

The wiring of the nervous system: setting up the hardware for behavior

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Behavior:

- Instinct: Programmed behavior
- Learned: Adaptability

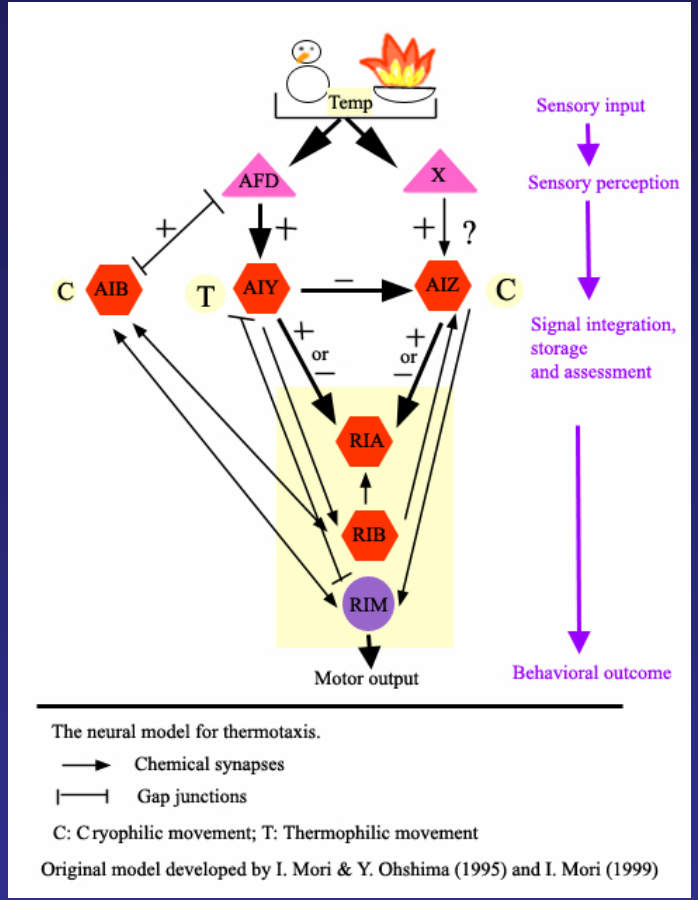
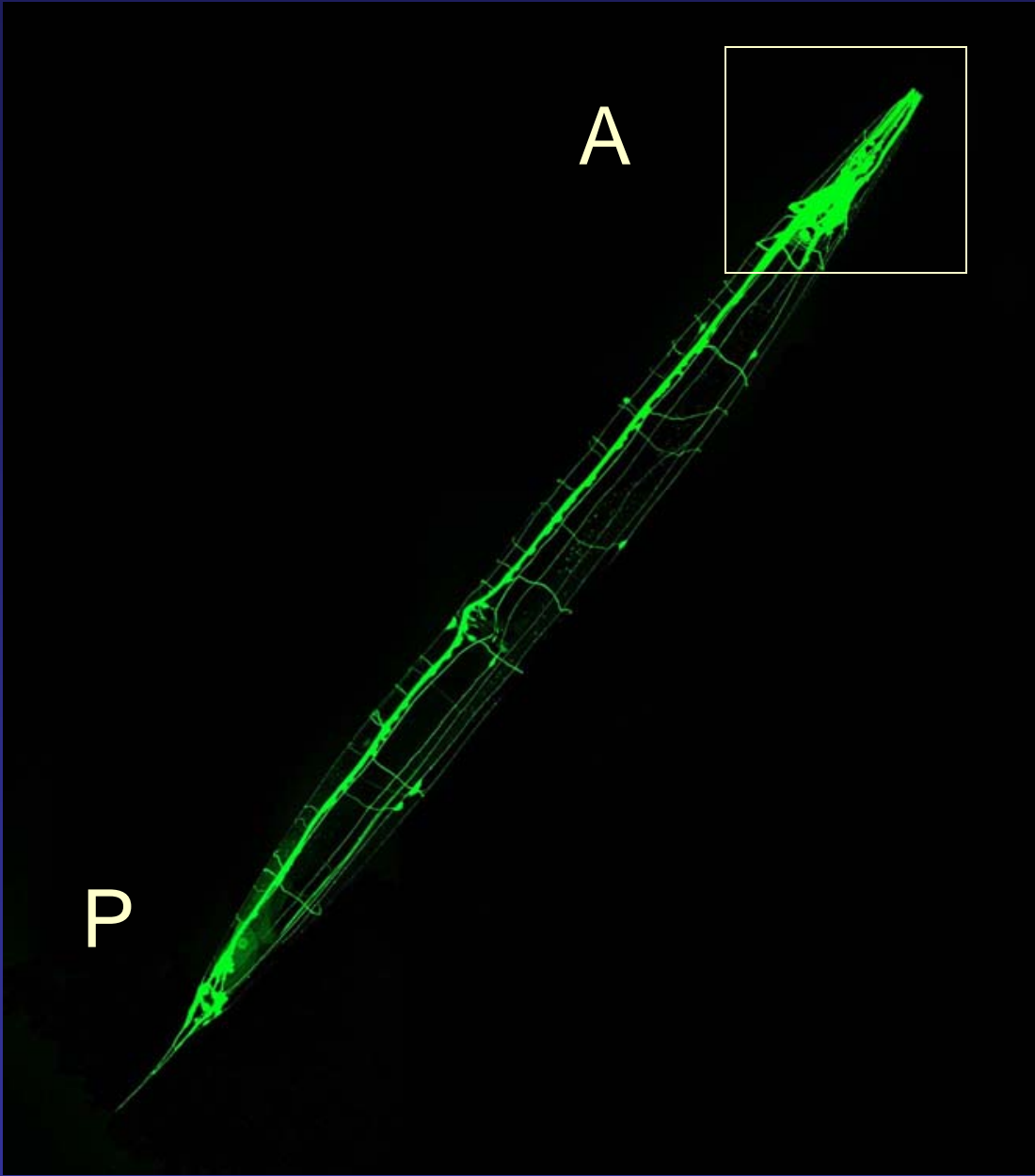
Genetic basis for both rooted in the brain architecture

