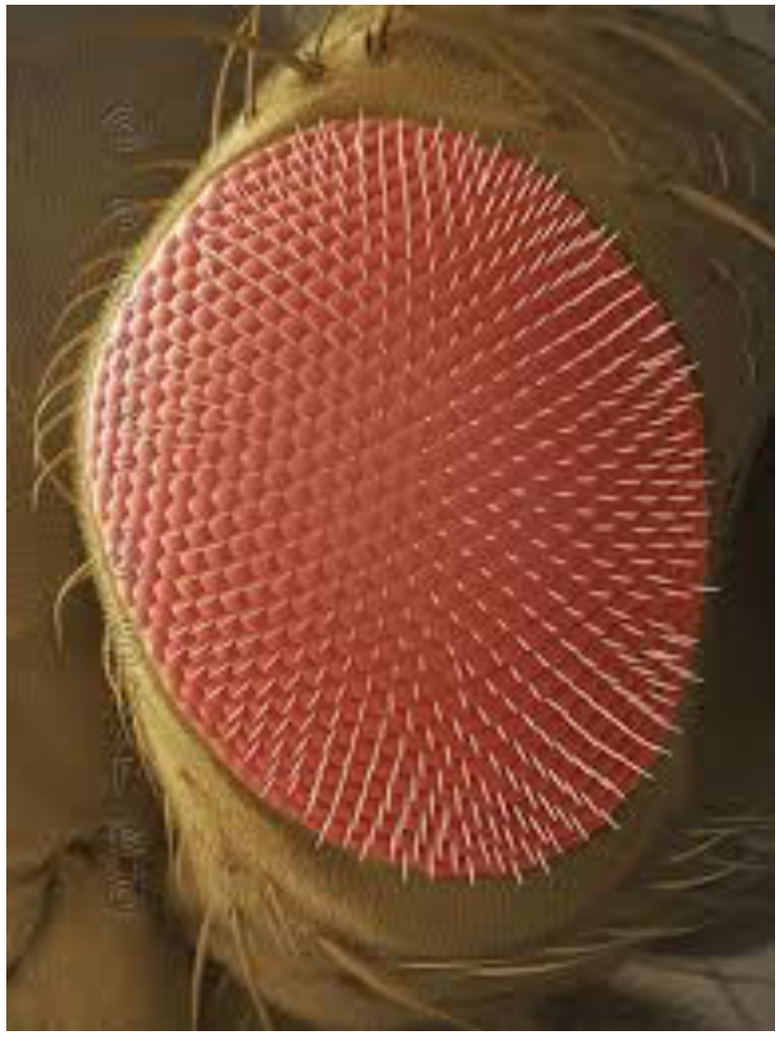
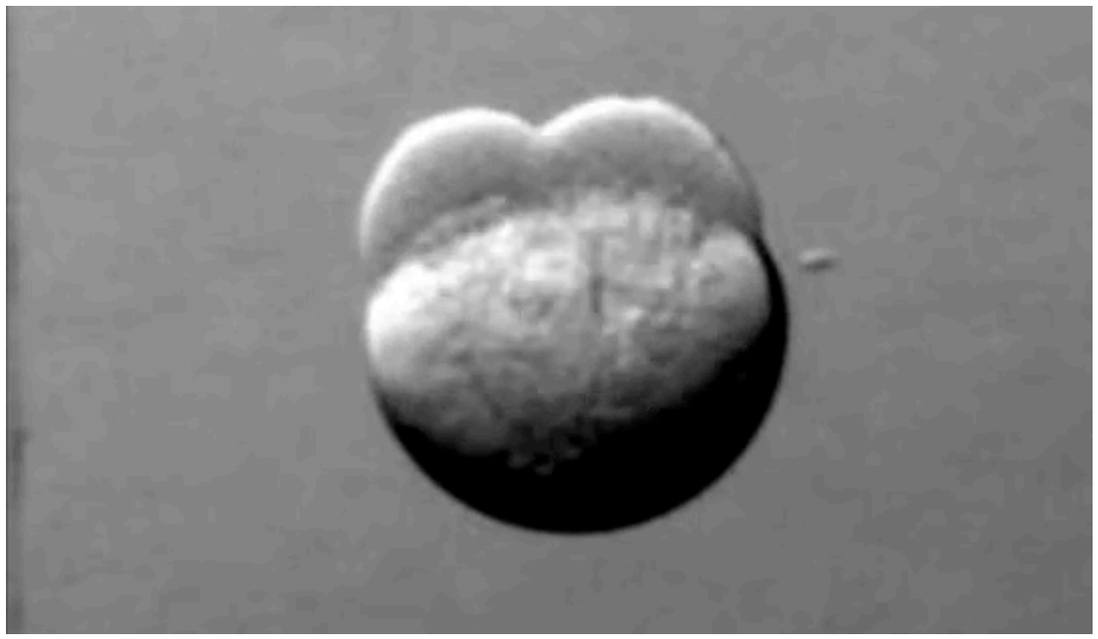
Developmental genetics

C. elegans



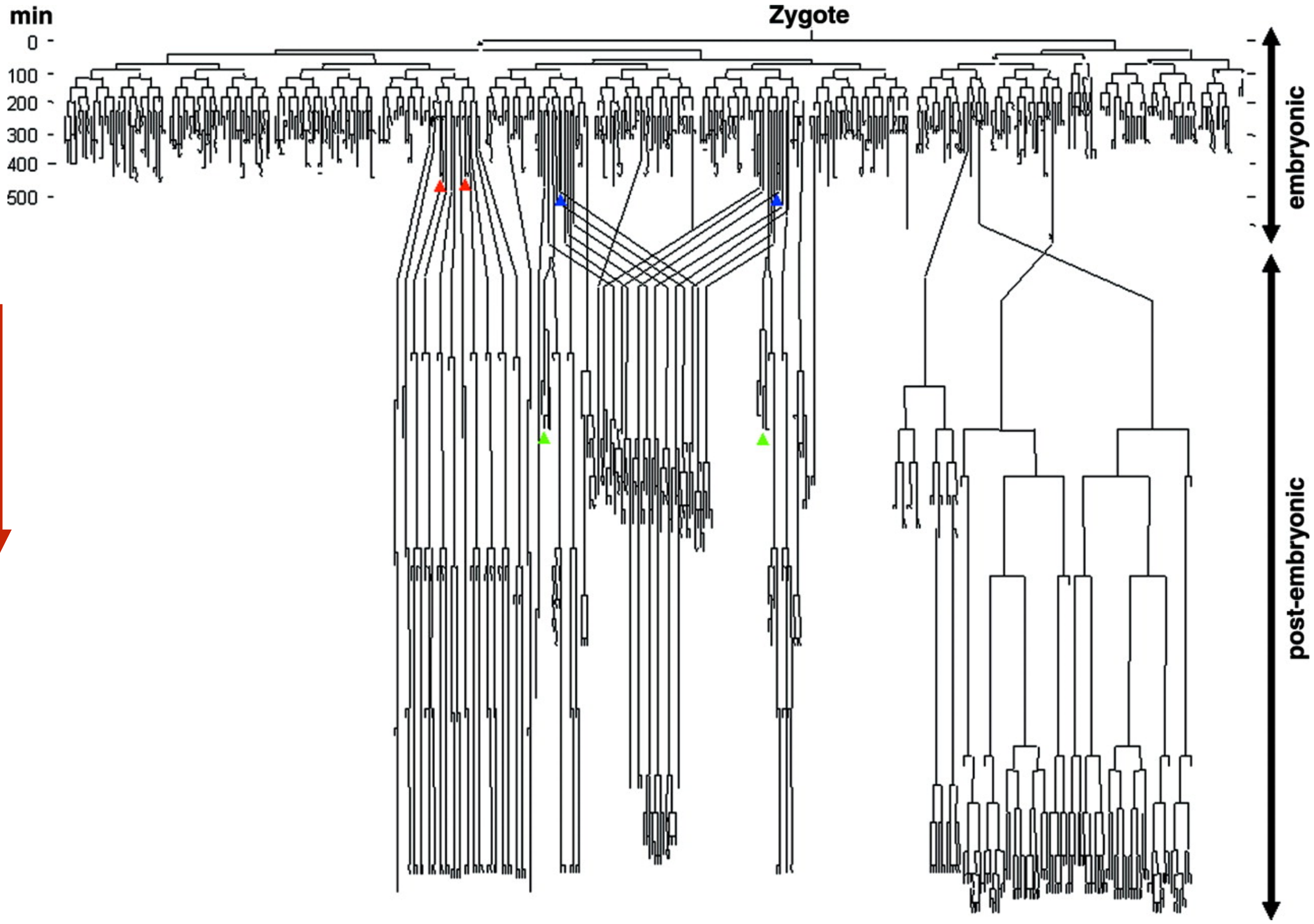
D. melanogaster

Developmental genetics is the study of how genes regulate the growth and development of an organism.



