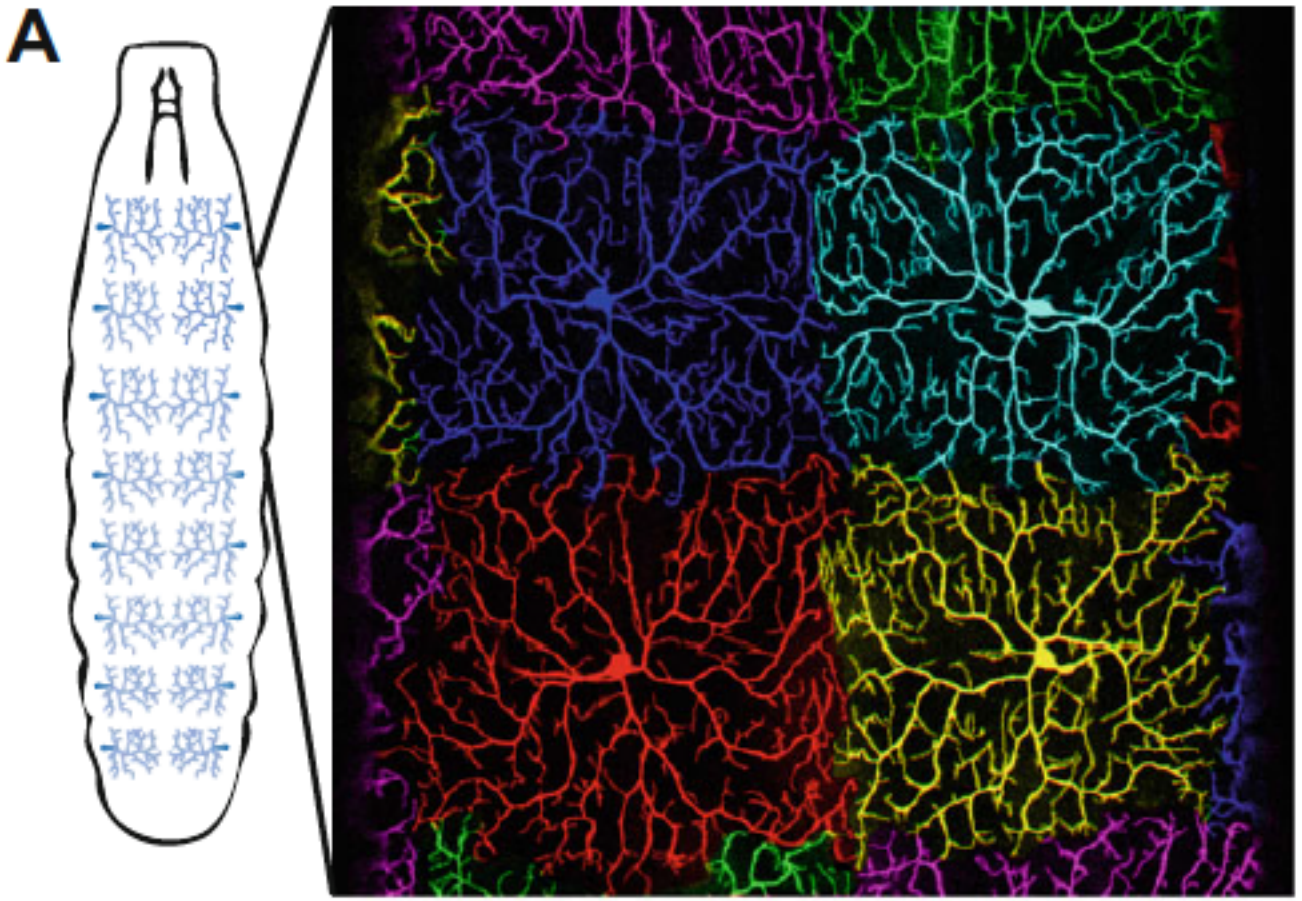




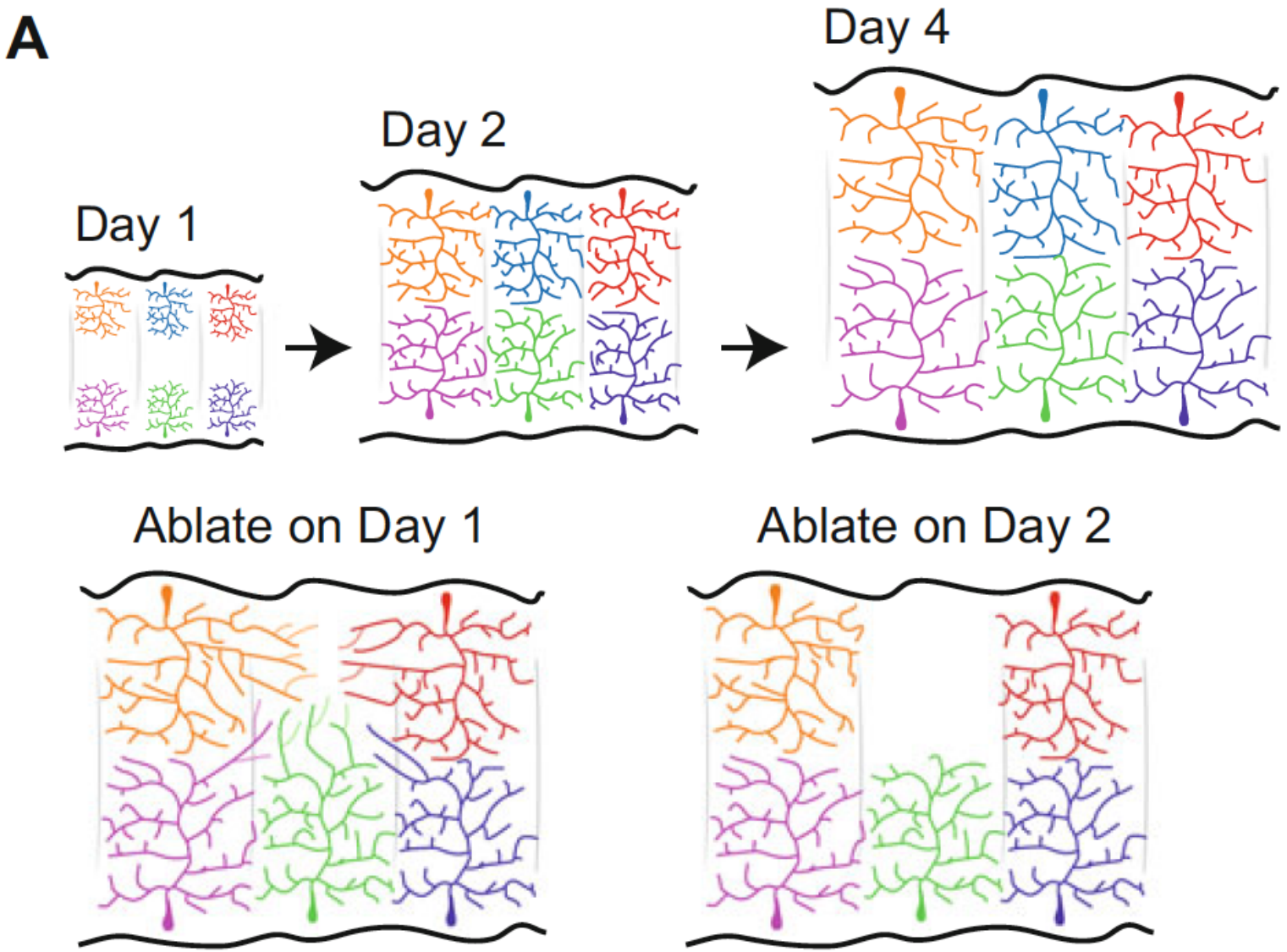






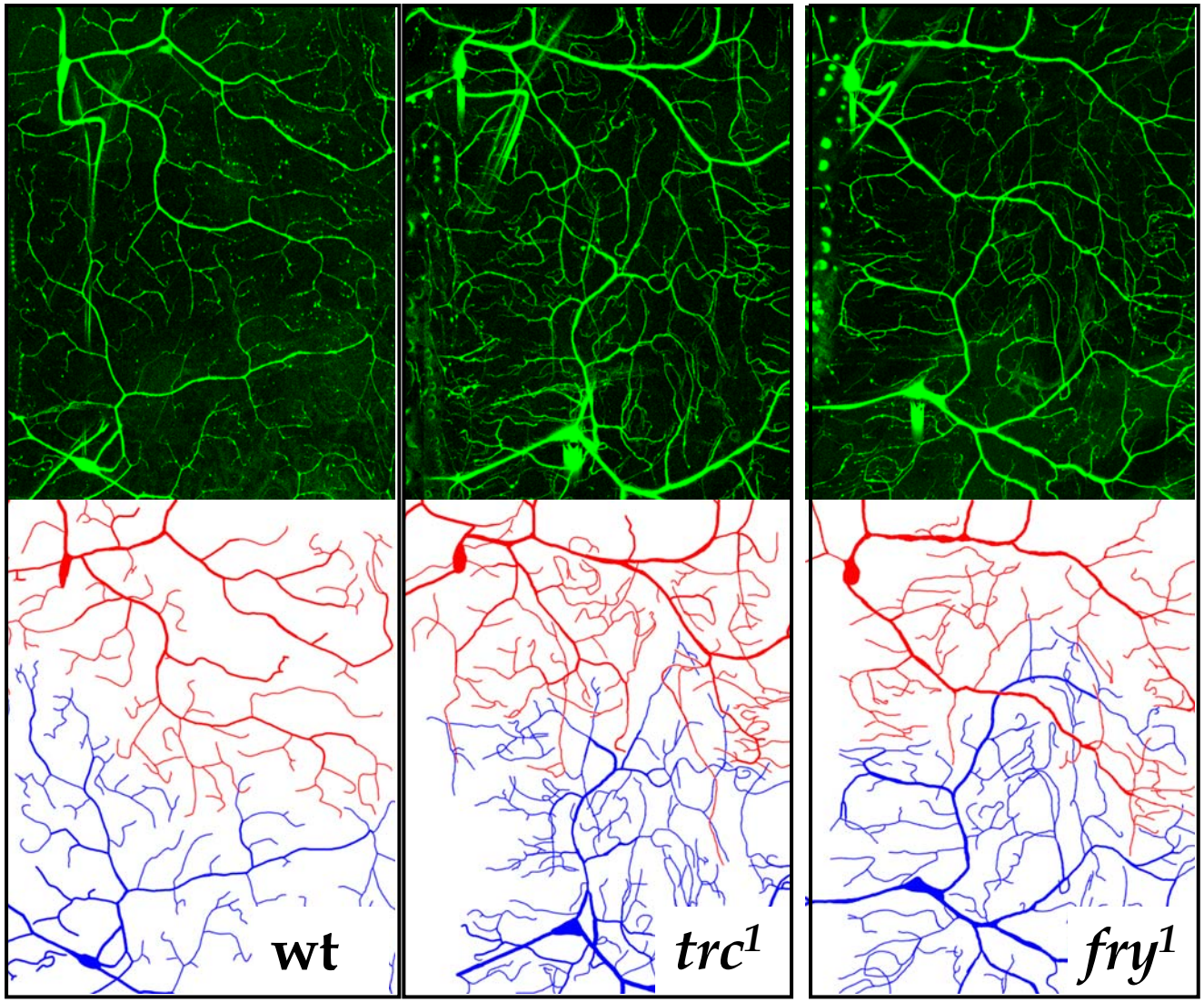


Parrish 2016



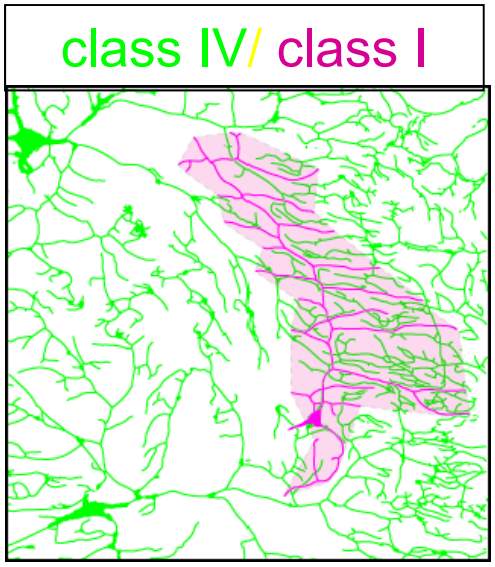
Parrish 2016

Dendritic tiling defect in *trc* and *fry* mutants



(Emoto et al., Cell, 2004)

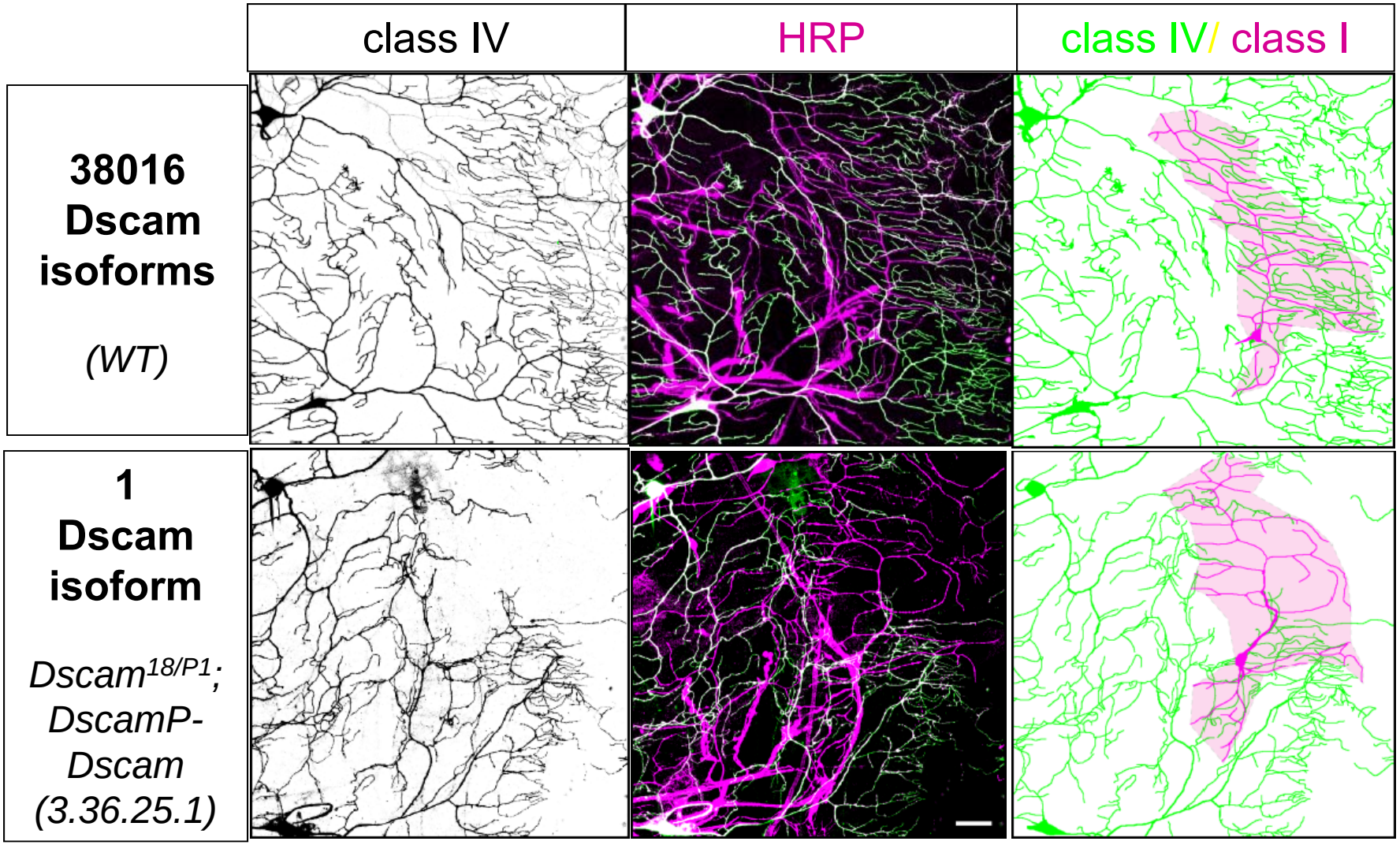
Does Dscam isoform diversity matter for co-existence?



"Diversity" larvae	"no choice" larvae
38016 Dscam isoforms	**1** Dscam isoform
↓	↓
Wild type	*Dscam*^{18}/*Dscam*^{P1}; *DscamP-Dscam(3.36.25.1)*

It is thought that each neuron chooses to express a small subset of Dscam isoforms stochastically

Expression of only one Dscam isoform is incompatible with co-existence of dendritic fields



(Soba et al., Neuron, 2007)

Summary

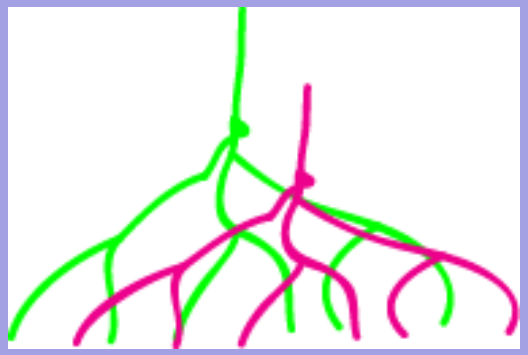
- Expression of a single Dscam isoform is sufficient for self-avoidance of dendrites of individual neurons

But: Diversity matters !

- Expression of the same Dscam isoform in class I and class IV da neurons impairs the co-existence of their dendritic fields

Co-existence of dendritic fields likely requires divergent Dscam isoform expression of individual da neurons

"Diversity" (wild type)



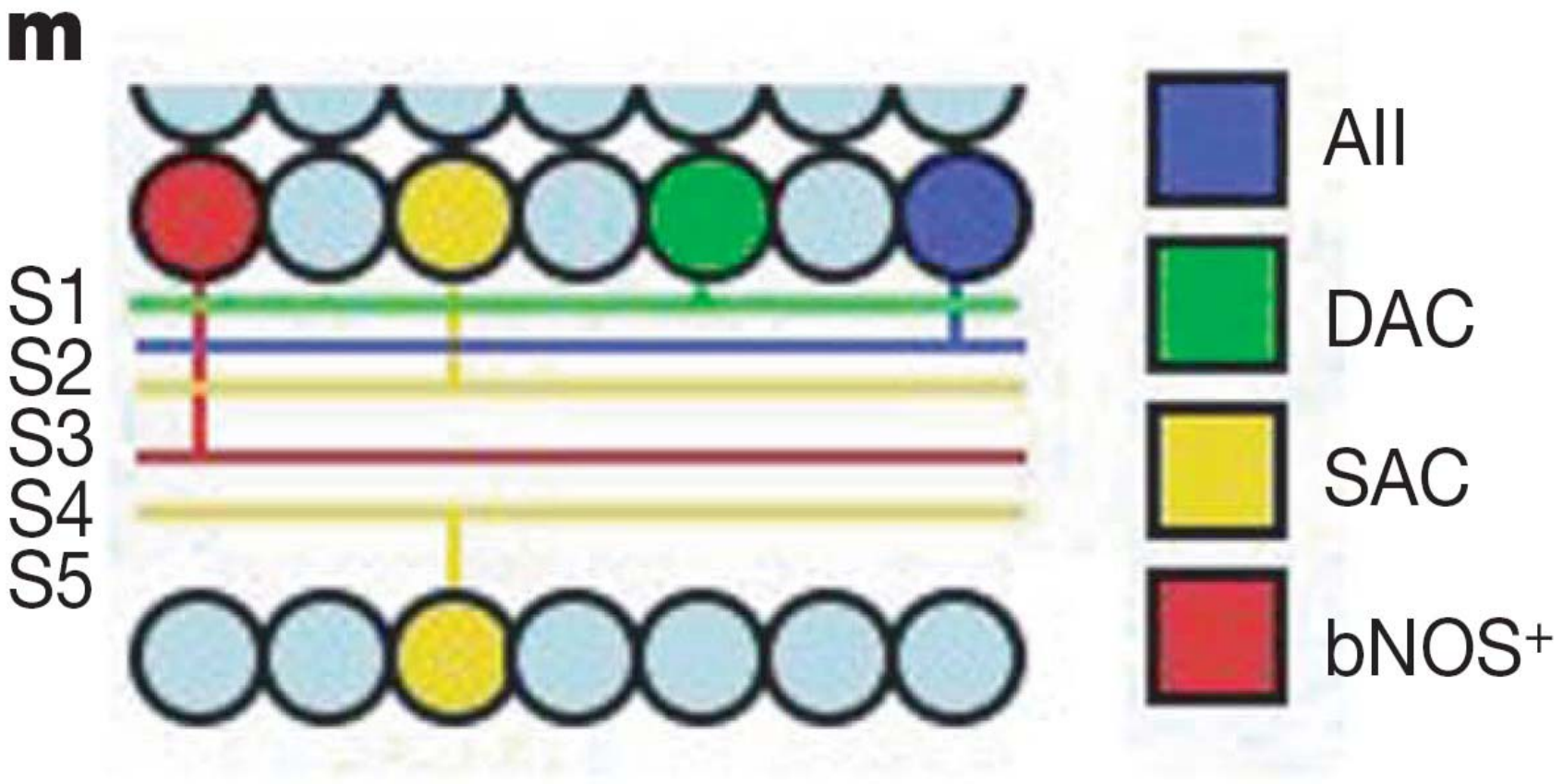
divergent Dscam isoform expression

"no choice"

common Dscam isoform expression

Is the role of Dscam in dendrite development evolutionarily conserved?