Laying out the hardware for behavior

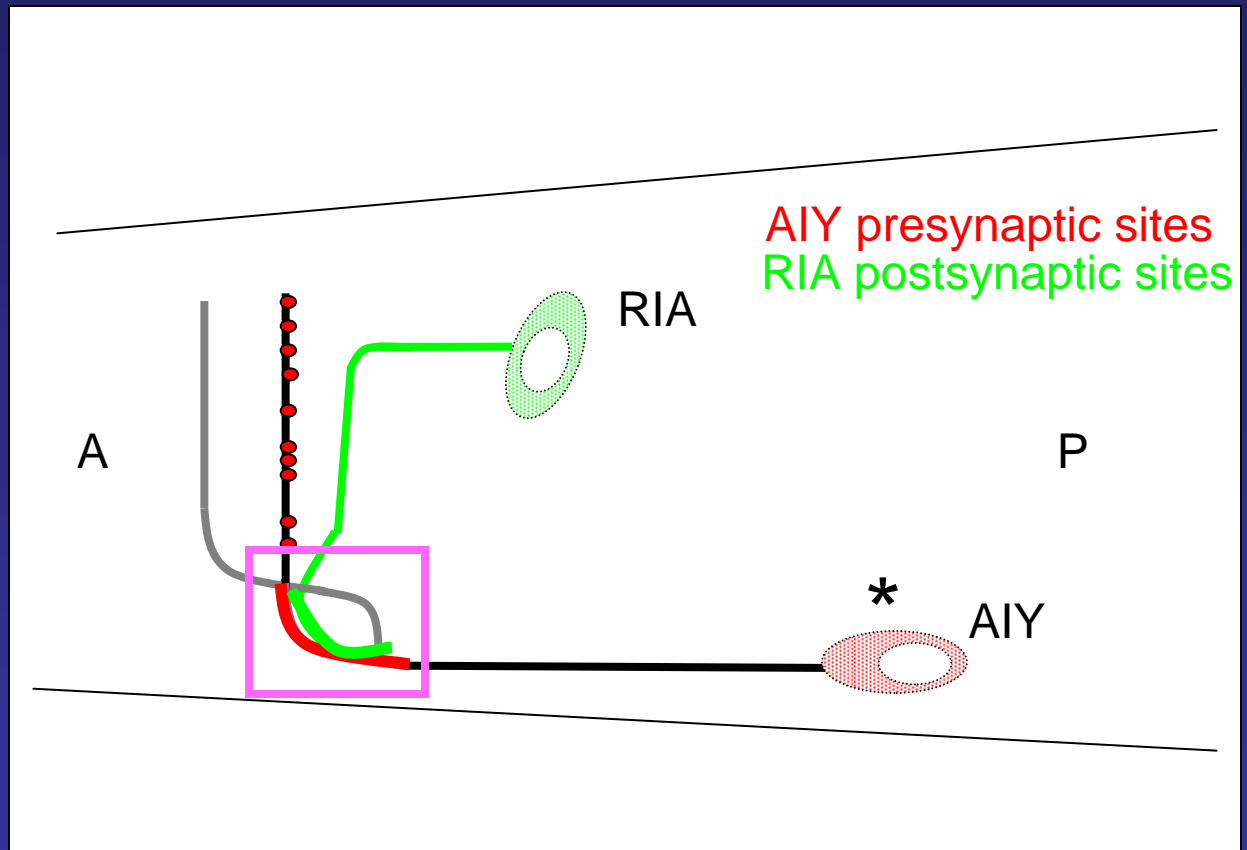
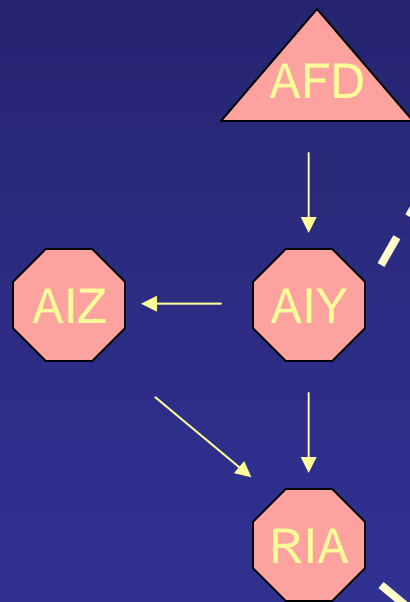
- Specification of cell fate
- Dendritic and axonal outgrowth: when, where and how
- Synaptic formation
- Coordinated developmental events lead to correct circuit assembly

Making things a bit easier: *C. elegans*

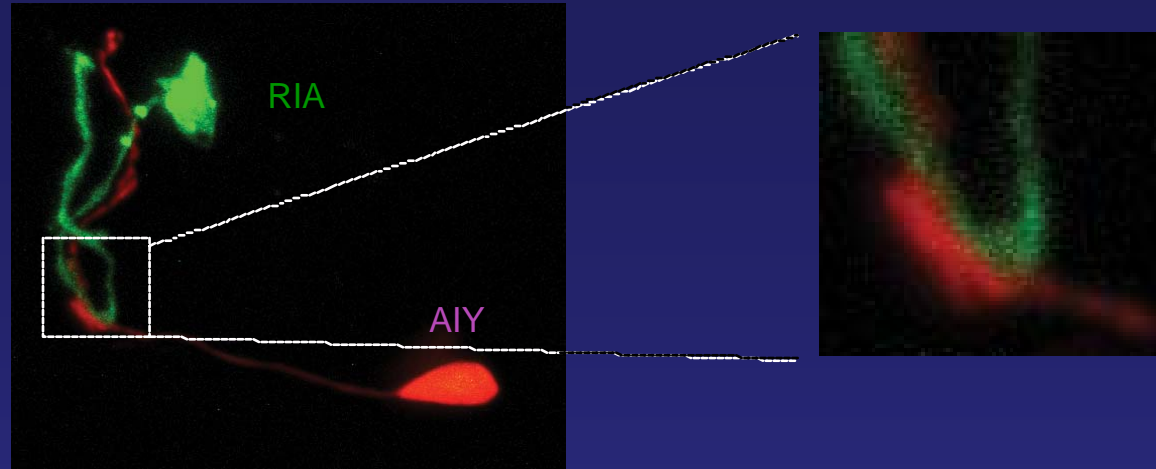
- In vivo system → Implications in behaviors
- 100 billion neurons → 302 neurons
- 100 trillion synapses → 5000 synapses



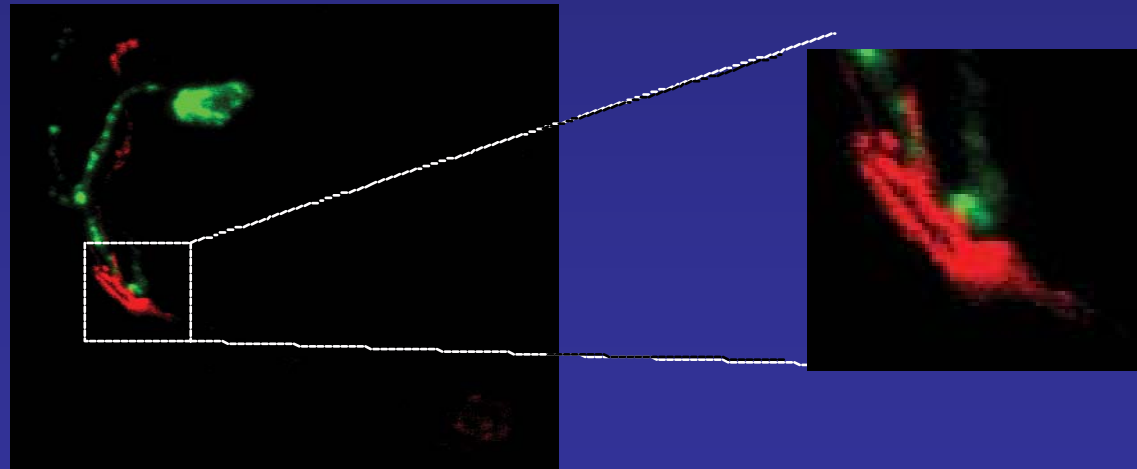
AIY innervates RIA in a stereotypical manner



