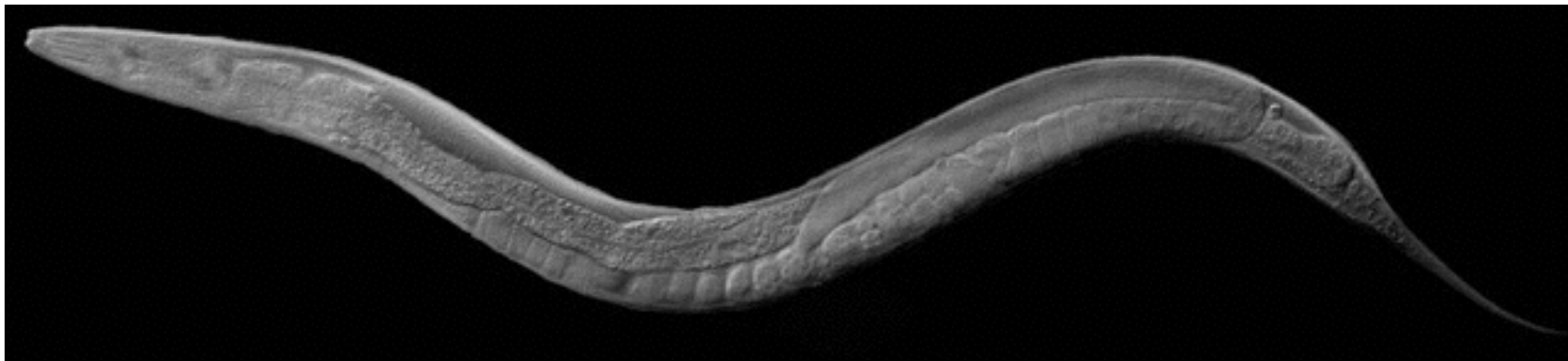
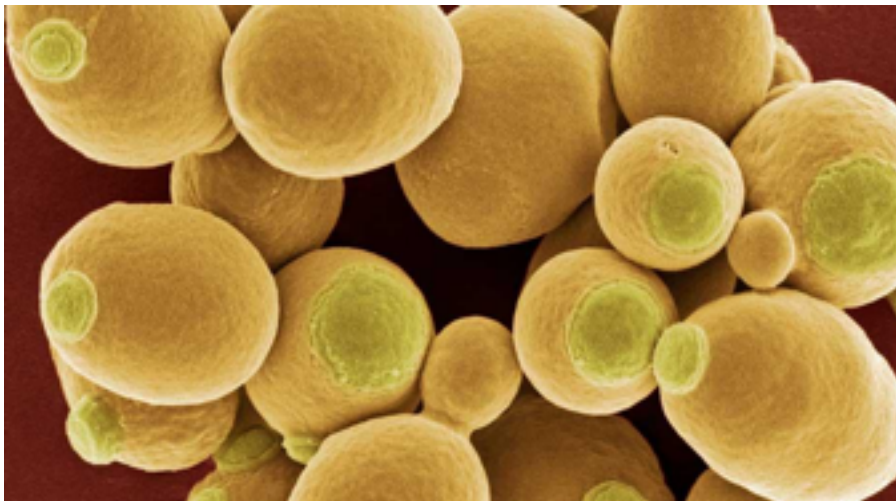


# Bio393: Genetic Analysis

Screens, selections, mutants, dosage



# Where do all those mutant strains come from?

## **Natural**

- Made by random errors of DNA repair, replication, transcription, recombination, etc.
- Made by natural mutagens (UV, etc.)
- Variants present in a population
- Rare or common

## **Induced**

- Made by mutagens (EMS, ENU, X-ray irradiation, etc.)

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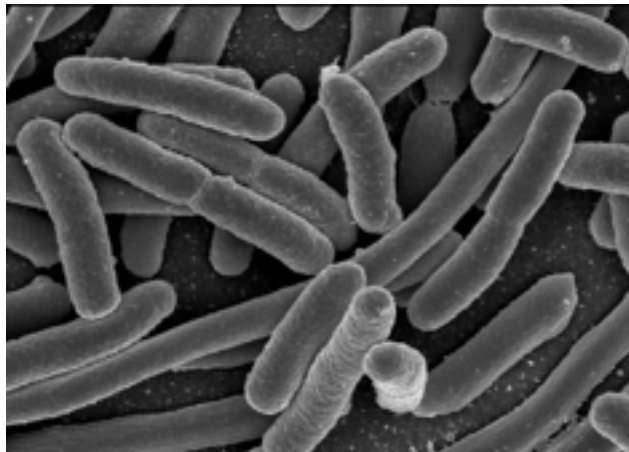
## Induced

- Made by mutagens (EMS, ENU, X-ray irradiation, etc.)

