cGAL, a Bipartite Expression System for Transgene Control in *C. elegans*

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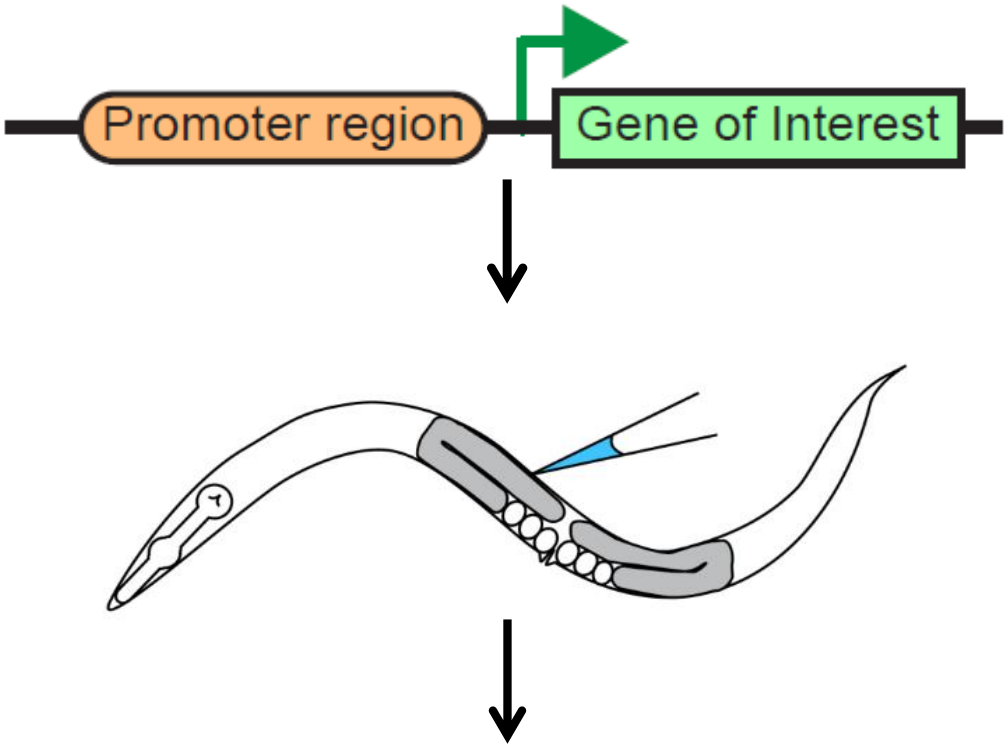
2019-06-23

