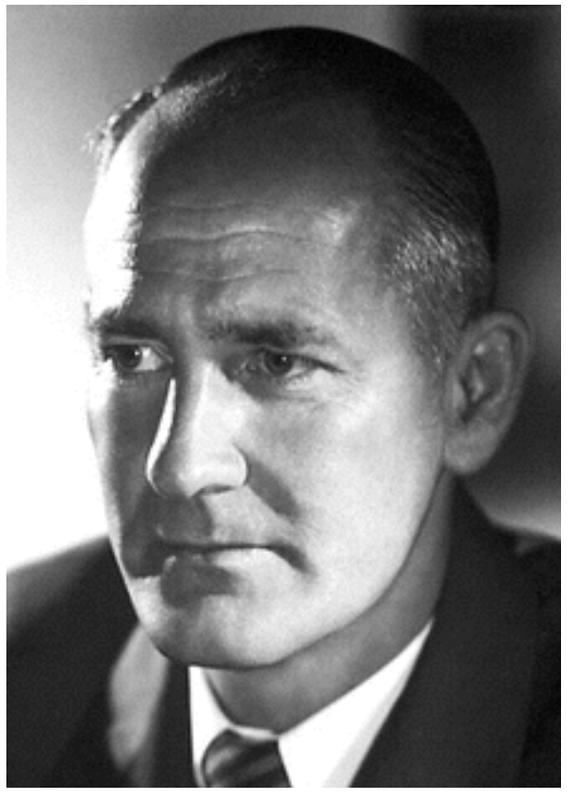
Bio393: Genetic Analysis

Genetic interactions: epistasis



George Beadle

Ed Tatum

Arginine mutant complementation experiment

	arg-a	*arg-b*	*arg-c*	*arg-d*	*arg-e*	*arg-f*	*arg-g*	*arg-h*	*arg-i*
arg-a		■	■		■			■	■
arg-b	■			■	■	■	■	■	■
arg-c	■			■	■	■	■	■	■
arg-d		■	■		■			■	■
arg-e	■	■	■	■		■	■		
arg-f		■	■		■			■	■
arg-g		■	■		■			■	■
arg-h	■	■	■	■		■	■		
arg-i	■	■	■	■		■	■		

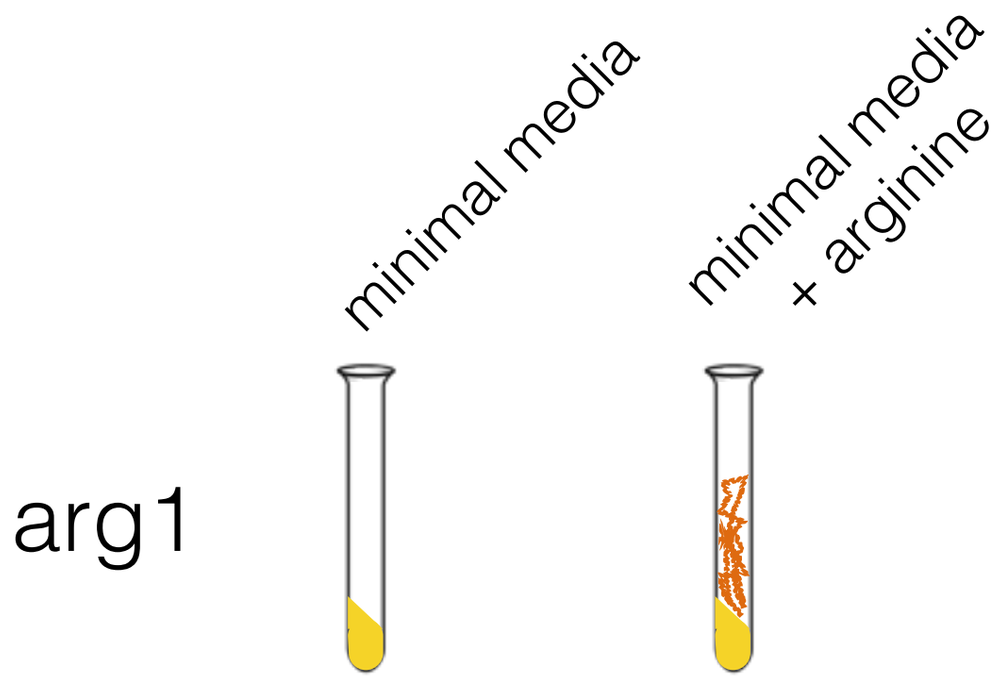
Arginine mutant complementation experiment

Three genes

arg1 = [a, d, f, g]

arg2 = [b, c]

arg3 = [e, h, i]



One gene - one enzyme hypothesis

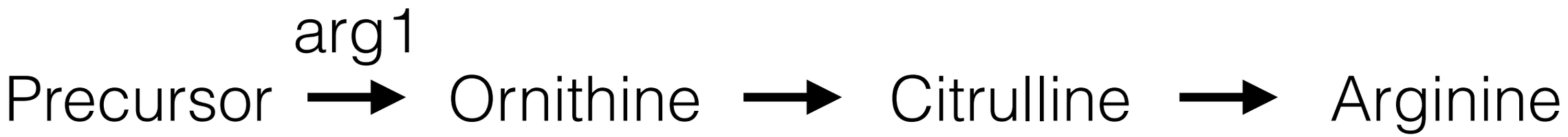
Precursor → Ornithine → Citrulline → Arginine