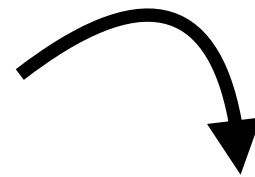
**Genomes are full of mutations**

# Two ways to isolate mutants: selection or screen

## Selection:



*E. coli*



**Complete  
media +  
drug**

**~24 hrs  
→**



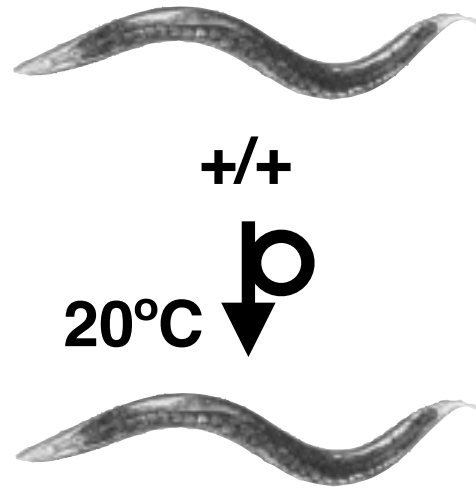
**Complete  
media +  
drug**

# **Two ways to isolate mutants: selection or screen**

**Selection:**

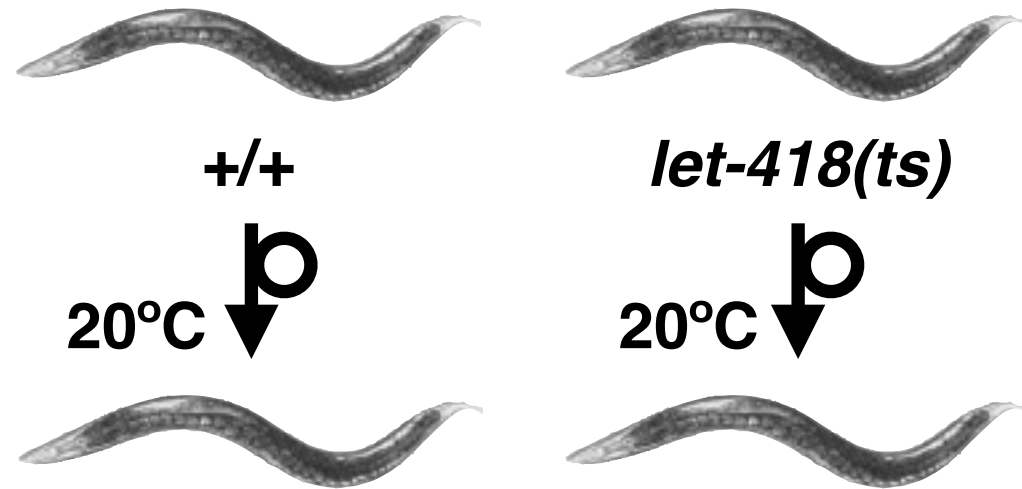
# Two ways to isolate mutants: selection or screen

## Selection:



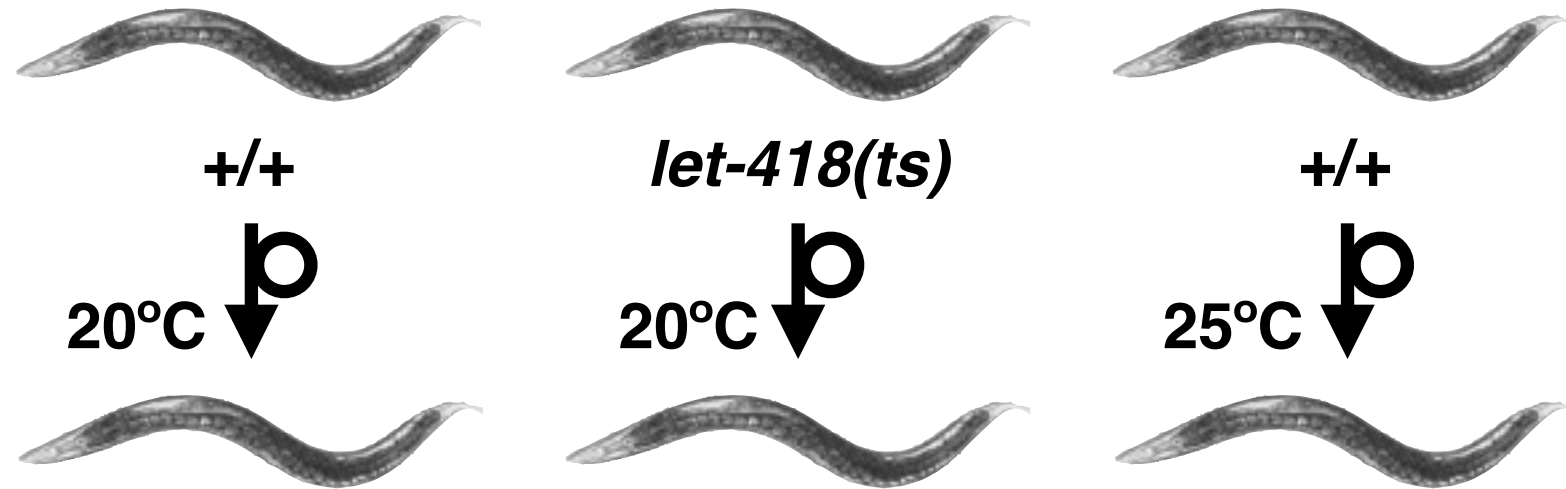
# Two ways to isolate mutants: selection or screen