Caltech

Classic *C. elegans* transgenesis

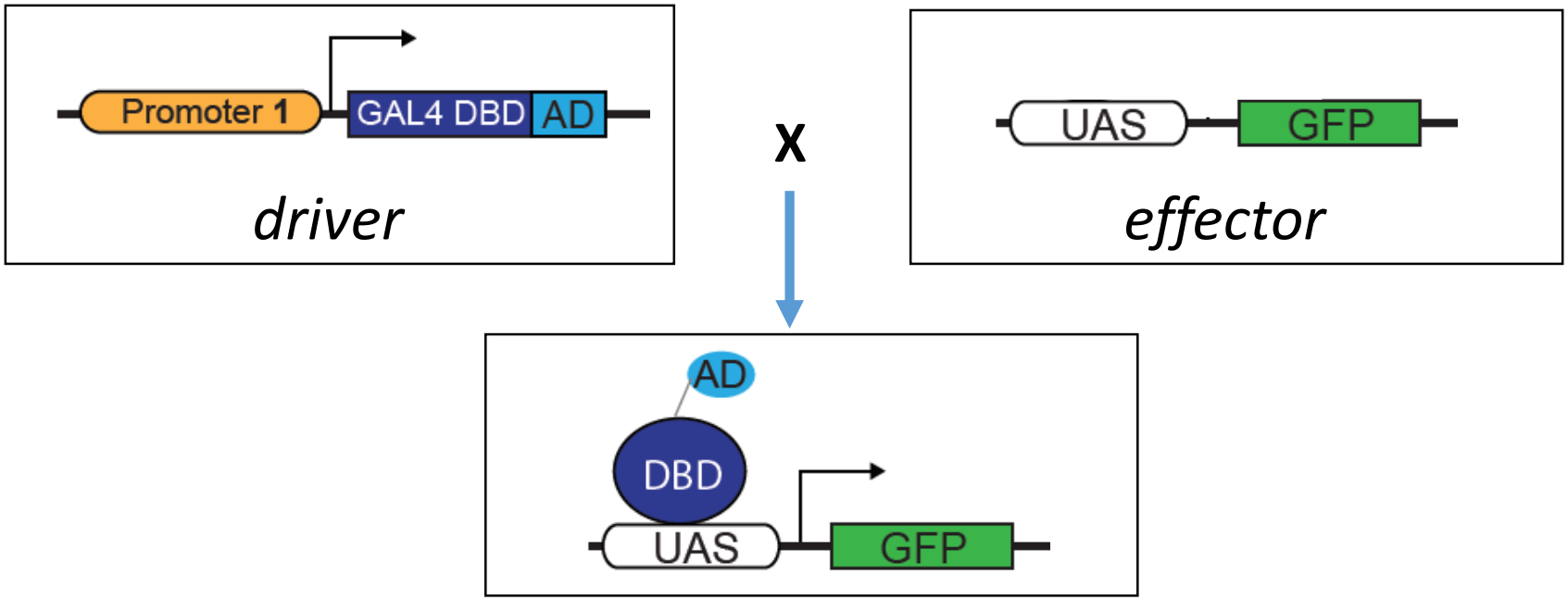


Manipulate gene activity and observe phenotypes

The GAL4-UAS system

From the yeast *S. cerevisiae*

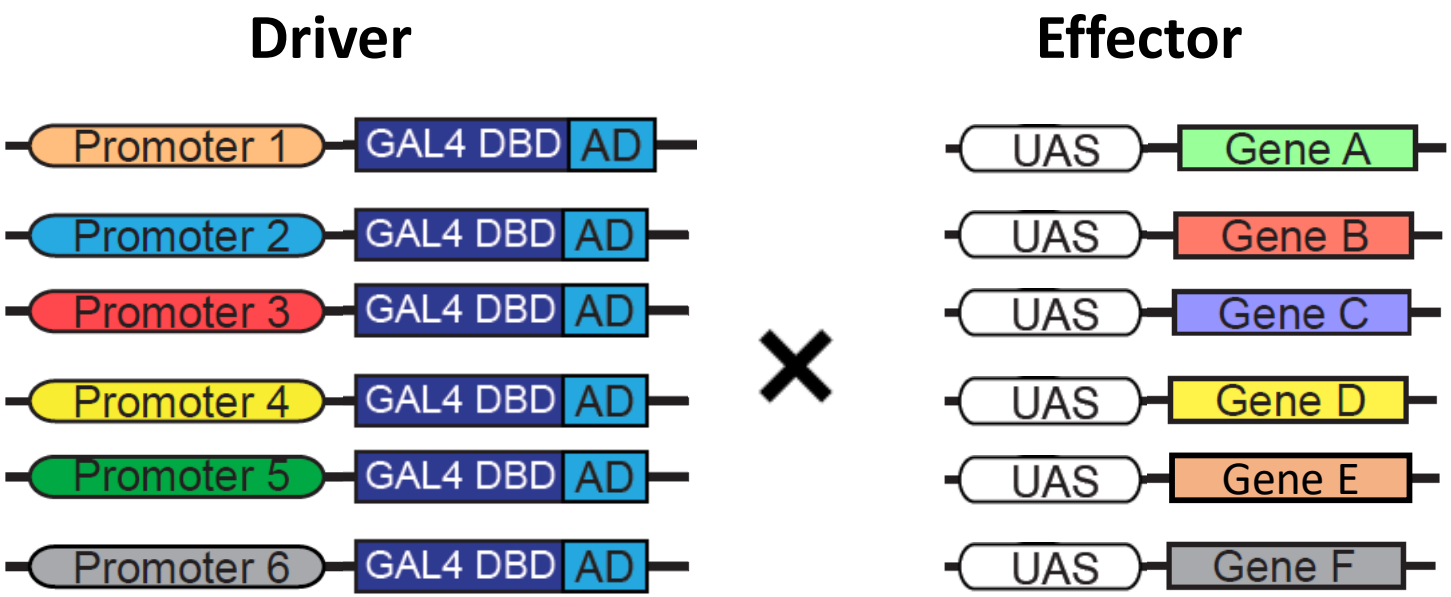
Widely used in *Drosophila* for transgene control.