Stratification of different amacrine neurites in the inner plexiform layer

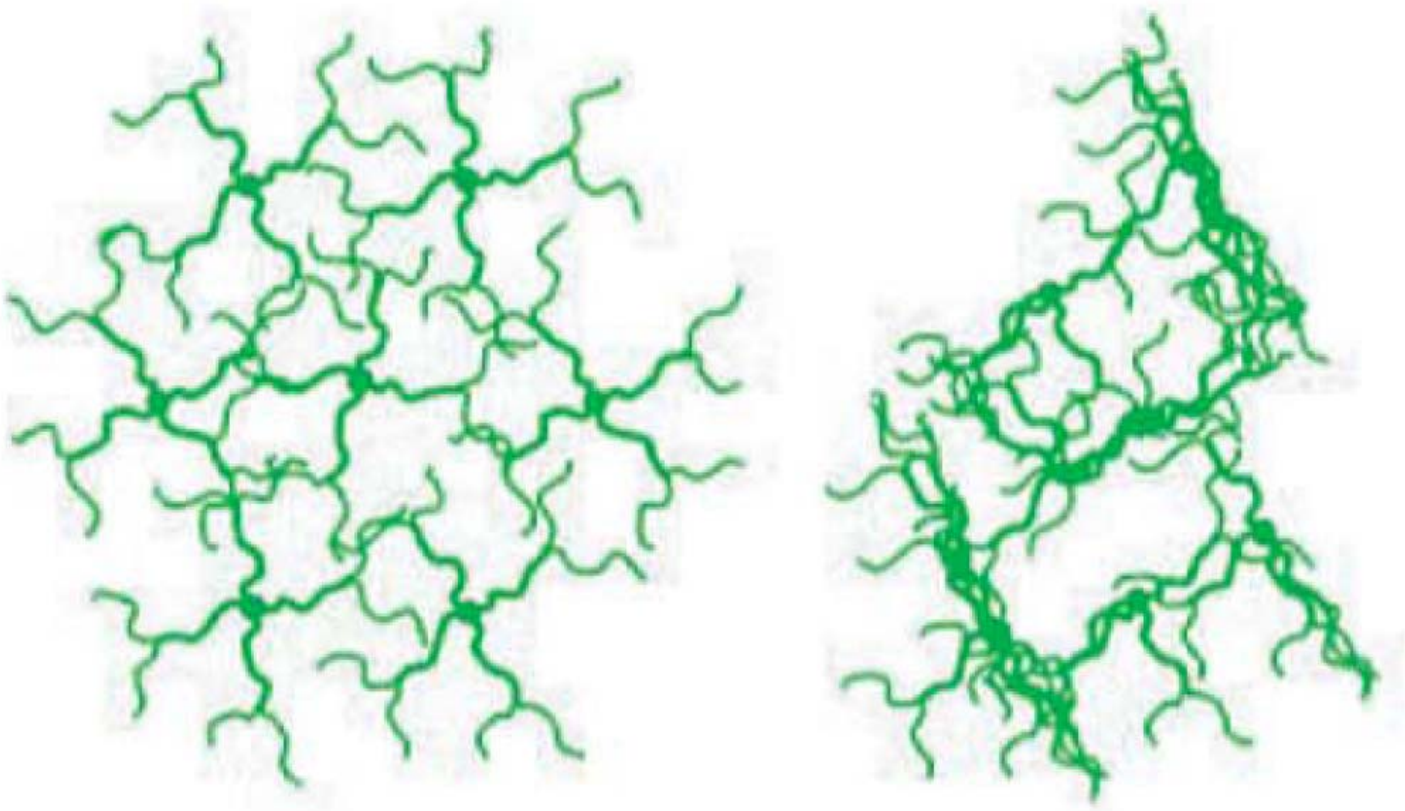


(Fuerst et al., Nature, 2008)

n *Dscam*-positive cell type

Wild-type retina

Dscam$^{-/-}$ retina

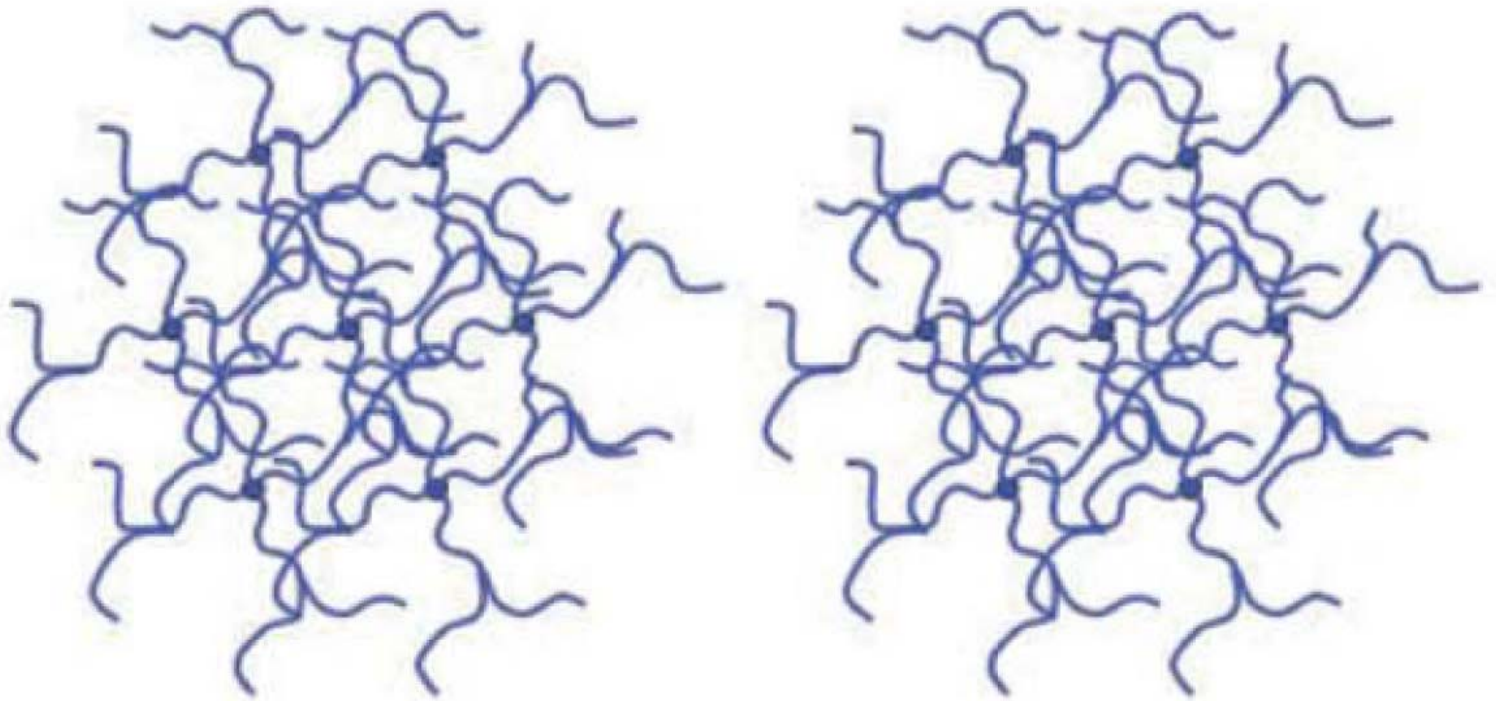


(Fuerst et al., Nature, 2008)

Dscam-negative cell type

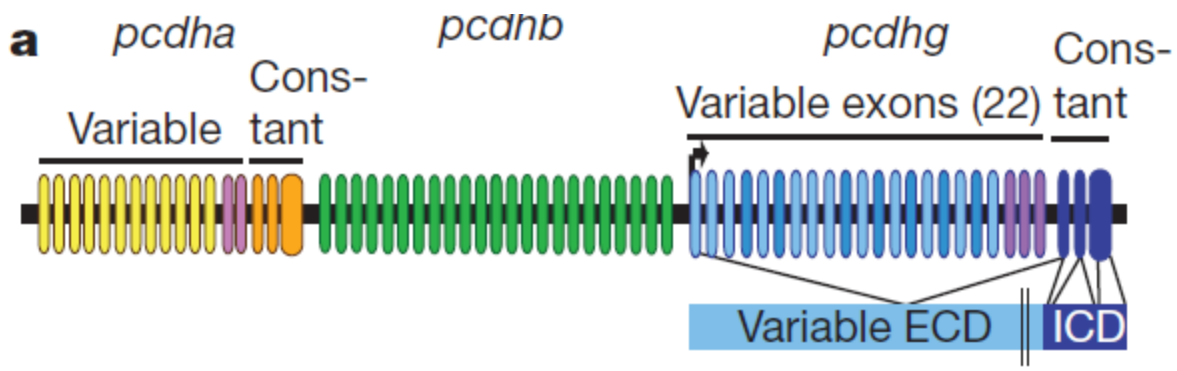
Wild-type retina

Dscam$^{-/-}$ retina



(Fuerst et al., Nature, 2008)

Protocadherins (Pcdh) mediates dendritic self-avoidance
Lefebvre et al., Nature, 2012 (J Sanes, T maniatis Labs)

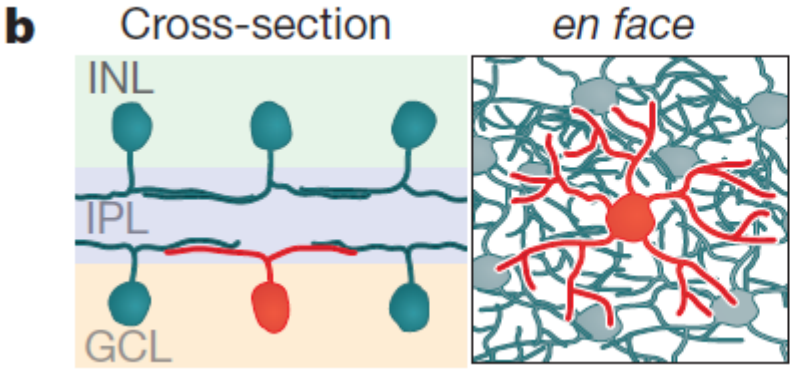


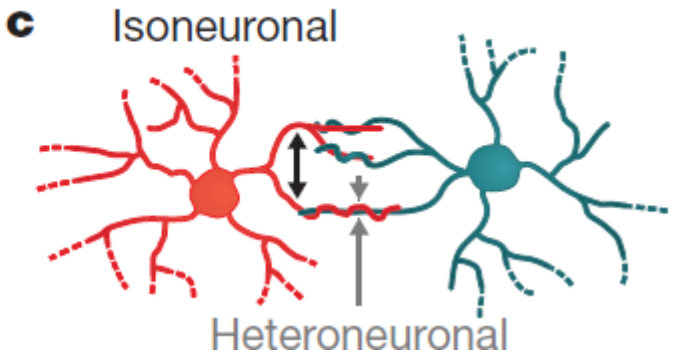
- Cluster of 58 *Pcdh* genes: 14 *Pcdha*, 22 *Pcdhb*, 22 *Pcdhg*

- Isoform specific homophilic adhesion

- Expressed Stochastically and combinatorially in single neurons

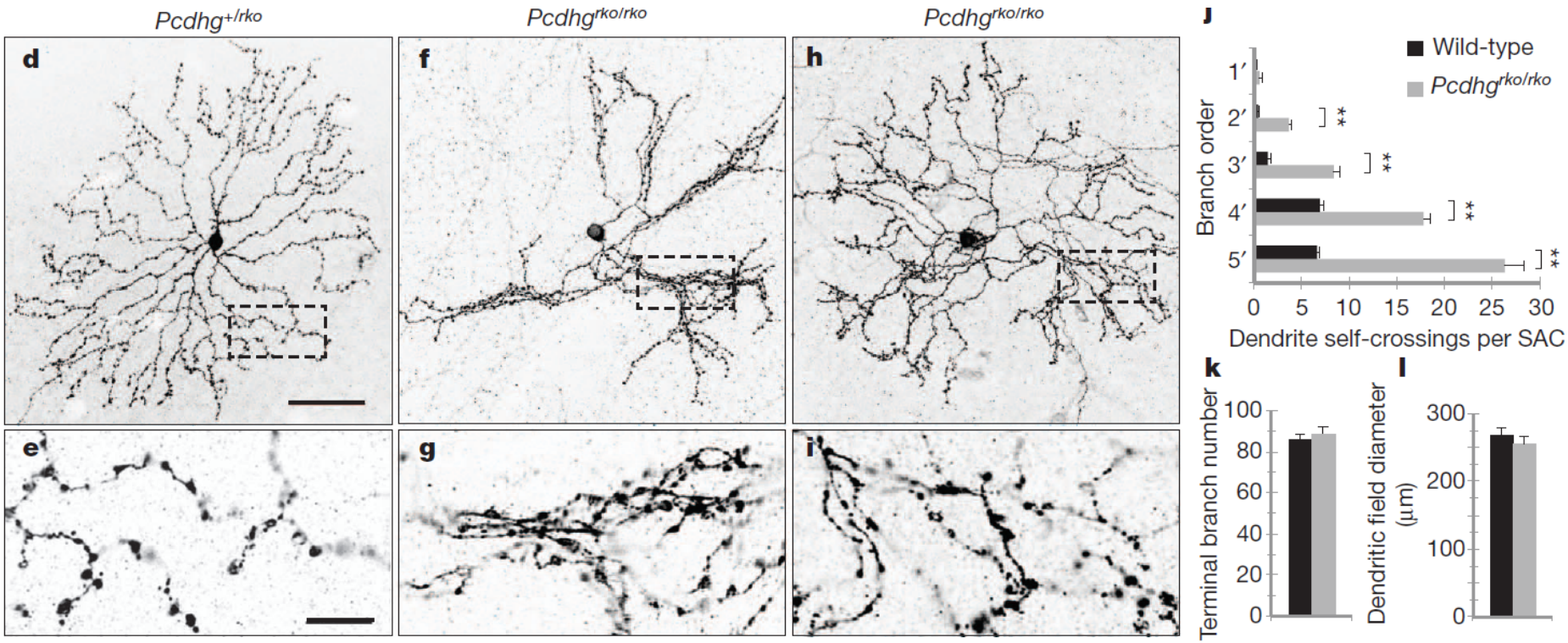
Dendrites of Starburst amacrine cells (SACs) self-avoid but interact with like neurons: they can discriminate self from non-self