## Selection:



# Two ways to isolate mutants: selection or screen

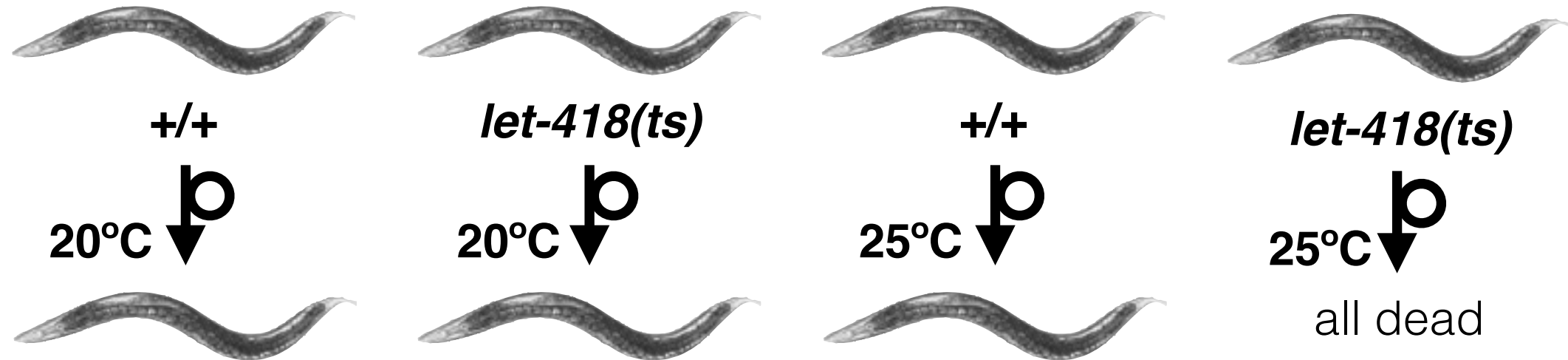
## Selection:





# Two ways to isolate mutants: selection or screen

## Selection:



# Two ways to isolate mutants: selection or screen

## Selection:



*+/+*

20°C ↓ **p**



*let-418(ts)*

20°C ↓ **p**



*+/+*

25°C ↓ **p**



*let-418(ts)*

25°C ↓ **p**

all dead

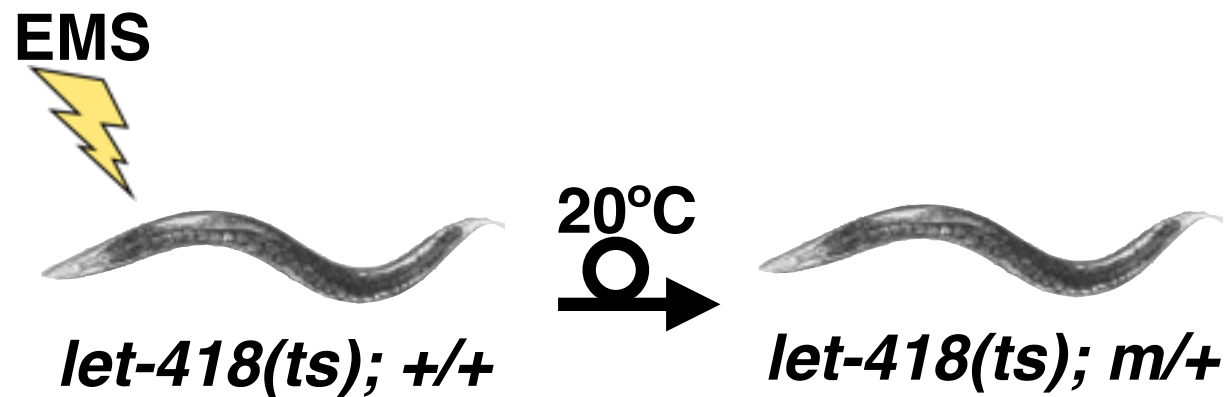
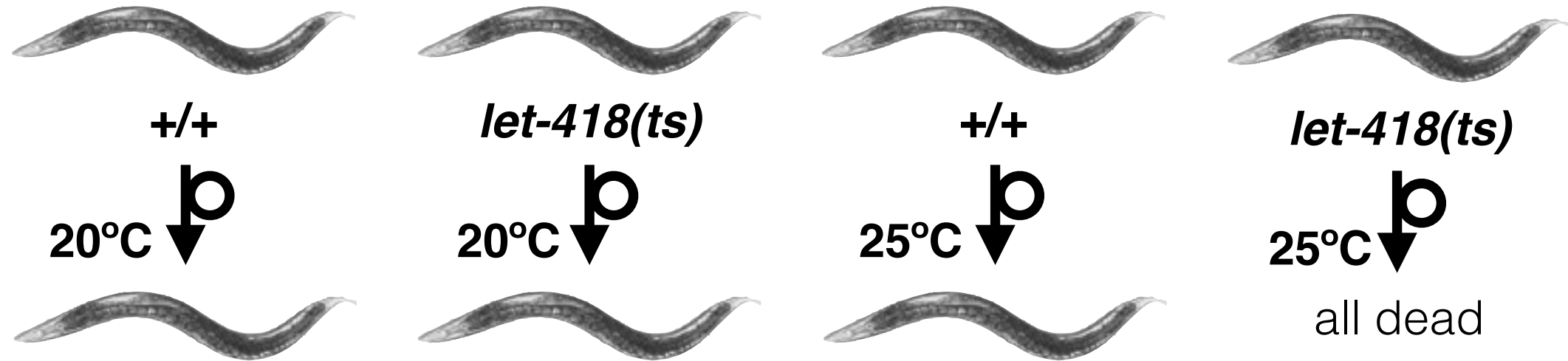
EMS