DBD: DNA Binding Domain

AD: Activation Domain

The GAL4-UAS system is efficient



100 neurons + 20 genes

= 120 constructs and 120 transgenes,

but the same 2,000 strains

Advantages of the GAL4-UAS system

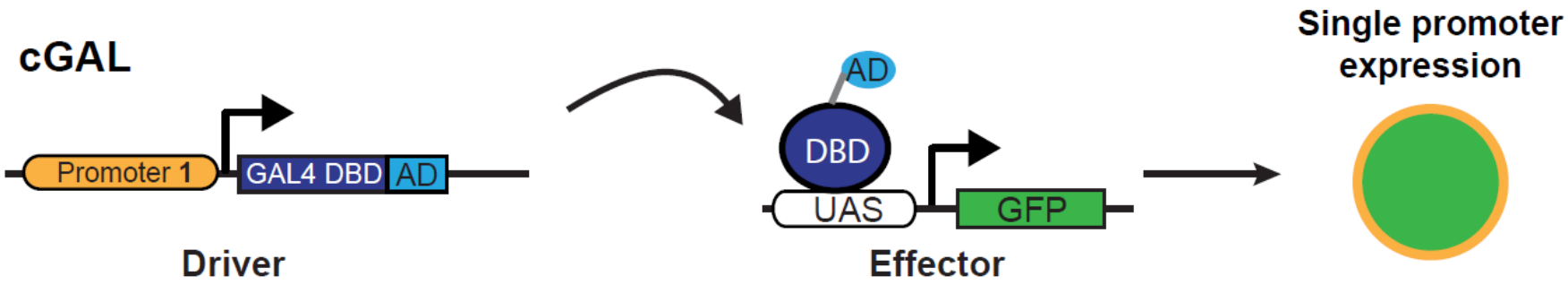
Efficient

Re-usable