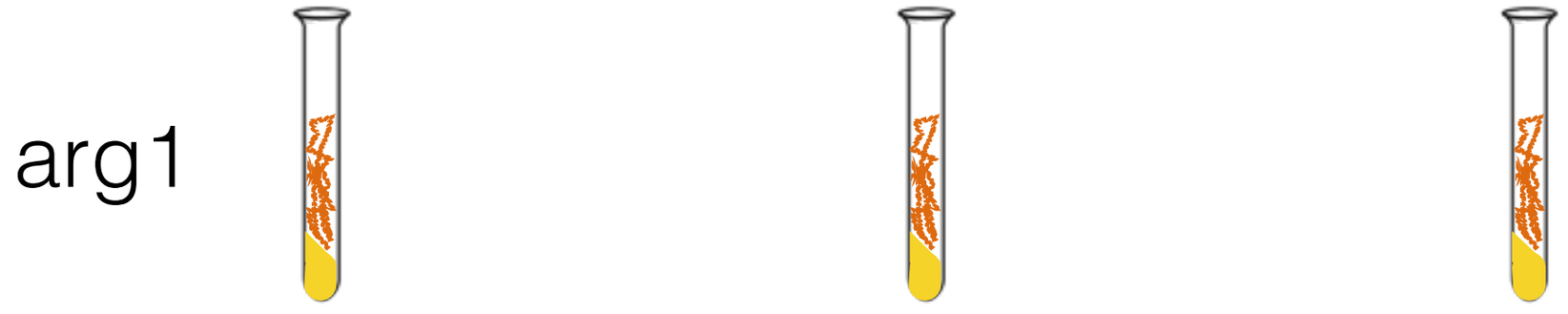
One gene - one enzyme hypothesis

Precursor → Ornithine → Citrulline → Arginine

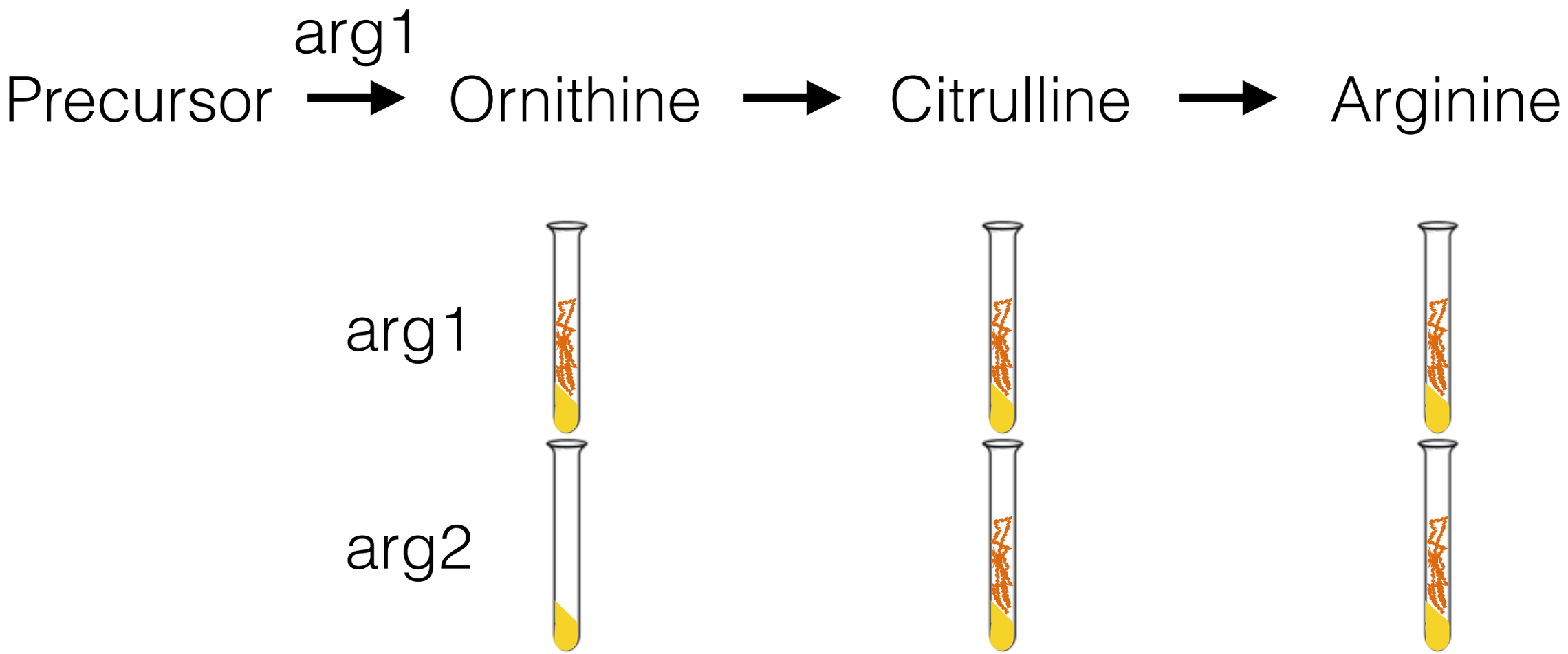
arg1

One gene - one enzyme hypothesis

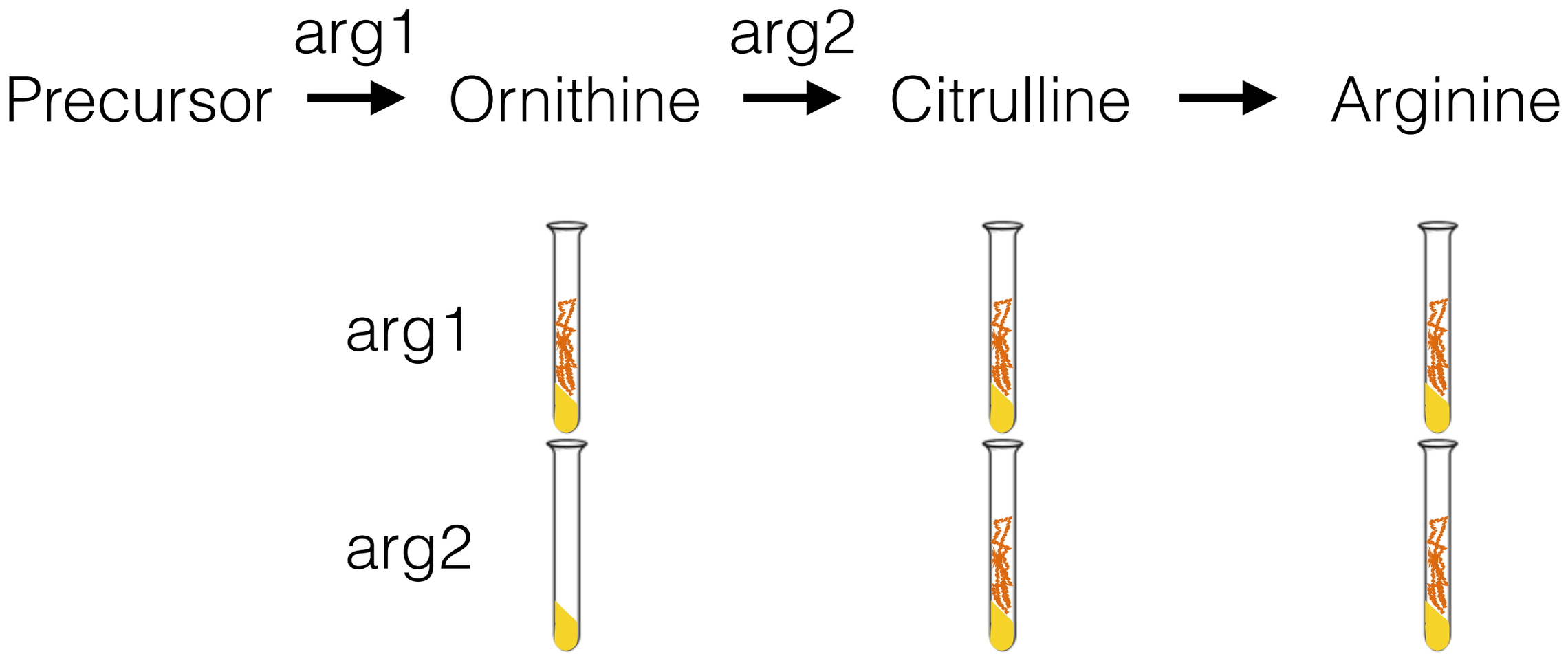




One gene - one enzyme hypothesis



One gene - one enzyme hypothesis



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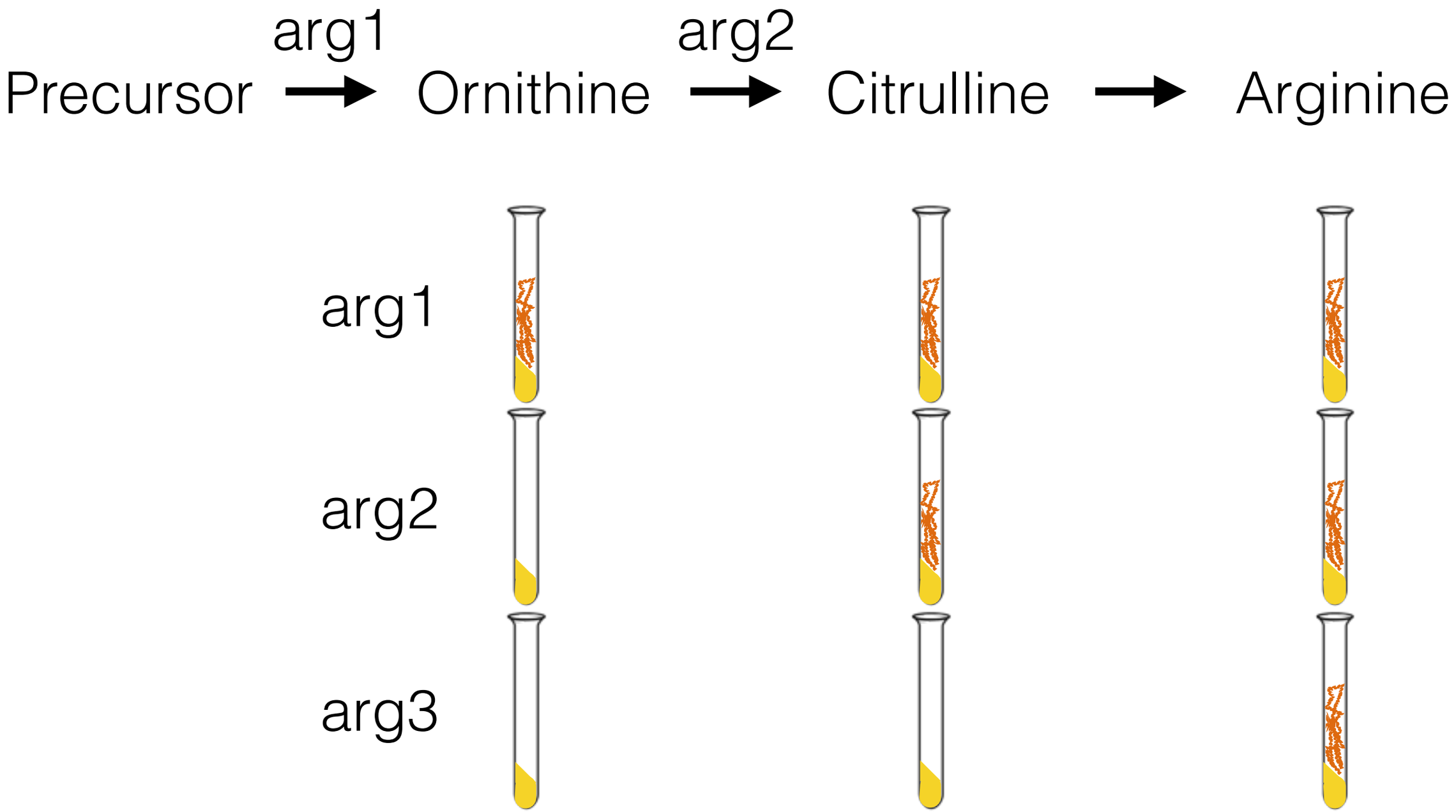

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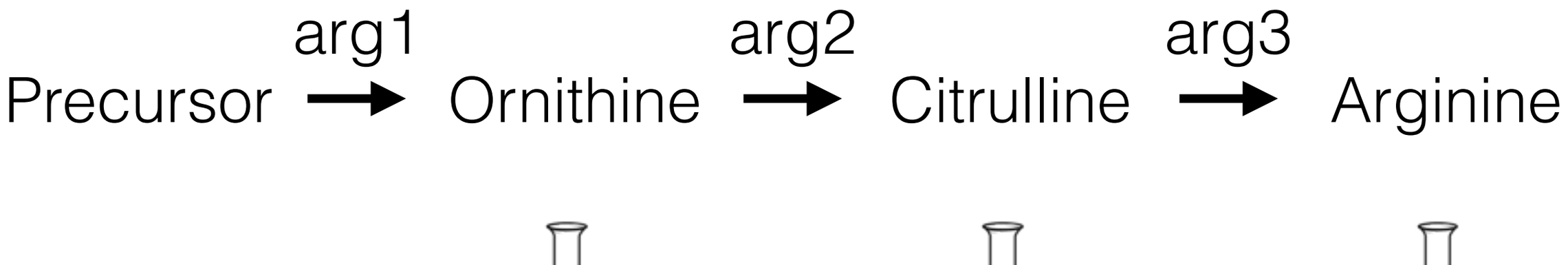