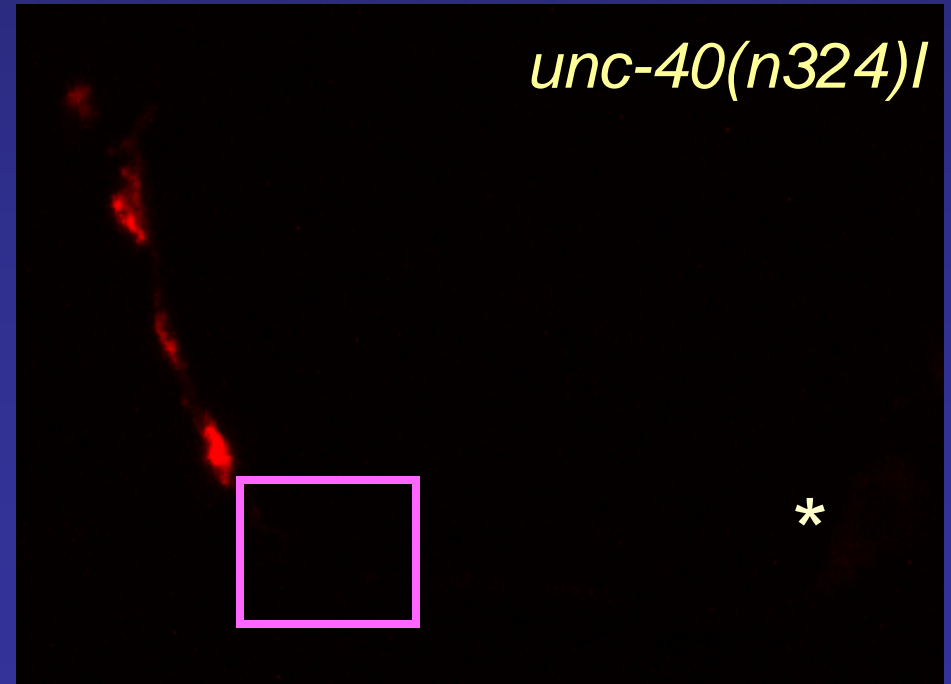
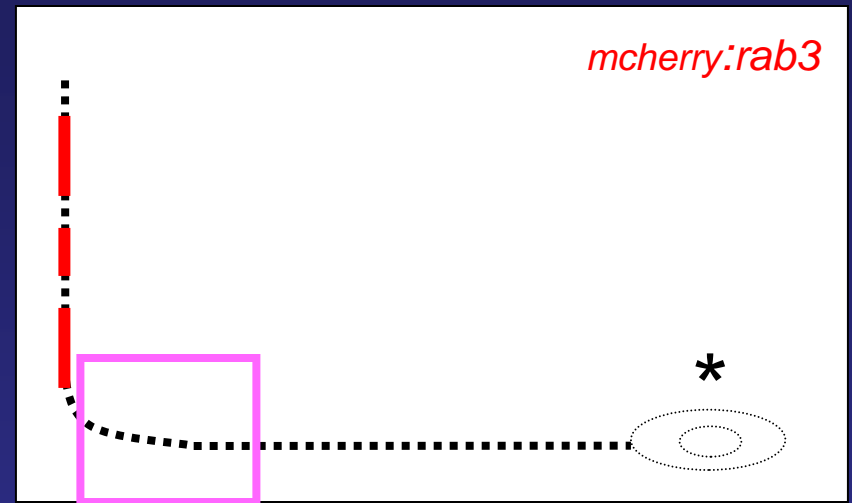
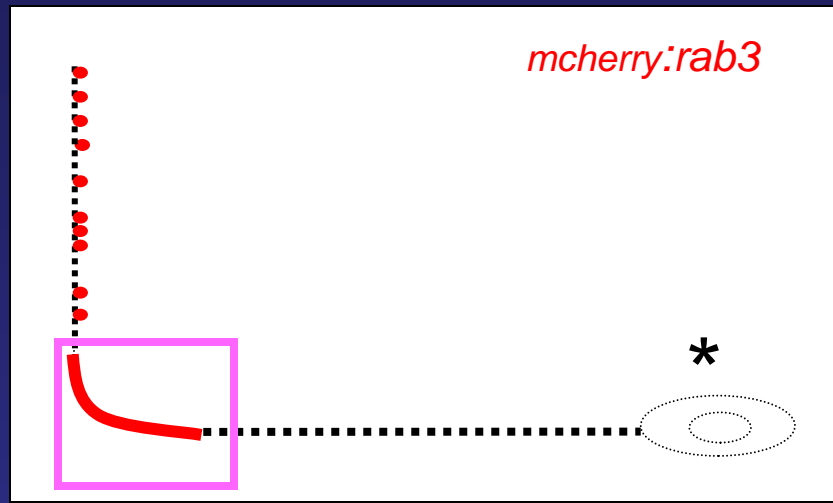
Cell-specific
Cytoplasmic markers



mcherry::rab-3 in AIY
glr-1::gfp in RIA

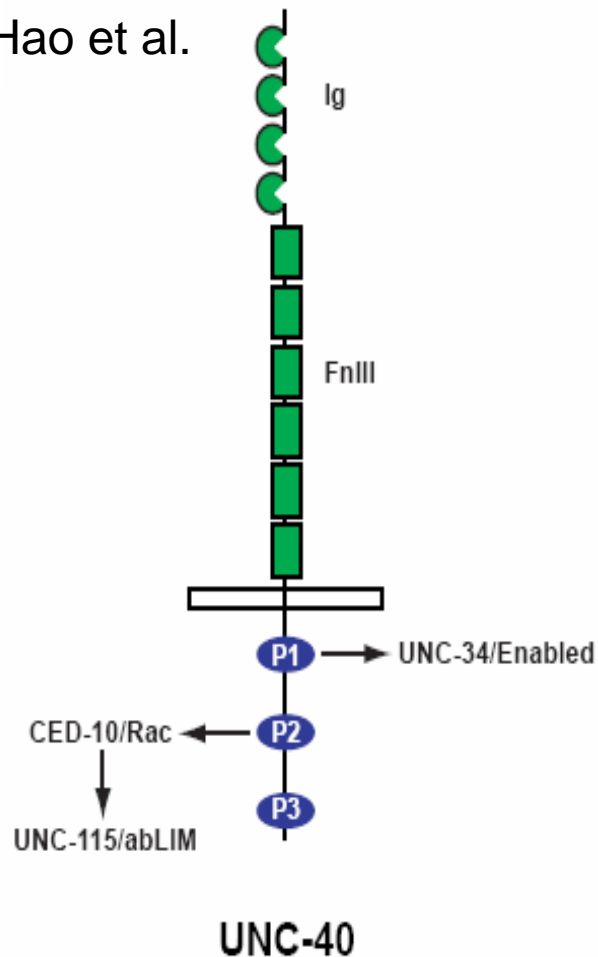


UNC-40 controls presynaptic vesicle cluster distribution in AIY



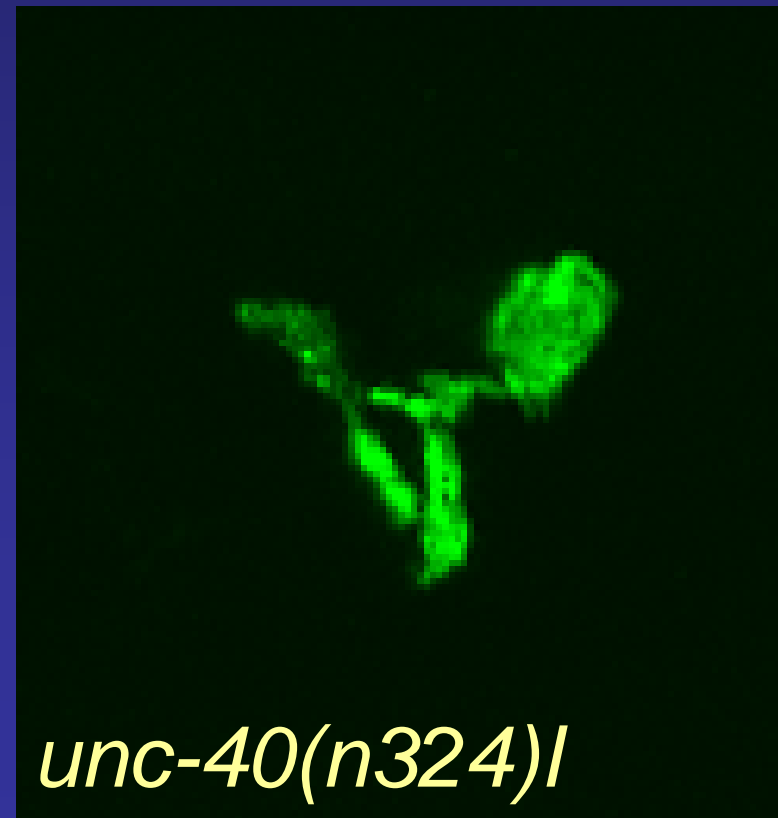
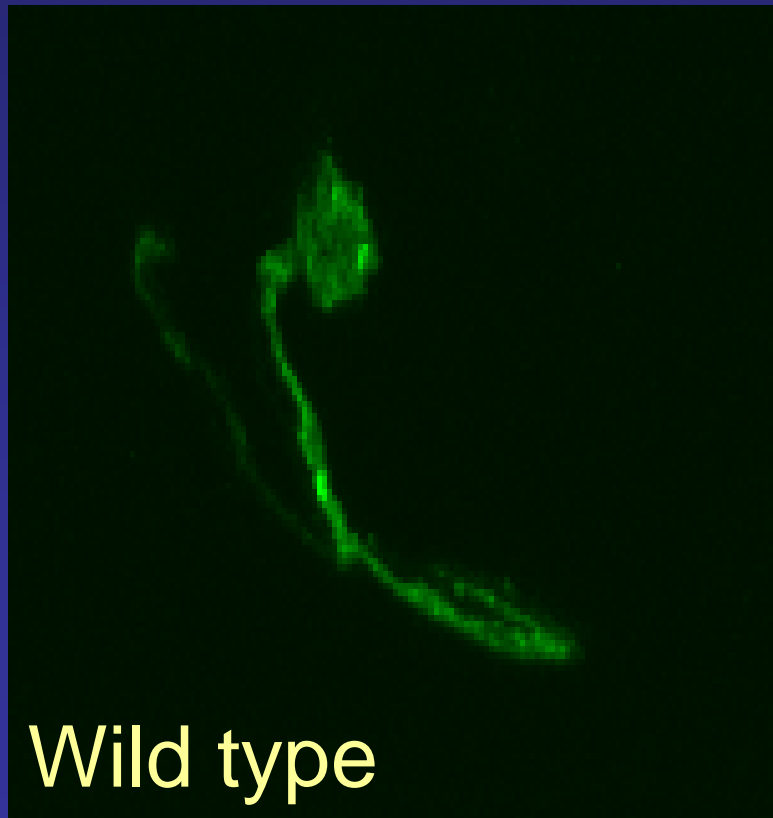
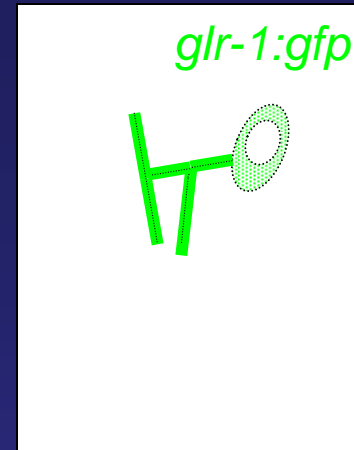
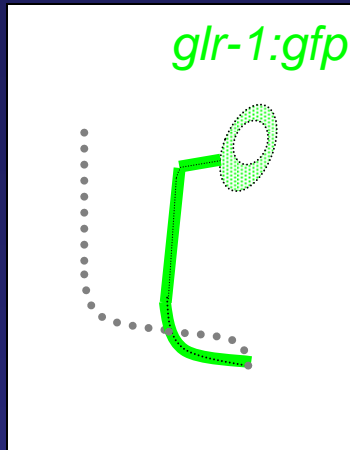
UNC-40/Frazzled/DCC