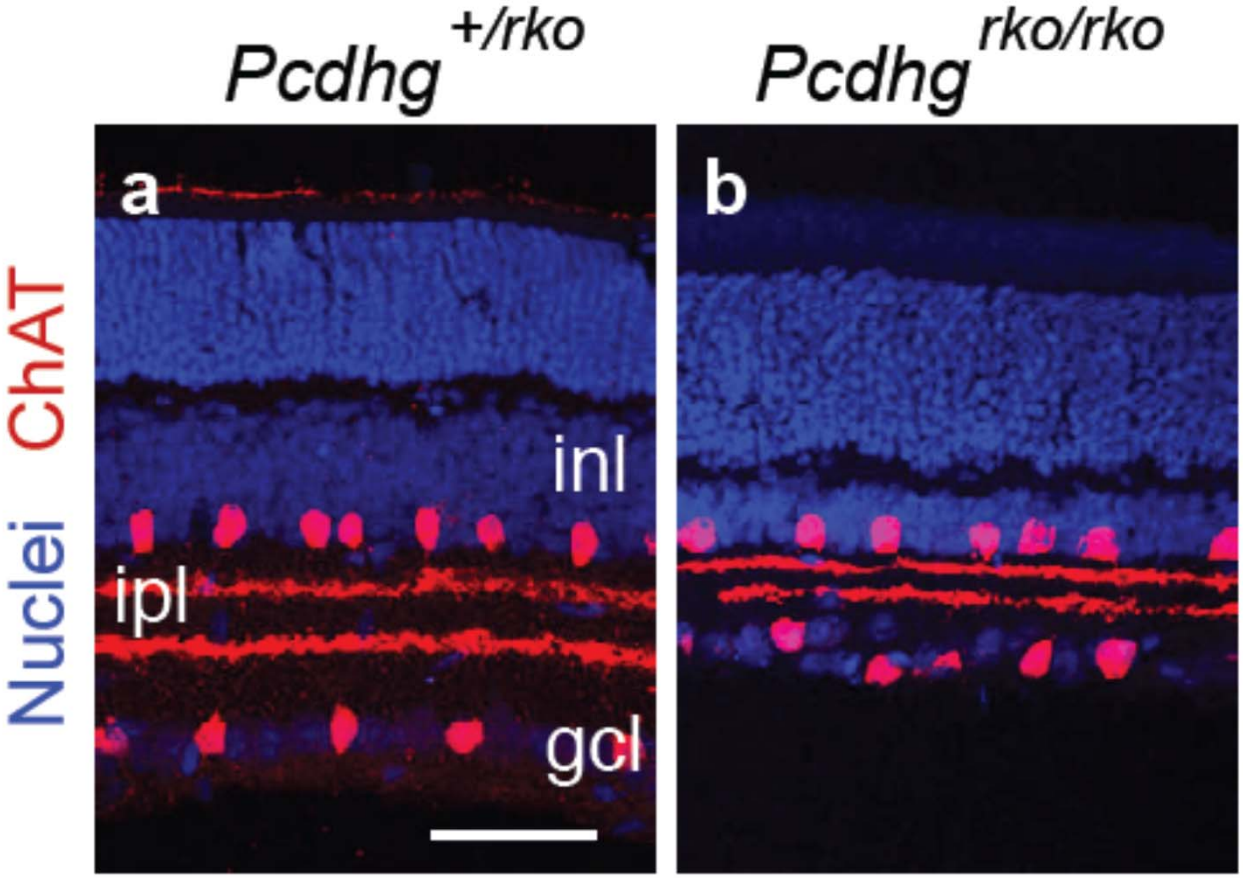
Lefebvre et al., Nature, 2012

Pcdhgs are required for self-avoidance of SAC dendrites



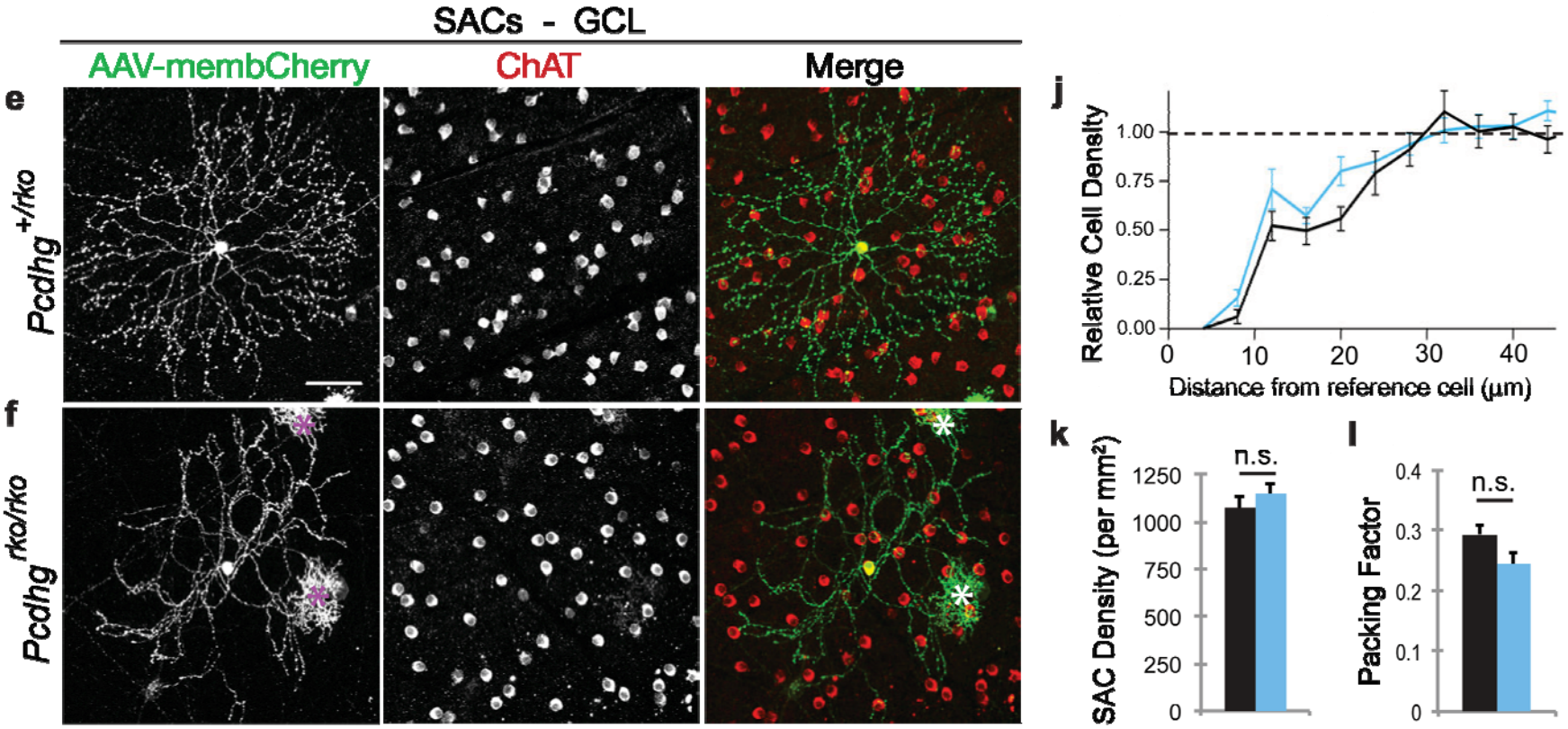
Lefebvre et al., Nature, 2012

Laminar targeting of SACs is not affected in the absence of Pcdhgs



Lefebvre et al., Nature, 2012

Mosaic arrangement of SACs is not affected in the absence of Pcdhgs



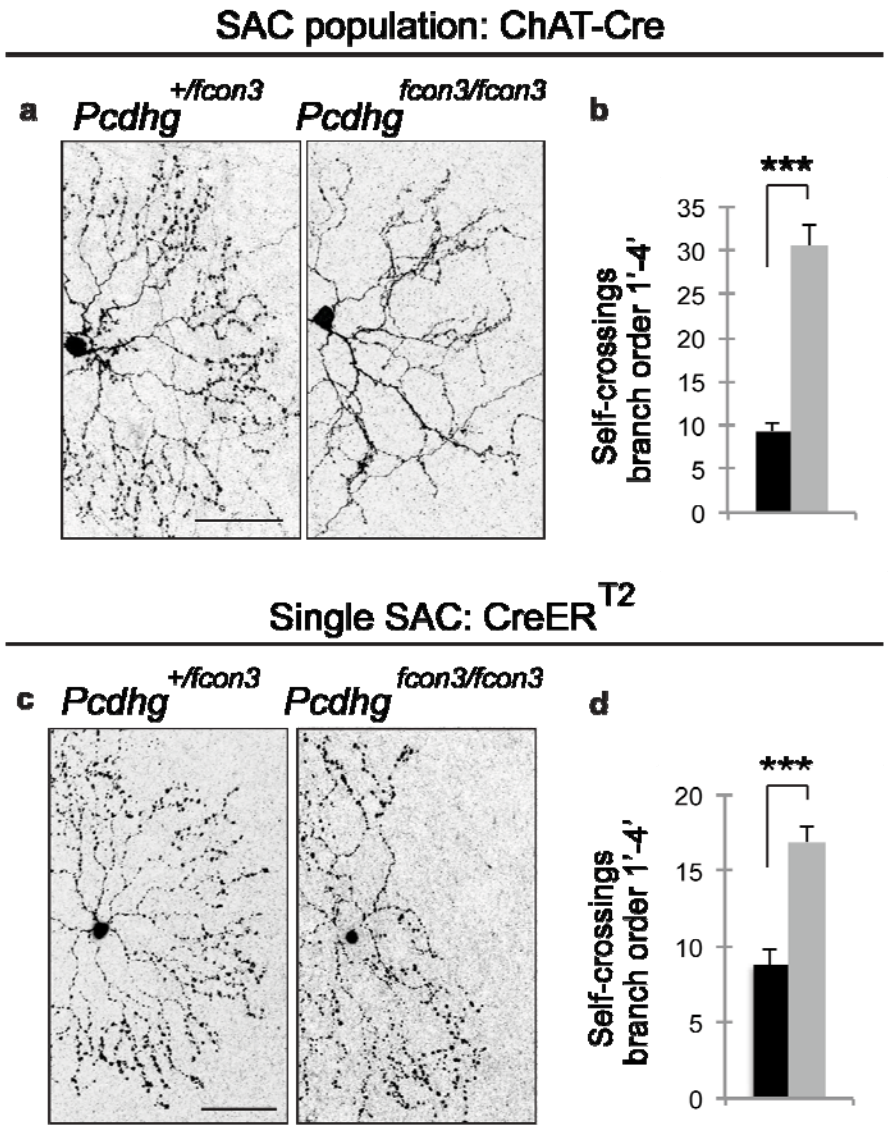
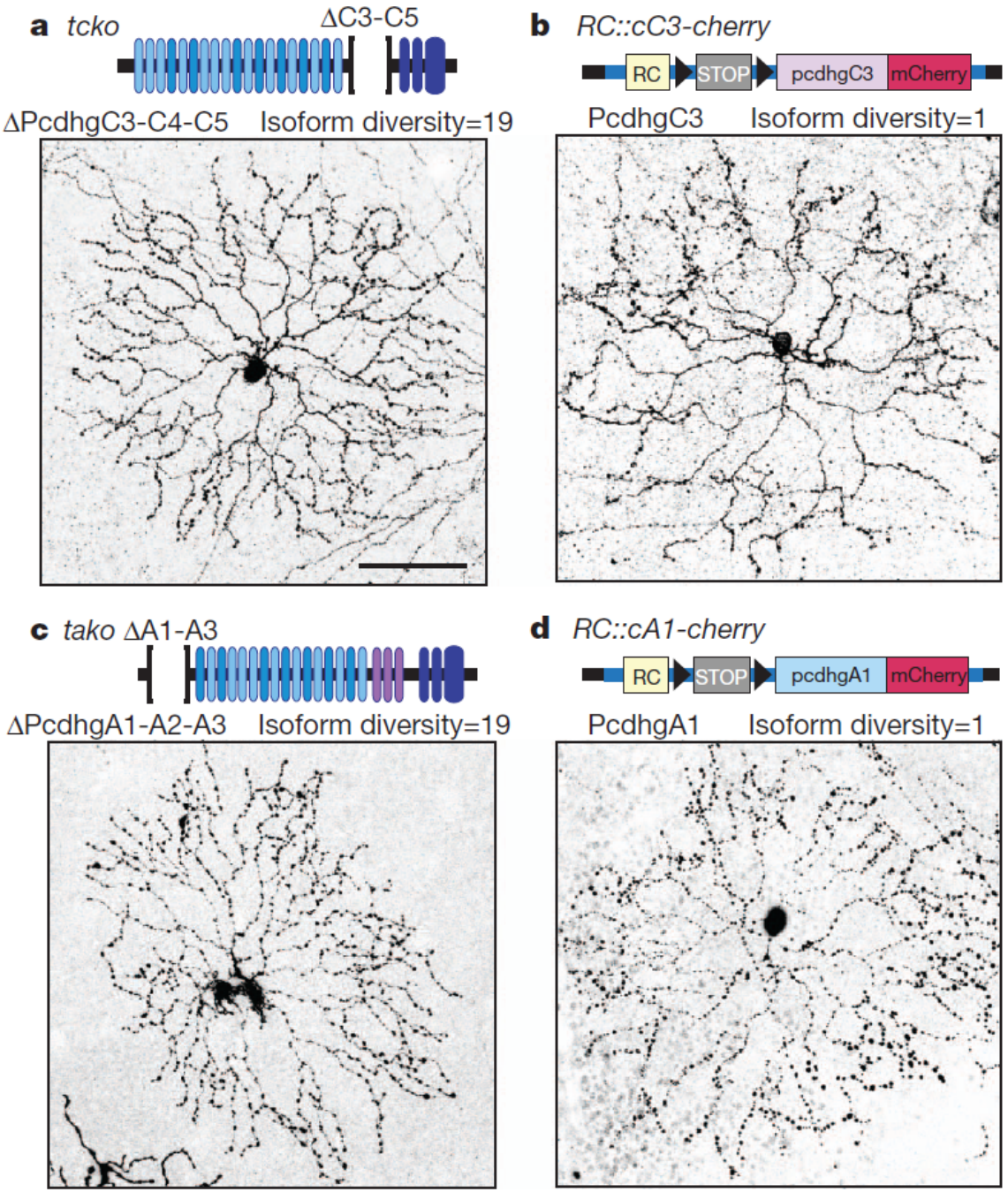
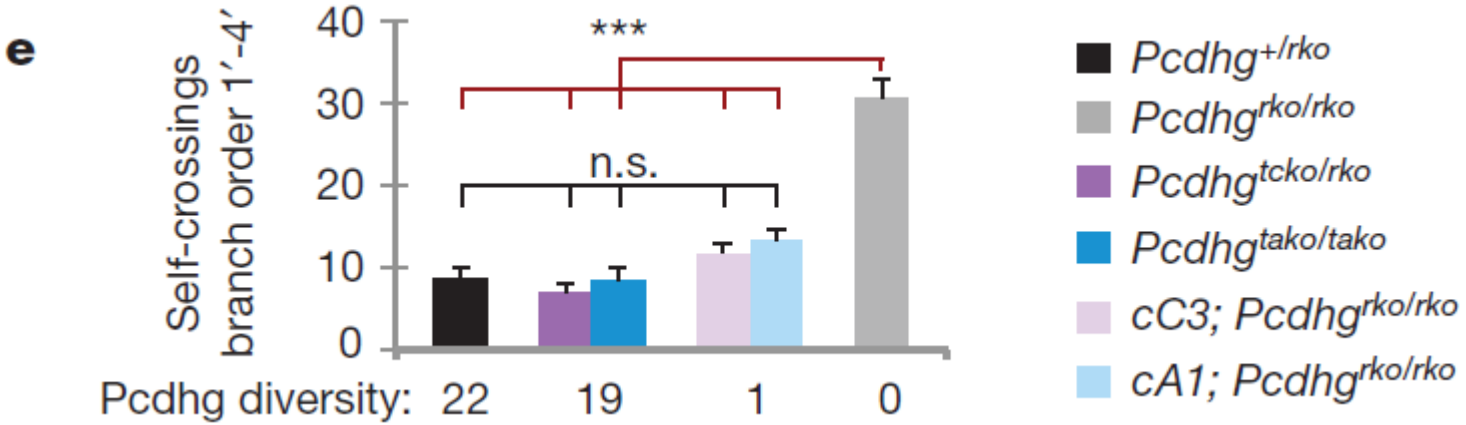


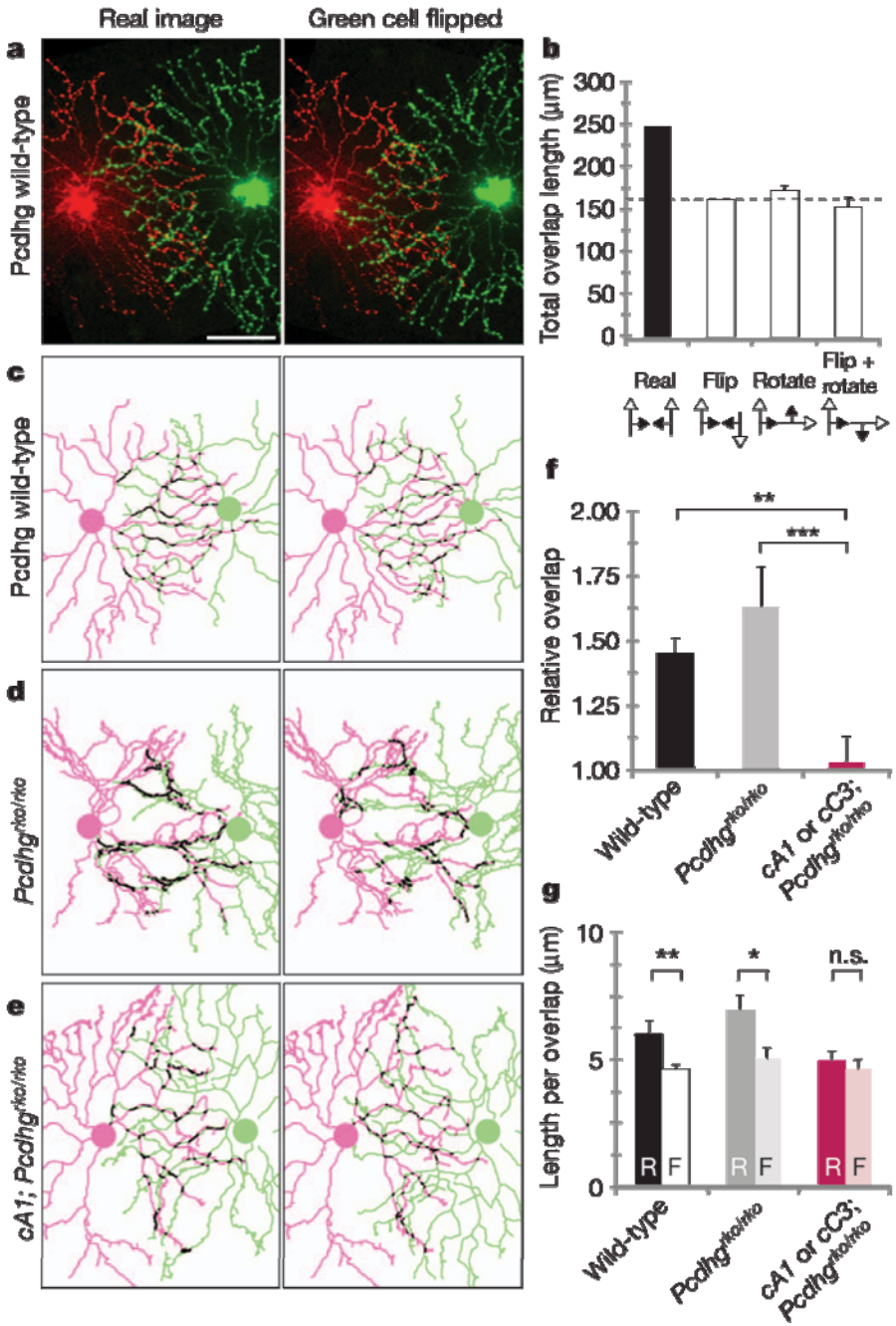
Figure S4. Selective removal of Pcdhgs in SAC population and in single SACs disrupts dendrite self-avoidance.


a tcko
ΔC3-C5
ΔPcdhgC3-C4-C5 Isoform diversity=19
b RC::cC3-cherry
RC
STOP
pcdhgC3
mCherry
PcdhgC3 Isoform diversity=1
c tako ΔA1-A3
ΔPcdhgA1-A2-A3 Isoform diversity=19
d RC::cA1-cherry
RC
STOP
pcdhgA1
mCherry
PcdhgA1 Isoform diversity=1

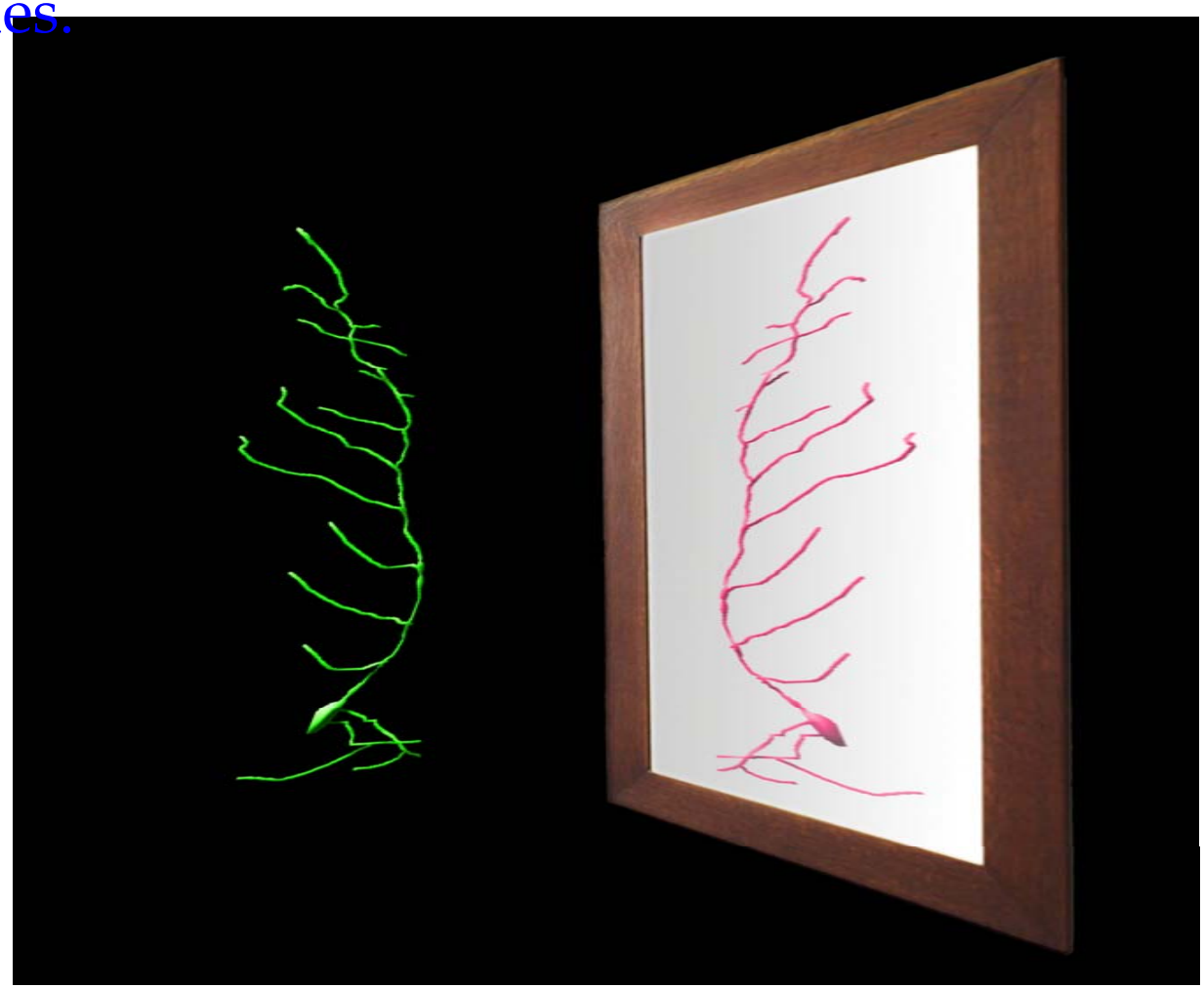
Single isoform is sufficient for dendrite self-avoidance



Lefebvre et al., Nature, 2012


Real image
Green cell flipped
a
Pcdhg wild-type
b
Total overlap length (µm)
300
250
200
150
100
50
0
Real
Flip
Rotate
Flip + rotate
c
Pcdhg wild-type
d
Pcdhg^tko/tko
e
cA1; Pcdhg^tko/tko
f
Relative overlap
2.00
1.75
1.50
1.25
1.00
**
***
Wild-type
Pcdhg^tko/tko
cA1 or cC3; Pcdhg^tko/tko
g
Length per overlap (µm)
10
5
0
**
*
n.s.
R
F
Wild-type
Pcdhg^tko/tko
cA1 or cC3; Pcdhg^tko/tko

How does a neuron self-recognize?
Fly and mammal use similar strategy but different molecules.