Standardized

Easy to incorporate new tools

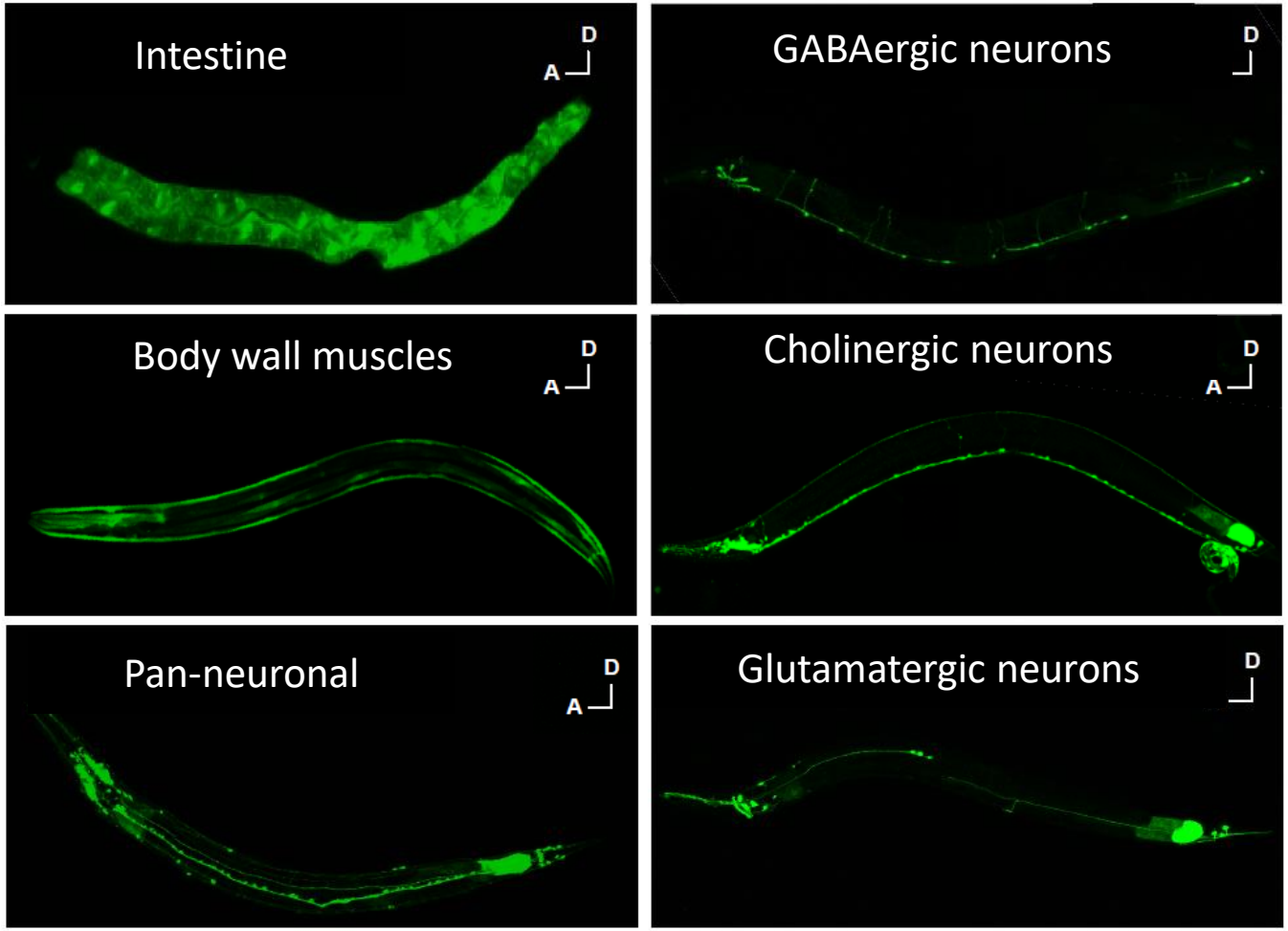
cGAL, a GAL4-based bipartite system for *C. elegans*



Wang and Liu *et al.*, 2017, Nature Methods

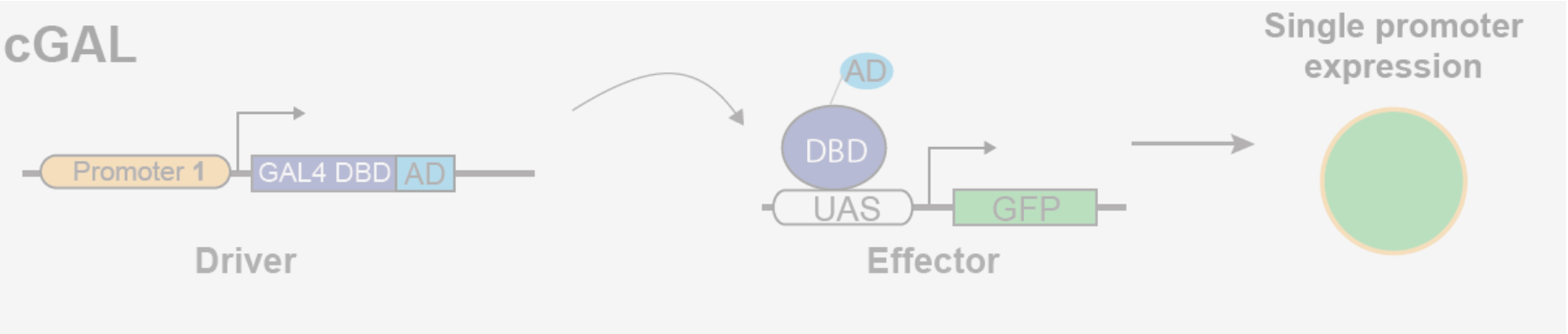
cGAL works robustly in different tissues