From Hao et al.



- Ig superfamily:
UNC-6/Netrin receptor
- Dorso-ventral cell mig.
and axon guidance
- Does **not** affect AIY
axon guidance, **only**
presynaptic patterning

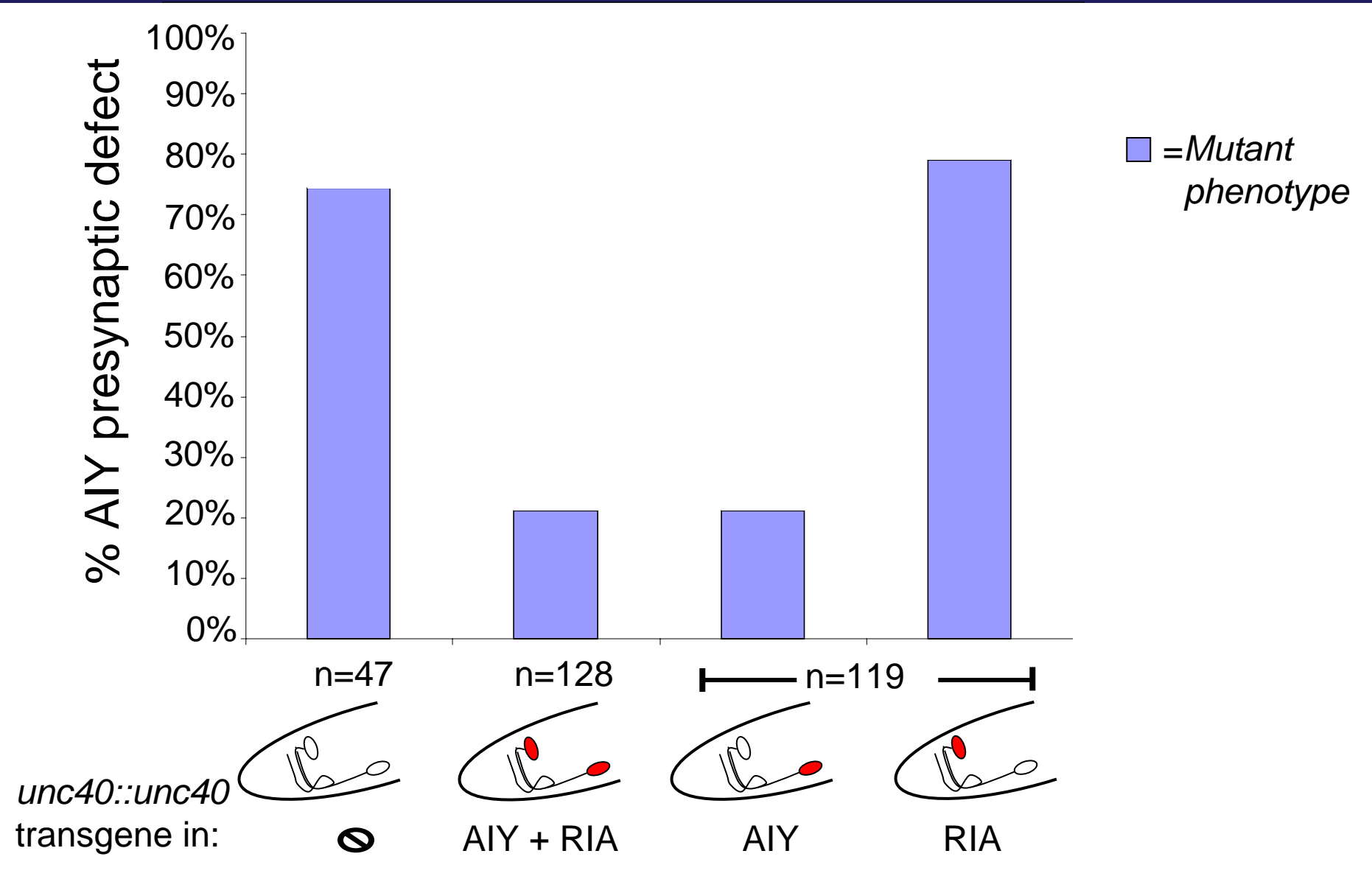
UNC-40 controls axon guidance in RIA



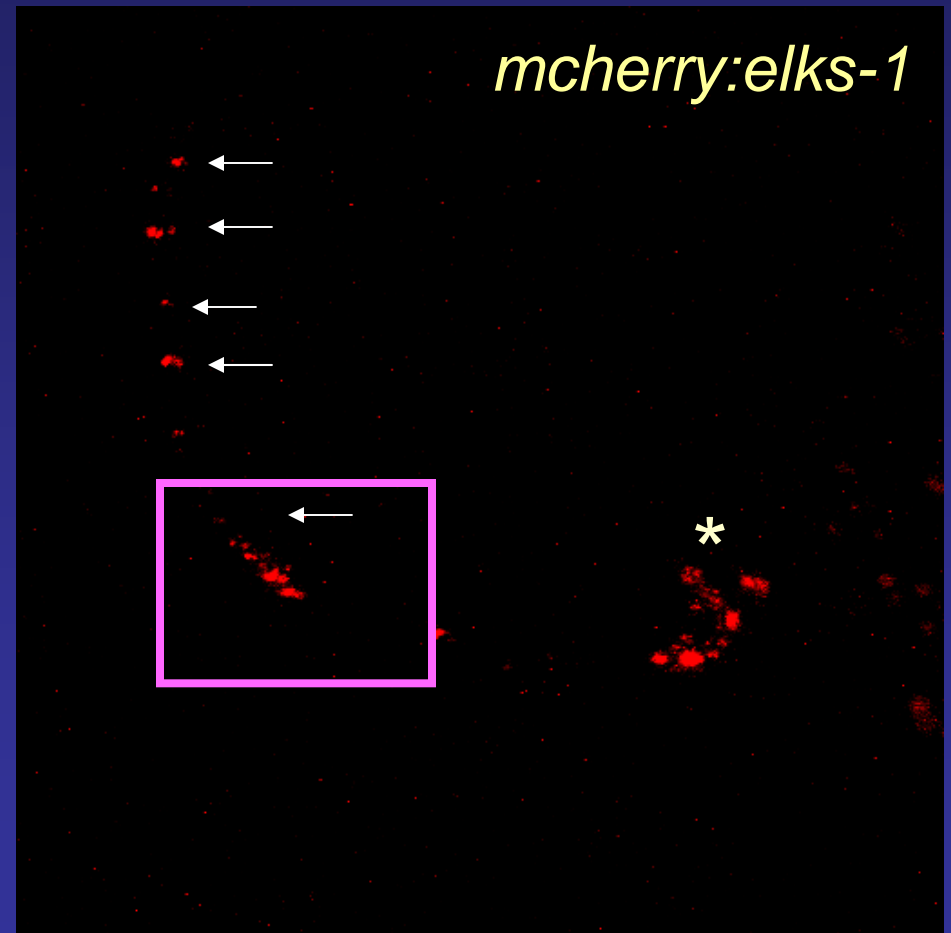
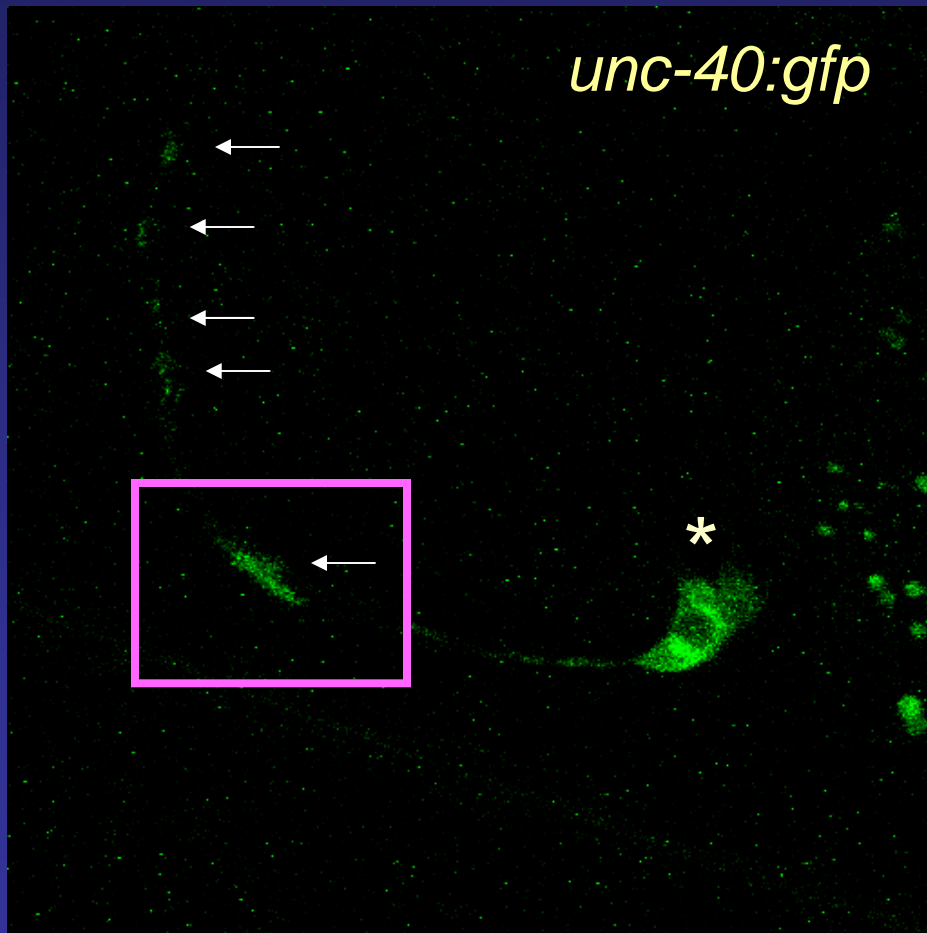
UNC-40 and AIY

1. UNC-40 effect in AIY is extrinsic and indirect
 - RIA is required for correct synaptic patterning in AIY