Cell location
Cell fate
Cell-cell communication
Maternal effects
Cell autonomy
Epistasis

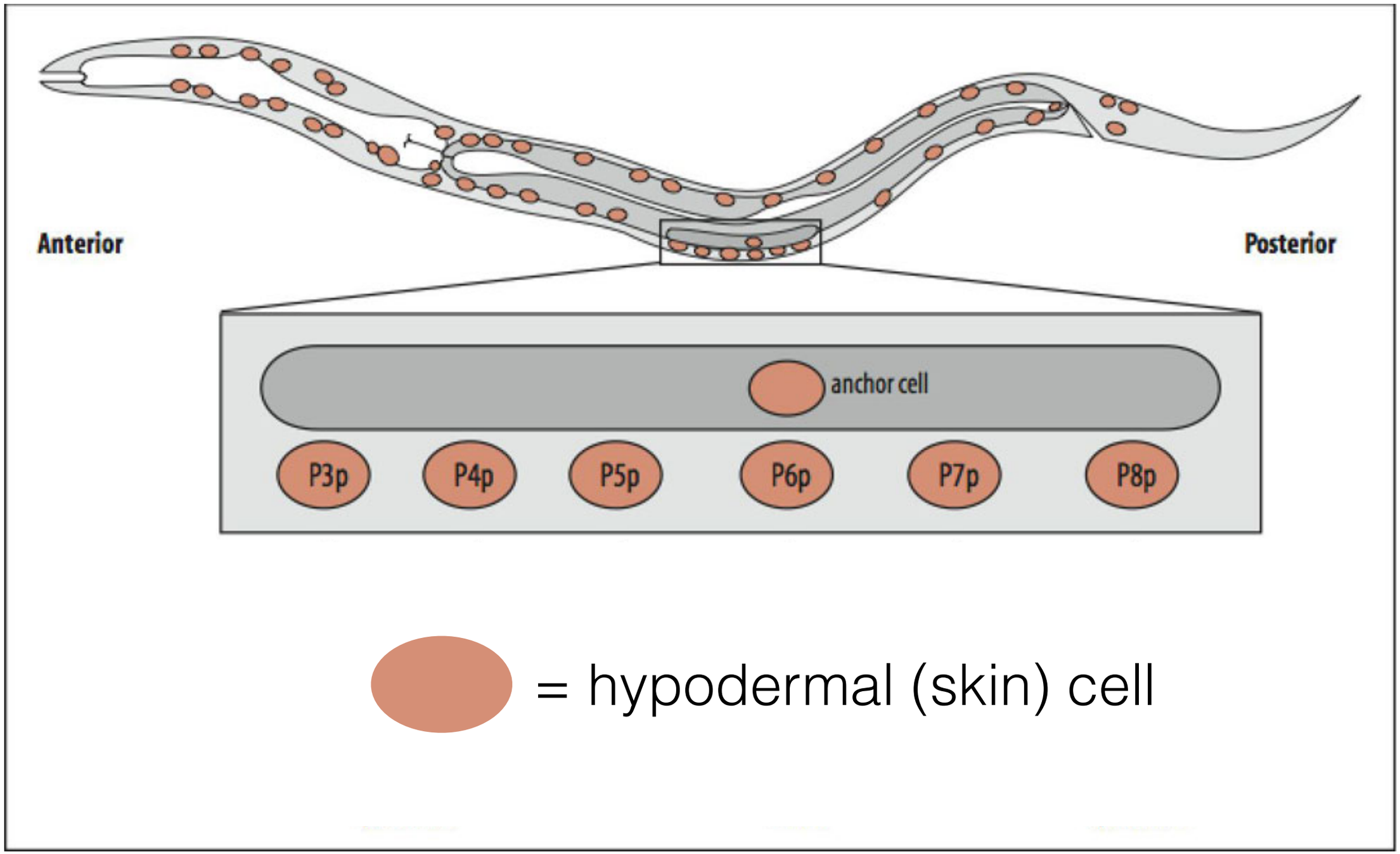
The cell lineage of *C. elegans* is known and invariant



The cell lineage of *C. elegans* is known and invariant

John Sulston

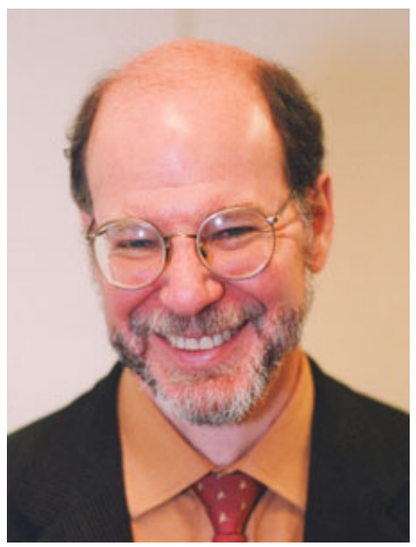
C. elegans vulval development



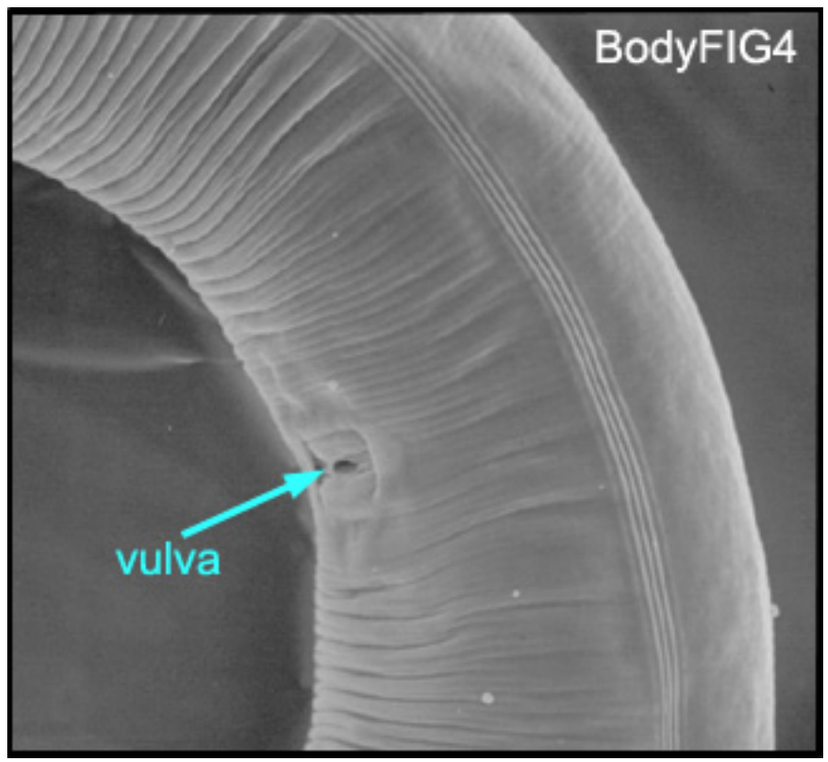
One of the best genetic screens ever

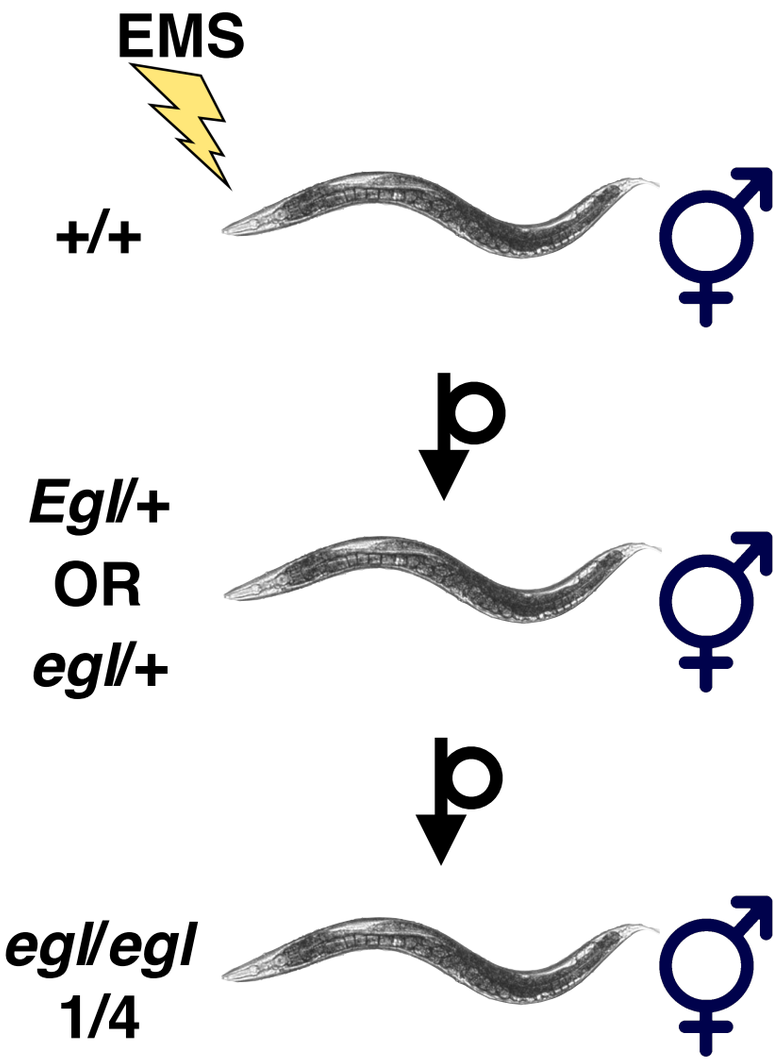
Let's say you screened for mutants that failed to lay eggs