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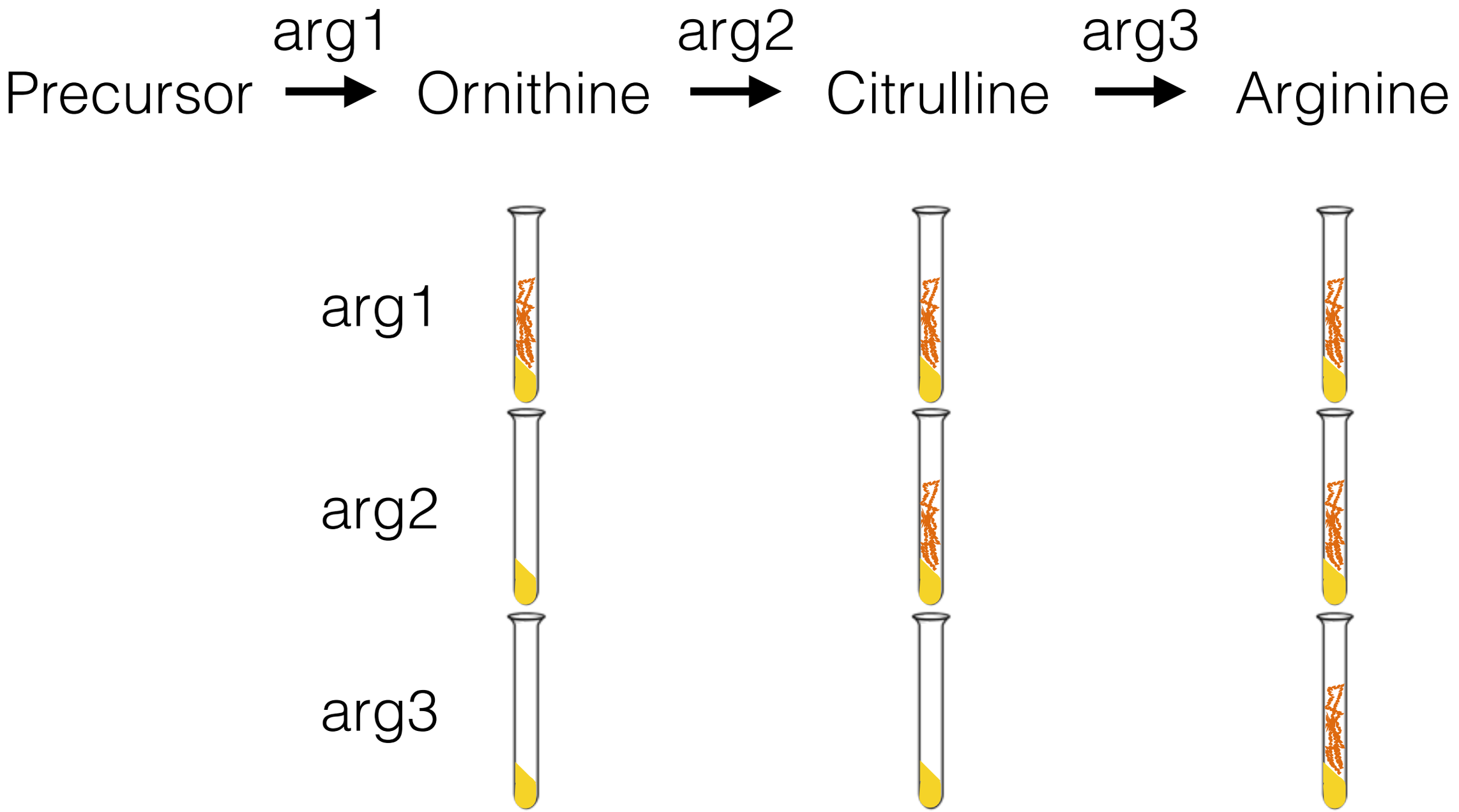
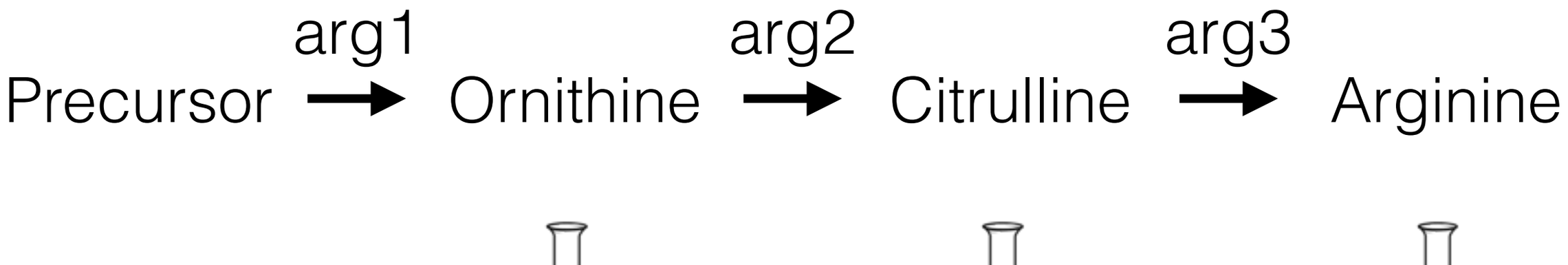


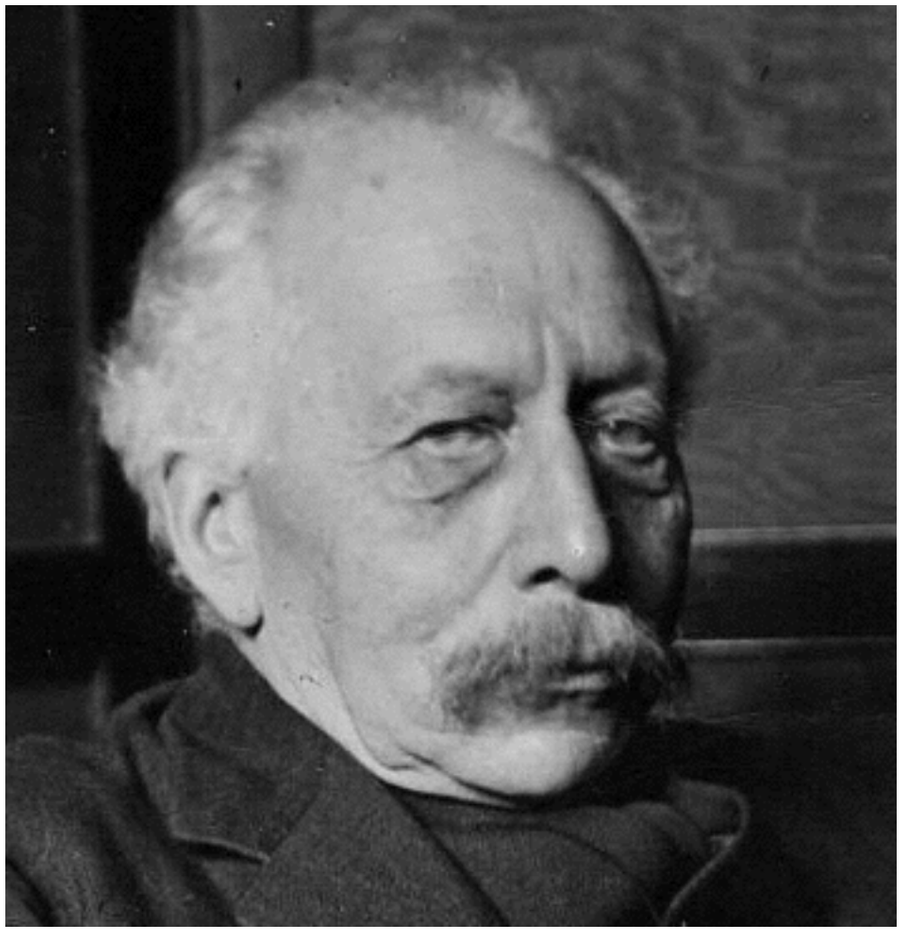
Mutants accumulate precursor for previous step

One gene - one enzyme hypothesis



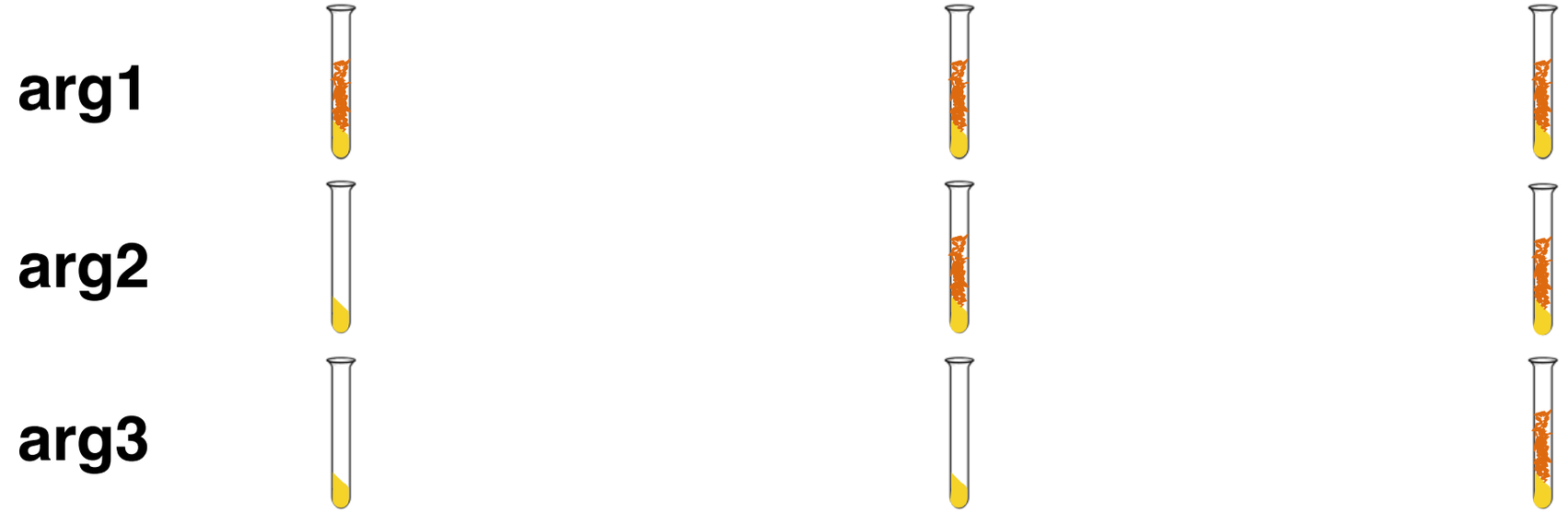
Mutants accumulate precursor for previous step