 - UNC-40 indirectly affects AIY by disrupting axon guidance in RIA
2. UNC-40 acts cell autonomously in AIY/RIA

UNC-40 acts cell autonomously in AIY



UNC-40 is enriched at presynaptic sites

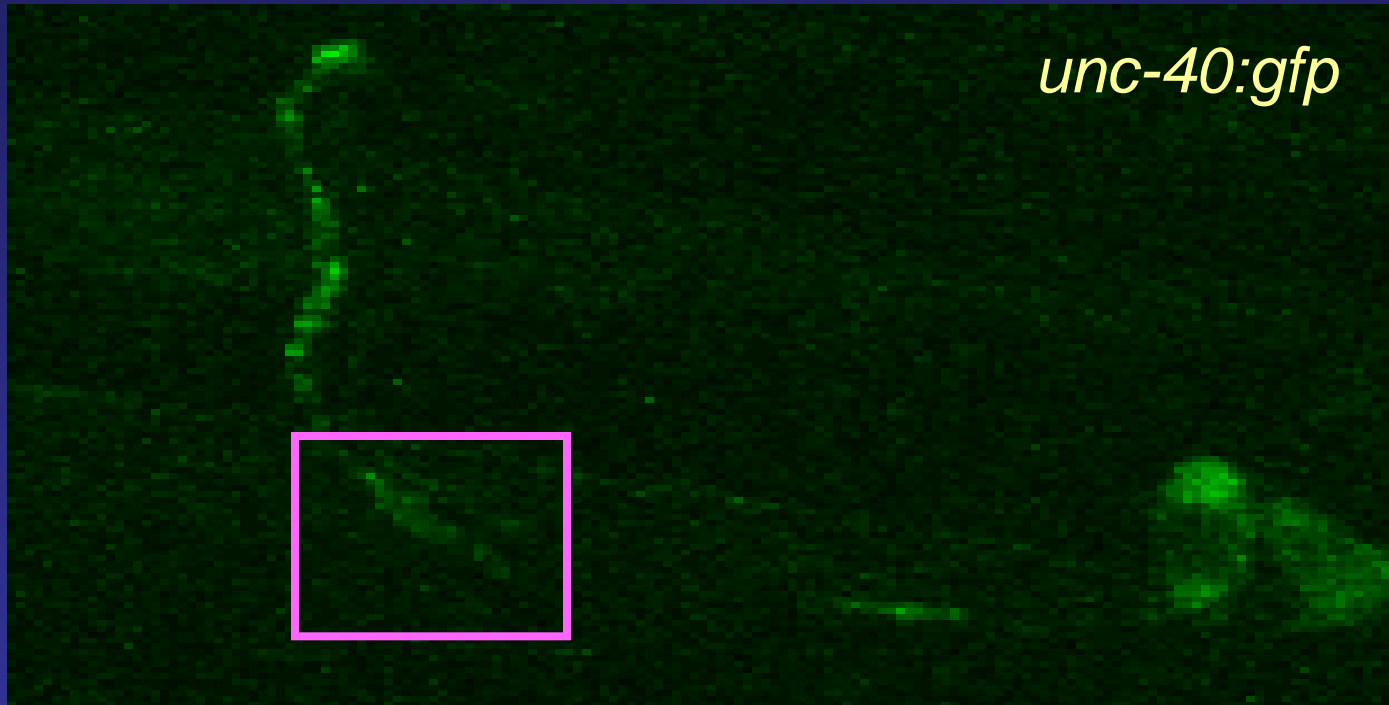


UNC-40/DCC as a molecular multitasker

- In RIA, UNC-40 controls axon guidance
- In AIY, UNC-40 directs correct presynaptic patterning
 - UNC-40 is enriched at AIY synaptic sites

What directs UNC-40 localization to synaptic sites?