Called Egl for egg-laying defective

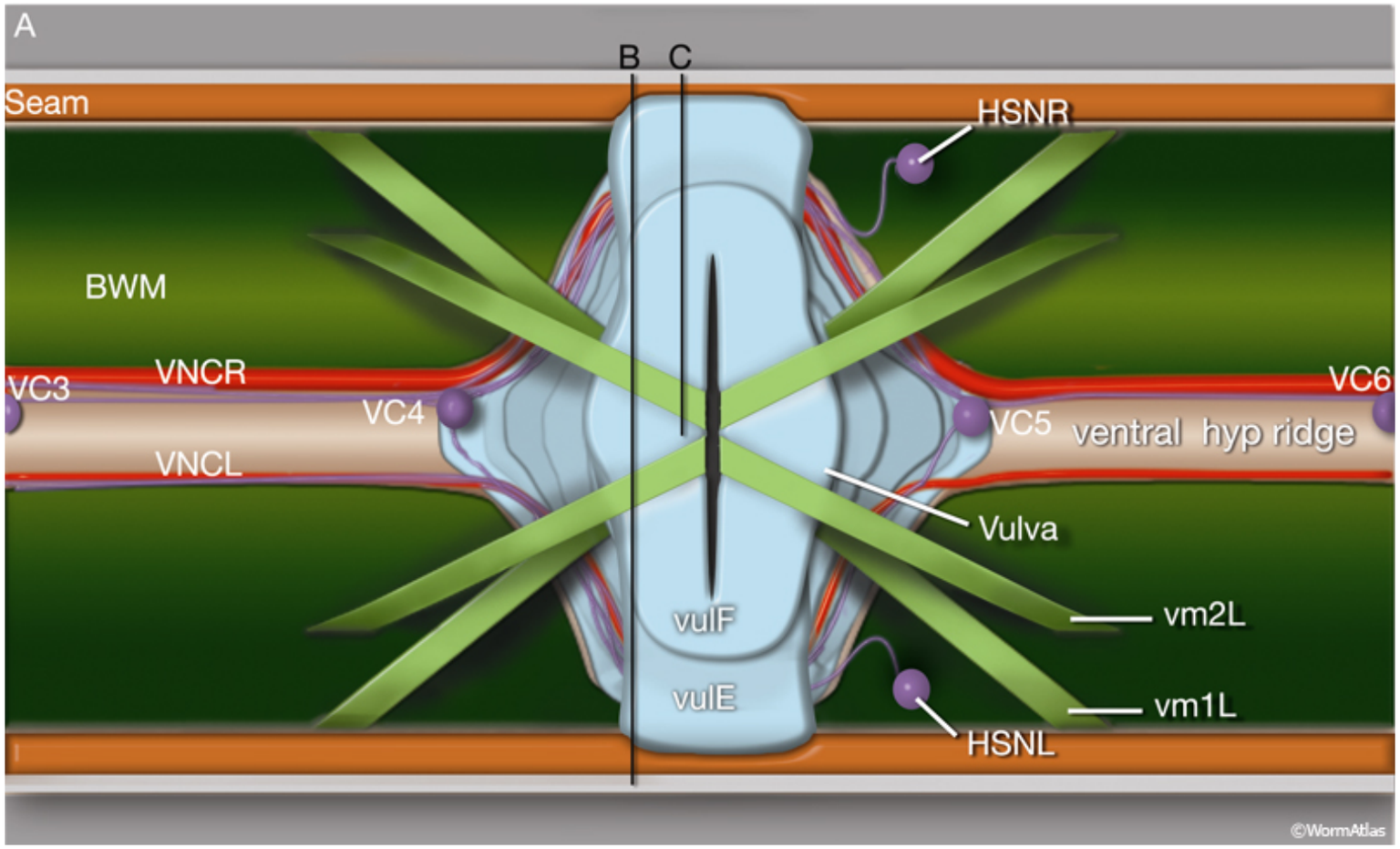


Bob Horvitz





One of the best genetic screens ever

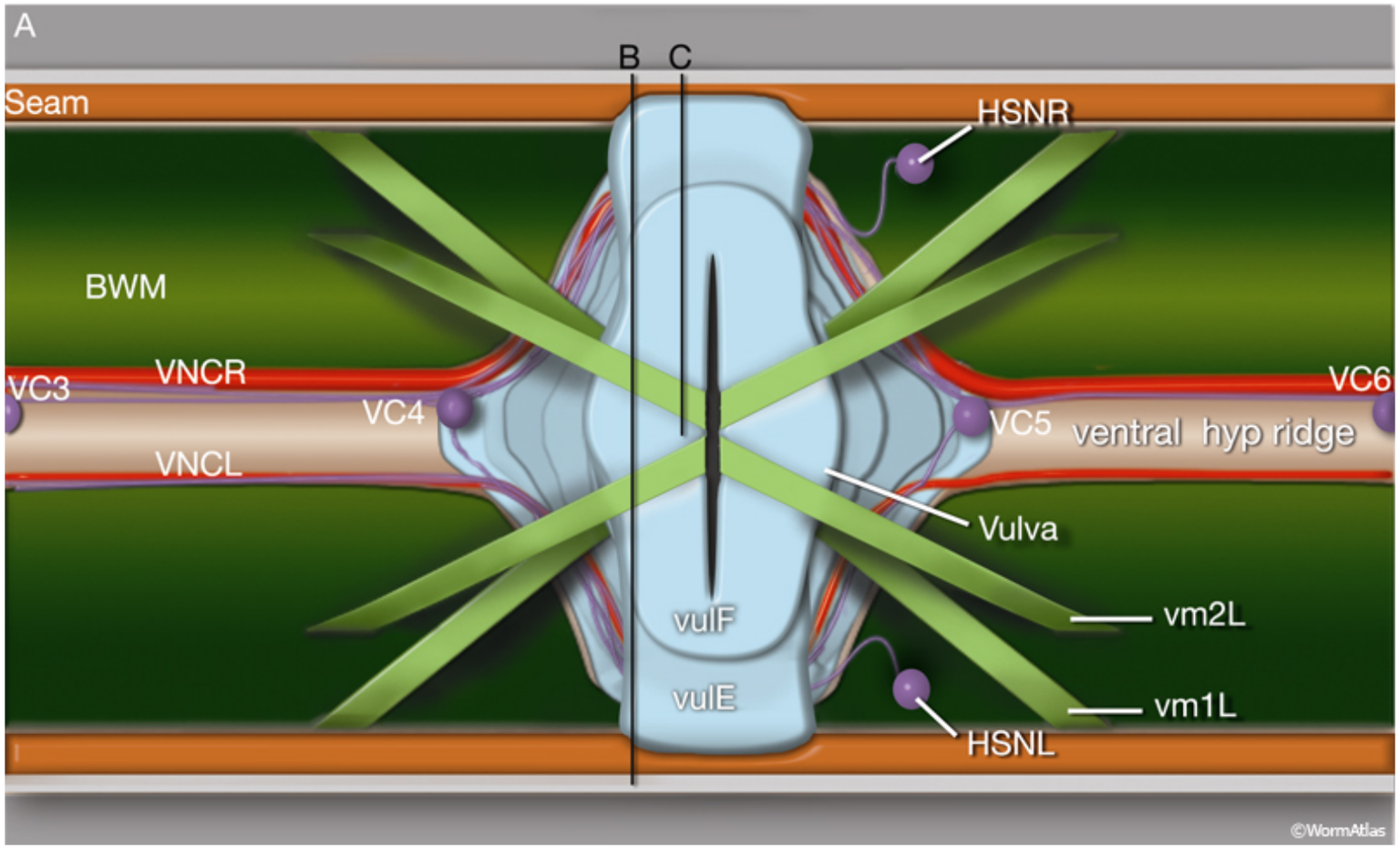


No neuron

egl-1 = inducer of programmed cell death

Hermaphrodite-Specific Neuron (HSN) inappropriately dies

One of the best genetic screens ever

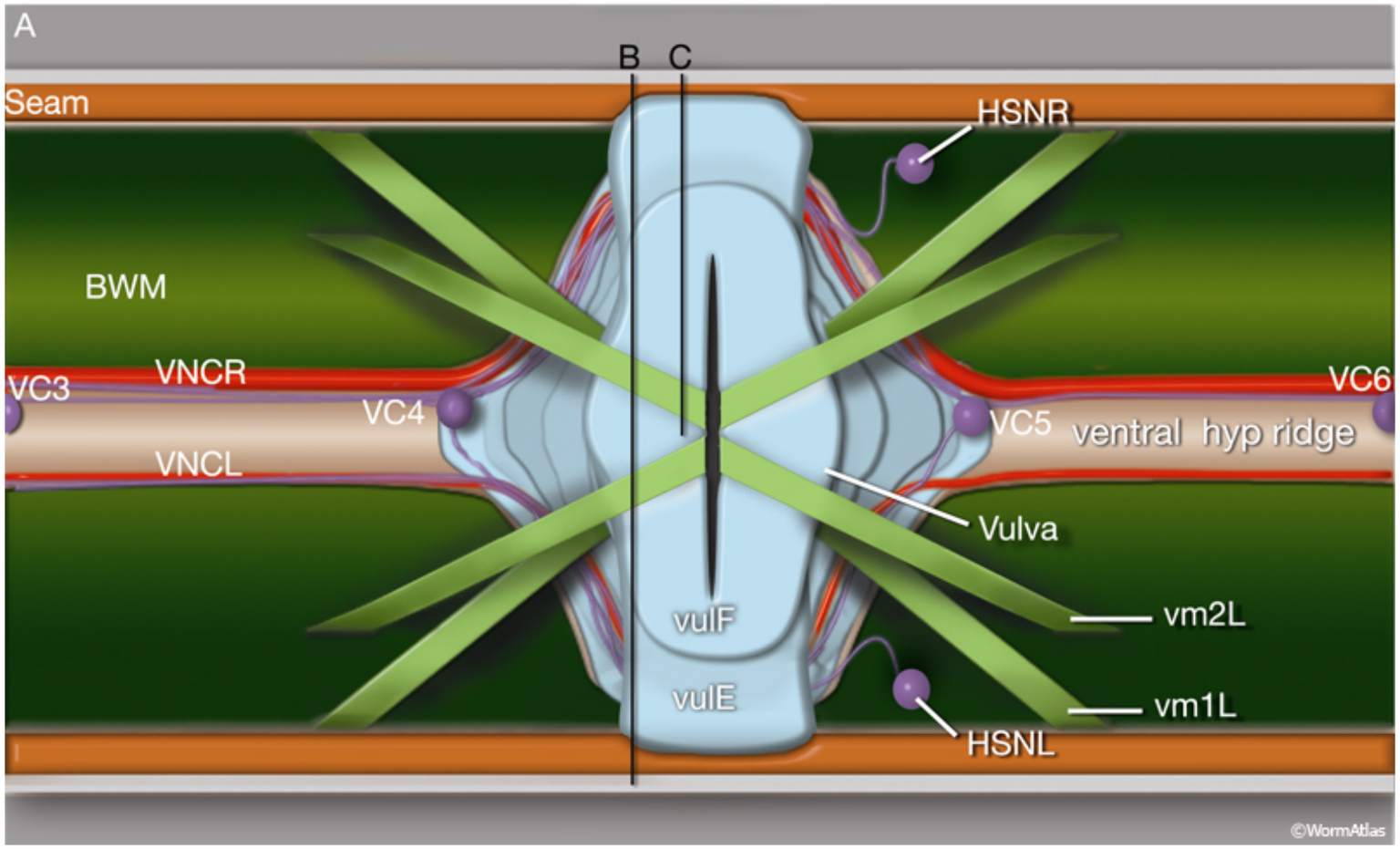


No neuron

tra-1 = inducer of sex determination