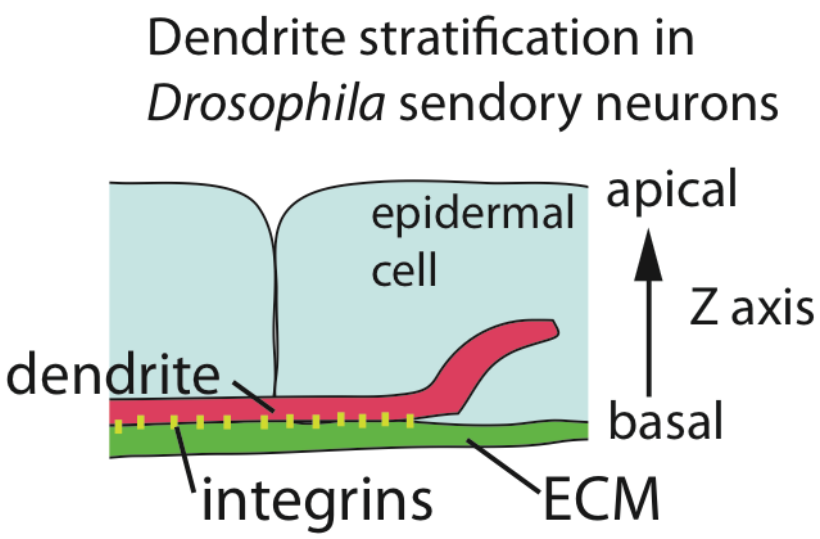
Three interactions that pattern dendritic arbors

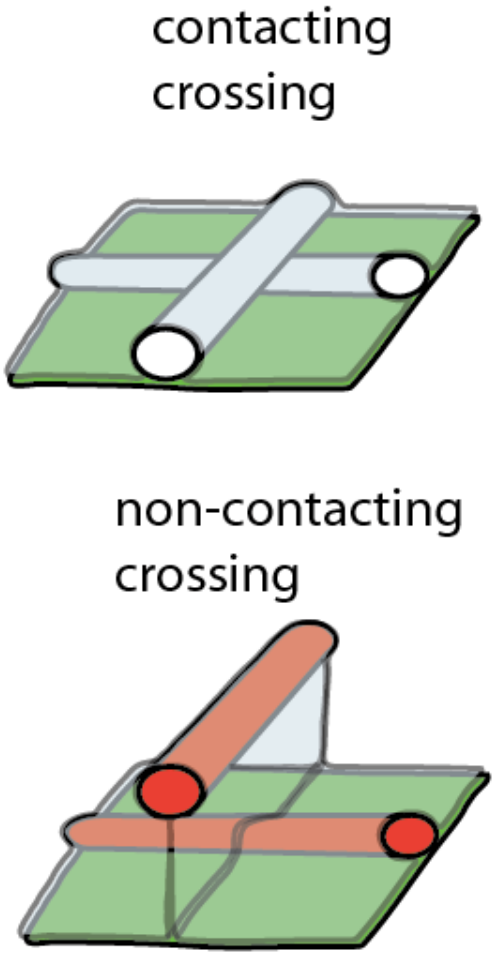
(3) Dendrites are tethered to ECM, a 2D space to facilitate the repulsion-mediated self-avoidance and tiling

(Kim et al., Neuron, 2012, Grueber lab)

(Han et al., Neuron, 2012)

Self-avoidance requires dendrites to be restricted in a 2D space to facilitate the Dscam-mediated repulsions between sister dendrites





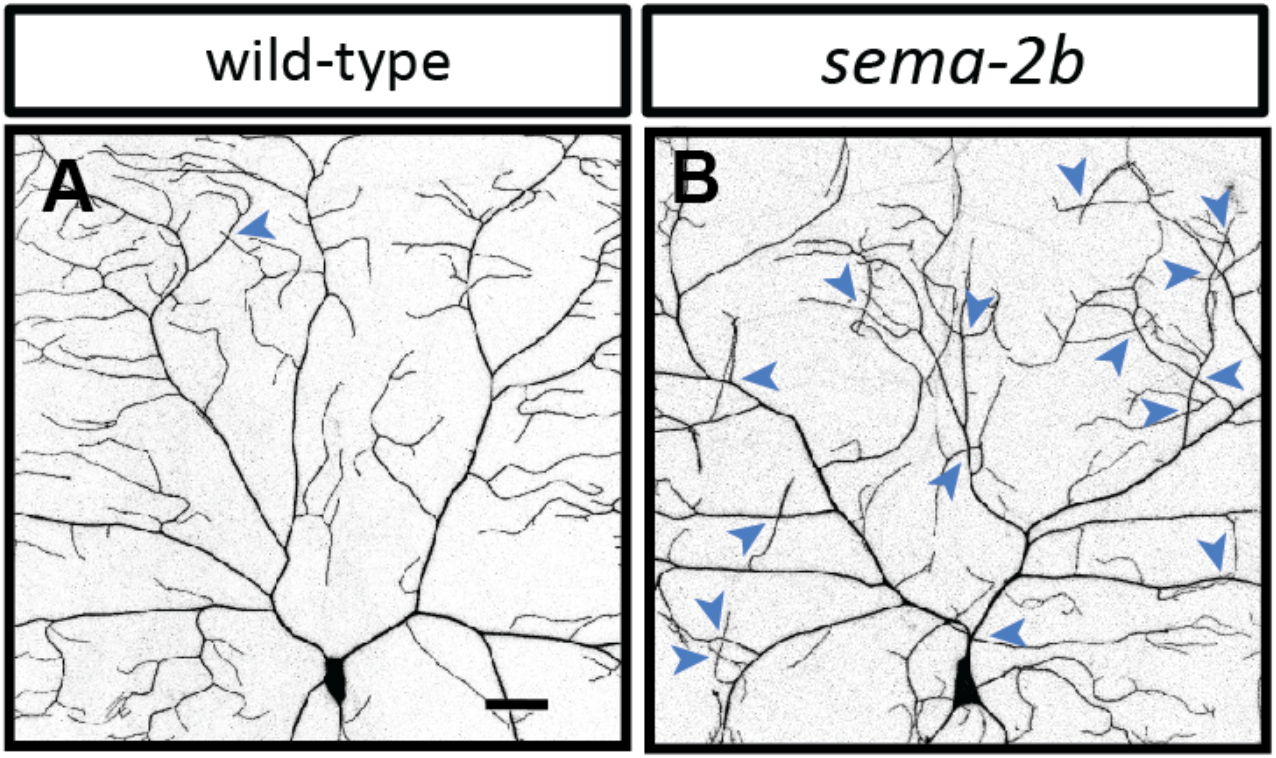
Kim et al., Neuron, 2012 (Grueber Lab)

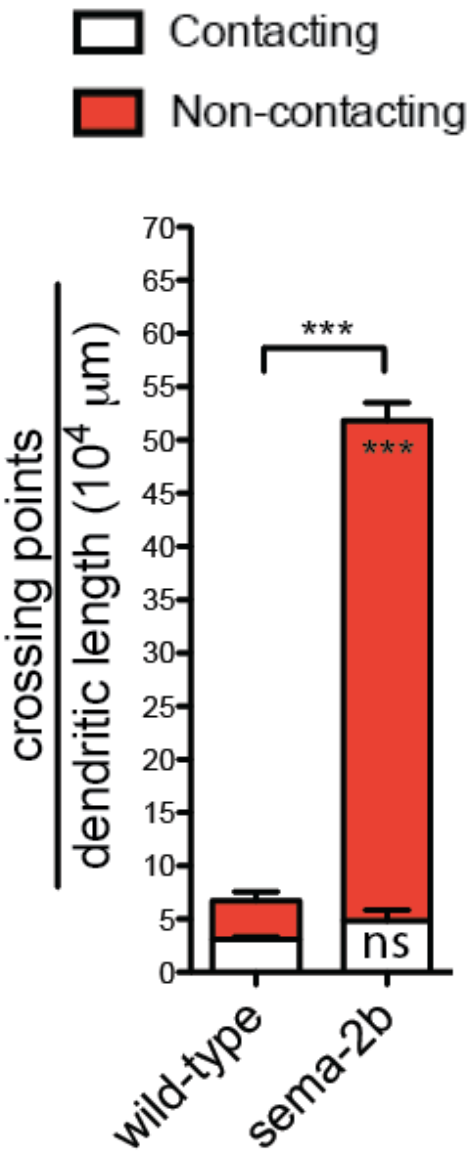
Han et al., Neuron, 2012

Molecules involved in restricting dendrites to 2D space

- Integrins (Kim et al., Neuron, 2012; Han et al., Neuron, 2012)
- Trc and Fry, components of Hippo kinase pathway (Han et al., Neuron, 2012)
- Ret kinase (Soba et al., eLife, 2015)
- Semaphorin-2b and Plexin B (Meltzer et al., Neuron, 2016)

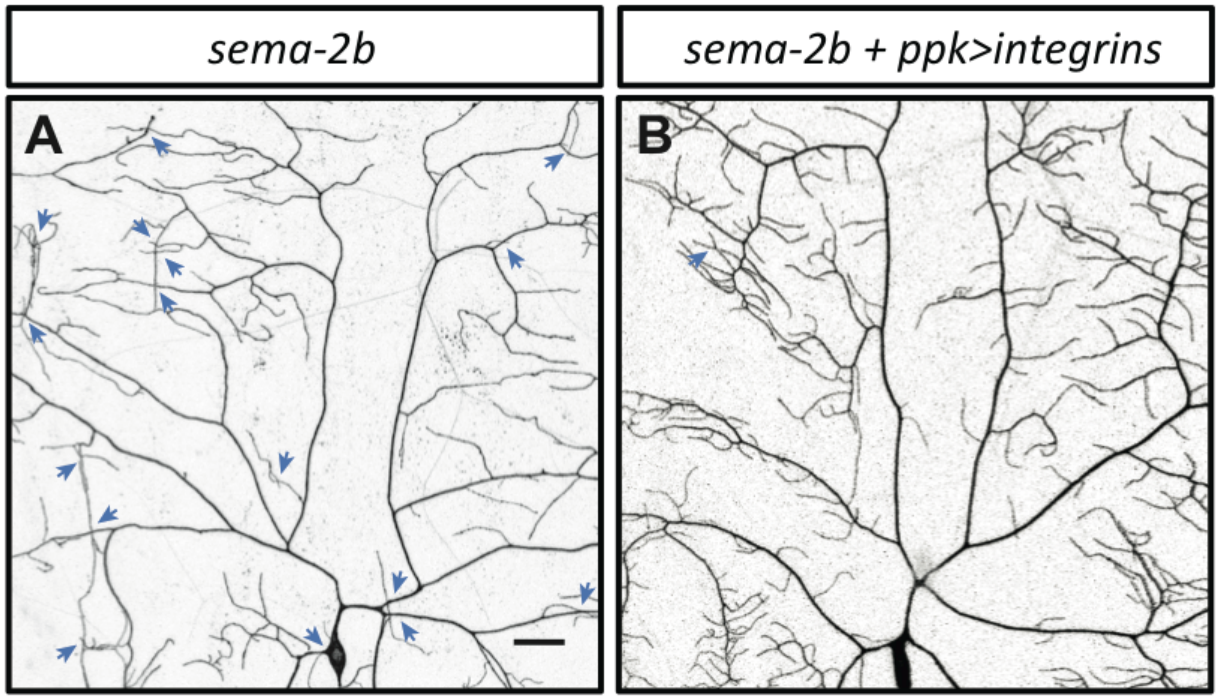
Non-contacting crossings increase in the *sema-2b* mutants

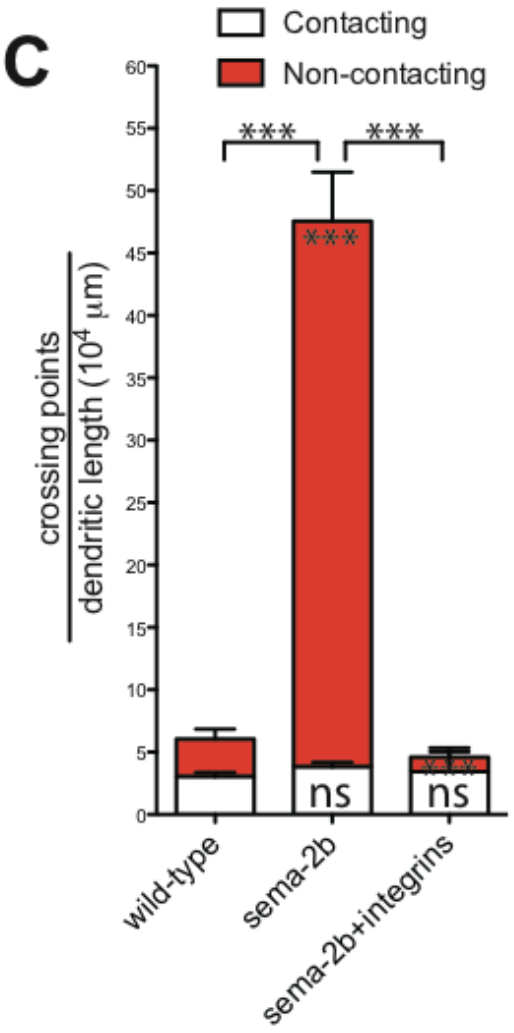




(Meltzer et al.,Neuron 2016)

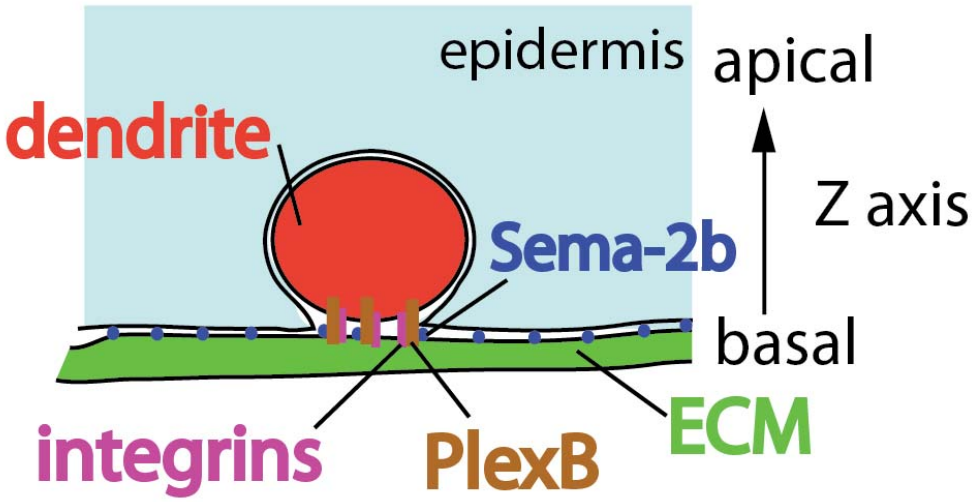
Integrin overexpression in neurons rescues their dendrite crossing phenotype

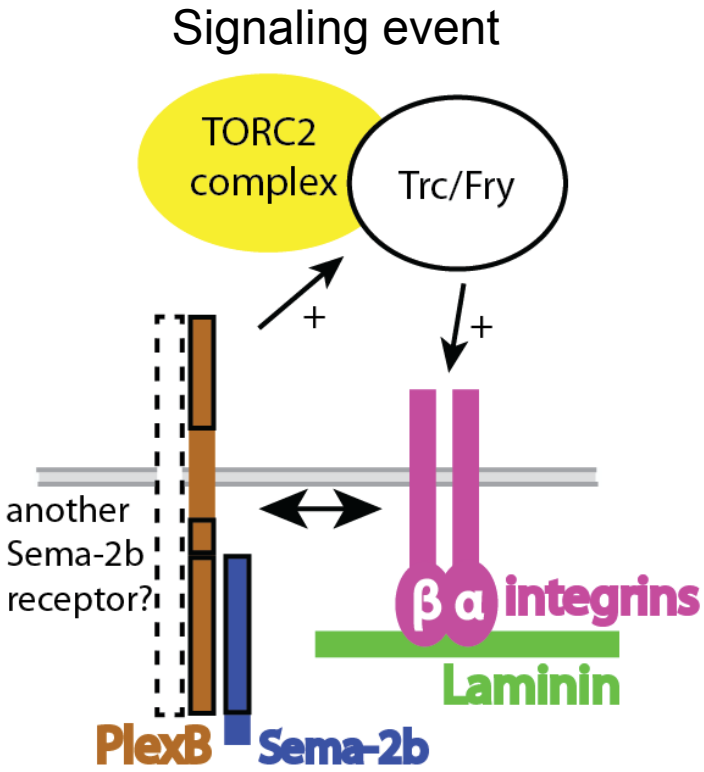




(Meltzer et al., Neuron 2016)

Epidermis-derived Semaphorin-2b promotes dendrite-substrate adhesion in *Drosophila* sensory neurons

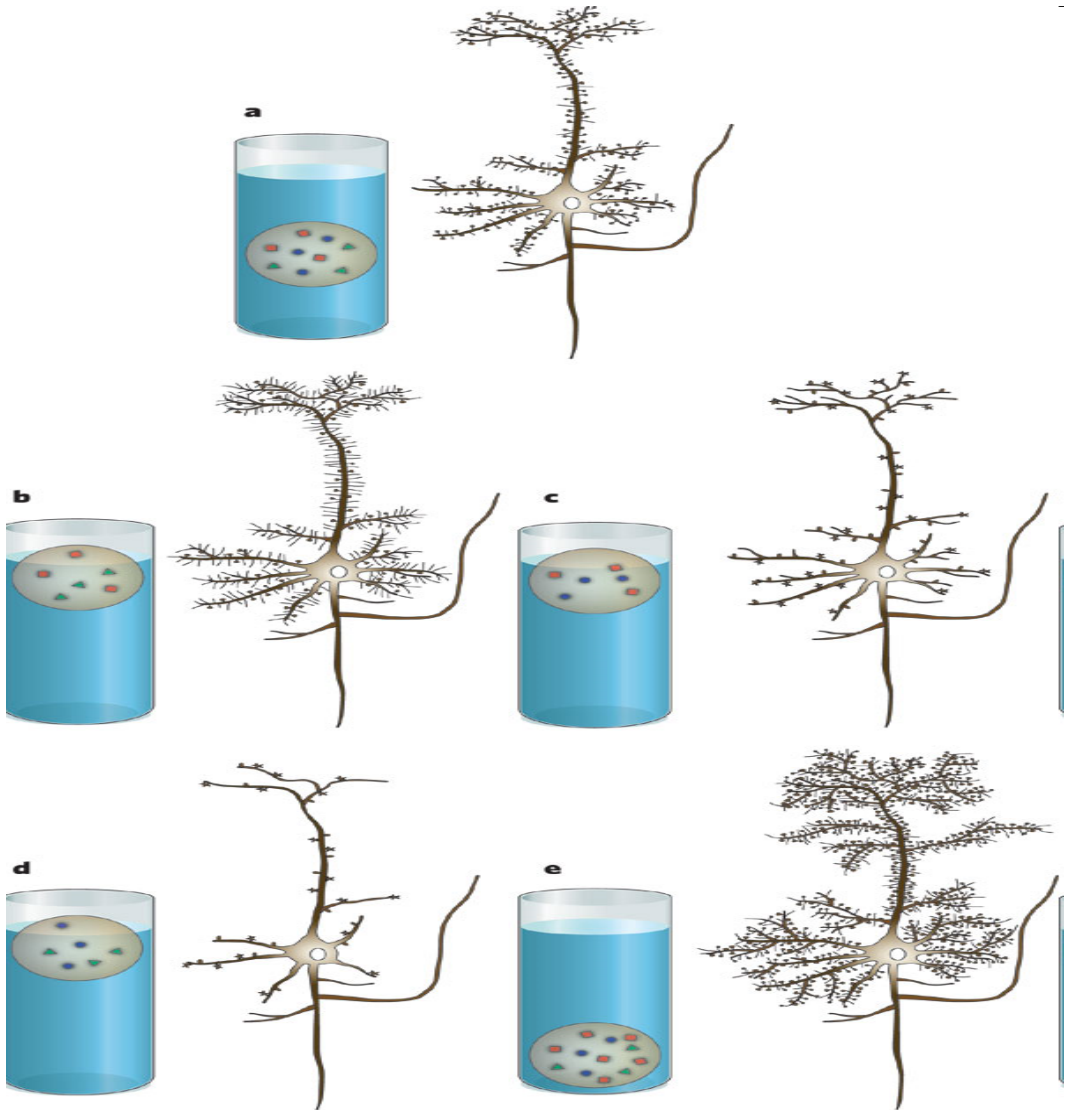




(Meltzer et al., Neuron, 2016)

Studies of mutations affecting dendrite morphogenesis may provide insights into the cause of certain neurological disorders.