Epistasis
the effect of one gene is dependent on another gene

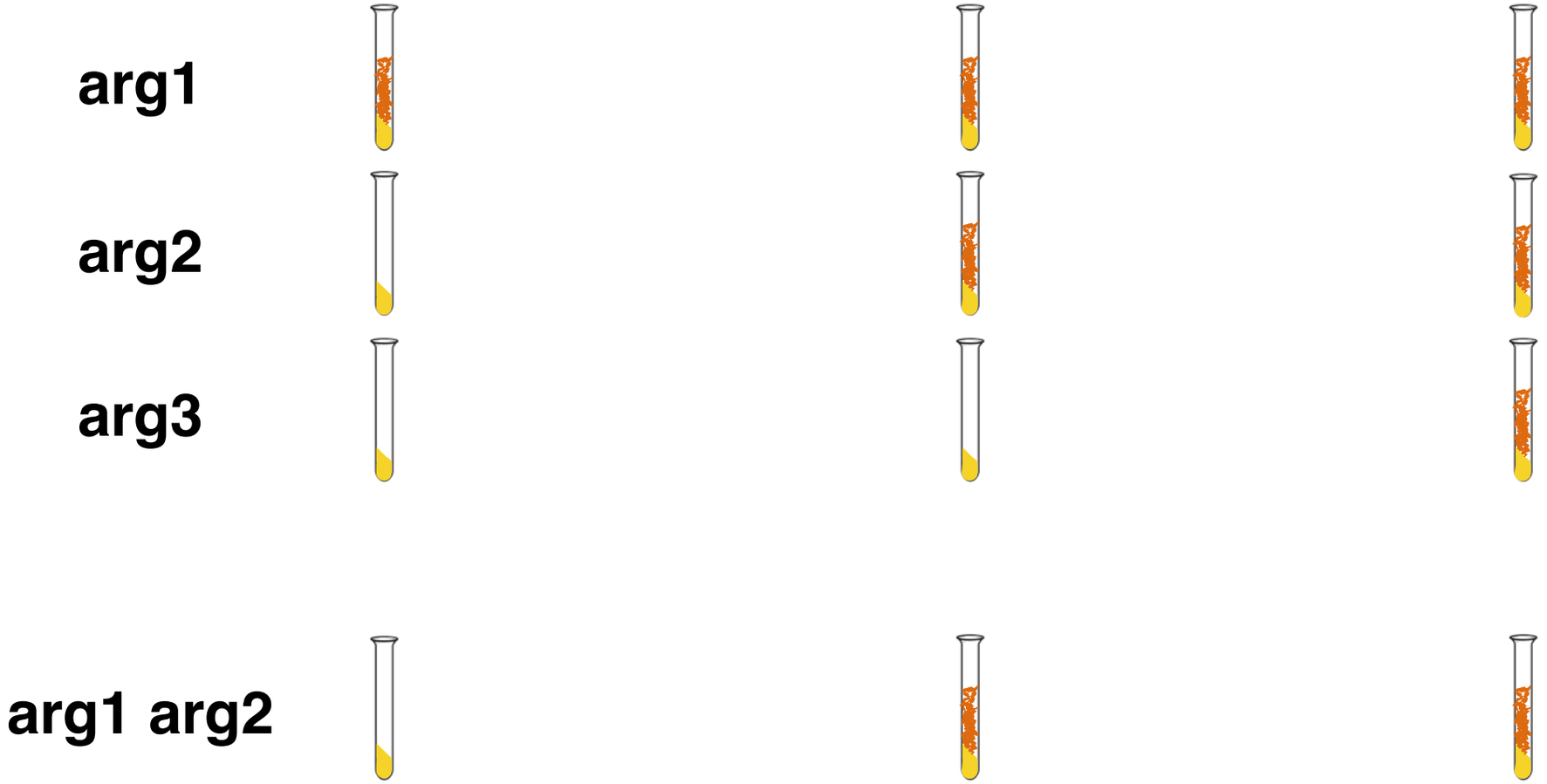


William Bateson

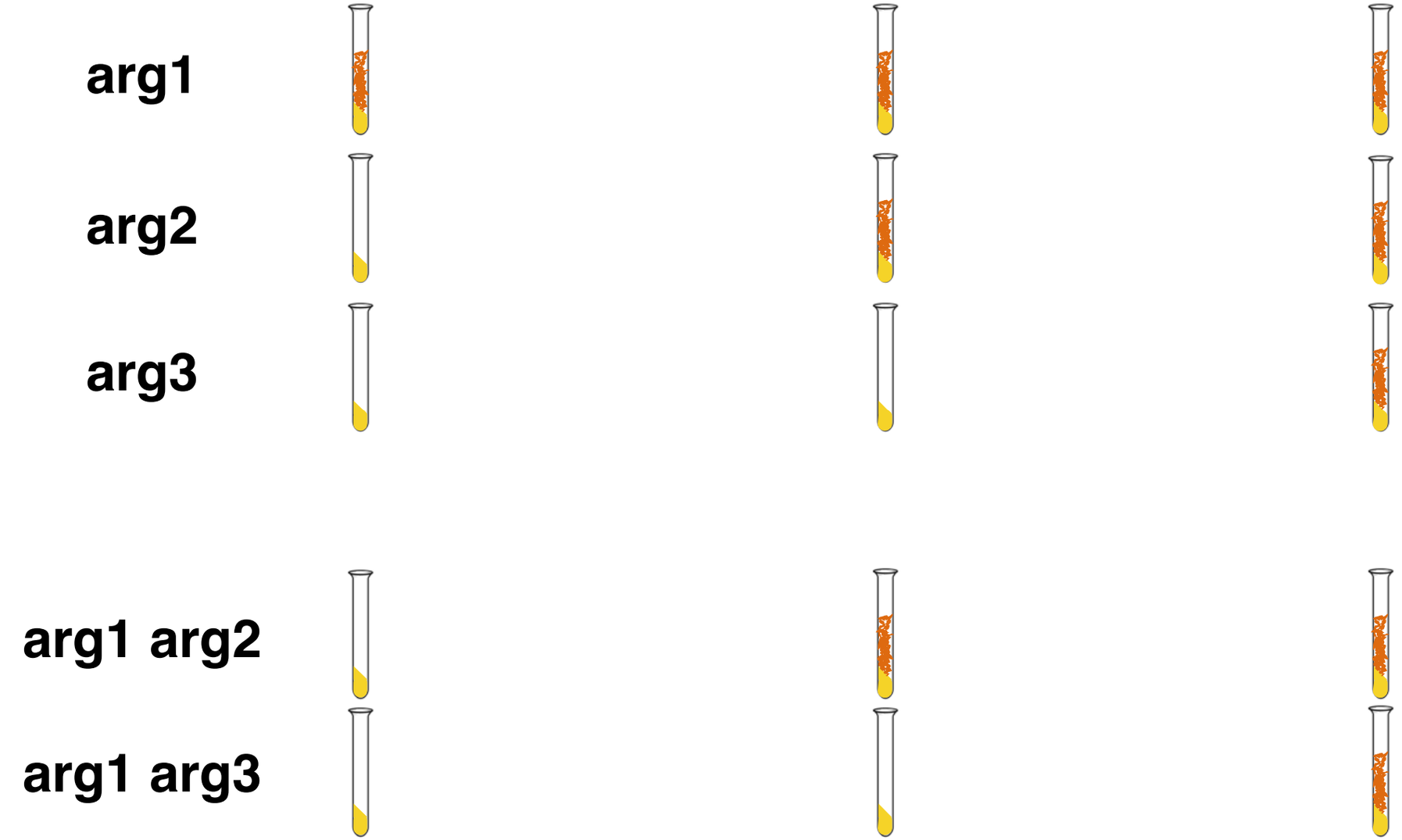
Biochemical epistasis



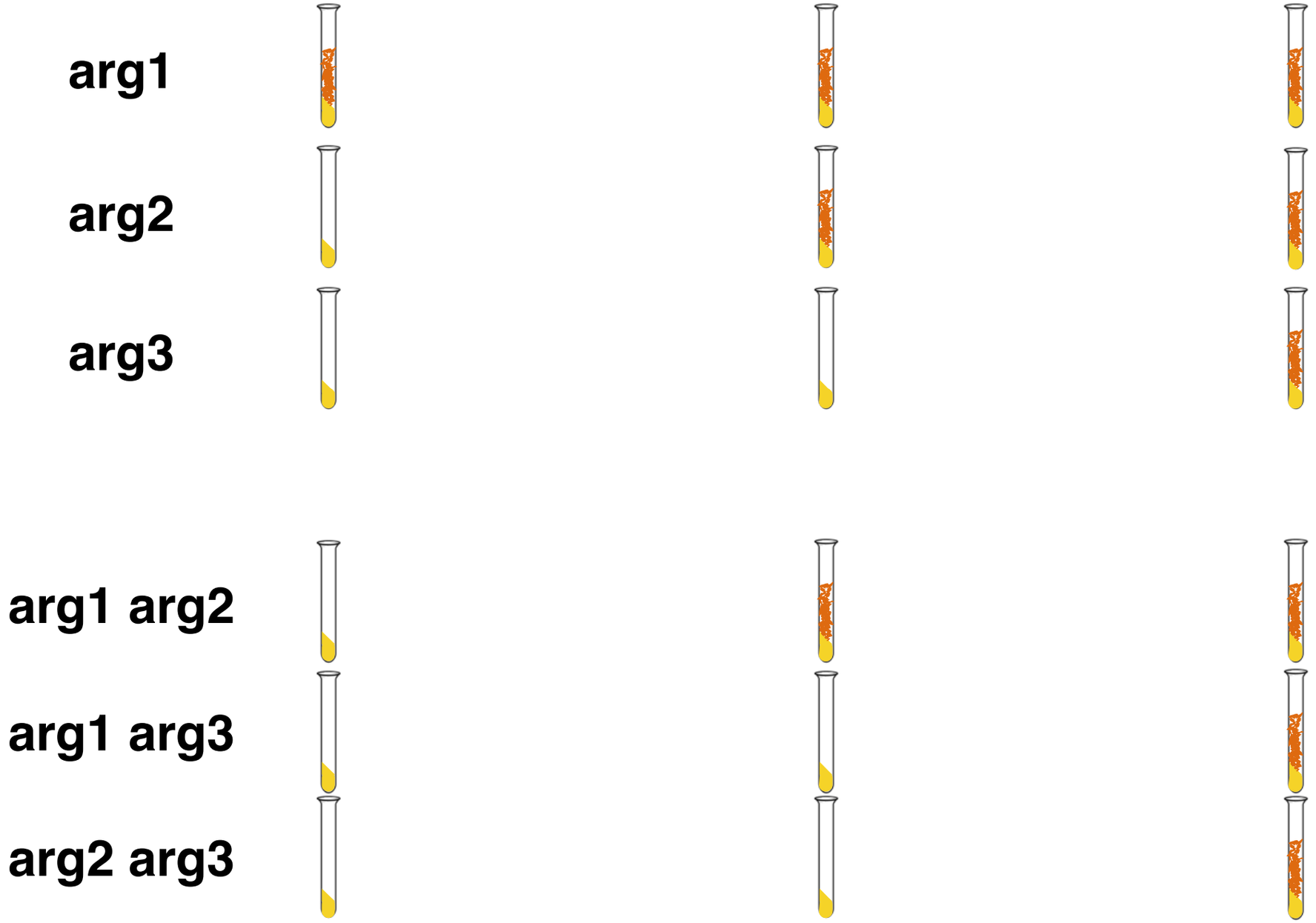
Biochemical epistasis



Biochemical epistasis



Biochemical epistasis



Approach to understanding biochemical epistasis

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1. Single mutants fail in a step in a biosynthesis pathway

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2. Double mutants fail in the most upstream step in a biosynthesis pathway