*let-418(ts); +/+*

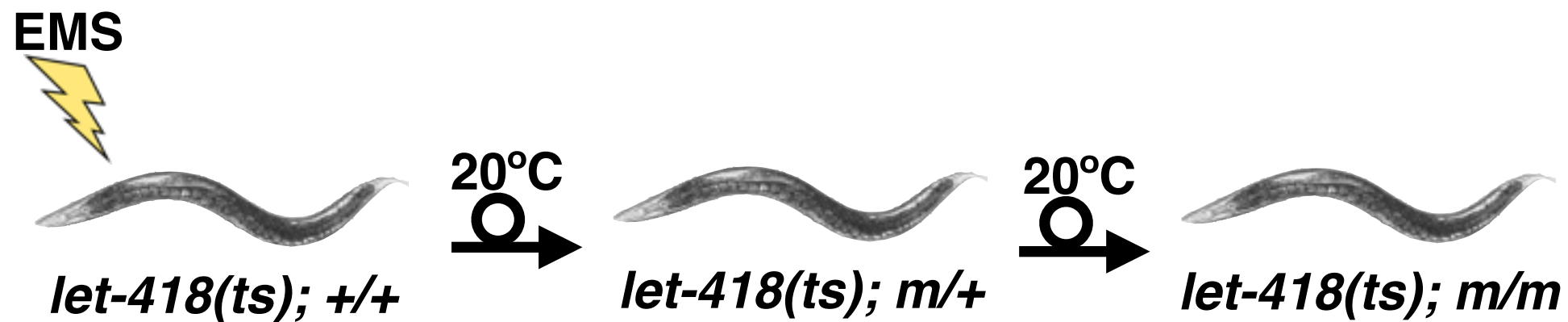
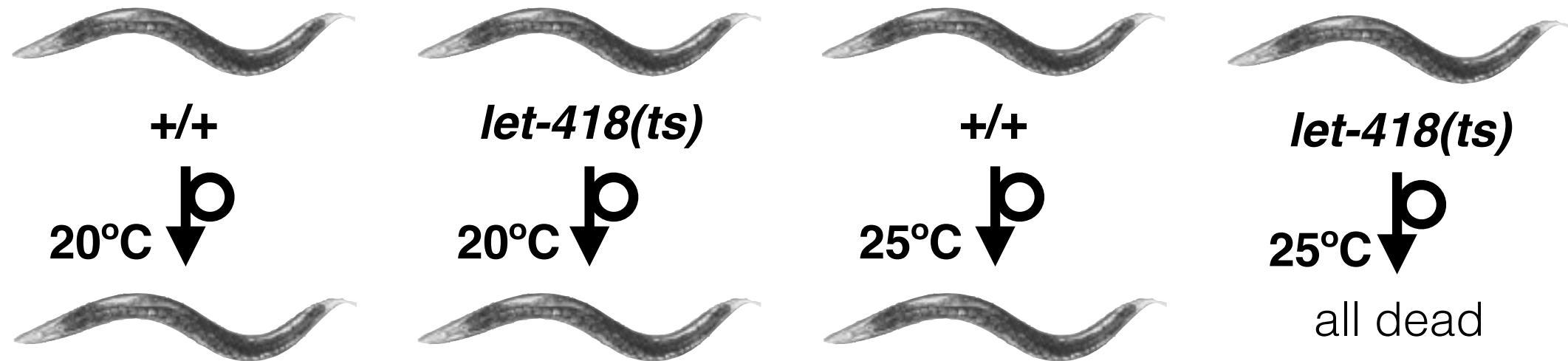
# Two ways to isolate mutants: selection or screen

## Selection:



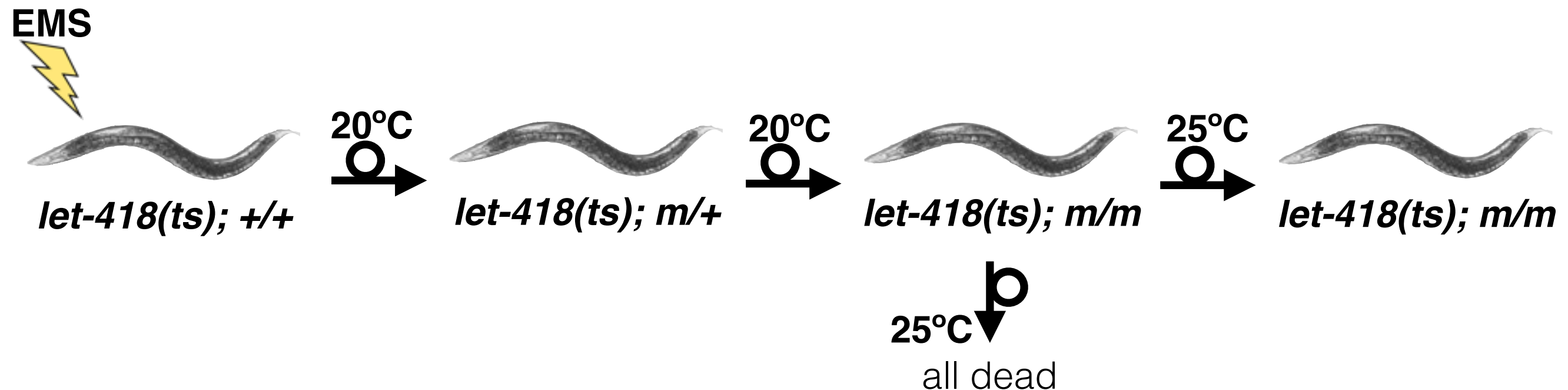
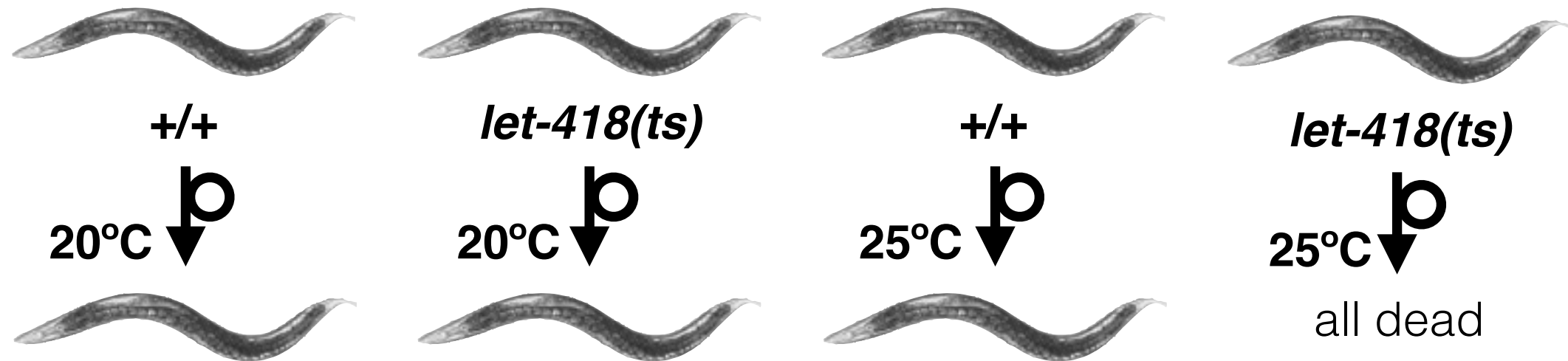
# Two ways to isolate mutants: selection or screen