Mutants are partially male so HSNs die

One of the best genetic screens ever

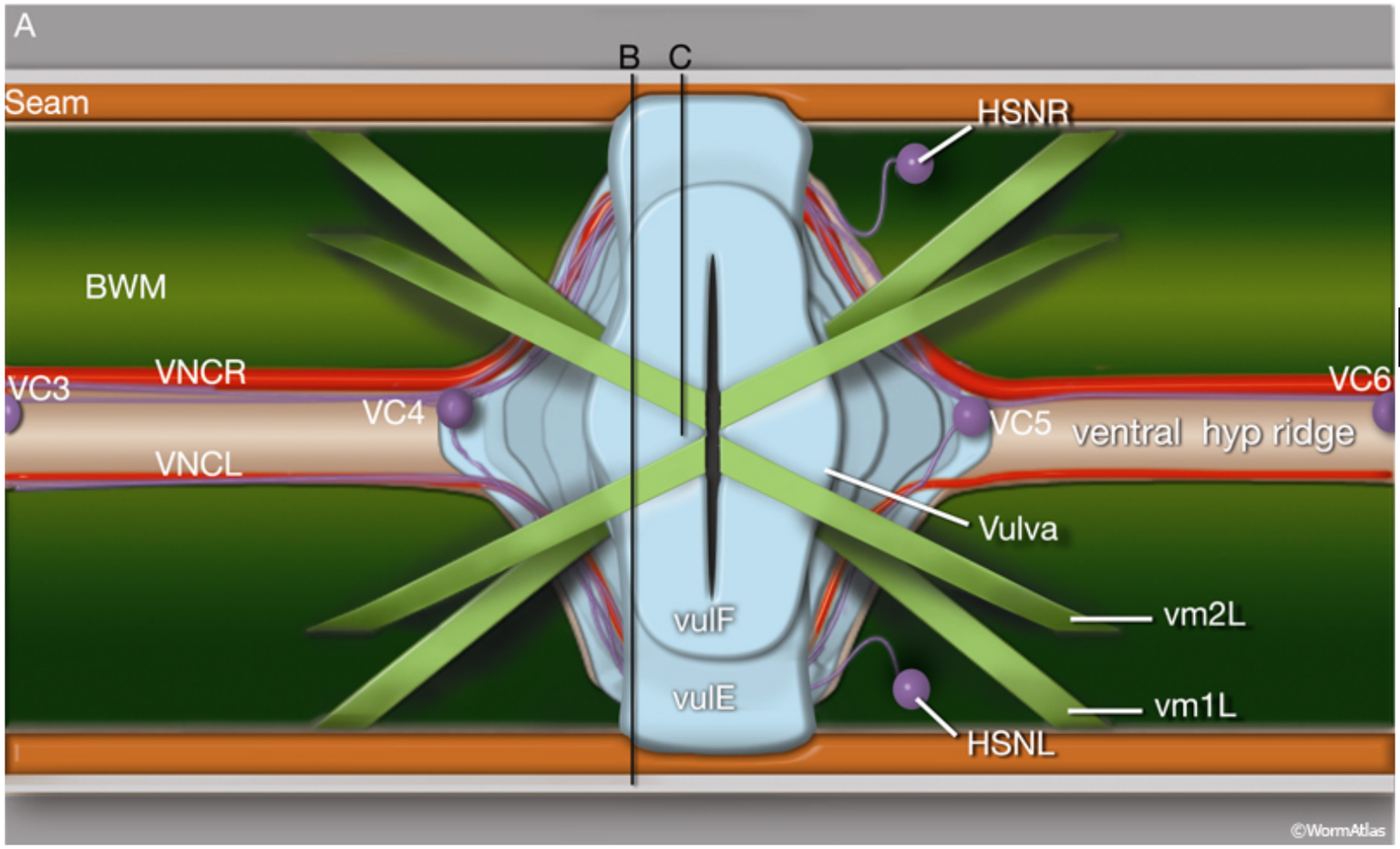


No neuron

No neuronal signaling

egl-6 = seratonin signaling from HSN is defective

One of the best genetic screens ever



No neuron

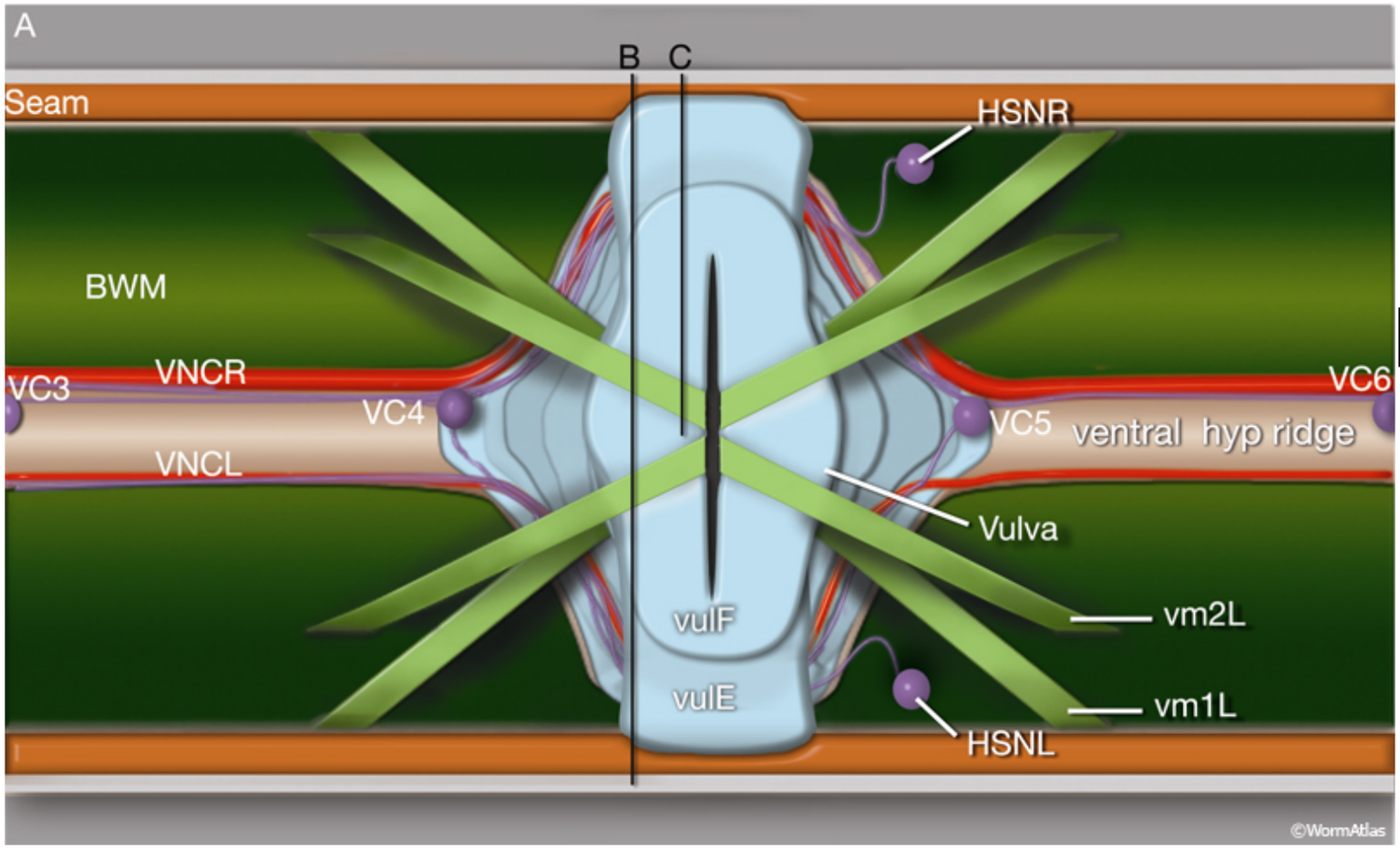
No neuronal signaling

No vulva

lin-3 = lineage defective gene 3

Vulval cells are not specified

One of the best genetic screens ever



No neuron