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3. What will the single and double mutants accumulate?

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Approach to understanding biochemical epistasis

1. Single mutants fail in a step in a biosynthesis pathway

2. Double mutants fail in the most upstream step in a biosynthesis pathway

3. What will the single and double mutants accumulate?

4. Pathways can be branched

Epistasis - one mutant phenotype trumps another

(A)

(B)

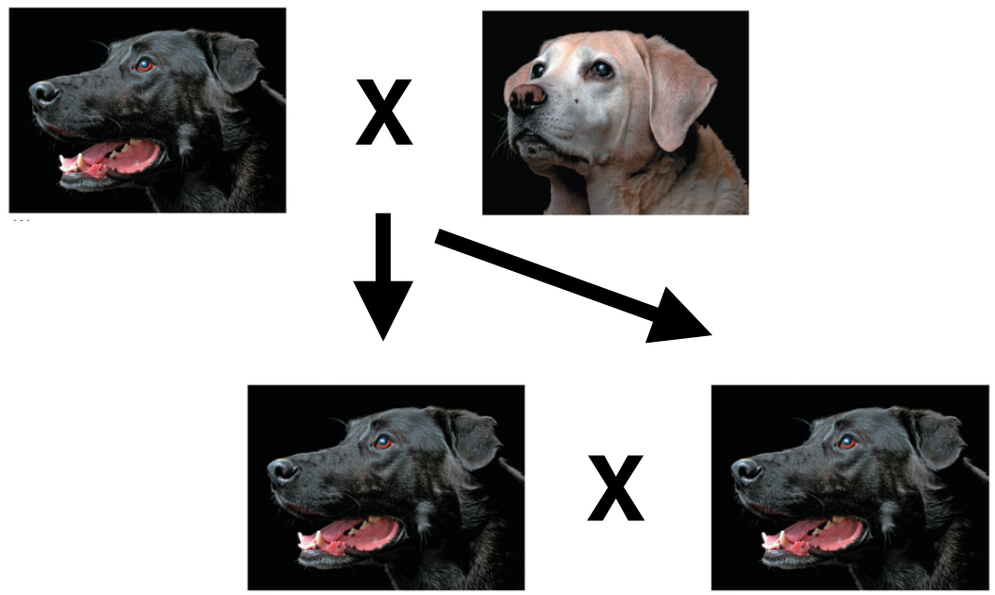
(C)

***LIFE 8e*, Figure 10.14**

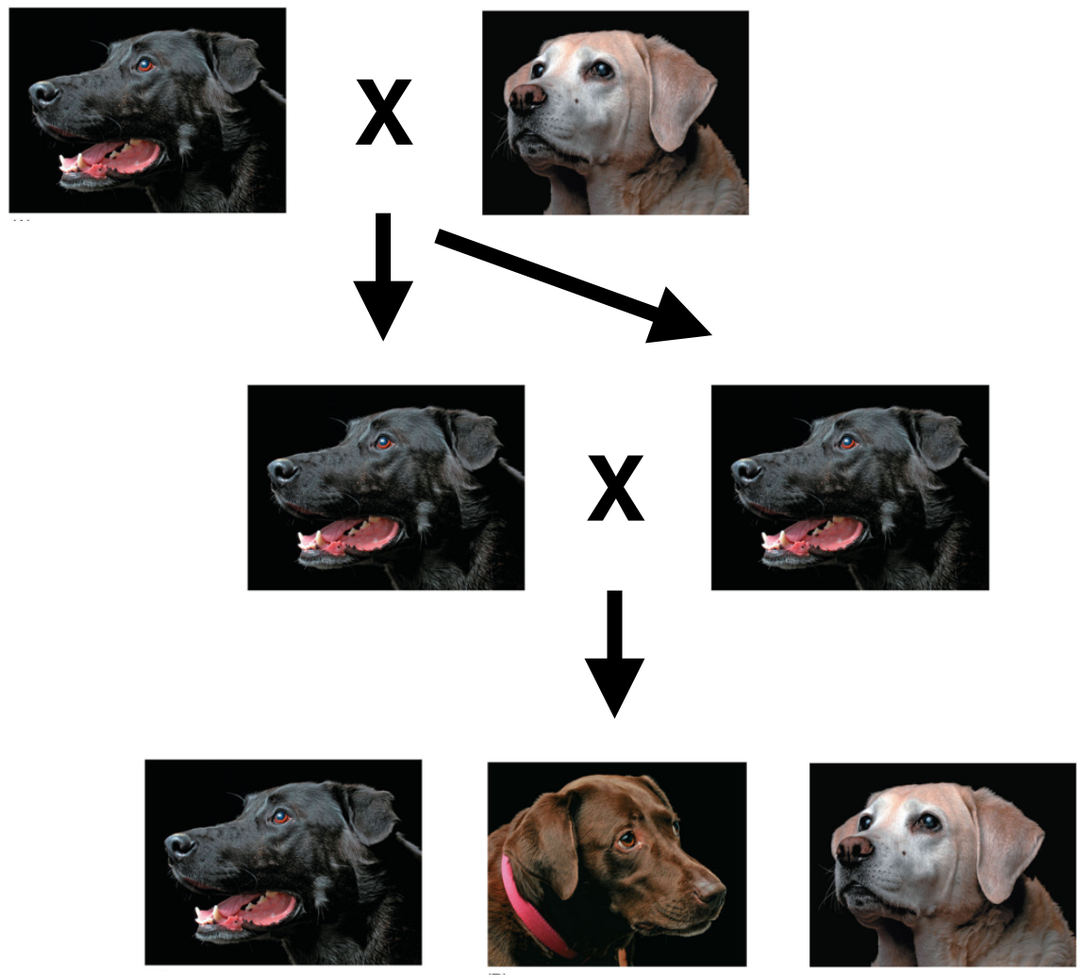
Epistasis - one mutant phenotype trumps another