## Selection:



# Two ways to isolate mutants: selection or screen

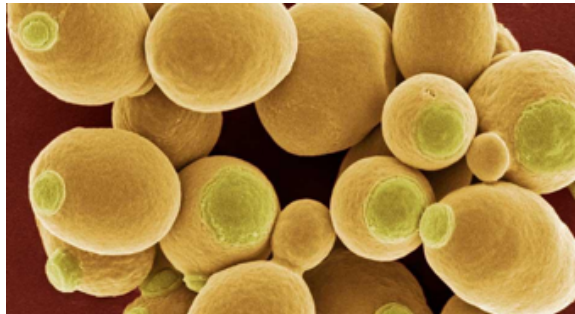
## Selection:



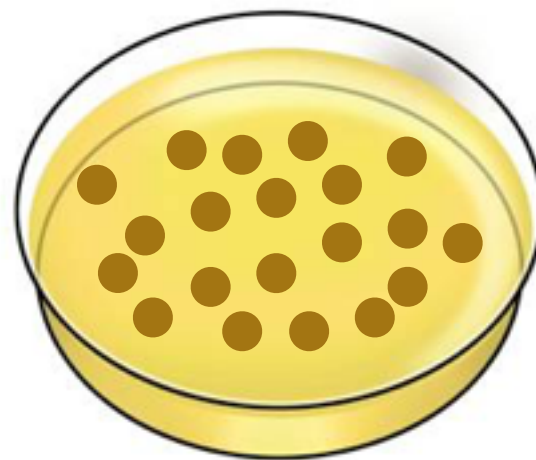
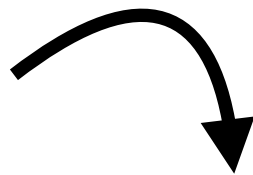
# Two ways to isolate mutants: selection or screen

## Screen:

EMS



*S. cerevisiae*

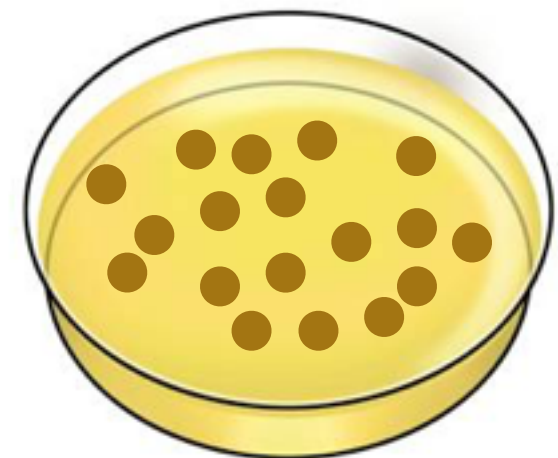


Complete  
media

Replica  
plate



~24 hrs

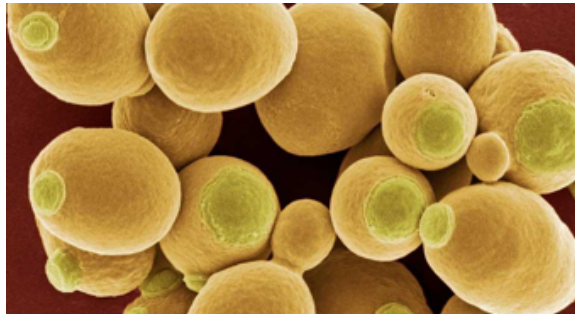


Media  
-adenine

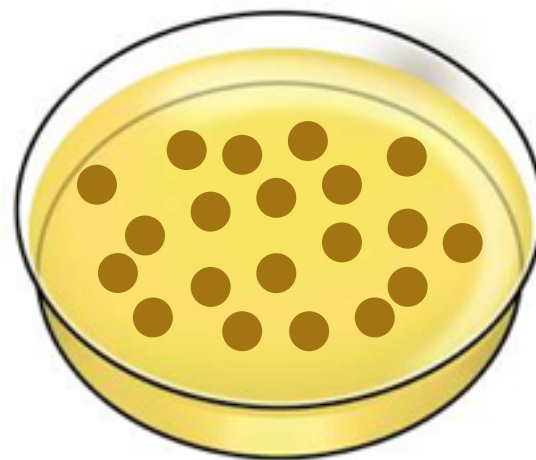
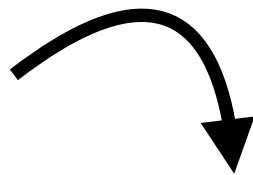
# Two ways to isolate mutants: selection or screen