Dendrite defects are often found to be associated with mental disorders



Fragile X

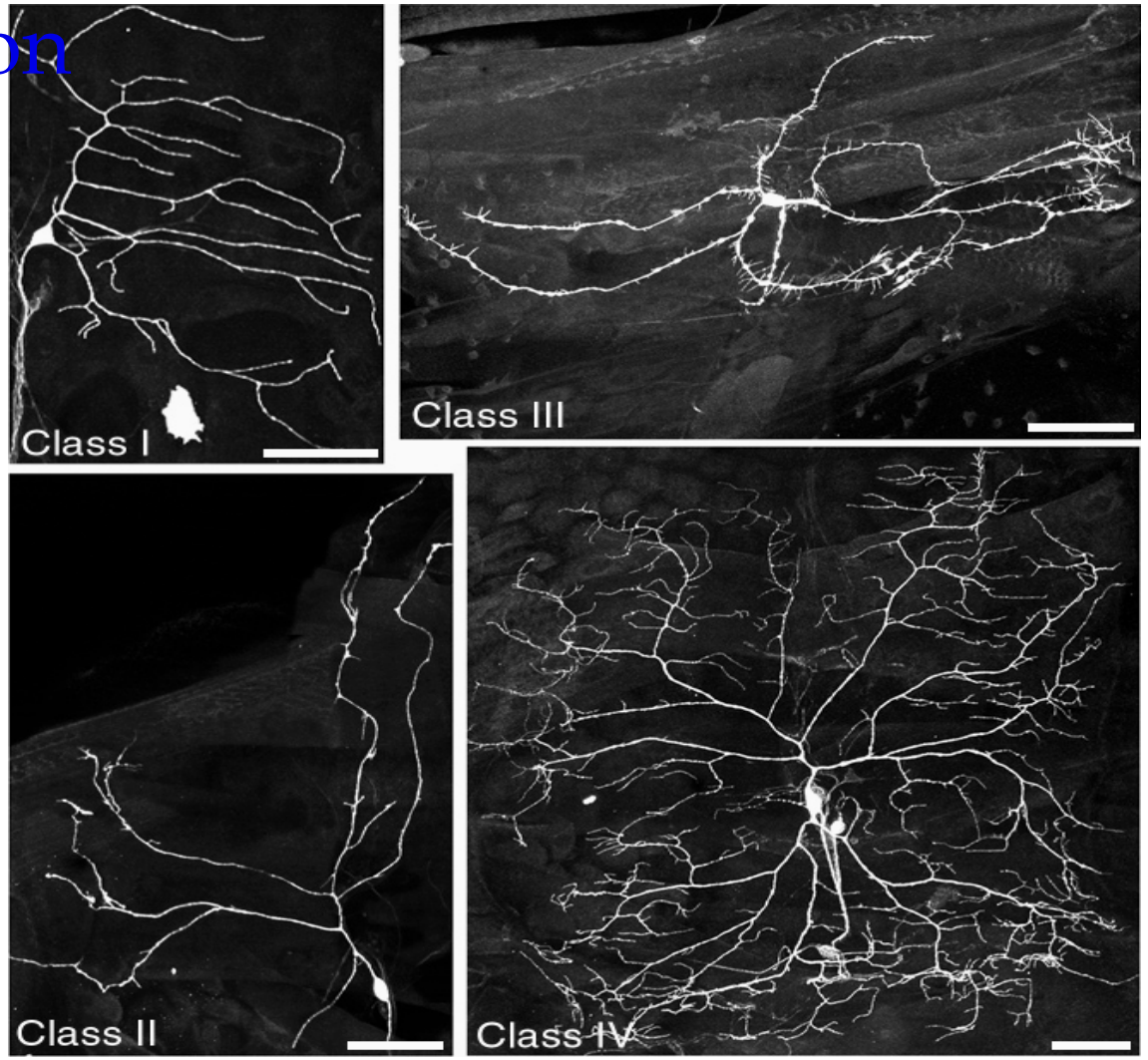
Angelman syndrome

Rett's syndrome

Mecp2 duplication

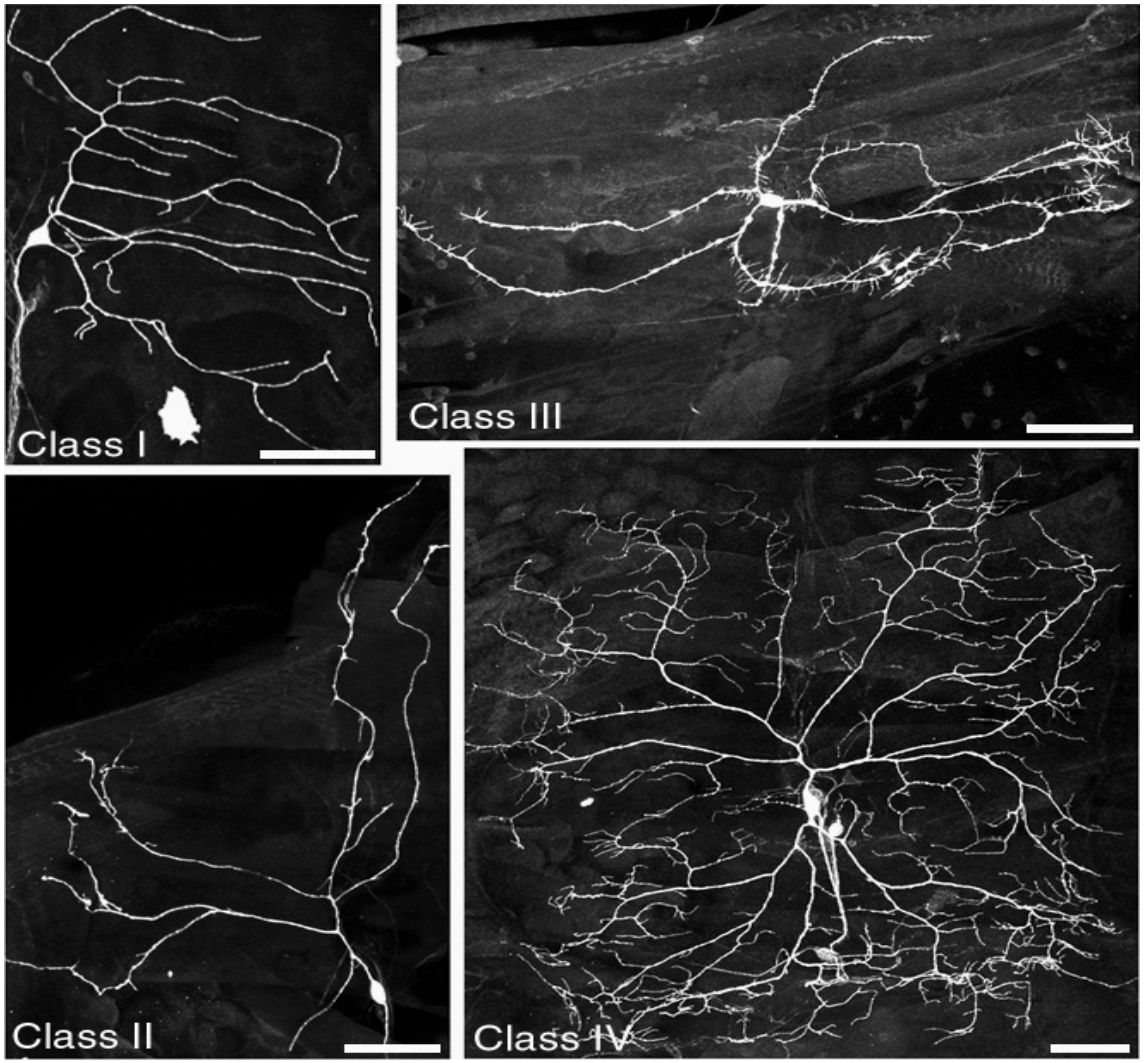
Ramocki& Zoghbi, Nature, 2008

Four classes of da neurons with distinctive dendritic morphology and function



Nociception, mediated by DmPiezo (Kim et al., Nature, 2012)

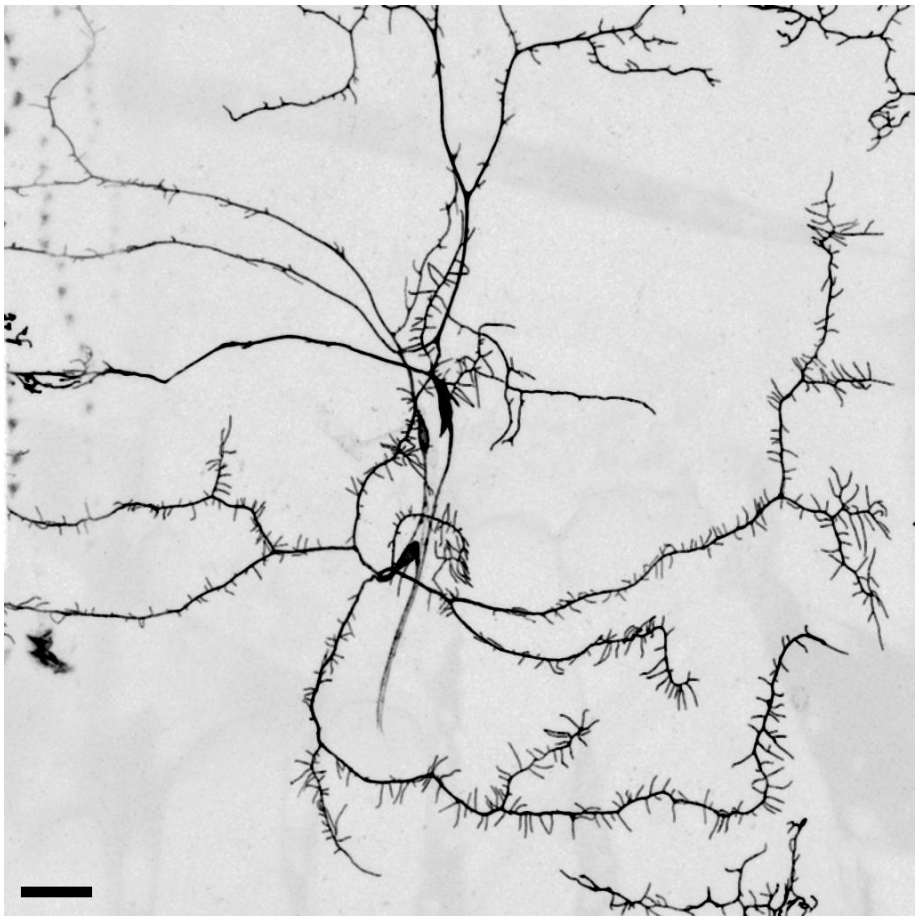
Four classes of da neurons with distinctive dendritic morphology and function

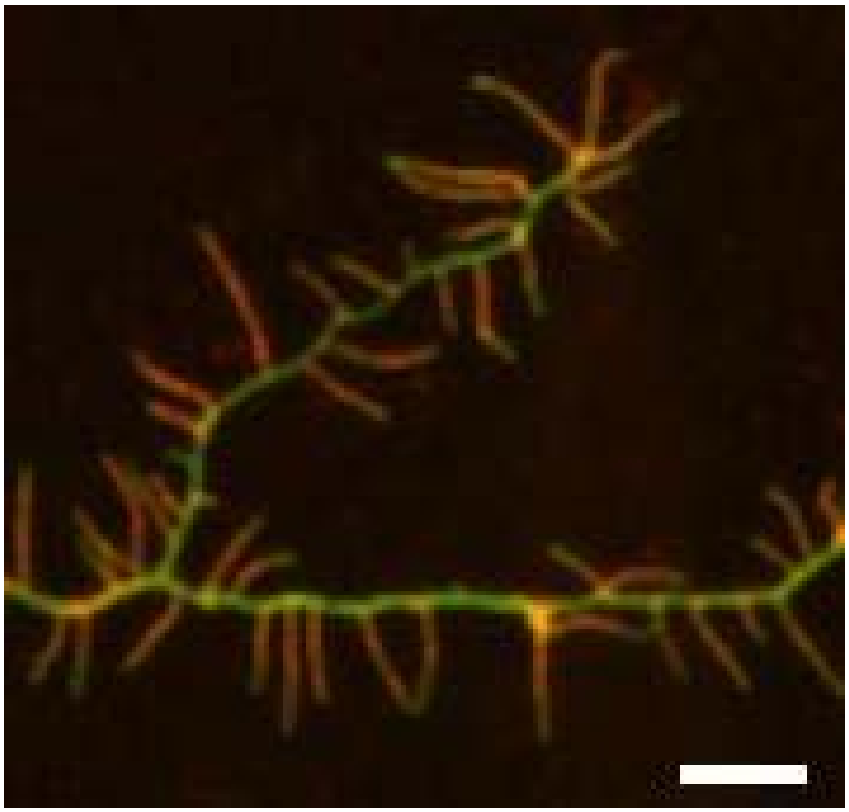


Gentle touch, mediated by NompC (Yan et al., Nature, 2013)

Nociception, mediated by DmPiezo (Kim et al., Nature, 2012)

The touch sensitive class III da neurons contain short, actin-rich terminal branches (the dendritic spikes)

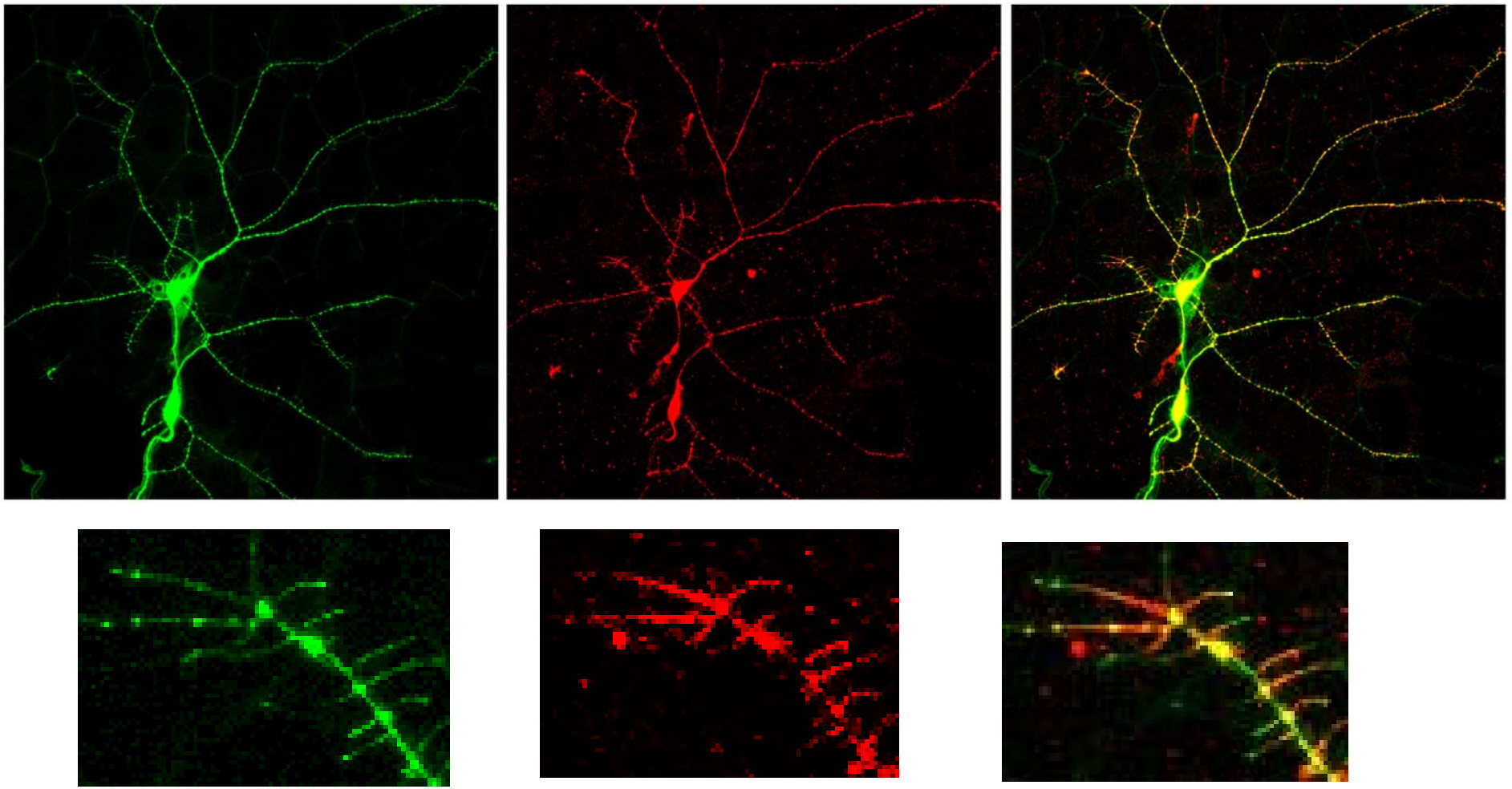




CD4-tdGFP
LifeActin-tdTOM

NompC is expressed in class III da neuron

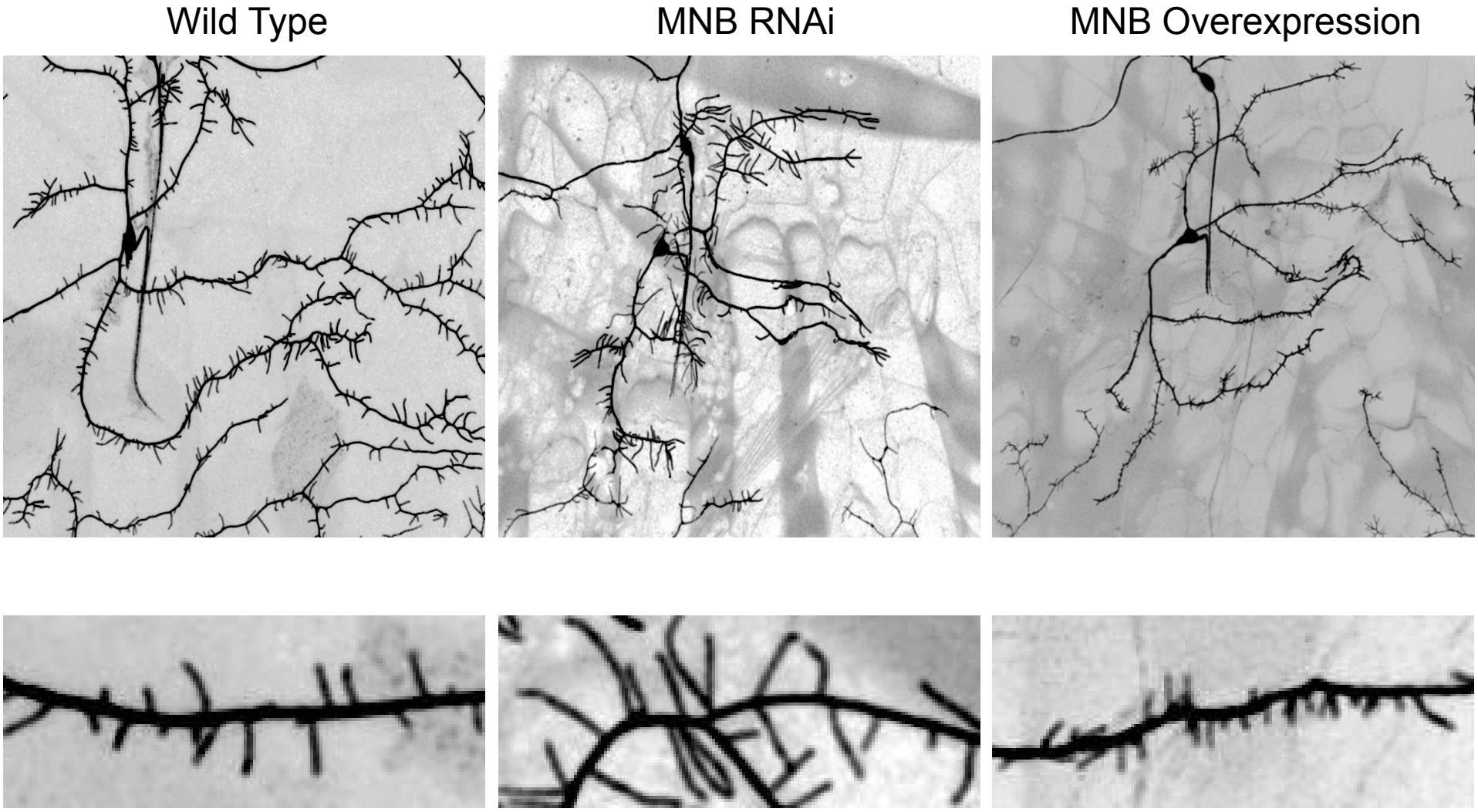
19-12 Gal4, UAS-CD4 td GFP/ NompC



Yan et al., Nature, 2013

In search of kinase mutants that affect dendritic spikes (Kassandra Ori-Mckenney)

The Importance of Minibrain Dosage



(Ori-McKenney et al., Neuron, 2016)

Minibrain *In Vivo* function

- Expressed in class III neurons
  - Contributes to overall dendrite outgrowth
  - Maintains terminal branch length

- Regulates microtubule dynamics
  - Knockdown = more MTs entering terminal branches
  - Overexpression = fewer dynamic MTs overall

Minibrain Kinase

- *Drosophila minibrain* was originally discovered in M. Heisenberg's lab based on its brain size phenotype