X

Epistasis - one mutant phenotype trumps another

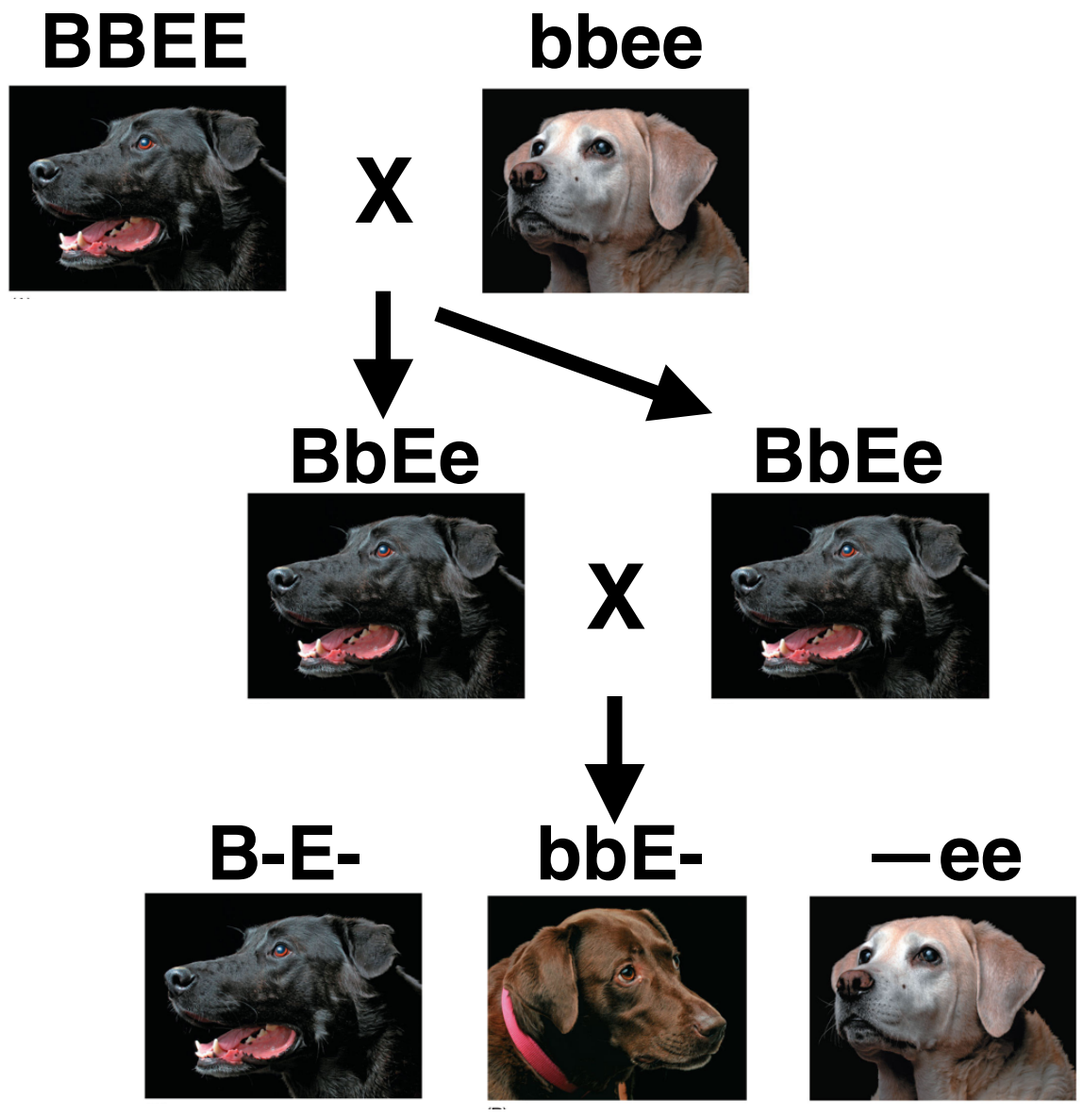


Epistasis - one mutant phenotype trumps another



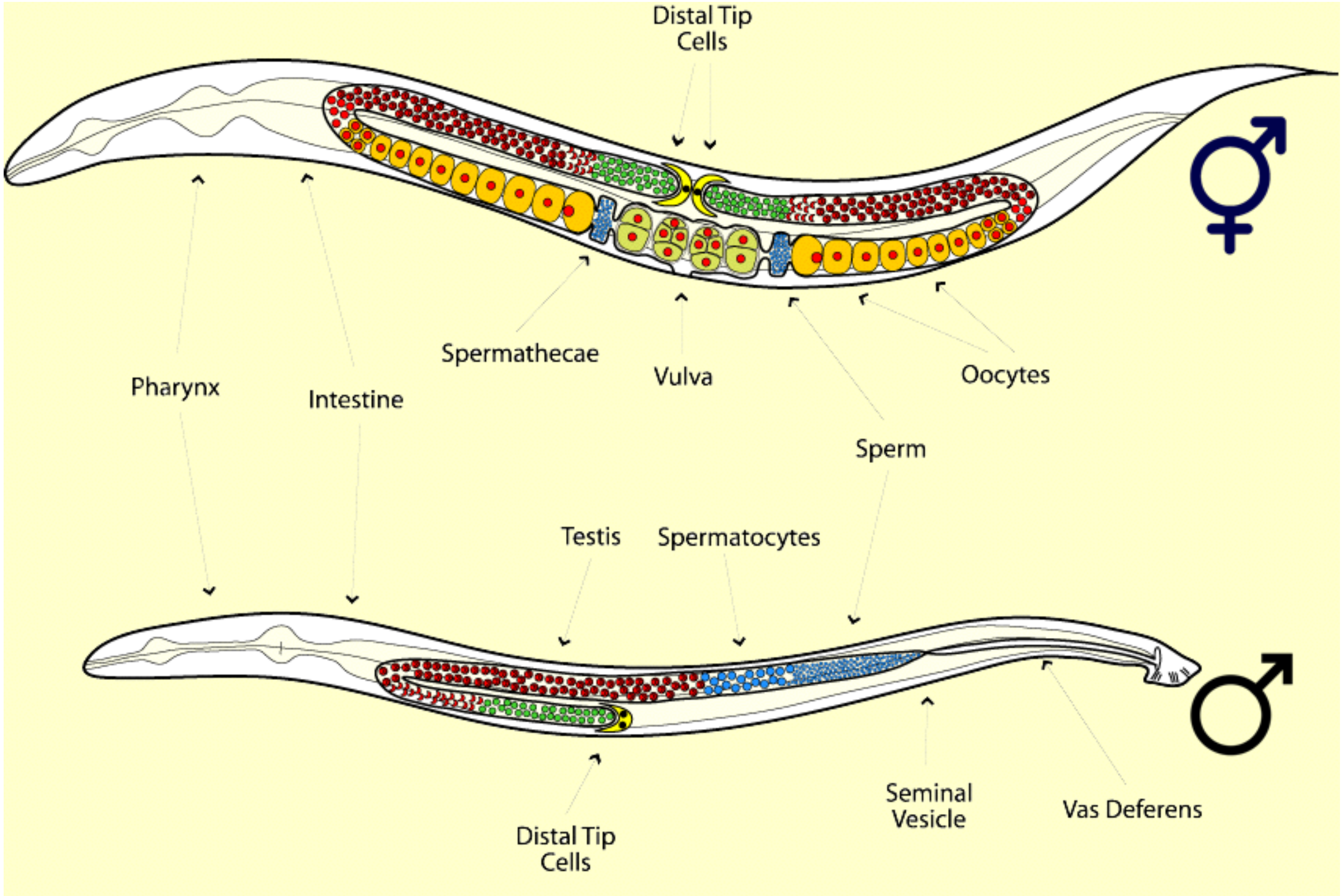
9 : 3 : 4

Epistasis - one mutant phenotype trumps another

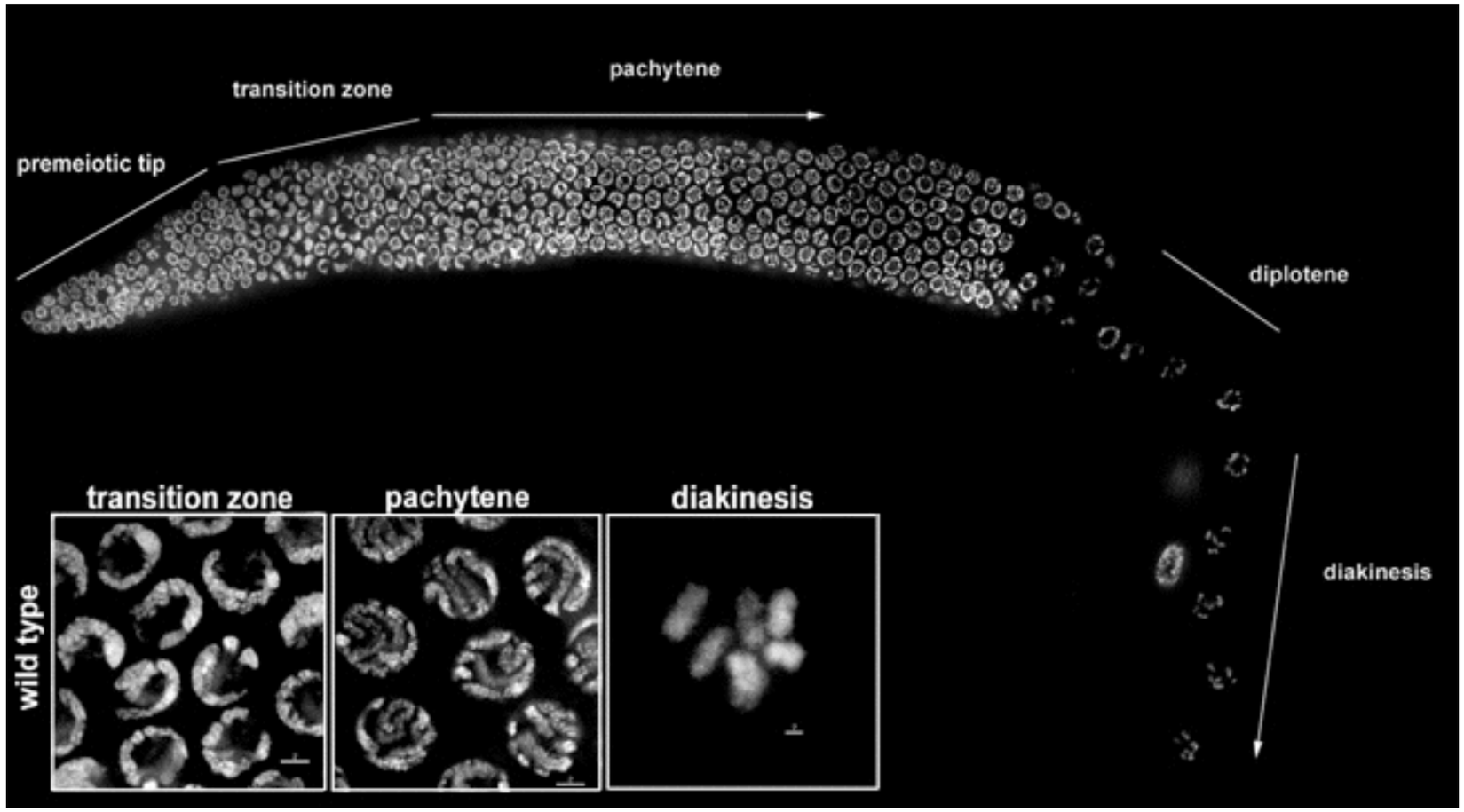


B = black
b = brown
E = color
e = no color

The *C. elegans* germline



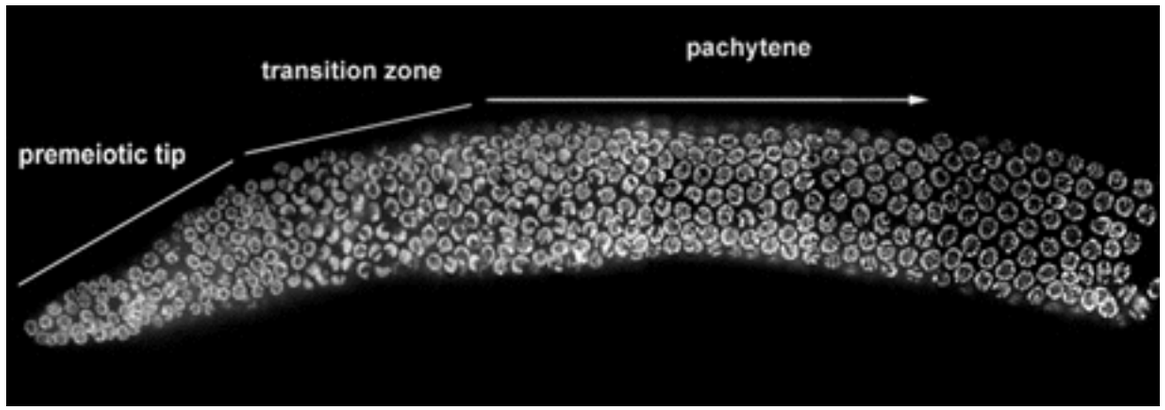
The *C. elegans* germline



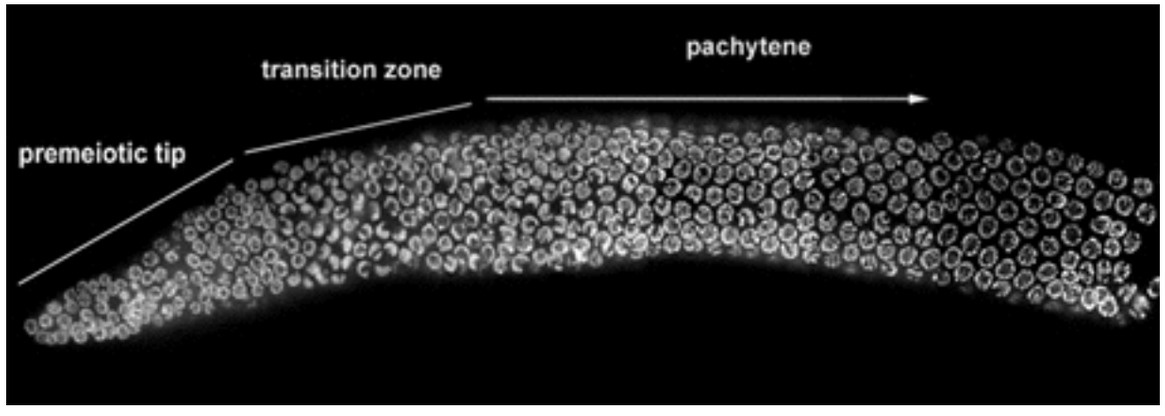
Judith Kimble

Lecture 6

C. elegans germline mutants

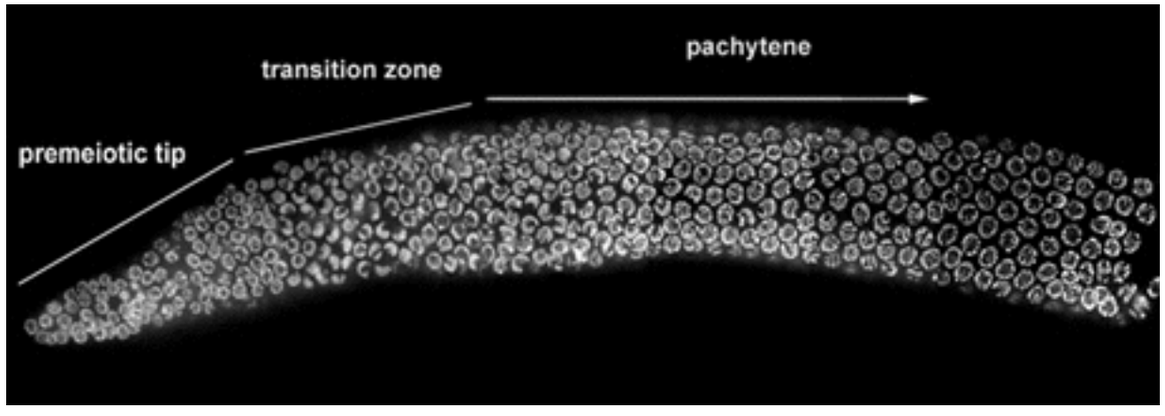


C. elegans germline mutants