## Screen:

EMS



*S. cerevisiae*

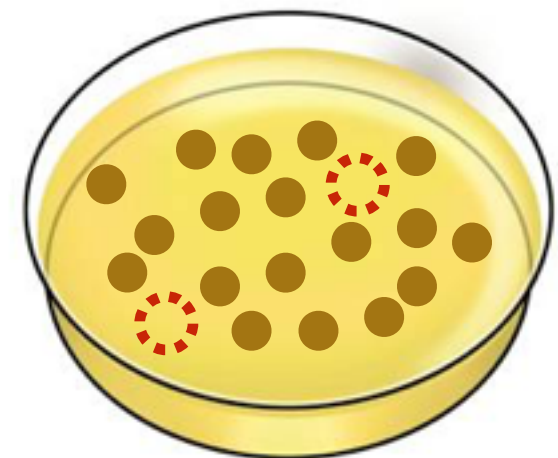


Complete  
media

Replica  
plate

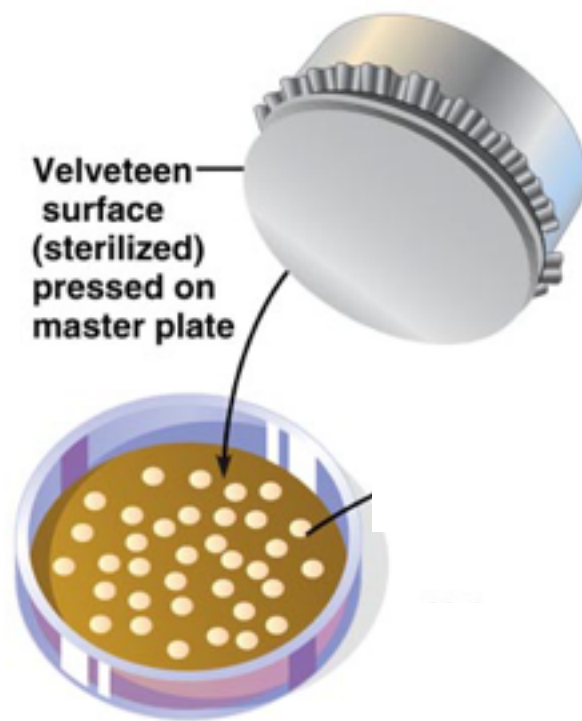


~24 hrs



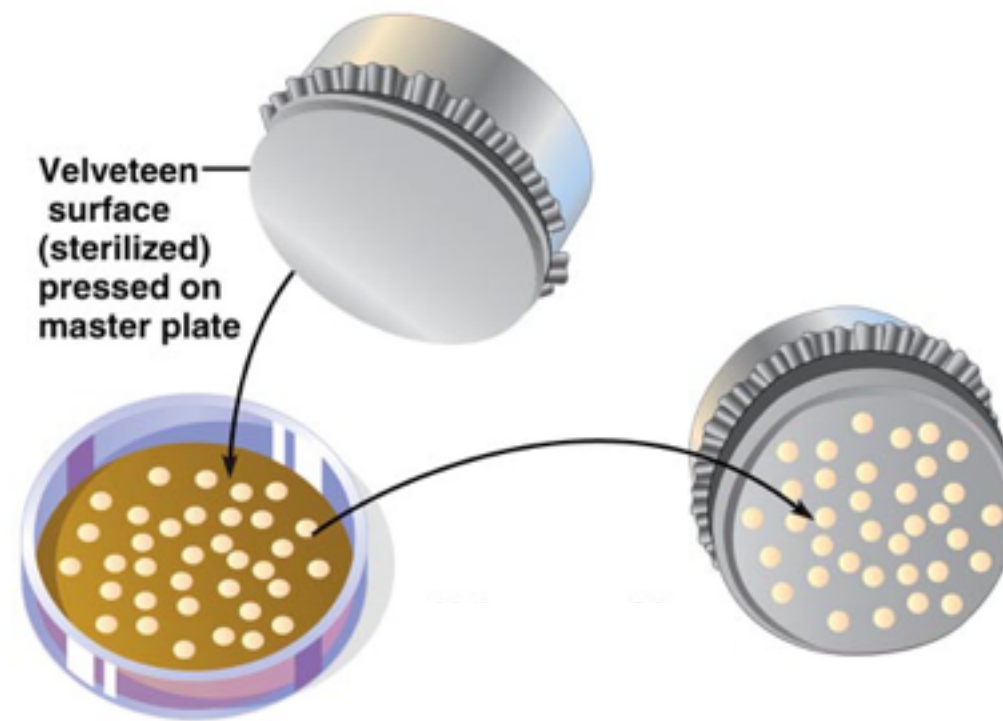
Media  
-adenine

# Replica plating

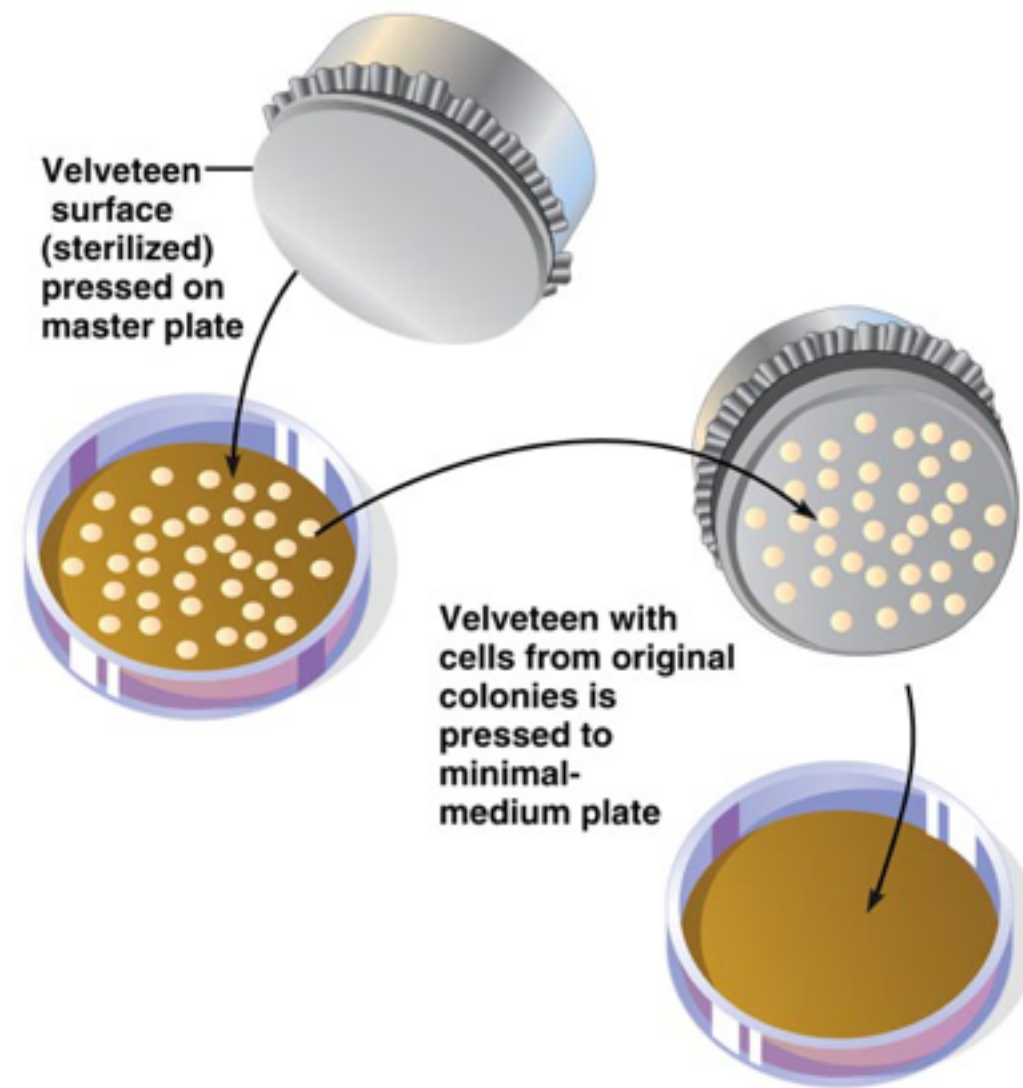