- 82% identical to mammalian homolog, DYRK1A, which is in the "Down syndrome critical region" of human chromosome 21 and has been strongly implicated in Down syndrome and Autism Spectrum Disorders

ASD risk genes

Table 1

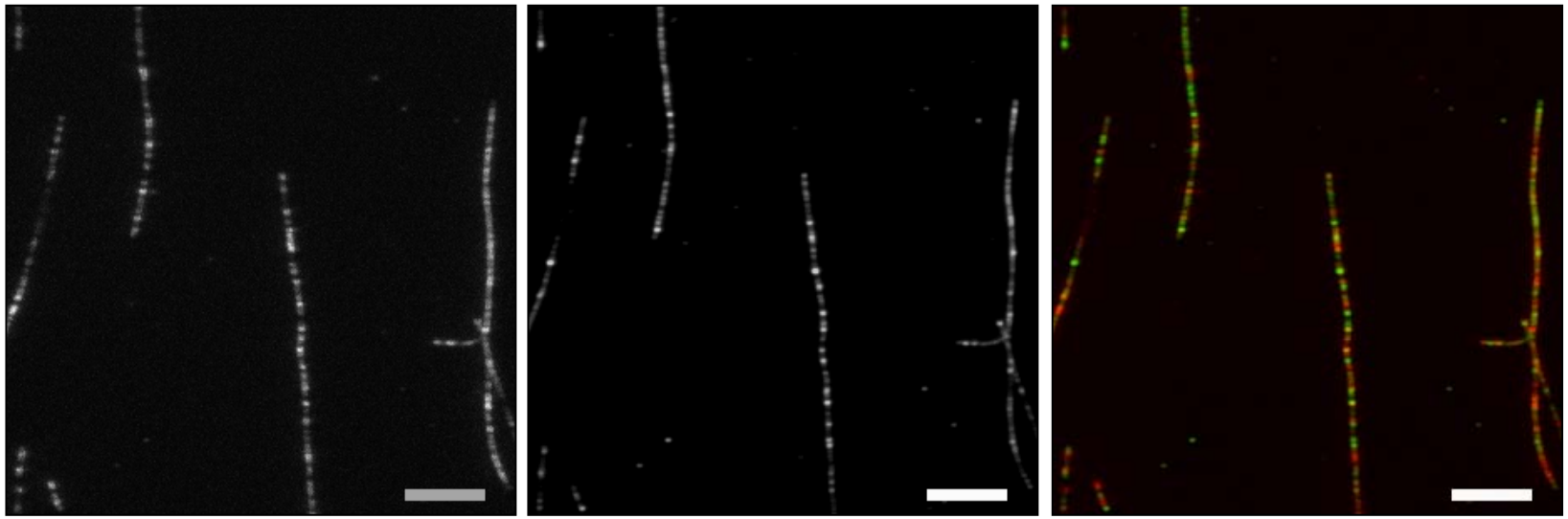
ASD risk genes discovered through recurrent *de novo* loss of function (dnLoF) mutations identified by whole-exome and whole-genome sequencing

Recurrent dnLoF[a]	False discovery rate[b]	Genes
7	<0.0005	*CHD8*
5	<0.005	*ARID1B, DYRK1A, SYNGAP1*
4	<0.01	*ADNP, ANK2, DSCAM, SCN2A*
3	<0.05	*CHD2, GRIN2B, KDM5B, POGZ, SUV420H1*
2	<0.2	*ANKRD11, ASXL3, ASH1L, BCL11A, CACNA2D3, CUL3, DIP2A, FOXP1, GIGYF1, ILF2, KATNAL2, KDM6B, MED13L, NCKAP1, PHF2, RANBP17, RIMS1, SPAST, TBR1, TCF7L2, TNRC6B, WAC, WDFY3, ZC3H4*

[a] De novo mutations were identified in Refs. [31,32*,33,34*,35*,36,37**,38,39,41,42].
[b] False discovery rate estimated as in Ref. [37**].

Willsey and State, CONB, 2015

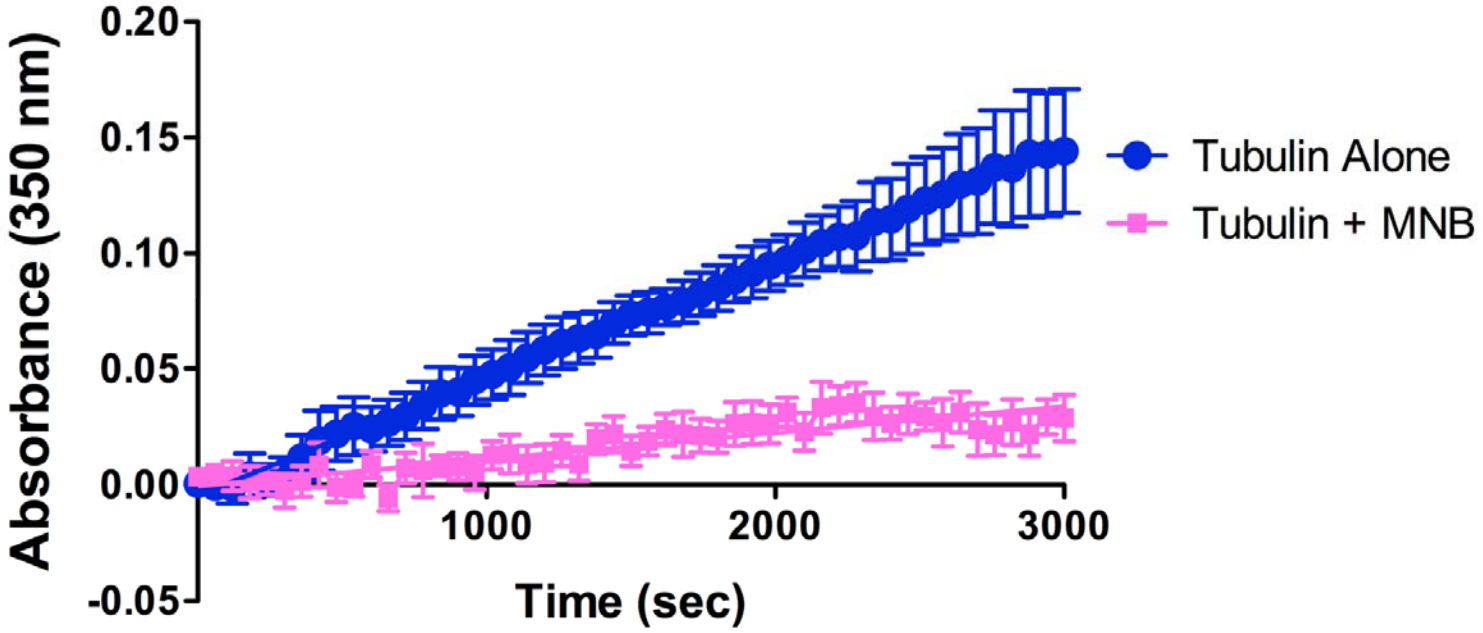
Purified Minibrain Kinase Binds Microtubules



Microtubules | Minibrain | Merge

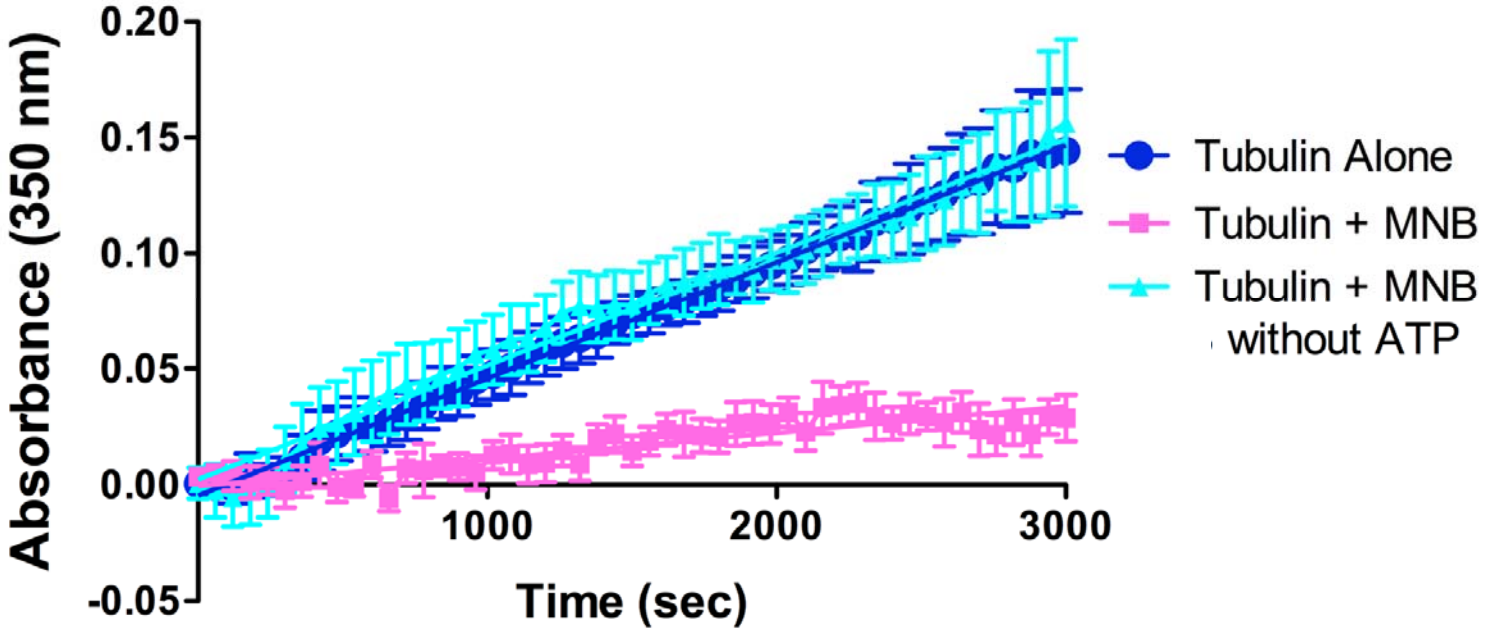
Blue or Red Taxol stabilized microtubules
Green = Minibrain

Minibrain Inhibits Microtubule Polymerization



25uM tubulin + 1mM GTP + 1mM ATP

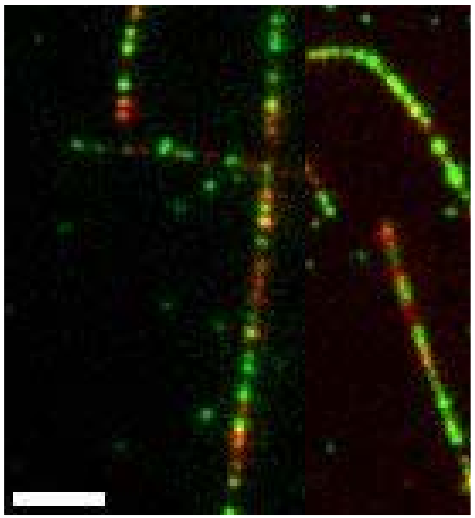
Minibrain Requires ATP to Inhibit MT Polymerization

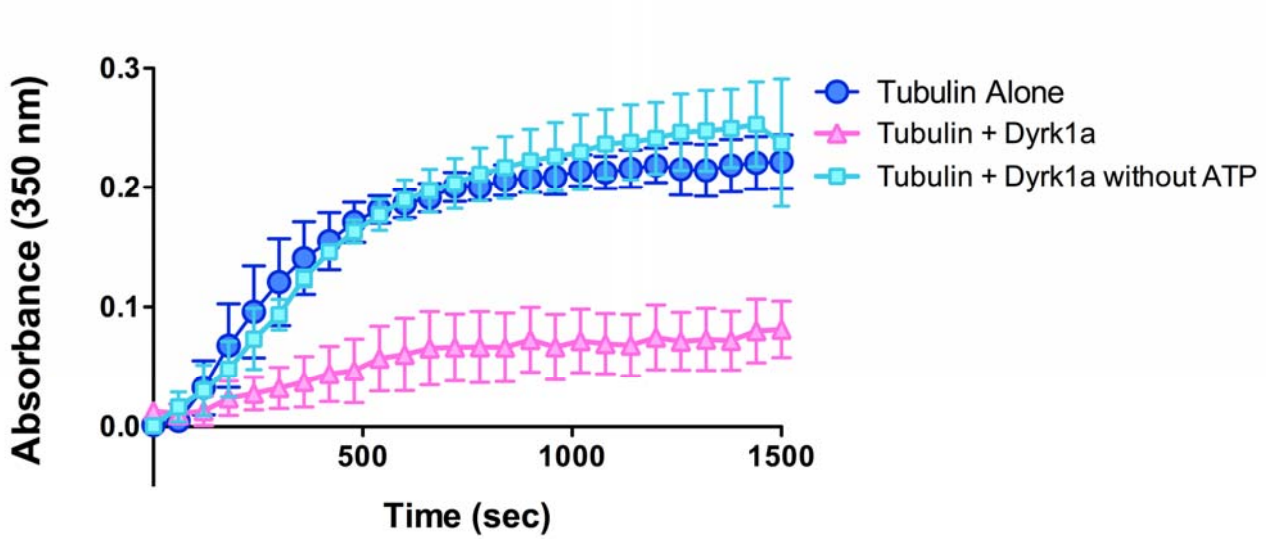


25uM tubulin + 1mM GTP + 1mM ATP (or 0mM ATP)

Conservation of Mechanism in Mammalian DYRK1a

MT/Dyrk1a





(Ori-McKenney et al., Neuron, 2016)

Minibrain Kinase

- *Drosophila minibrain* was originally discovered in M. Heisenberg's lab based on its brain size phenotype

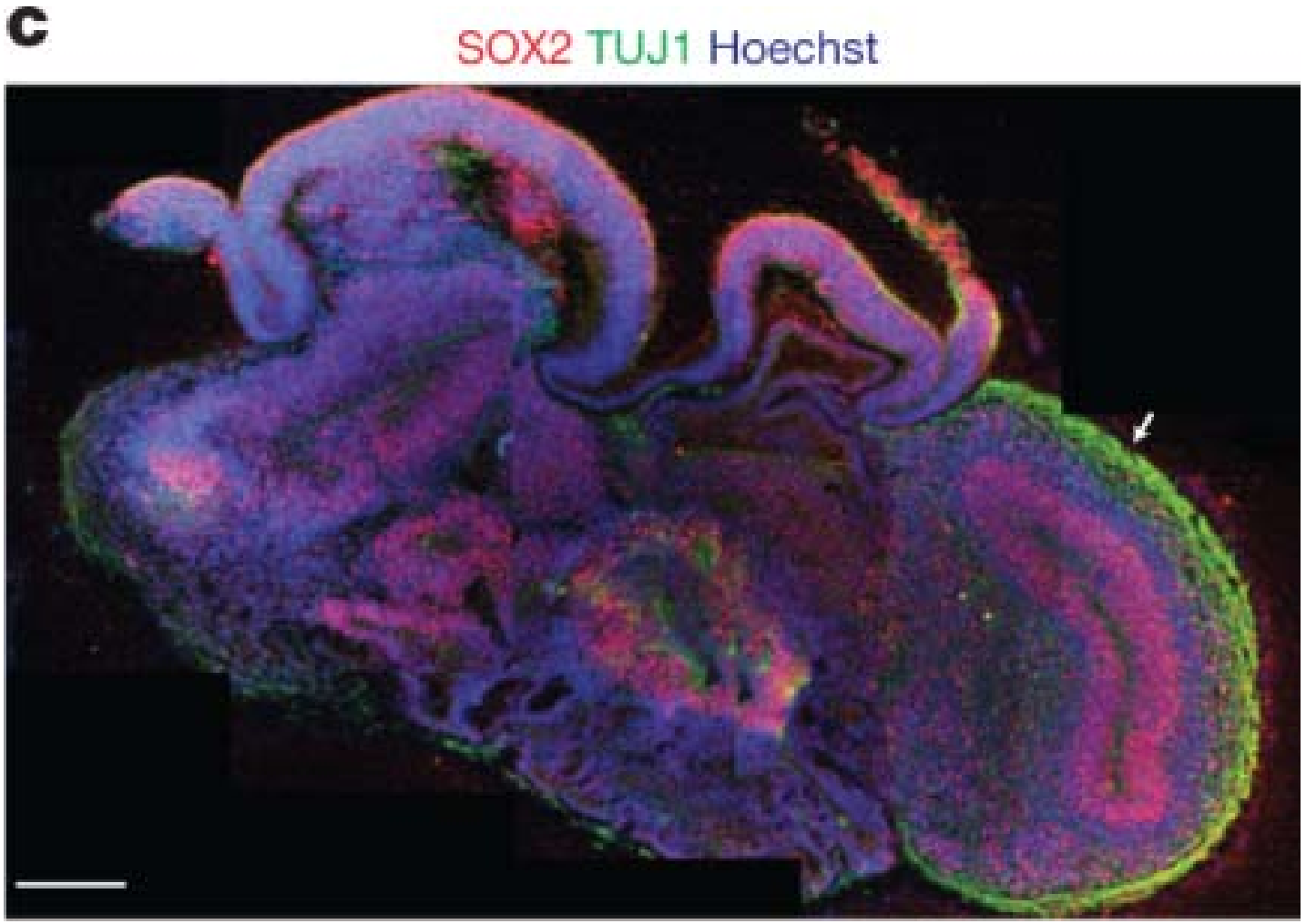
- 82% identical to mammalian homolog, DYRK1A, which is in the "Down syndrome critical region" of human chromosome 21 and has been strongly implicated in Down syndrome and Autism Spectrum Disorders

- MNB/DYRK1A controls dendrite morphology by regulating microtubule polymerization

Timothy syndrome is associated with activity-dependent dendritic retraction in rodent and human neurons (Kery et al., Nature Neurosci. 2013, Ricardo Dotmetsch lab)

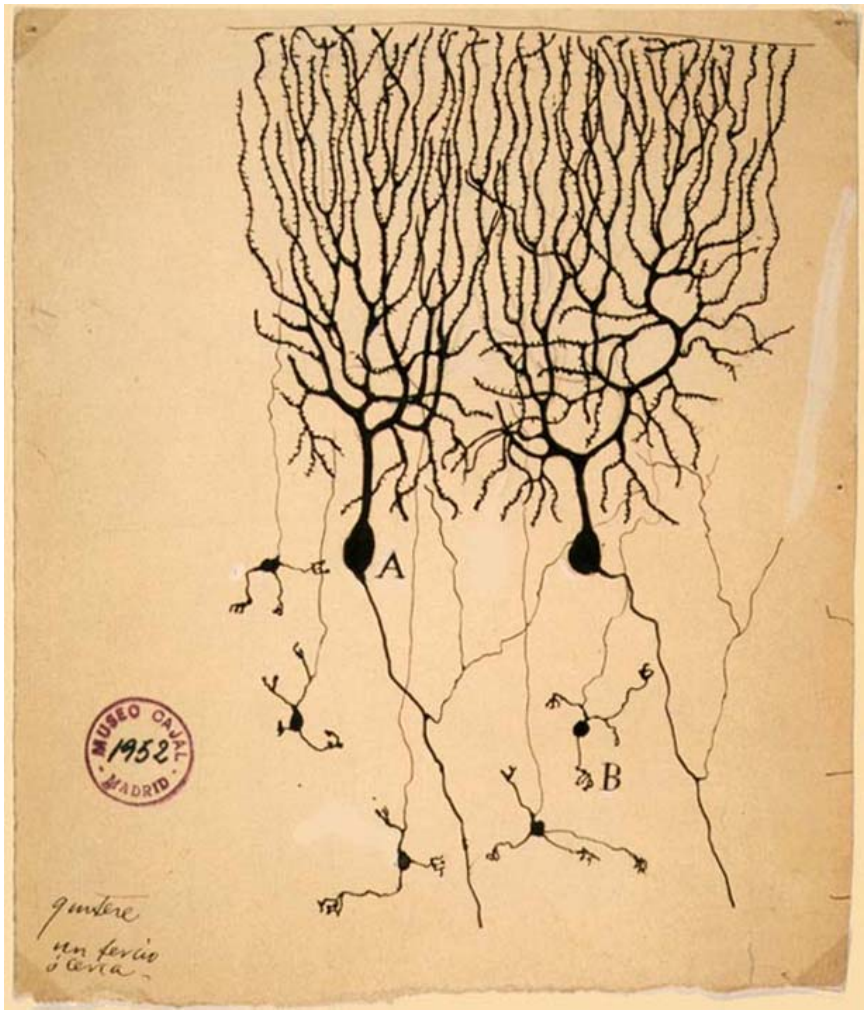
- One approach to study the cellular mechanism of autism spectrum disorder susceptibility gene is to use induced pluripotent stem cell (iPSC)-derived neurons from individuals with the syndrome.