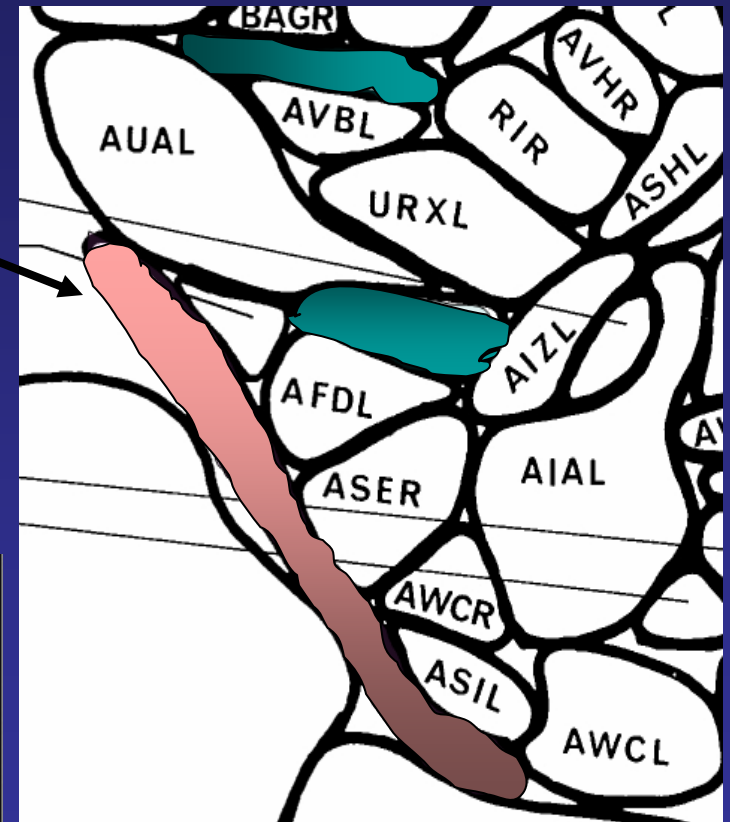
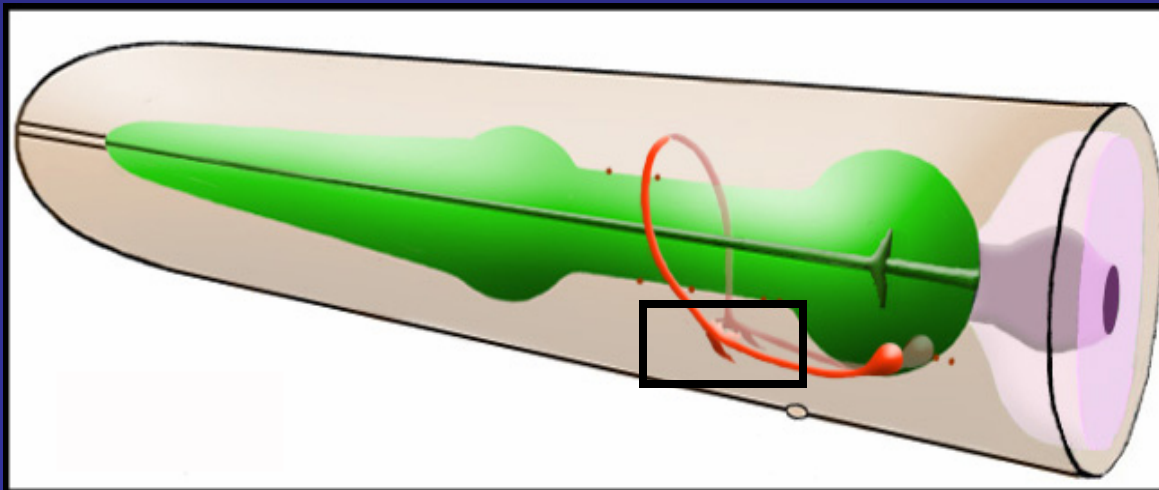
UNC-6/Netrin is required for UNC-40 synaptic enrichment