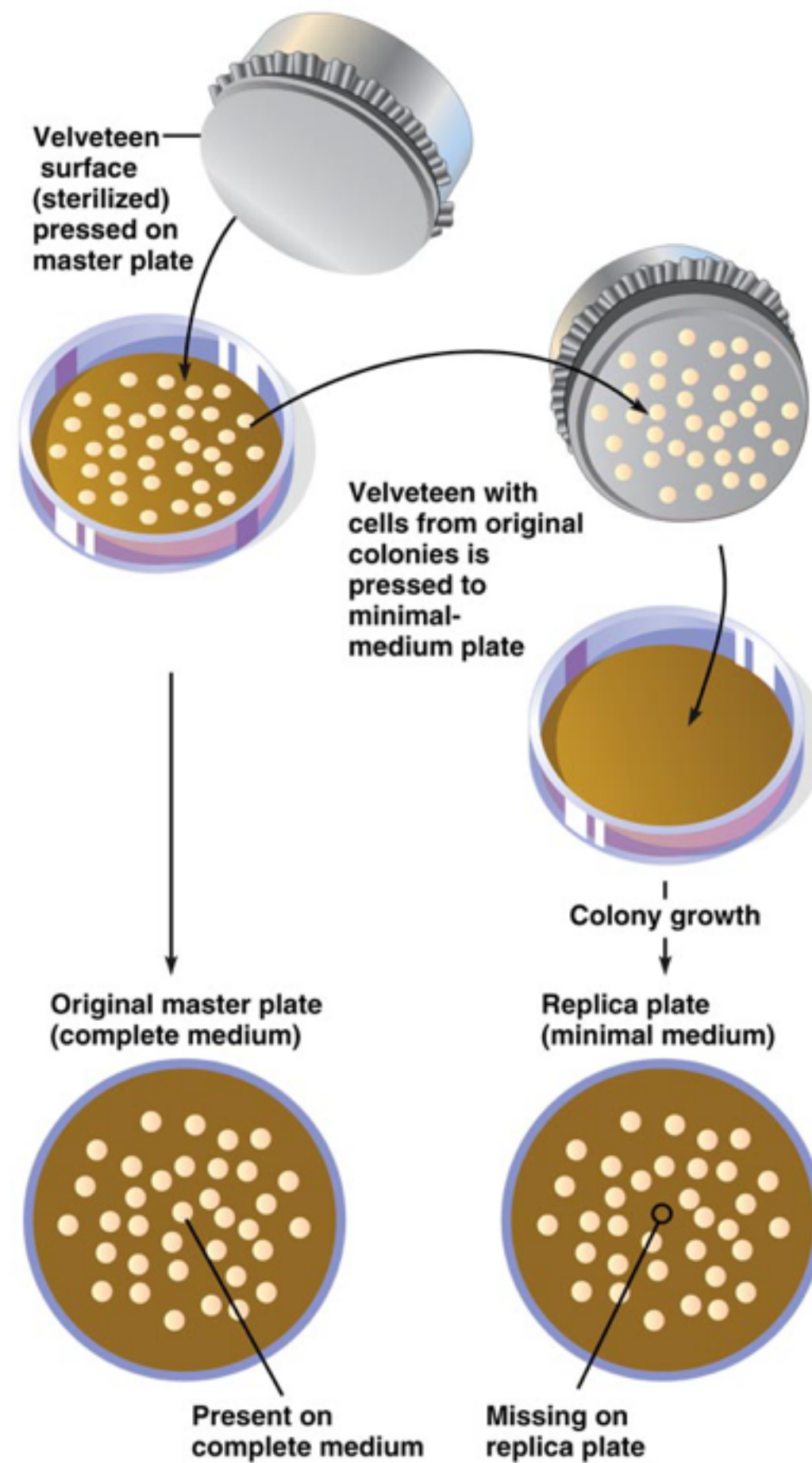
# Replica plating



# Replica plating



# Replica plating



# Two ways to isolate mutants: selection or screen

**Screen:**



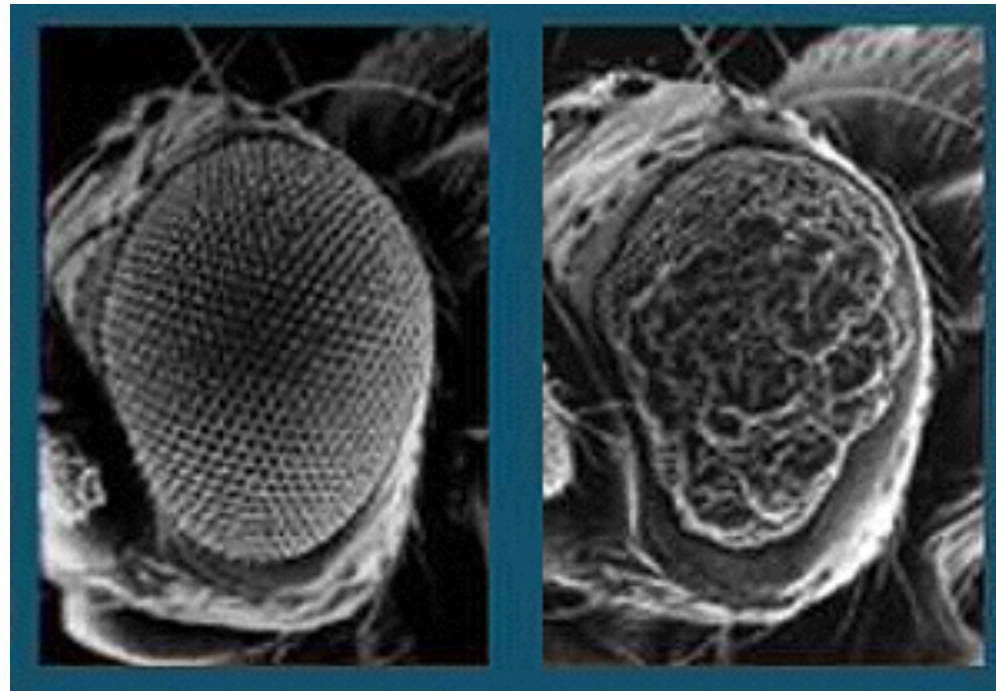
***D. melanogaster***

# Two ways to isolate mutants: selection or screen

**Screen:**



***D. melanogaster***