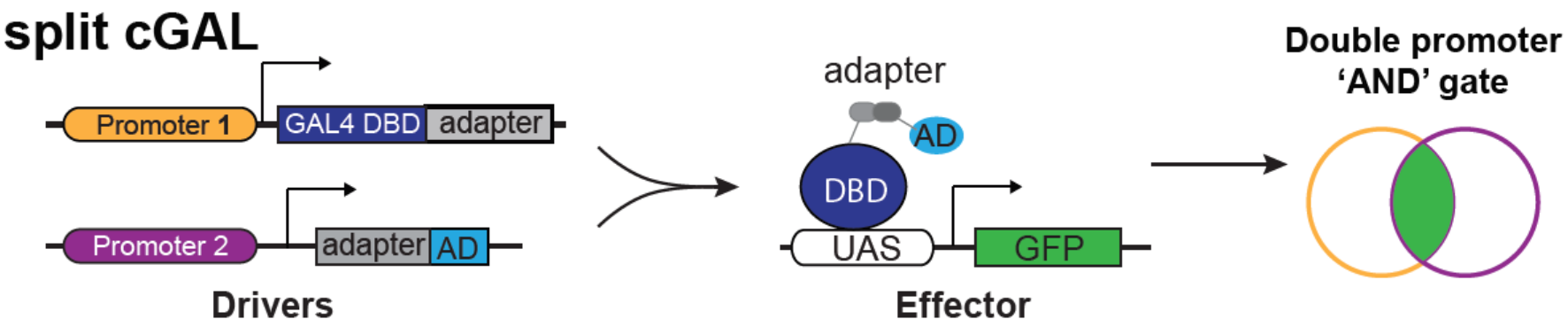
Tissue specific cGAL driver > UAS::gfp



Wang and Liu *et al.*, 2017, Nature Methods

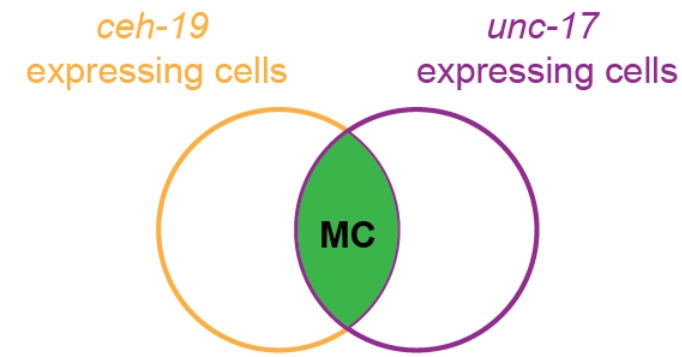
Intersectional split cGAL grants more precise control