No neuronal signaling

No vulva

Vulval muscle fails to function

Vulval opening fails to form

Uterus doesn’t connect to vulva

One of the best genetic screens ever

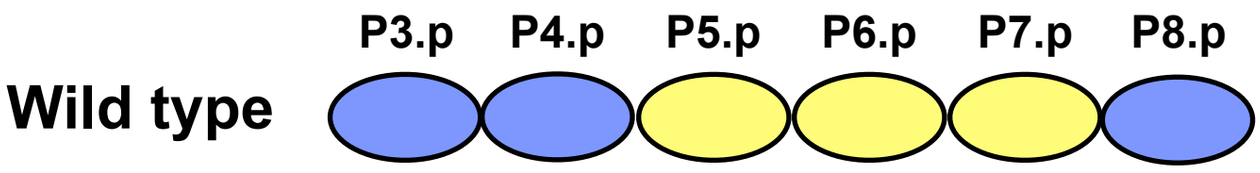
C. elegans

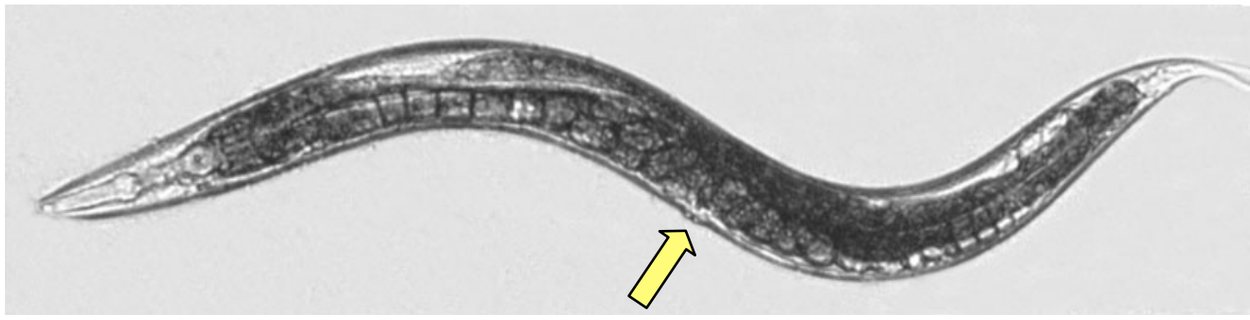
Sydney Brenner

H. Robert Horvitz

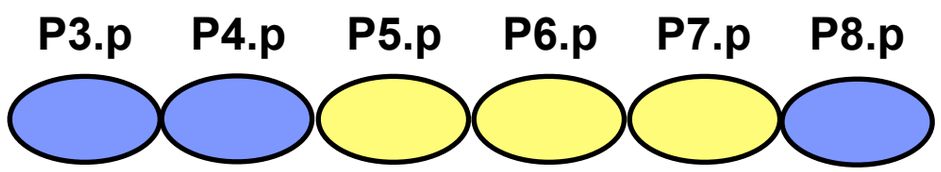
John E. Sulston

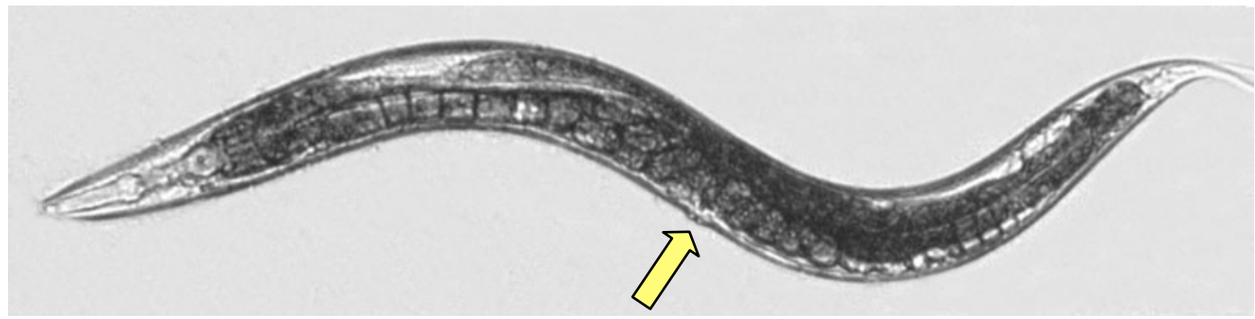
Three cells express vulval fates in wild-type animals