glp-1(0) = all meiotic germ cells

C. elegans germline mutants



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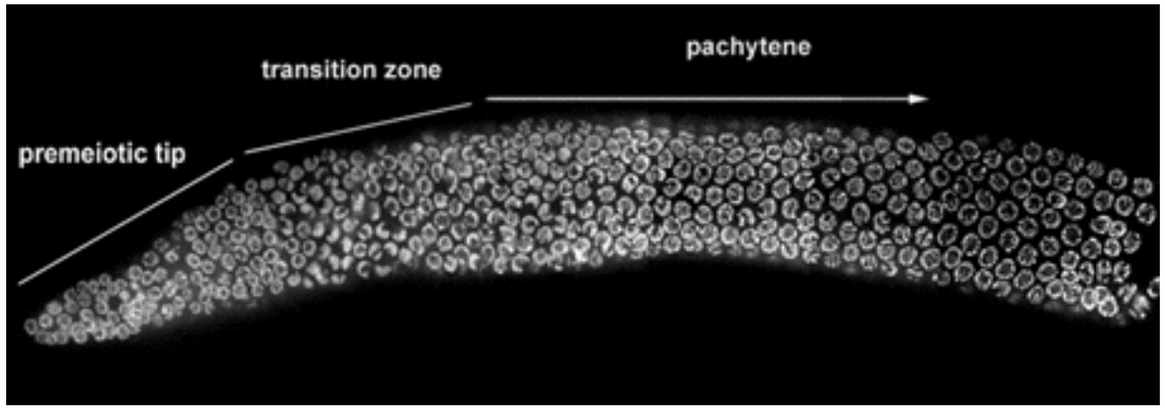
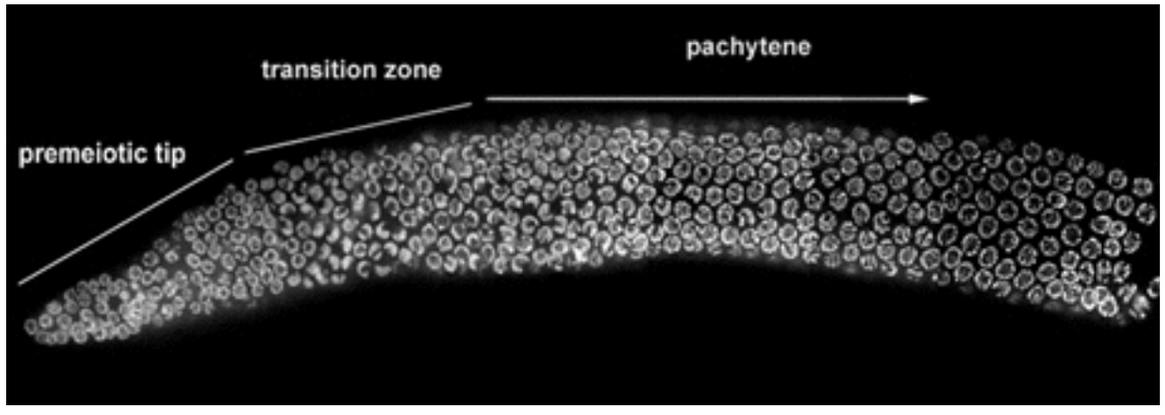
C. elegans germline mutants



glp-1(0) = all meiotic germ cells

glp-1(gf) = all mitotic germ cells

C. elegans germline mutants



glp-1(0) = all meiotic germ cells

glp-1(gf) = all mitotic germ cells

glp-1 → **germ cell proliferation**

C. elegans germline mutants

Mutant	Phenotype
glp-1(0)	meiotic cells
glp-1(gf)	mitotic cells
lag-2(0)	meiotic cells
fbf-1(0)	meiotic cells
gld-1(0)	mitotic cells