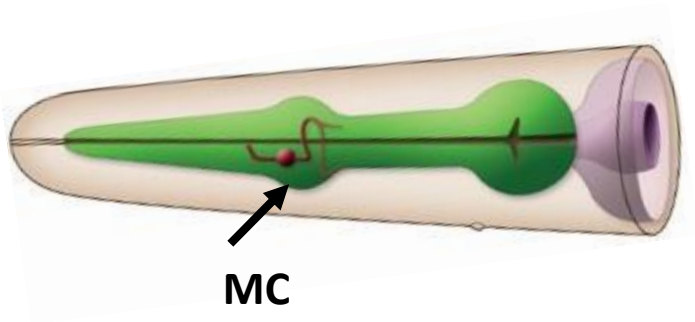




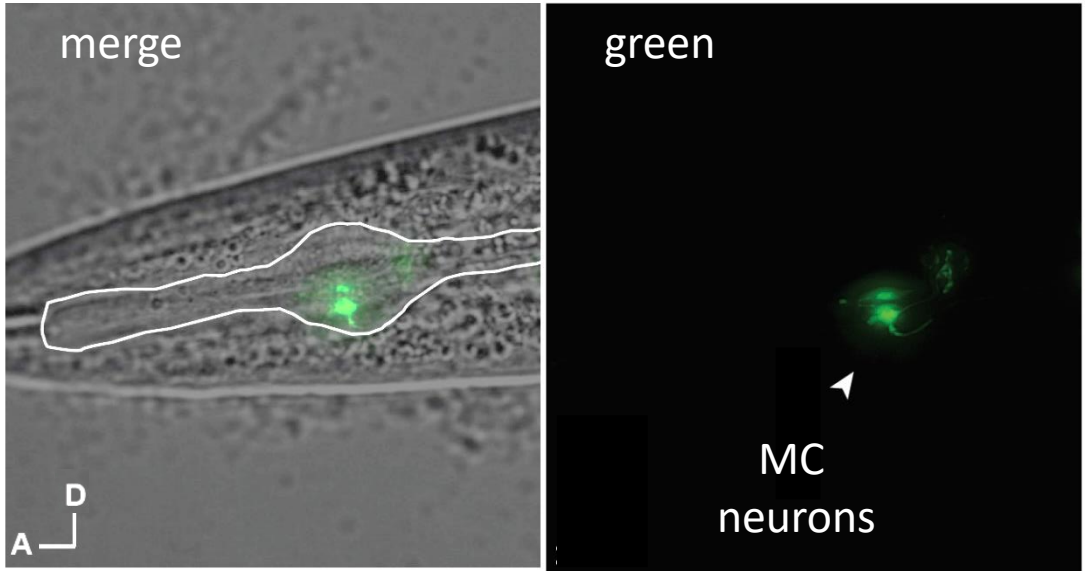
Wang and Liu *et al*., 2018, PNAS

Split cGAL can spatially restrict expression to single neuron types





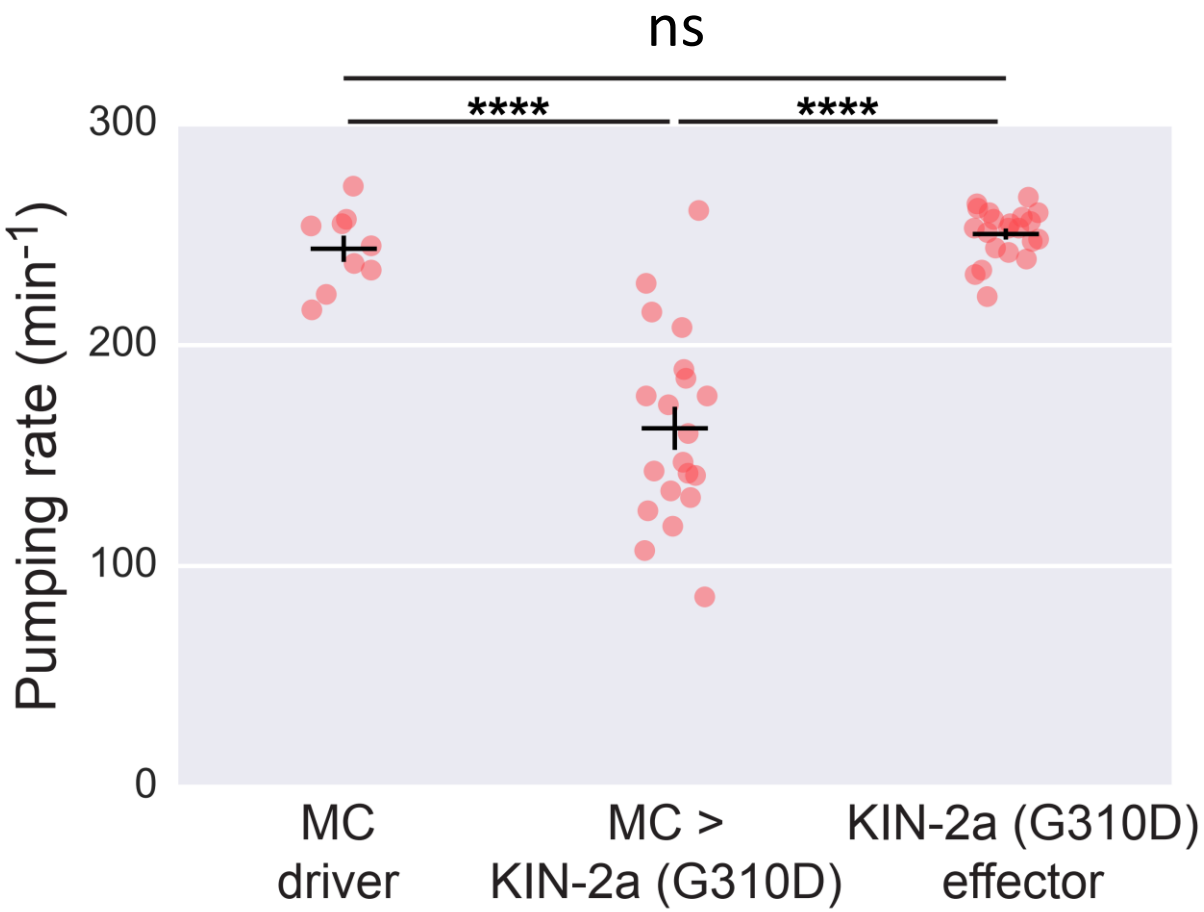