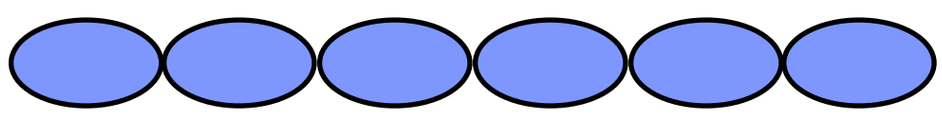




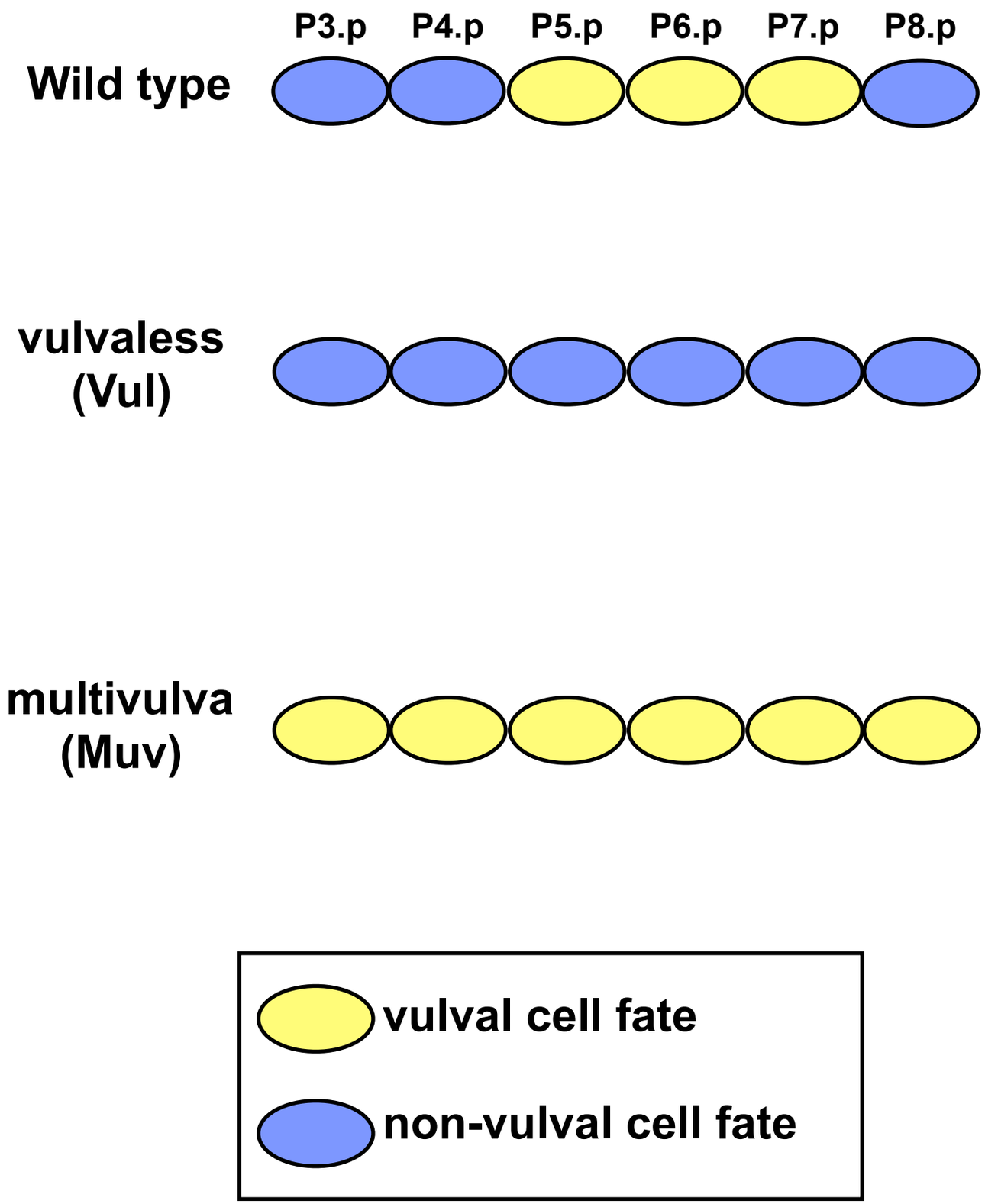
No cells express vulval fates in vulvaless mutants

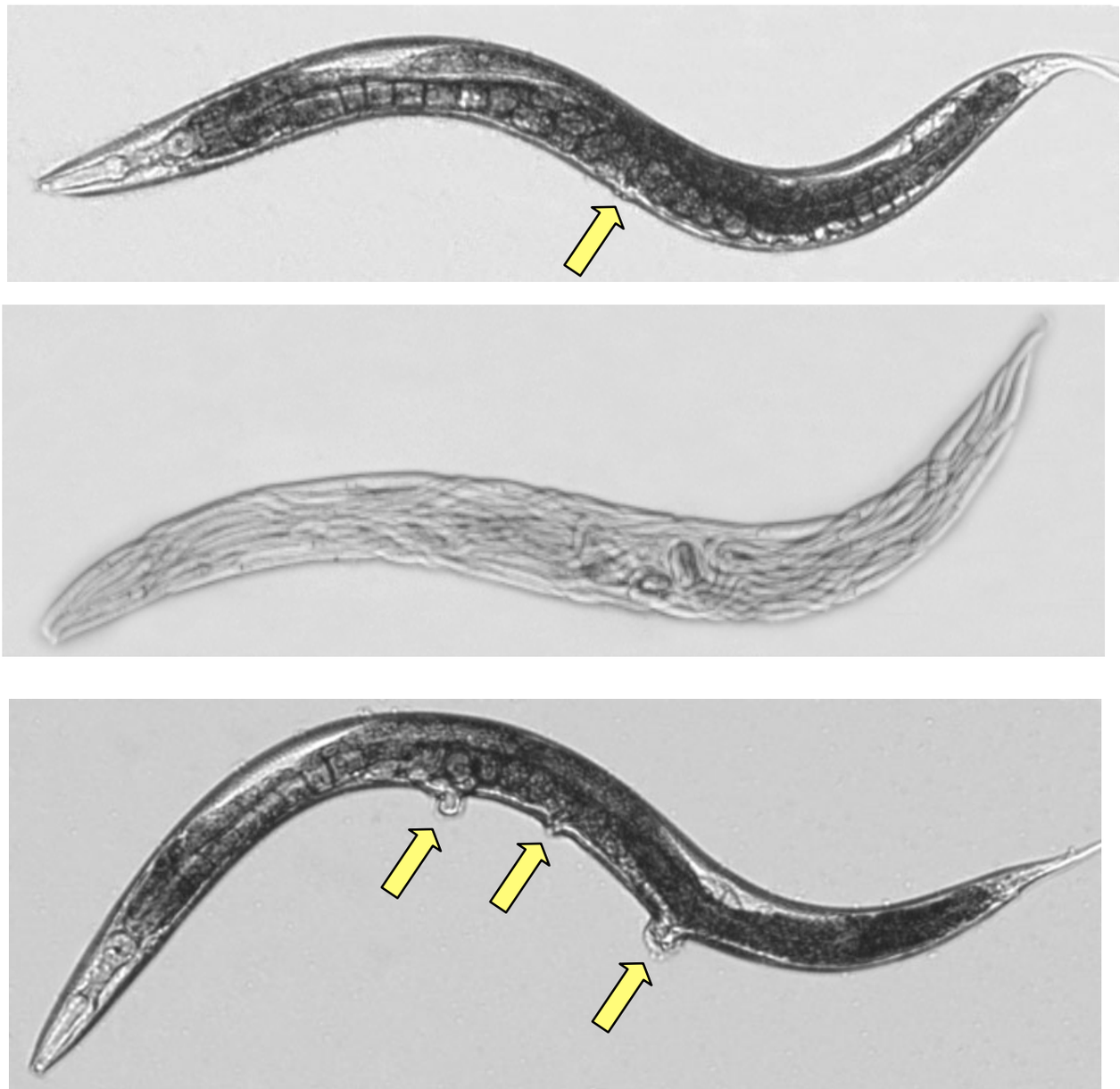






Six cells express vulval fates in multivulva mutants





Vulval mutants

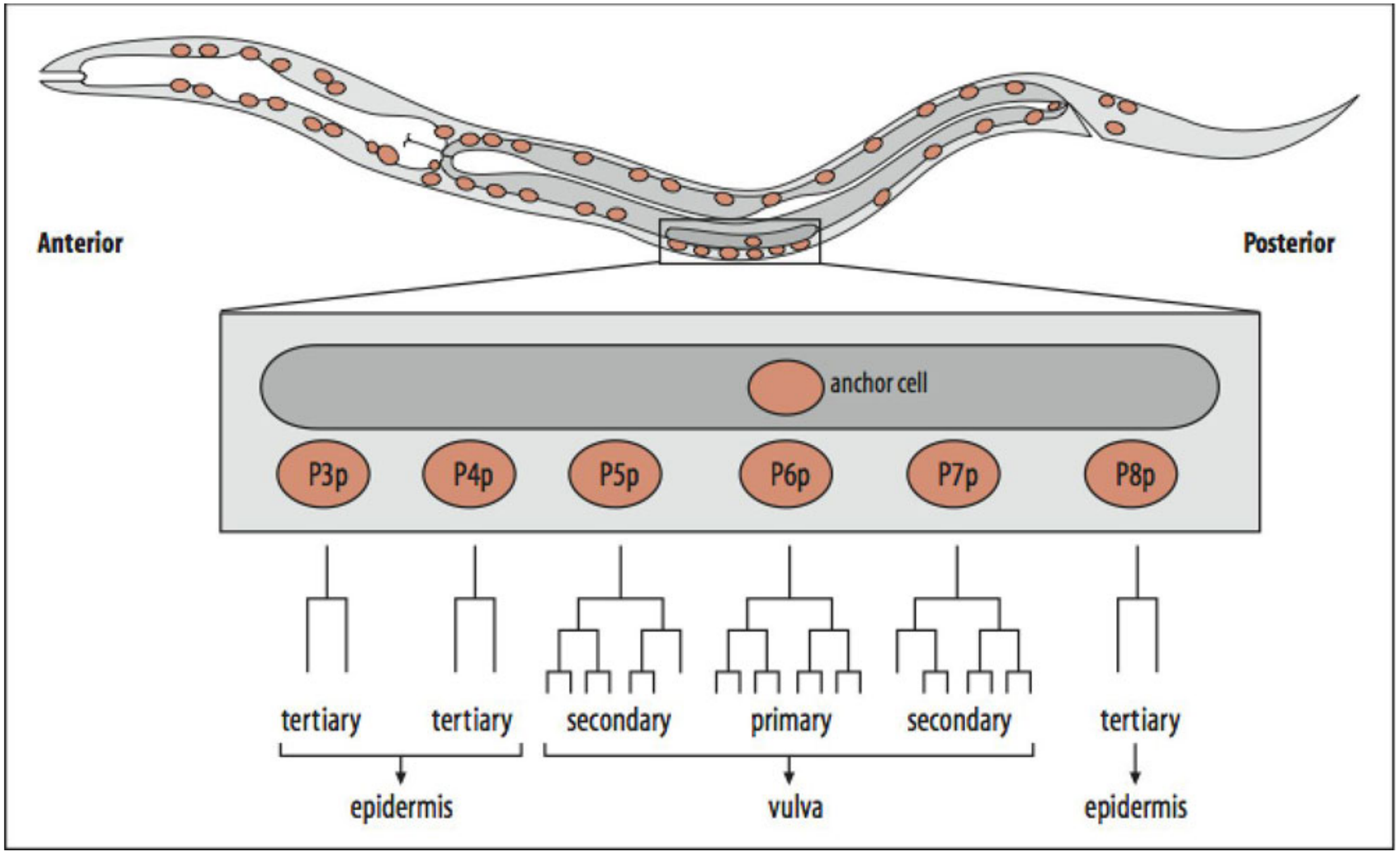
Mutant	Phenotype
lin-1(0)	Muv
lin-3(0)	Vul
let-60(0)	Vul
let-60(gf)	Muv
let-23(0)	Vul
let-23(gf)	Muv