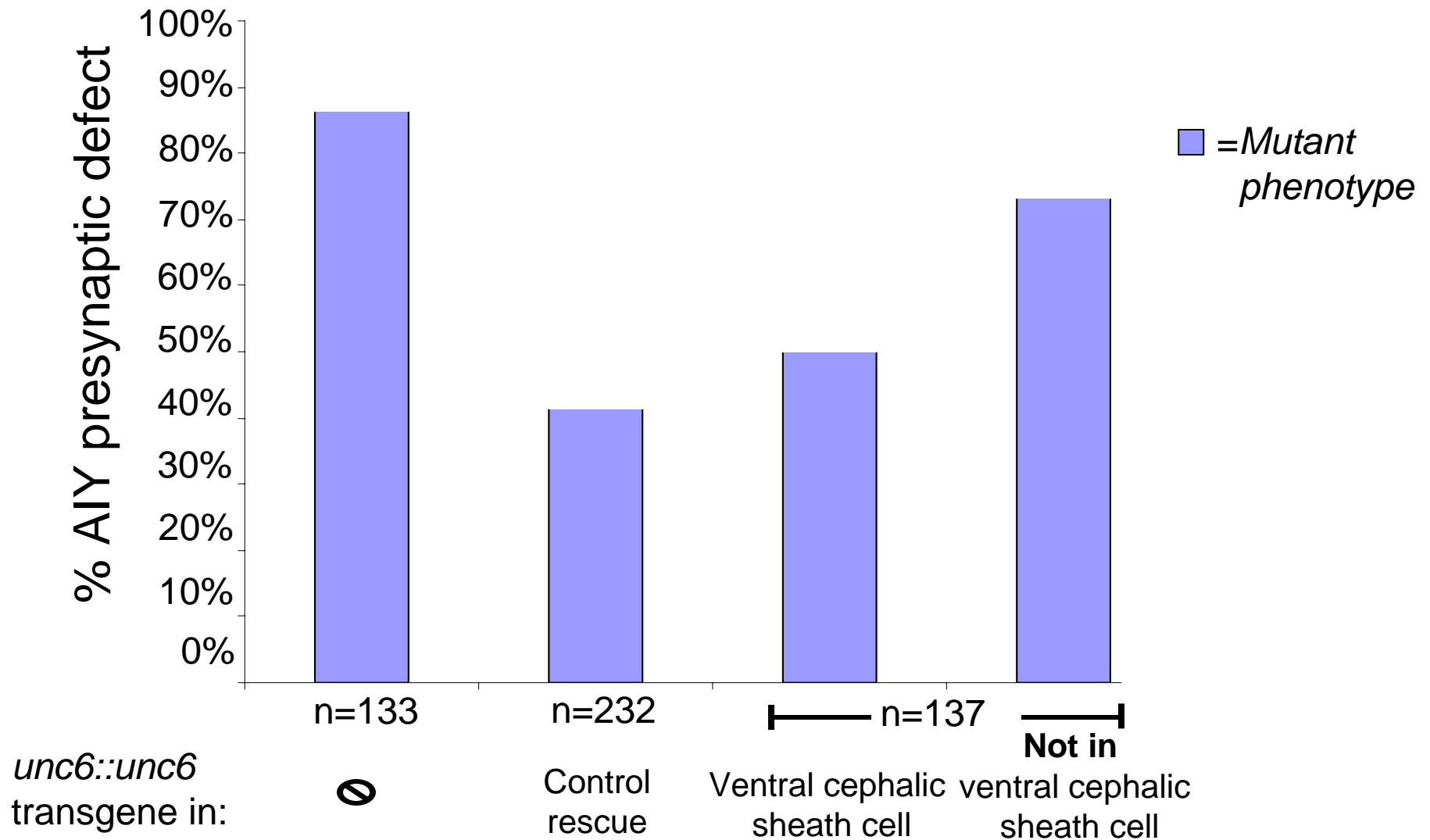
unc-6(ev400)X

UNC-6 is expressed by cephalic ventral sheath cells

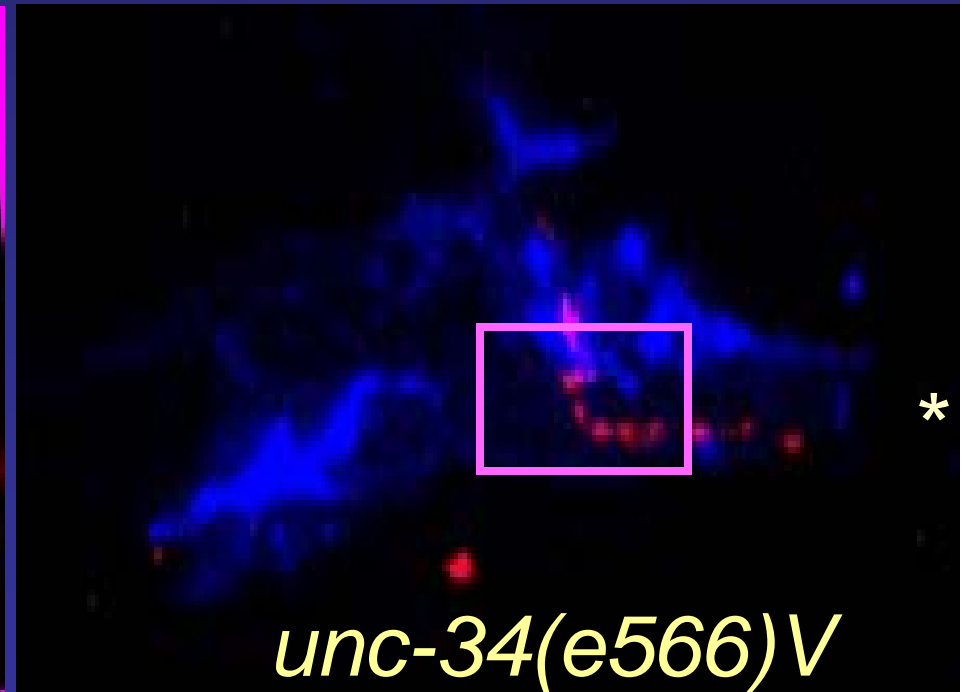
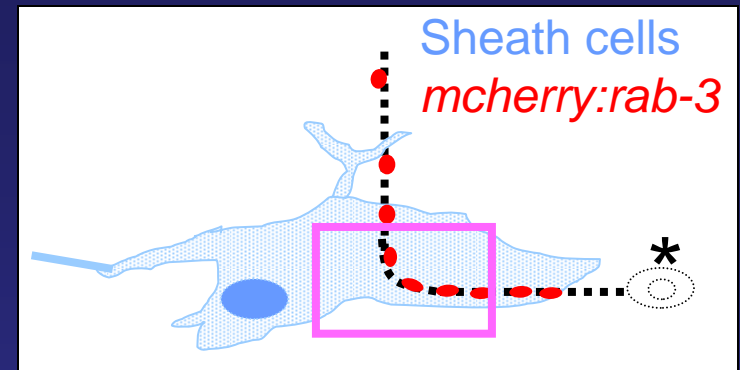
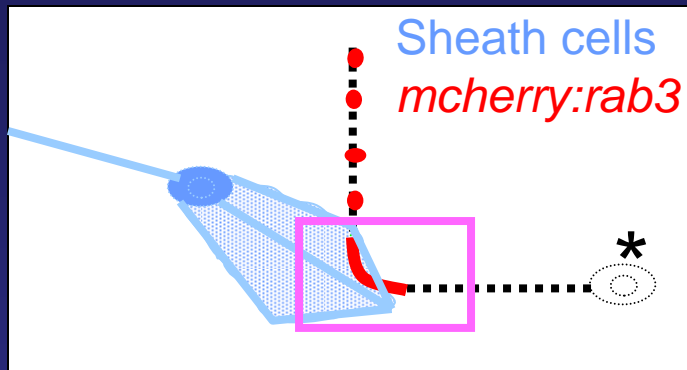
- UNC-6 is expressed in **ventral** cephalic sheath cells
- UNC-6 expression is **never** observed in **dorsal** cephalic sheath



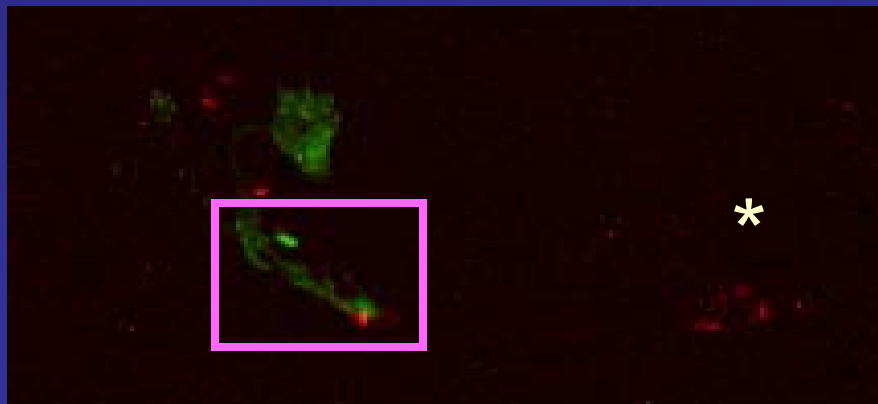
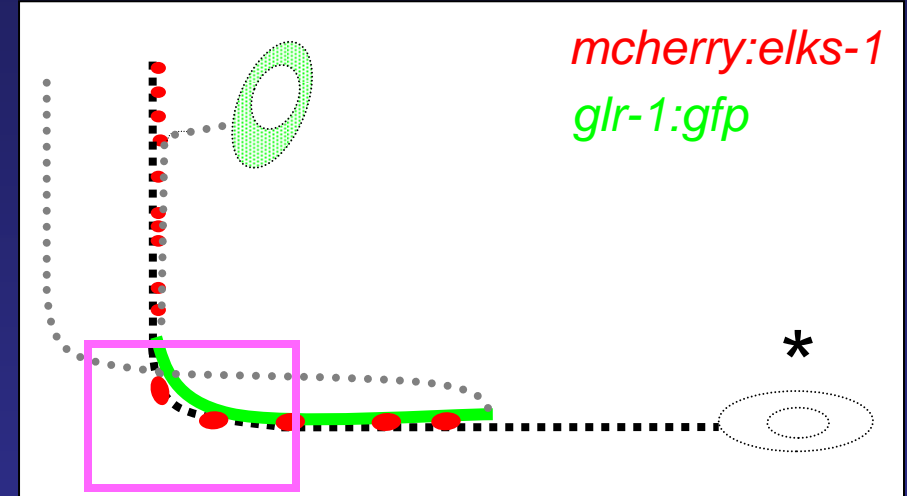
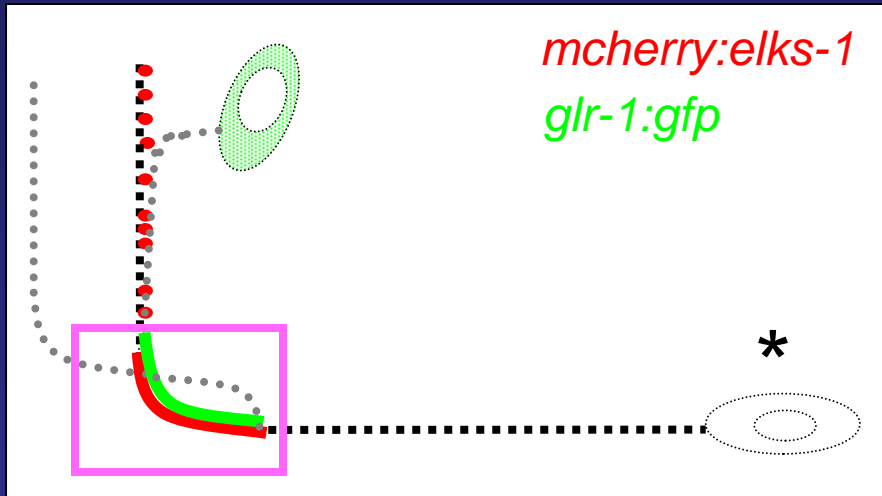
UNC-6 partially rescues when expressed in the ventral cephalic sheath cells