MC split cGAL driver > UAS::gfp



Wang and Liu *et al*., 2018, PNAS

PKA in MC neurons is required for normal pumping

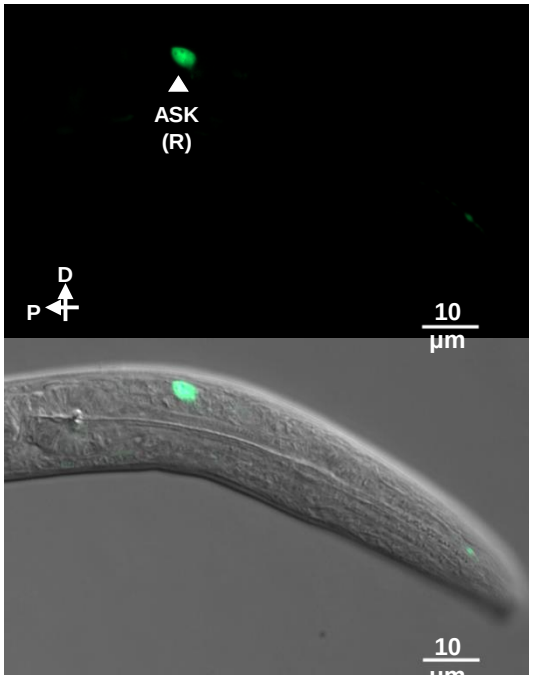
MC split cGAL driver > UAS::PKA(dn)