Double mutants defined the vulval pathway

Mutant genotypes	Phenotype
lin-1(0)	Muv
lin-3(0)	Vul
let-60(0)	Vul
let-60(gf)	Muv
let-23(0)	Vul
let-23(gf)	Muv
lin-3(0); let-23(gf)	Muv
lin-3(0); let-60(gf)	Muv
let-23(0); let-60(gf)	Muv
let-23(gf); let-60(0)	Vul
let-60(0); lin-1(0)	Muv
let-23(0); lin-1(0)	Muv

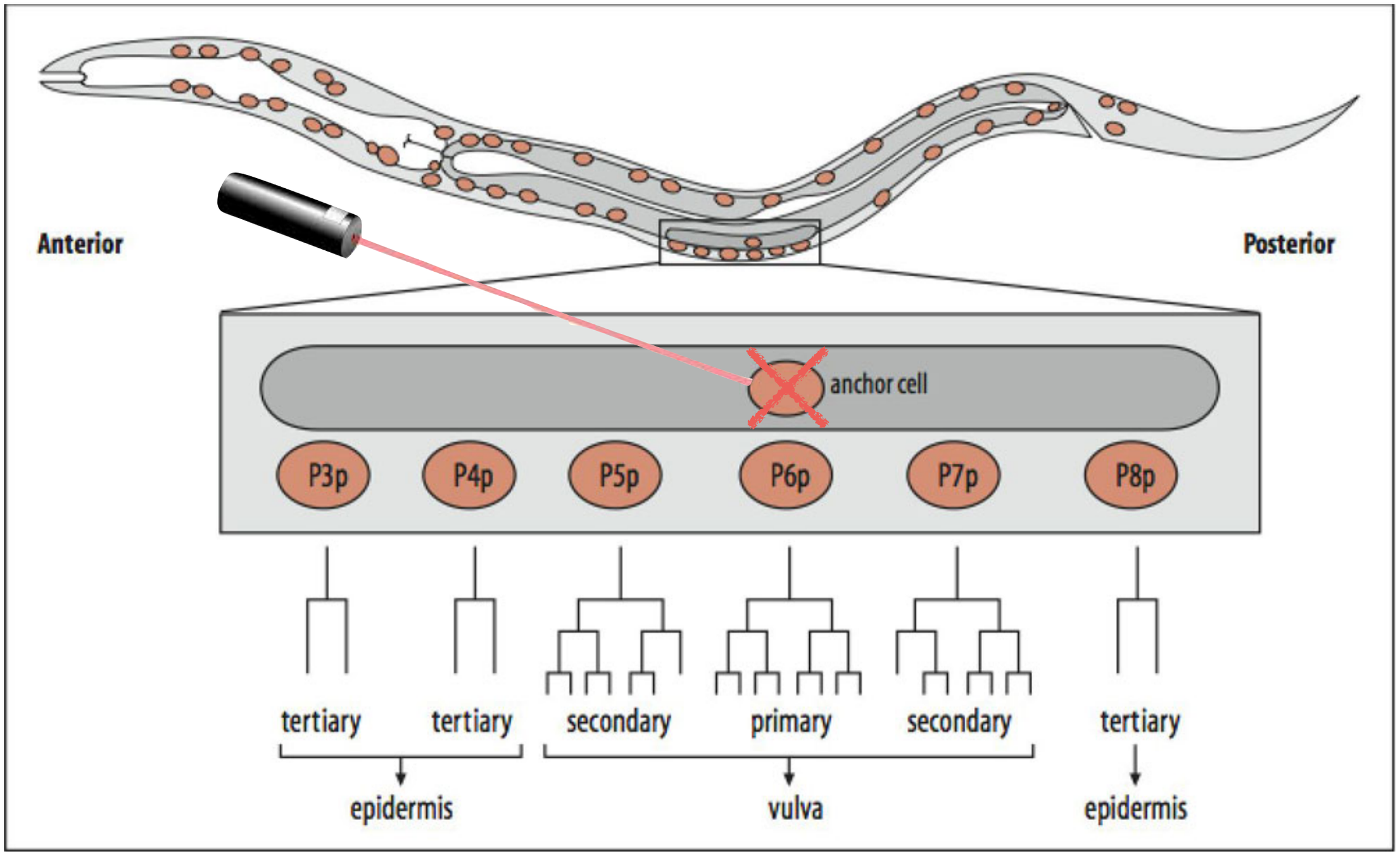
lin-3 → ***let-23*** → ***let-60*** ⊣ ***lin-1*** ⊣ **vulval fate**

What is the source of the inductive signal?



How do we determine that the AC is necessary and sufficient for vulval development (primary or secondary cells)?

Ablation removes cells (necessary)

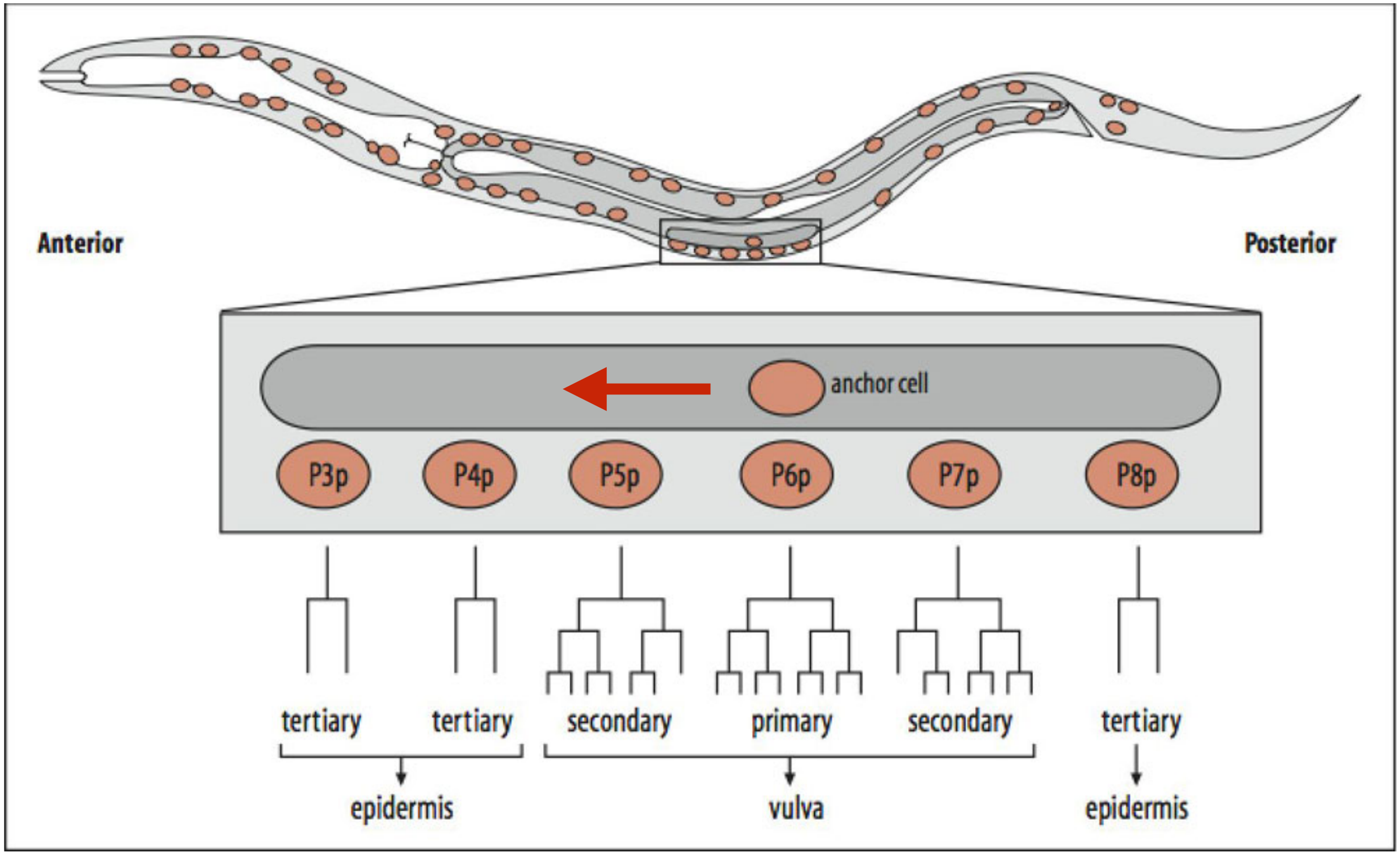


No AC leads to no vulval cell specification and a vulvaless phenotype

All other vulval mutants are epistatic to AC ablation

Mutant genotypes	Phenotype
AC ablation	Vul
lin-1(0)	Muv
lin-3(0)	Vul
let-60(gf)	Muv
let-23(gf)	Muv
AC ablation*; let-23(gf)*	Muv
AC ablation*; let-60(gf)*	Muv
AC ablation*; lin-1(0)*	Muv