***glp-1* → GSC prolif.**

C. elegans germline mutants

Mutant	Phenotype
glp-1(0)	meiotic cells
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lag-2(0)	meiotic cells
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glp-1 → **GSC prolif.**

lag-2 → **GSC prolif.**

C. elegans germline mutants

Mutant	Phenotype
glp-1(0)	meiotic cells
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lag-2(0)	meiotic cells
fbf-1(0)	meiotic cells
gld-1(0)	mitotic cells

glp-1 → **GSC prolif.**

lag-2 → **GSC prolif.**

fbf-1 → **GSC prolif.**

C. elegans germline mutants

Mutant	Phenotype	
glp-1(0)	meiotic cells	***glp-1*** → **GSC prolif.**
glp-1(gf)	mitotic cells	
lag-2(0)	meiotic cells	***lag-2*** → **GSC prolif.**
fbf-1(0)	meiotic cells	***fbf-1*** → **GSC prolif.**
gld-1(0)	mitotic cells	***gld-1*** ⊣ **GSC prolif.**

How do these genes work together?

Mutant	Phenotype
glp-1(0)	meiotic cells
glp-1(gf)	mitotic cells
lag-2(0)	meiotic cells
fbf-1(0)	meiotic cells
gld-1(0)	mitotic cells
glp-1(0); lag-2(0)	meiotic cells

How do these genes work together?

Mutant	Phenotype
glp-1(0)	meiotic cells
glp-1(gf)	mitotic cells
lag-2(0)	meiotic cells
fbf-1(0)	meiotic cells
gld-1(0)	mitotic cells
glp-1(0); lag-2(0)	meiotic cells

You can only do epistasis tests with mutants that have opposing phenotypes

How do these genes work together?

Mutant	Phenotype
glp-1(0)	meiotic cells
glp-1(gf)	mitotic cells
lag-2(0)	meiotic cells
fbf-1(0)	meiotic cells
gld-1(0)	mitotic cells
glp-1(gf); lag-2(0)	mitotic cells

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gld-1(0)	mitotic cells
glp-1(gf); lag-2(0)	mitotic cells

glp-1 → **GSC prolif.**

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glp-1(gf); lag-2(0)	mitotic cells

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Which phenotype is epistatic?

How do these genes work together?

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gld-1(0)	mitotic cells
glp-1(gf); lag-2(0)	mitotic cells

glp-1 → **GSC prolif.**

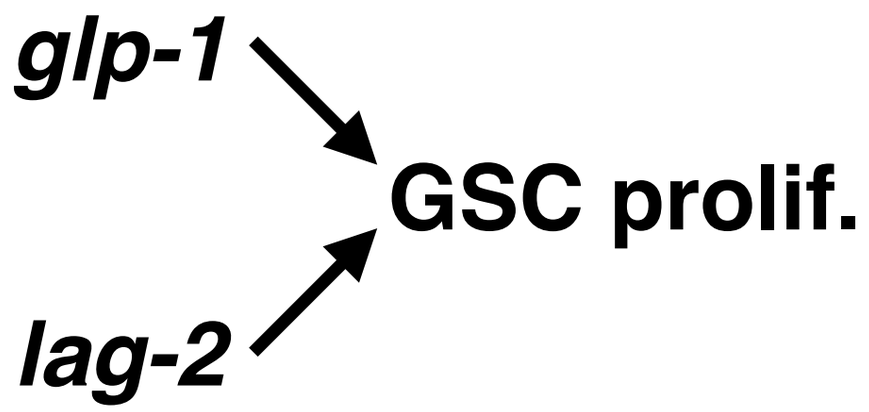
lag-2 → **GSC prolif.**

Which phenotype is epistatic?

lag-2 → ***glp-1*** → **GSC prolif.**

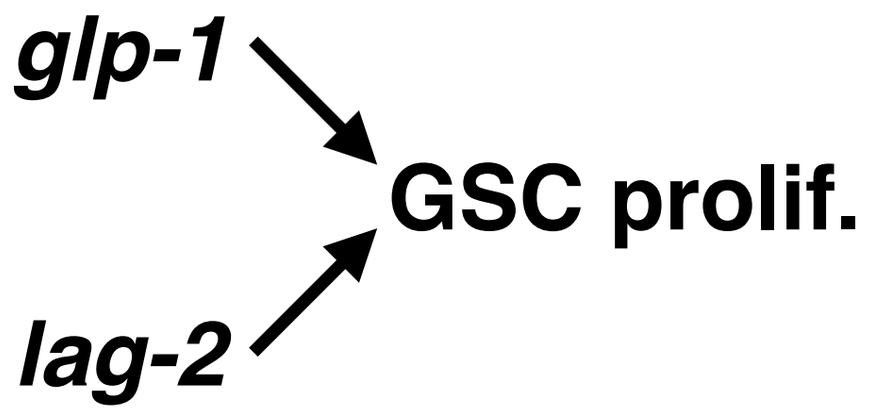
Parallel gene action can NEVER be formally excluded by phenotype alone

lag-2 → ***glp-1*** → **GSC prolif.**



Parallel gene action can NEVER be formally excluded by phenotype alone

lag-2 → ***glp-1*** → **GSC prolif.**



Null alleles have to be used

Approach to understanding regulatory epistasis

Approach to understanding regulatory epistasis

1. Decide what is the output phenotype; keep it consistent

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2. Look at single mutants and make a model with output

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1. Decide what is the output phenotype; keep it consistent

2. Look at single mutants and make a model with output

3. Look at double mutants and make a model with output and respect to single mutant models - epistatic gene acts downstream

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3. Look at double mutants and make a model with output and respect to single mutant models - epistatic gene acts downstream

4. Remember parallel but don't assume it is always parallel (*i.e.* make linear models for regulatory epistasis)

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1. Decide what is the output phenotype; keep it consistent

2. Look at single mutants and make a model with output

3. Look at double mutants and make a model with output and respect to single mutant models - epistatic gene acts downstream

4. Remember parallel but don't assume it is always parallel (*i.e.* make linear models for regulatory epistasis)

5. Remember two negatives make a positive

How do these genes work together?

Mutant	Phenotype
glp-1(0)	meiotic cells
glp-1(gf)	mitotic cells
lag-2(0)	meiotic cells
fbf-1(0)	meiotic cells
gld-1(0)	mitotic cells
glp-1(gf); lag-2(0)	mitotic cells
glp-1(gf); fbf-1(0)	meiotic cells
glp-1(0); gld-1(0)	mitotic cells
fbf-1(0); gld-1(0)	mitotic cells
lag-2(0); fbf-1(0)	meiotic cells
lag-2(0); gld-1(0)	mitotic cells

glp-1 → **GSC prolif.**

lag-2 → **GSC prolif.**

fbf-1 → **GSC prolif.**

gld-1 ⊣ **GSC prolif.**

lag-2 → ***glp-1*** → **GSC prolif.**

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glp-1(gf); fbf-1(0)	meiotic cells
glp-1(0); gld-1(0)	mitotic cells
fbf-1(0); gld-1(0)	mitotic cells
lag-2(0); fbf-1(0)	meiotic cells
lag-2(0); gld-1(0)	mitotic cells

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gld-1(0)	mitotic cells
glp-1(gf); lag-2(0)	mitotic cells
glp-1(gf); fbf-1(0)	meiotic cells
glp-1(0); gld-1(0)	mitotic cells
fbf-1(0); gld-1(0)	mitotic cells
lag-2(0); fbf-1(0)	meiotic cells
lag-2(0); gld-1(0)	mitotic cells

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lag-2 → ***glp-1*** → ***fbf-1*** → **GSC prolif.**

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lag-2(0)	meiotic cells
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glp-1(gf); lag-2(0)	mitotic cells
glp-1(gf); fbf-1(0)	meiotic cells
glp-1(0); gld-1(0)	mitotic cells
fbf-1(0); gld-1(0)	mitotic cells
lag-2(0); fbf-1(0)	meiotic cells
lag-2(0); gld-1(0)	mitotic cells

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fbf-1(0)	meiotic cells
gld-1(0)	mitotic cells
glp-1(gf); lag-2(0)	mitotic cells
glp-1(gf); fbf-1(0)	meiotic cells
glp-1(0); gld-1(0)	mitotic cells
fbf-1(0); gld-1(0)	mitotic cells
lag-2(0); fbf-1(0)	meiotic cells
lag-2(0); gld-1(0)	mitotic cells

glp-1 → **GSC prolif.**

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lag-2 → ***glp-1*** → ***fbf-1*** ⊣ ***gld-1*** ⊣ **GSC prolif.**