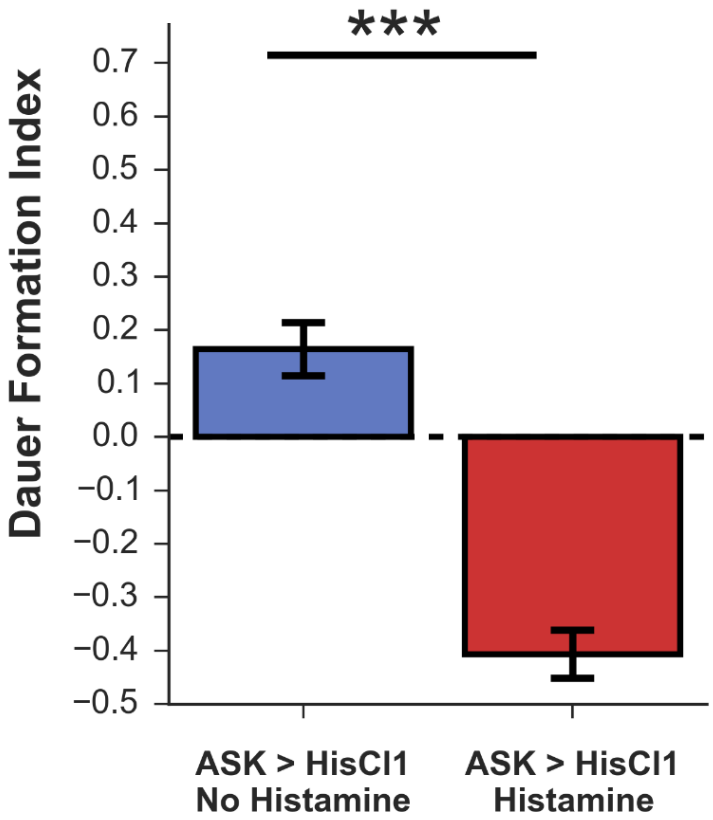


Wang and Liu *et al*., 2018, PNAS

Inhibition of ASK pheromone-sensing neurons inhibits dauer entry

ASK driver > UAS::gfp





C. Chai, 961C

Applications of cGAL/split cGAL

Sternberg Lab:

Dauer entry

J.S. Lee, 194
M. Cao, 712C
C. Chai, 961C

Sleep

H. Wang, 48

Male mating

C. Chen, 685C

Heat shock response

S. J. Walton, 1054C

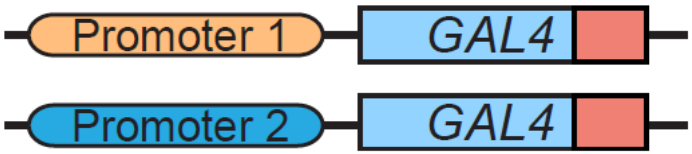
Other Labs:

L. Chauve, 93, neuronal stress

A.L. Zacharias, 435B, Wnt signaling

C. Ayuso & P. Askjaer, microPublication, 2019, cGAL with FLP/FRT

Current cGAL driver library



Total: 30 integrated drivers, including

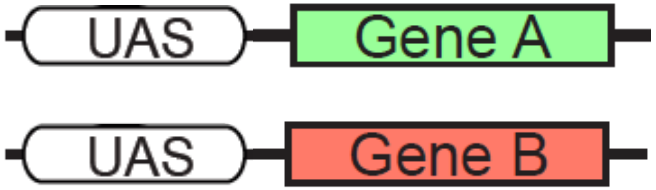
Major tissues (neuron, muscle, intestine, and hypodermis)

Neuron classes (e.g. Cholinergic and GABAergic neurons)

Single neuron types (e.g. ADF, ALA, DVA, DVC, RIA, etc…)

See Jun Young (Daniel) Oh's Poster 838C for details

Current cGAL effector library



Total: 33 integrated effectors, including

Neuronal manipulation (ChR2, Chrimson, HisCl1)

Calcium Indicators (GCaMP6, GCaMP7)

Cell ablations (miniSOG, ICE)

More …

See Jun Young (Daniel) Oh's Poster 838C for details

Summary

We developed the cGAL bipartite system for *C. elegans*;

We generated a set of cGAL drivers and effectors.

We successfully applied cGAL to study dauer formation, sleep, male mating, and heat shock response;

Future plans

Make drivers for all neurons

Make more effectors

Use cGAL for brain-wide functional circuit mapping

Further engineer the cGAL system (e.g. an inhibitory cGAL and single copy cGAL)

Acknowledgments

PI: Paul Sternberg

cGAL team
Jonathan Liu
Jun Young (Daniel) Oh
Shahla Gharib
Cynthia Chai
Chun-Hao Chen
Mengyi Cao
James Lee
Pei-Yin Shih
Stephanie Nava
Minyi Tan
& other lab members

Poster 838C
Sunday, June 23
3:00 - 4:00 PM

NIH NIGMS K99
NIH NIMH R21
Della Martin Postdoc Fellowship

Caltech

NIH

cGAL DNA samples available!