Altering ventral sheath cell position affects AIY synaptic rich region



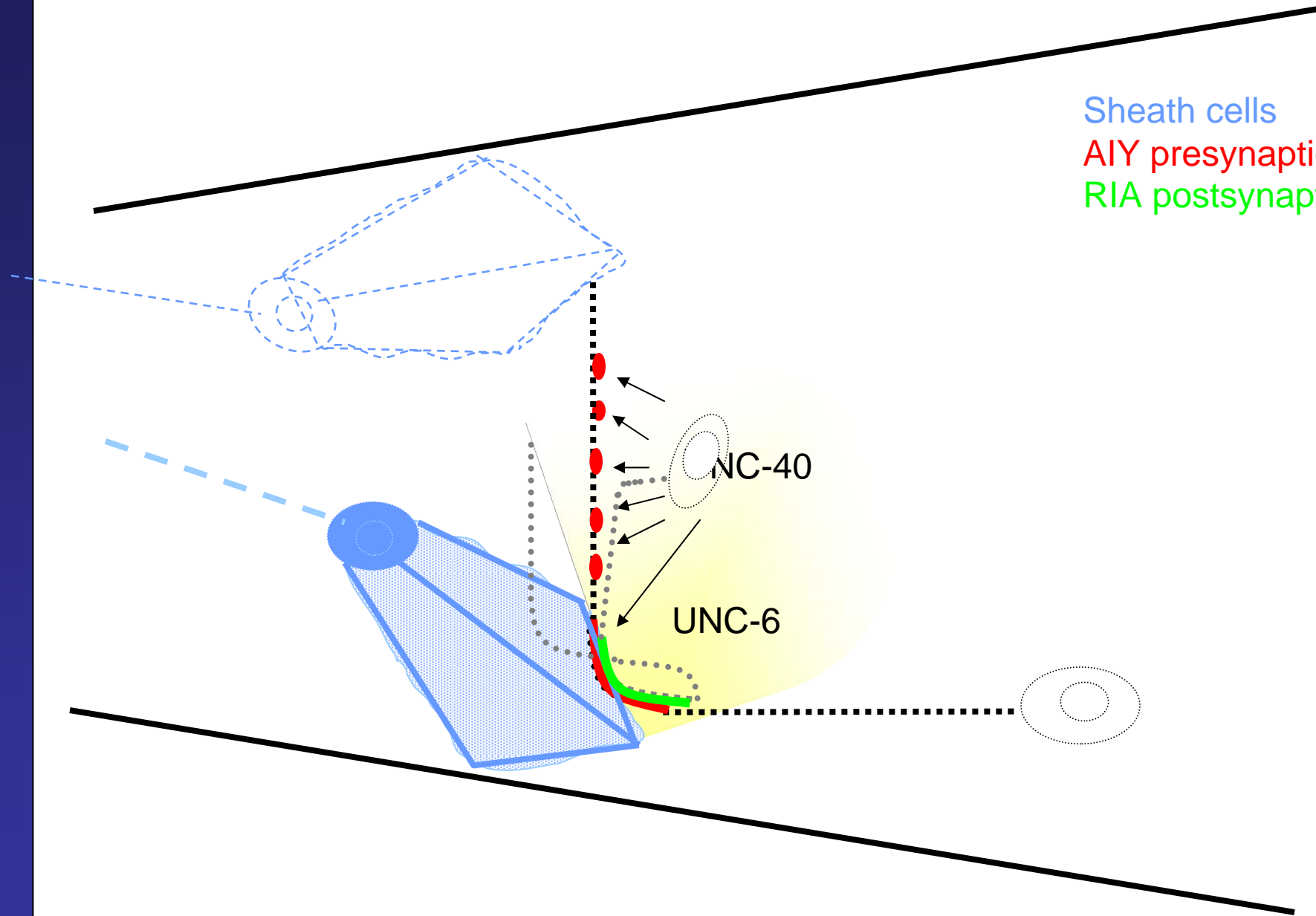
Altering ventral sheath cell position affects AIY synaptic rich region and RIA axon guidance



Wild type

unc-34 (e566)V

Sheath cells
AIY presynaptic
RIA postsynaptic



Summary

- UNC-40 is a synaptic targeting protein in AIY
- UNC-40 is a molecular multitasker:
 - Controls different pathways in cell-specific manner
 - RIA: axon guidance
 - AIY: synaptic targeting
- Ventral cephalic sheath cells act as guidepost cells by orchestrating circuit formation in the *C. elegans* nerve ring

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Kohara lab
CGC and Knockout consortium

Damon Runyon
Cancer Research
Foundation

Science and Puerto Rico: CienciaPR

- Resource network
- >750 members
- Promotes research among minorities
- Networking/collaboration/mentoring tool

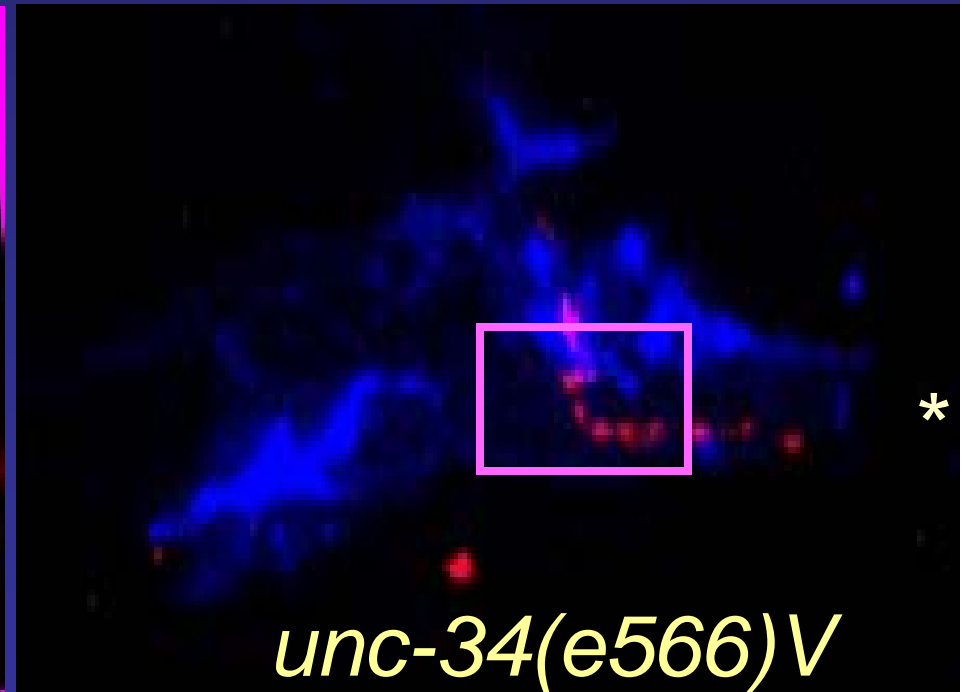
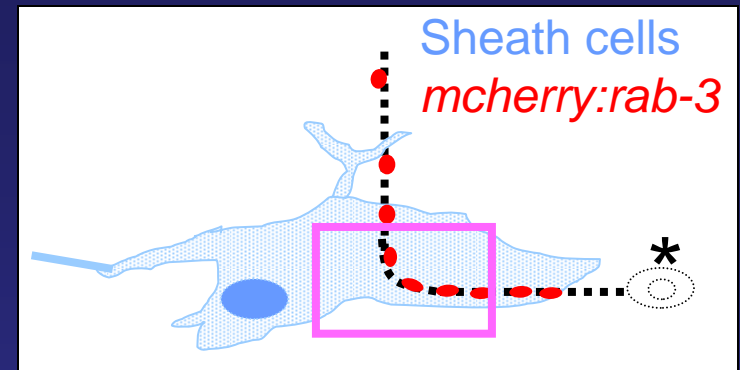
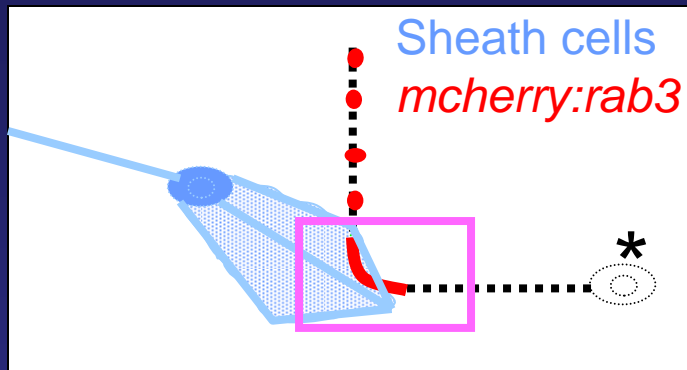
<http://www.cienciapr.org>

- Searchable directory
- Summer research opportunities for minority scientists
- Message boards
- Calendar of activities
- RSS feeds with funding news

<http://www.cienciapr.org>

- One year:
 - 750 members
 - >5000 hits daily
 - >50 countries
- Team of 8 volunteers
- 10 news articles on lay science in Puerto Rican newspapers
- Mentoring relationships

Altering ventral sheath cell position affects AIY synaptic rich region



Sheath cells
AIY presynaptic
RIA postsynaptic