Cerebral organoids model human brain development and microcephaly



Lancaster et al., Nature, 2013 (J Knoblich lab)

Axon regeneration vs. dendrite regeneration after injury



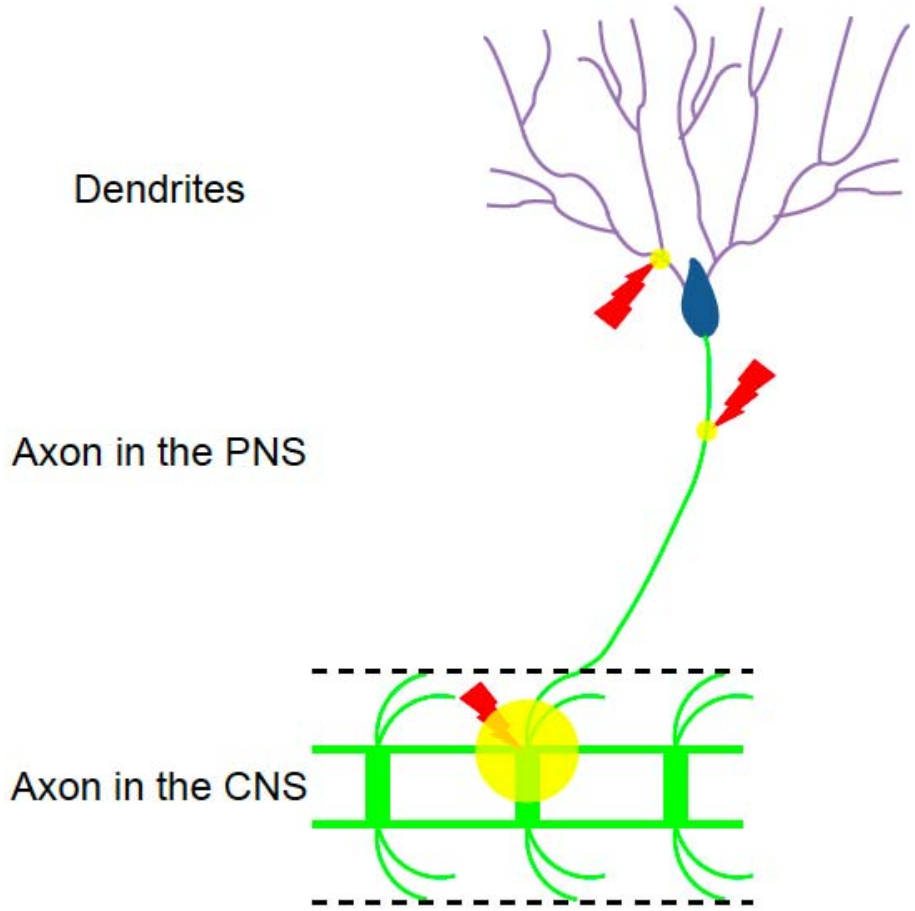
Santiago Ramón y Cajal, 1899

Dendrite regeneration: an interesting and little studied problem

- Axon regeneration: 1644 publications
- Dendrite regeneration: 8 publications

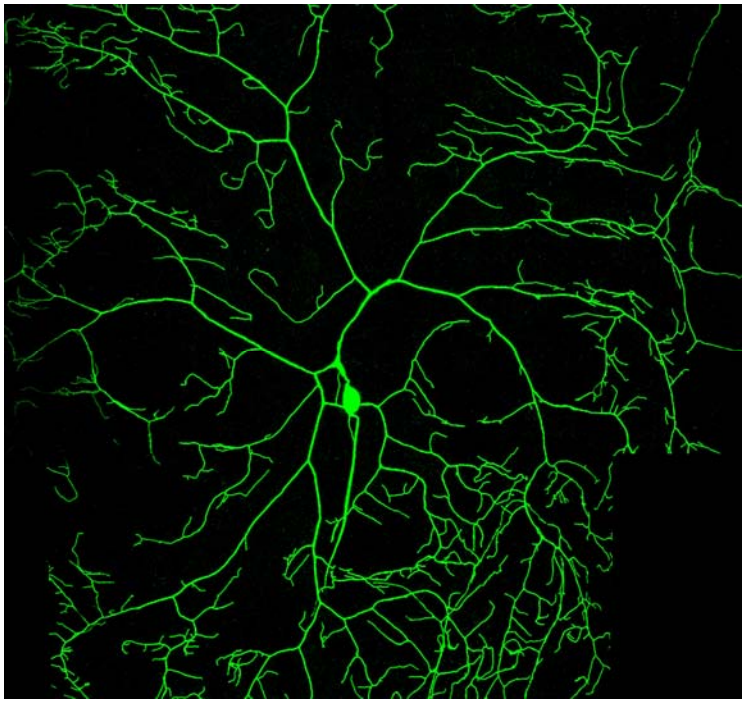
PubMed search on 11/16/2016

Study of axon and dendrite regeneration by using da neurons (Yuanquan Song)

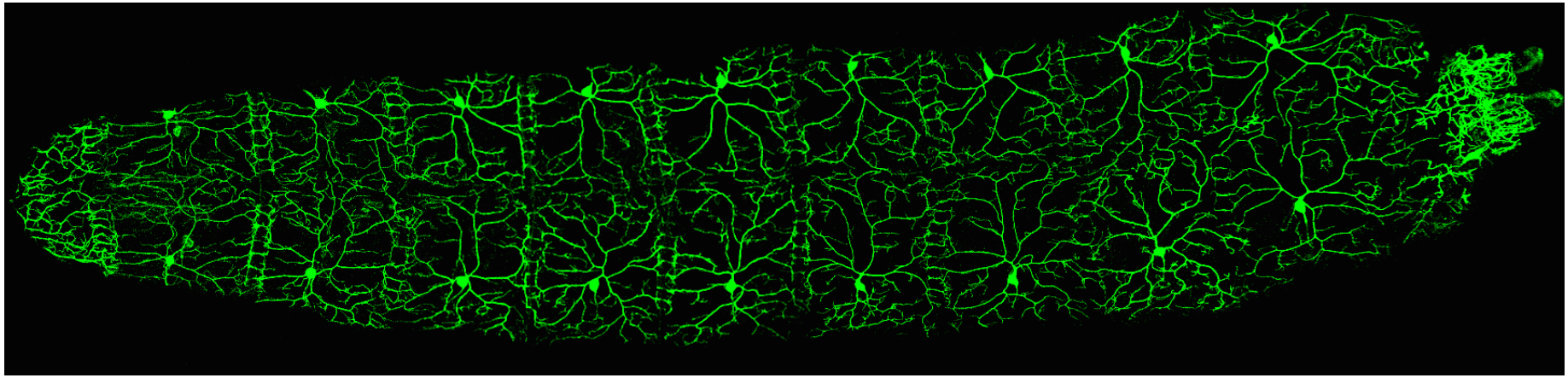


Song et al., Genes & Dev., 2012

Using *Drosophila* da neuron to study dendrite morphogenesis and regeneration



Drosophila larval class IV dendritic arborization (da) neuron--- a type of sensory neuron that innervates larval body wall.



Axon regeneration of da neuron

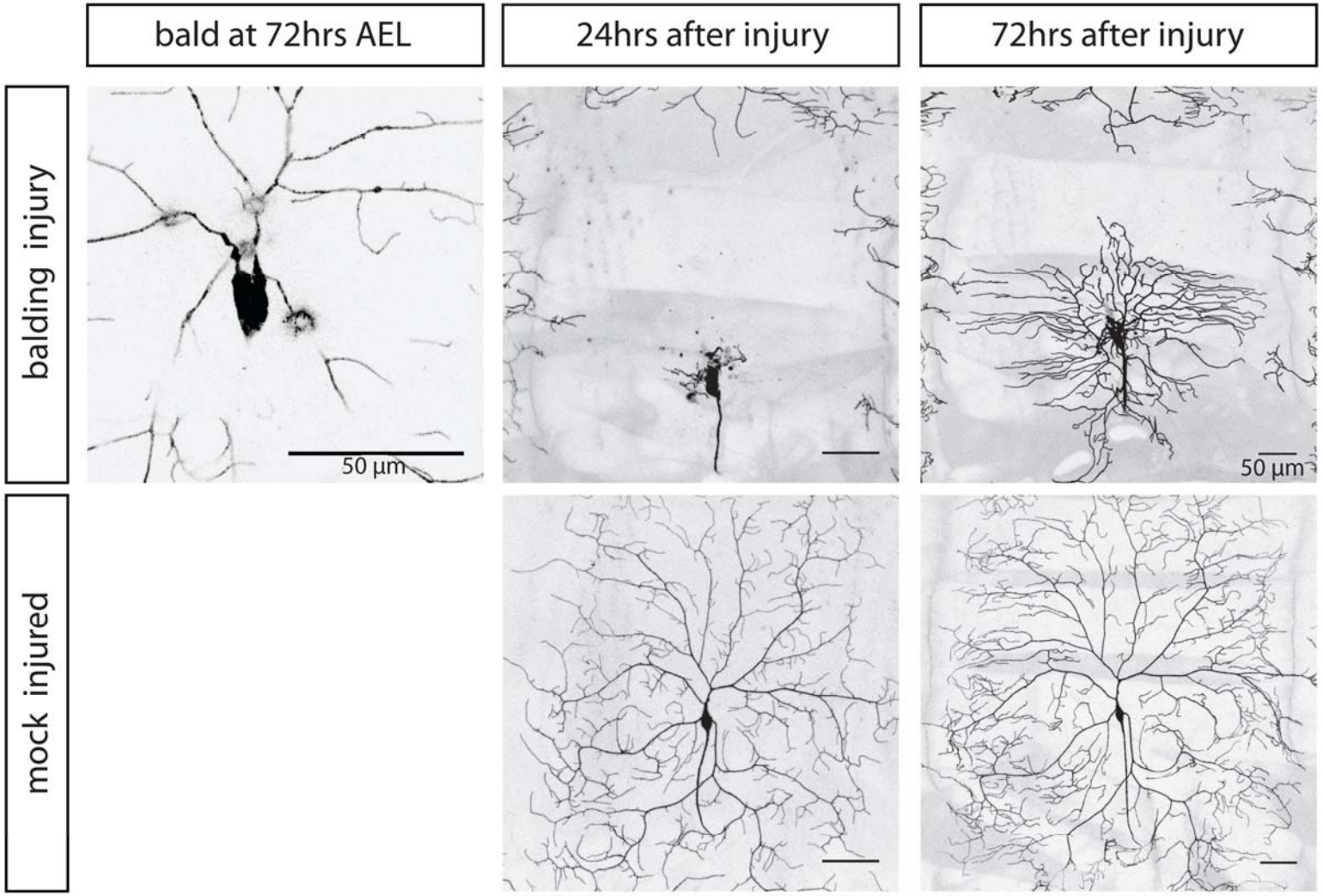
- Class IV da neuron axon regenerates substantially in the PNS but poorly in the CNS—resembles mammalian DRG neurons

- Activation of the AKT/PTEN/mTOR pathway enhances da neuron axon regeneration—an example of evolutionarily conserved mechanism
  (Song et al., Genes & Dev., 2012)

- Screen for novel regulators of axon regeneration by using the da neuron: identification of the Rtca RNA repair and splicing pathway as evolutionarily conserved regulators
  (Song et al., Nat. Neurosci., 2015)

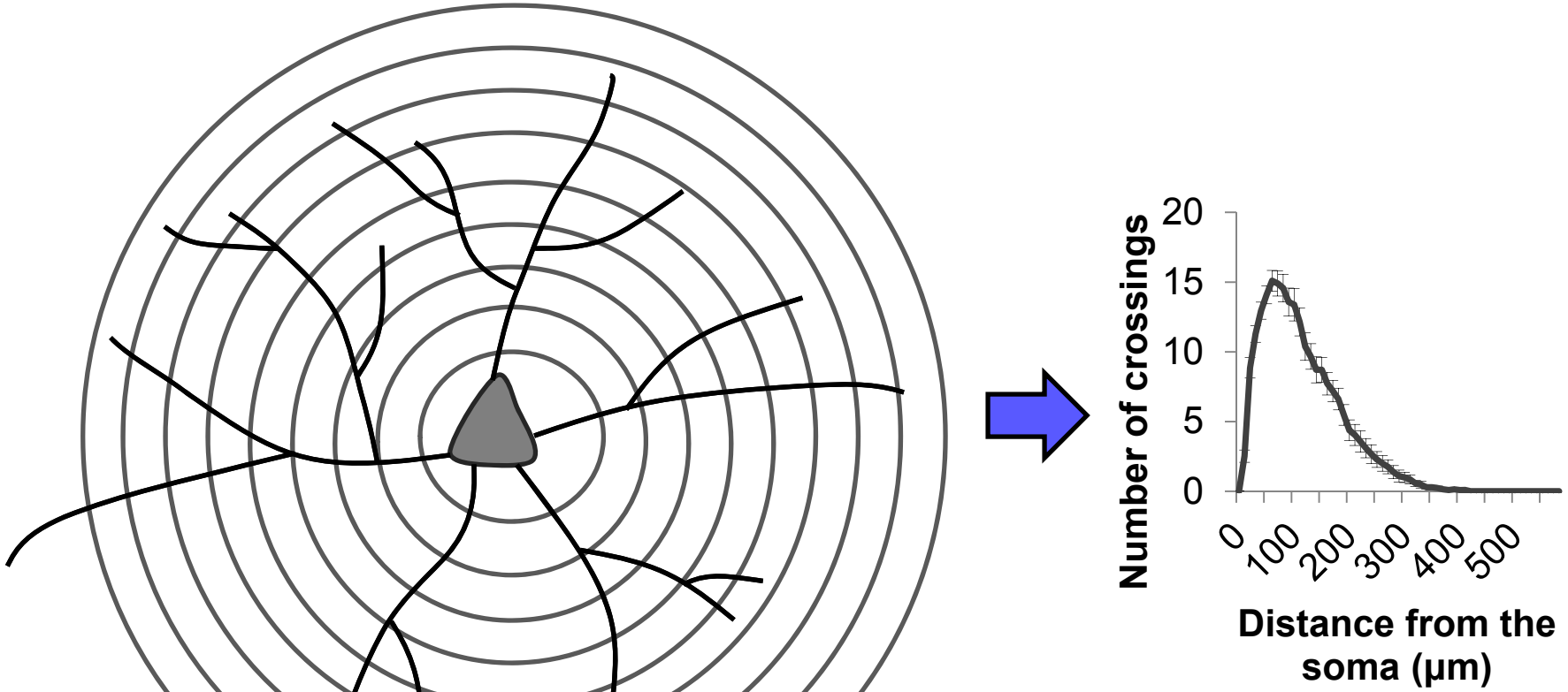
Dendrite regeneration
(Katie Thompson-Peer; Laura Devault)

Class IV da neuron can regenerate its dendritic arbor after injury

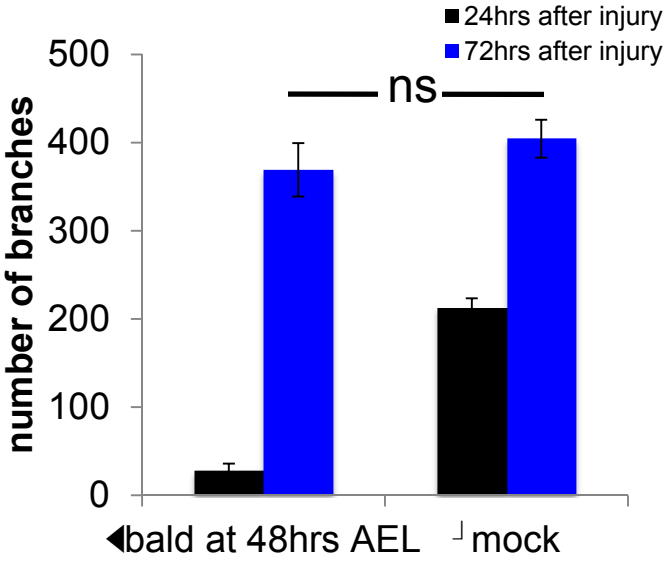


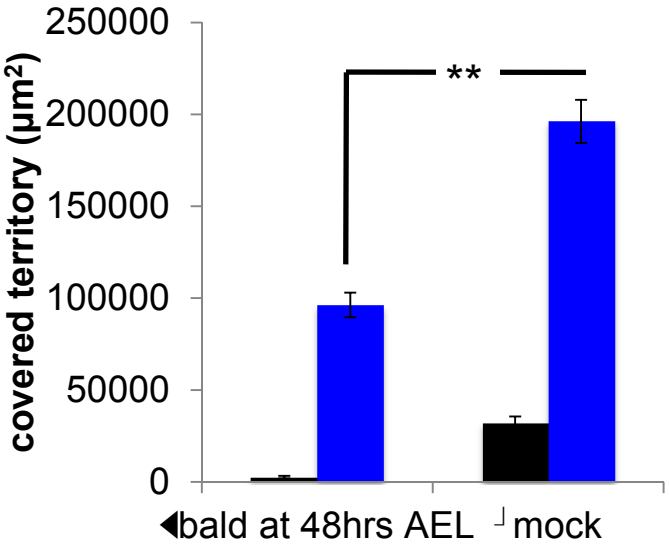
(Thompson-Peer et al., G&D, 2016)

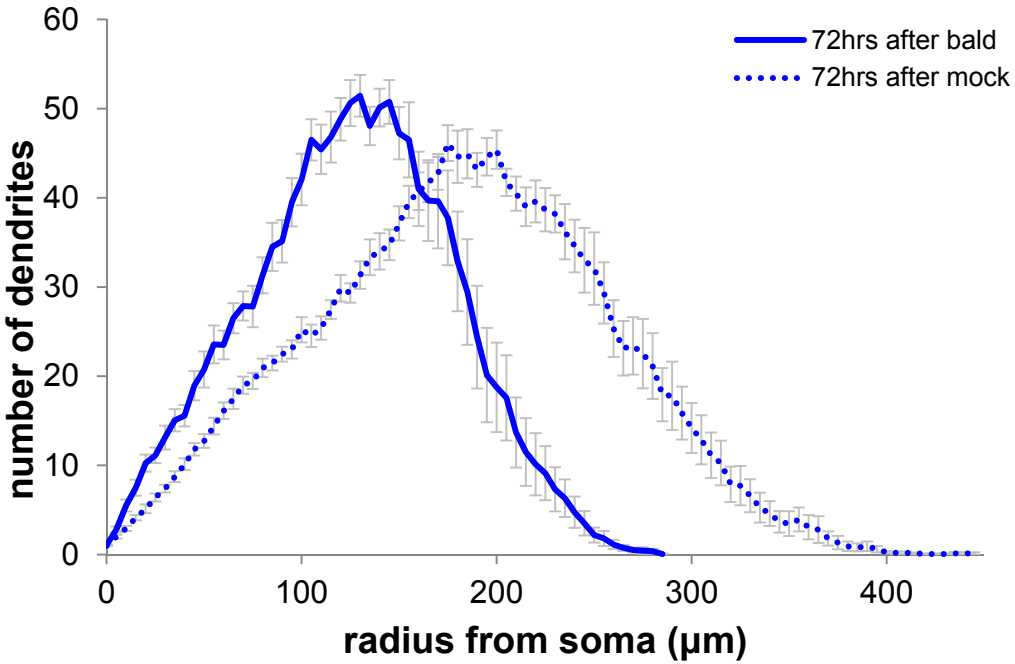
Sholl Analysis



bald@48hr AEL: recover branch # but not arbor size







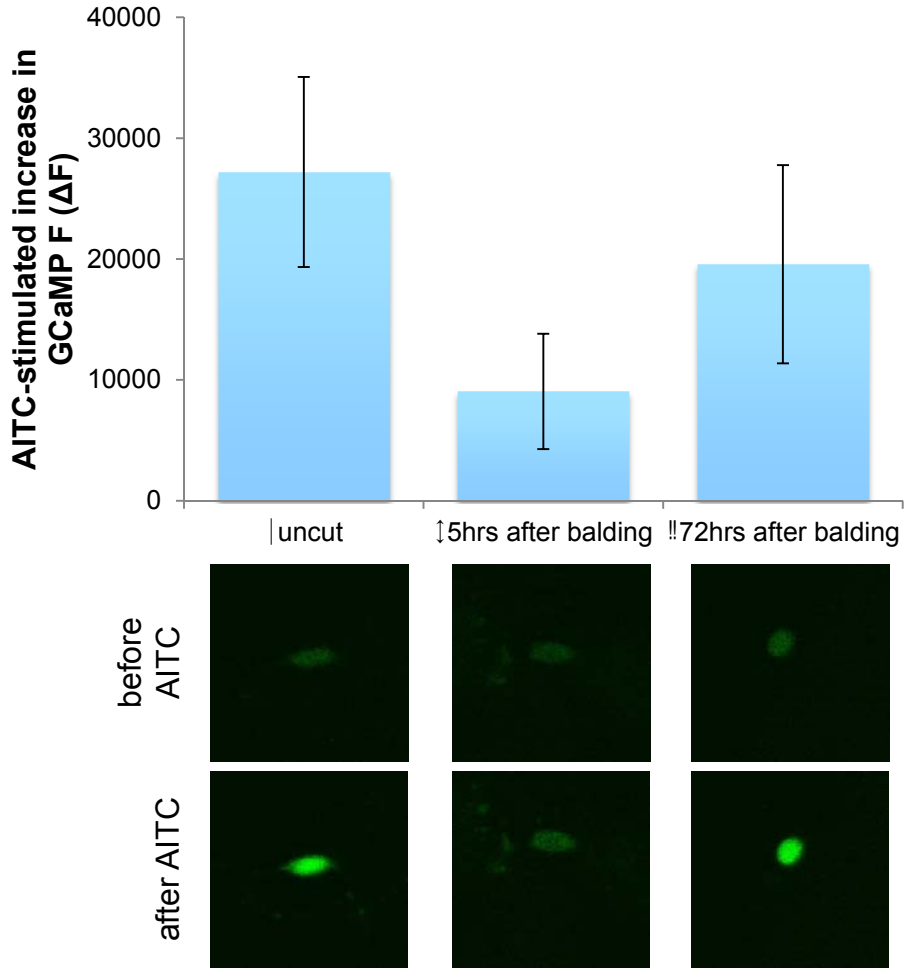
ablate surrounding neurons
n=16 for each

The quality of regeneration: do the injured neuron and its regenerated dendrites retain their neuronal-type specificity?