Moving the AC moves the vulva (sufficient)

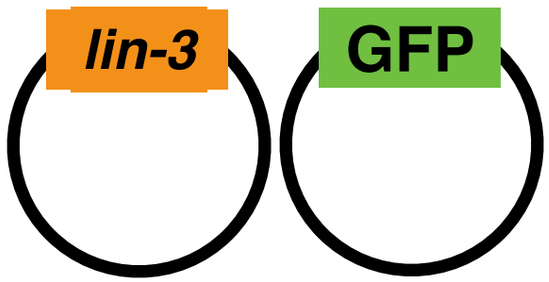


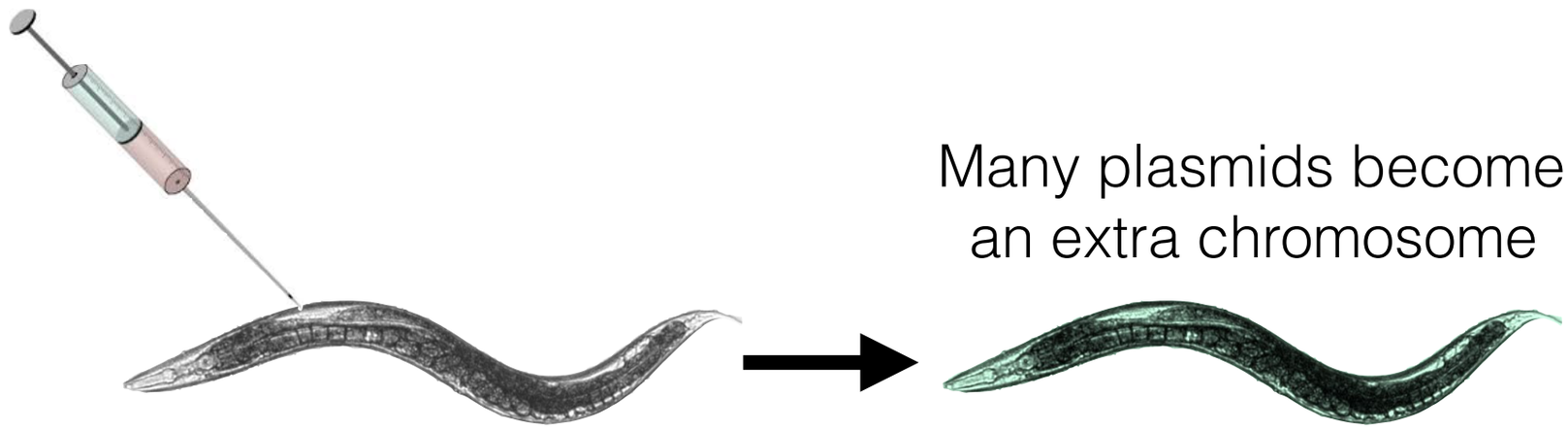
dig-1 displaced gonad mutants

AC ablation and loss of *lin-3* have the same phenotype and epistatic relationships

Mutant genotypes	Phenotype
AC ablation	Vul
lin-3(0)	Vul
lin-1(0)	Muv
let-60(gf)	Muv
let-23(gf)	Muv
AC ablation*; let-23(gf)*	Muv
AC ablation*; let-60(gf)*	Muv
AC ablation*; lin-1(0)*	Muv
lin-3(0); let-23(gf)	Muv
lin-3(0); let-60(gf)	Muv
lin-3(0); lin-1(0)	Muv

LIN-3 is expressed in the AC; does it function there?





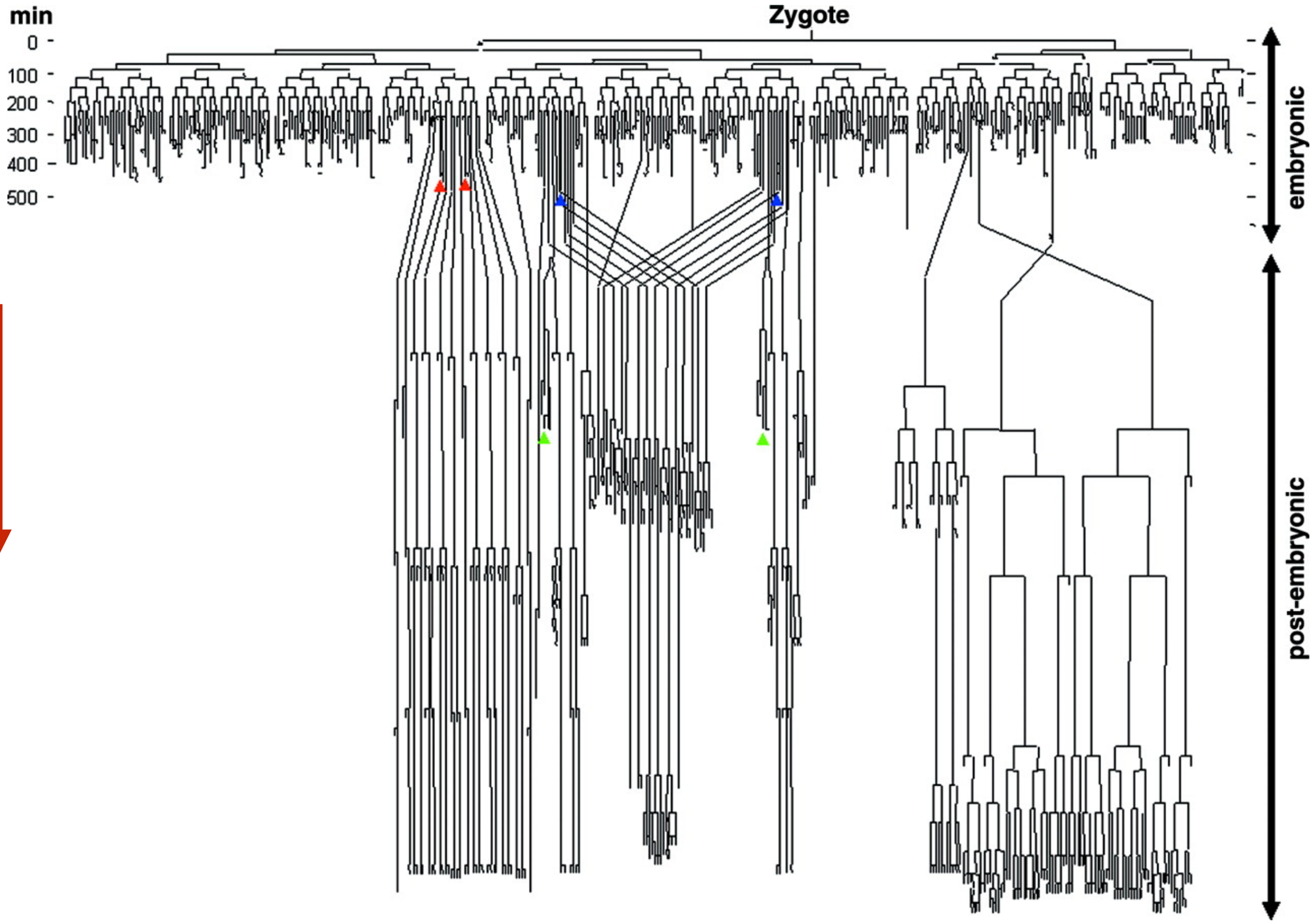
lin-3(0)
Vul

Many plasmids become an extra chromosome

lin-3(0); lin-3(+++)
Wild-type or Muv

Genotype	Phenotype	
lin-3(0)	Vul	
lin-3(0); lin-3(+++)	Wild-type	
lin-3(0); vulval cell:lin-3(+++)	Vul	Expression of *lin-3* in vulval cells
lin-3(0); intestine:lin-3(+++)	Vul	Expression of *lin-3* in the intestine
lin-3(0); neurons:lin-3(+++)	Vul	Expression of *lin-3* in the neurons
lin-3(0); AC:lin-3(+++)	Wild-type	Expression of *lin-3* in the AC

The cell lineage of *C. elegans* is known and invariant



A Ras pathway promotes vulval fates