The expression levels of cell type specific transcription factors, trafficking of the correct ion channels into the dendrites, etc, appeared to be unchanged.

(Thompson-Peer et al., G&D, 2016)

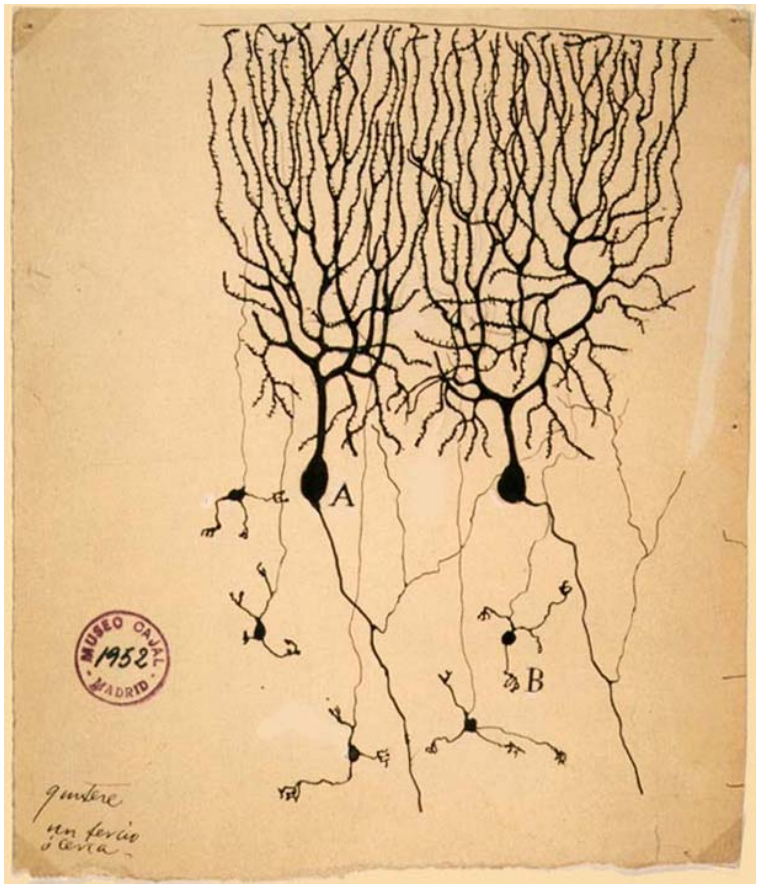
Are the regenerated dendrites functional?

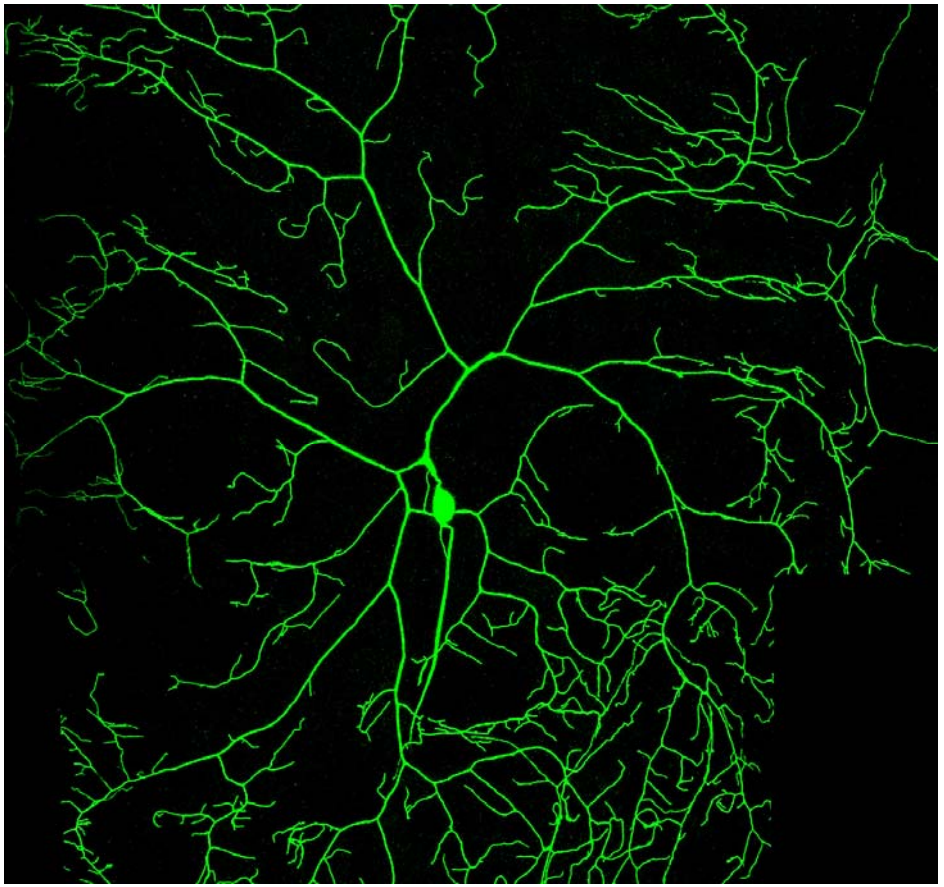


Response to AITC (wasabi)

The regenerated dendrites do have defects: self-avoidance of the regenerated dendrites is affected

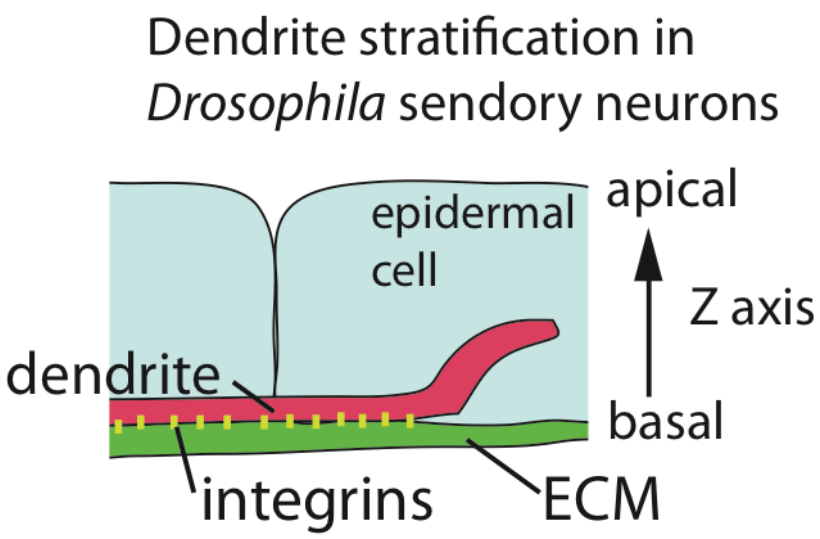
Self-avoidance---repulsions between sister dendrites of a neuron

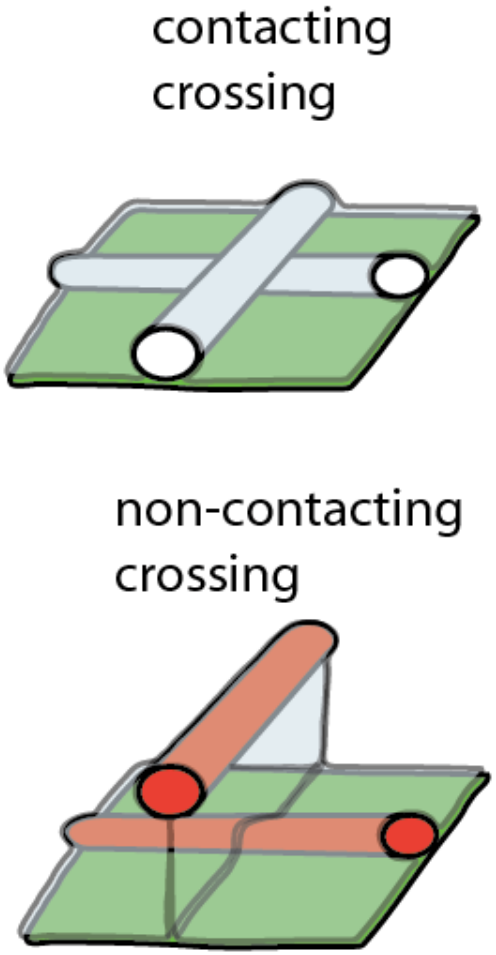




Santiago Ramón y Cajal, 1899.

Self-avoidance requires dendrites to be restricted in a 2D space to facilitate the Dscam-mediated repulsions between sister dendrites





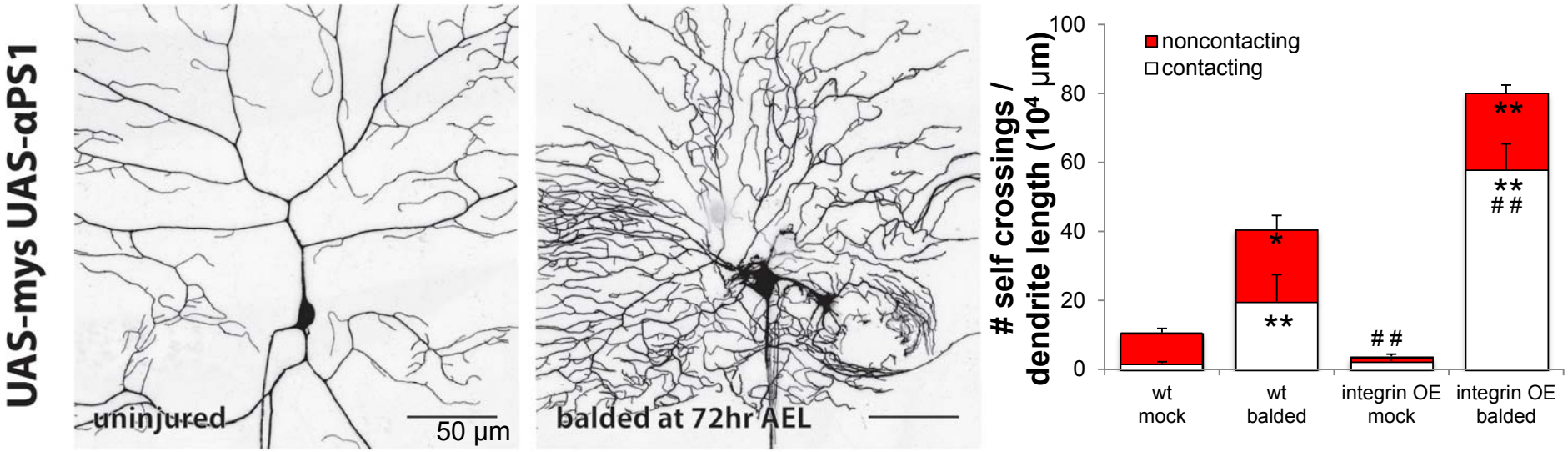
Kim et al., Neuron, 2012 (Grueber Lab)

Han et al., Neuron, 2012

Molecules involved in restricting dendrites to 2D space

- Integrins (Kim et al., Neuron, 2012; Han et al., Neuron, 2012)
- Trc and Fry, components of Hippo kinase pathway (Han et al., Neuron, 2012)
- Ret kinase (Soba et al., eLife, 2015)
- Semaphorin-2b and Plexin B (Meltzer et al., Neuron, 2016)

Regenerated class IV da neuron has self-avoidance defects that are not corrected by over-expressing Integrin



* p < 0.05 versus mock
** p < 0.01 versus mock
p < 0.01 versus wt

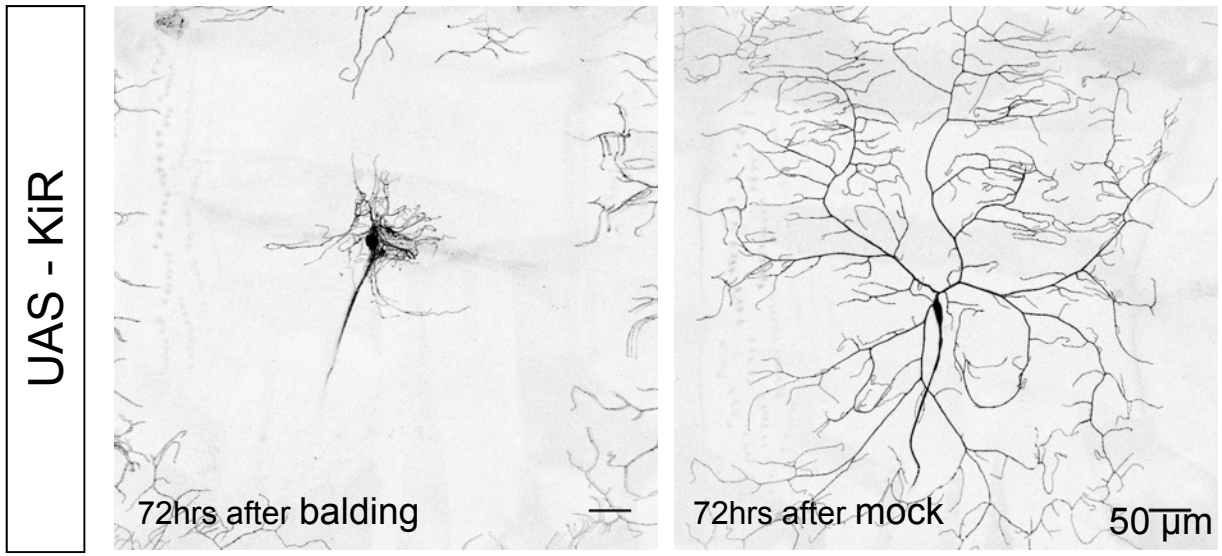
(Thompson-Peer et al., G&D, 2016)

Comparison of the mechanisms underlying axon regeneration & dendrite regeneration

- Axon and dendrite regeneration share some mechanisms (e.g. AKT/PTEN/mTOR pathway, dRtca) but not others (e.g. *bantam* miRNA, Dlk). (Song et al., G &D, 2012; Nat Neurosci, 2015); Stone et al., Cell Report, 2014 (Rolls lab))

- Identification of dendrite regeneration regulators (Thompson-Peer et al., G&D, 2016)

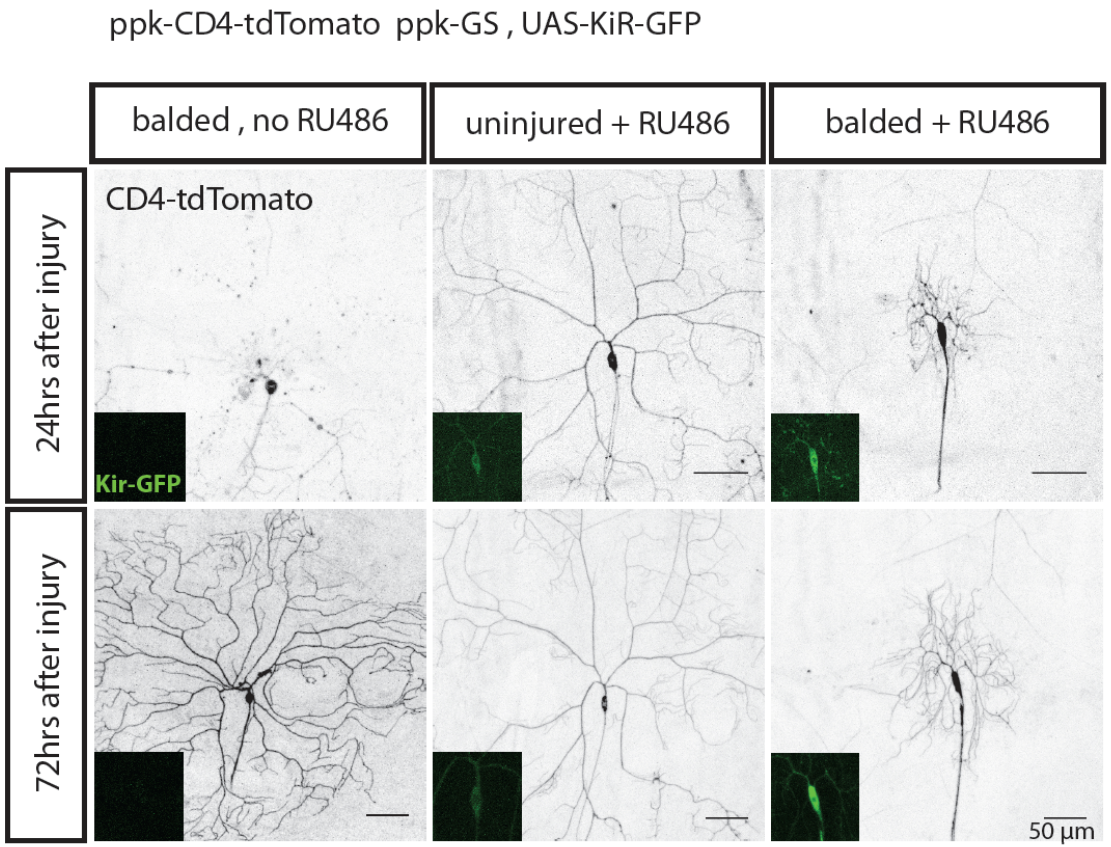
Activity control of regeneration

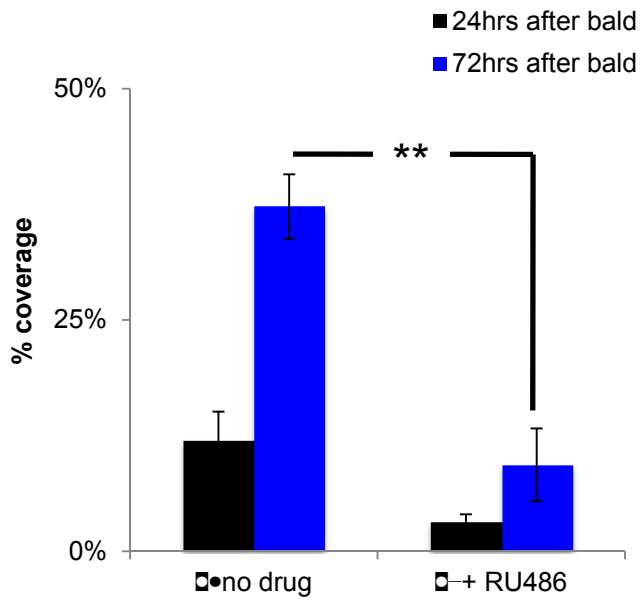


(Thompson-Peer et al., G&D, 2016)

bald@72hr AEL

Activity control of regeneration





RU486 applied ~24hrs before balding

(Thompson-Peer et al., G&D, 2016)

Summary---using class IV da neurons to study dendrite regeneration

- Class IV da neuron regenerates the same number of branches but covers smaller area
- The regenerated dendrites retain many of the normal properties and are functional
- However, self-avoidance is affected
- Identification of regulators of dendrite regeneration---activity is a potent regulator