# ***Drosophila* have balancer chromosomes**



# ***Drosophila* have balancer chromosomes**



Every balancer chromosome:

# ***Drosophila* have balancer chromosomes**

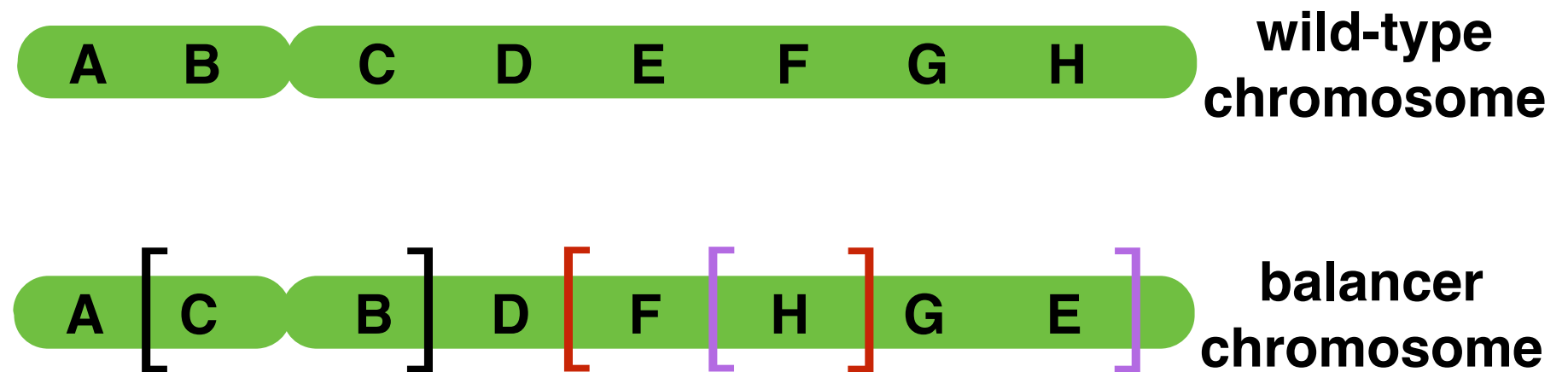


Every balancer chromosome:

1. has many inversions to eliminate recombination



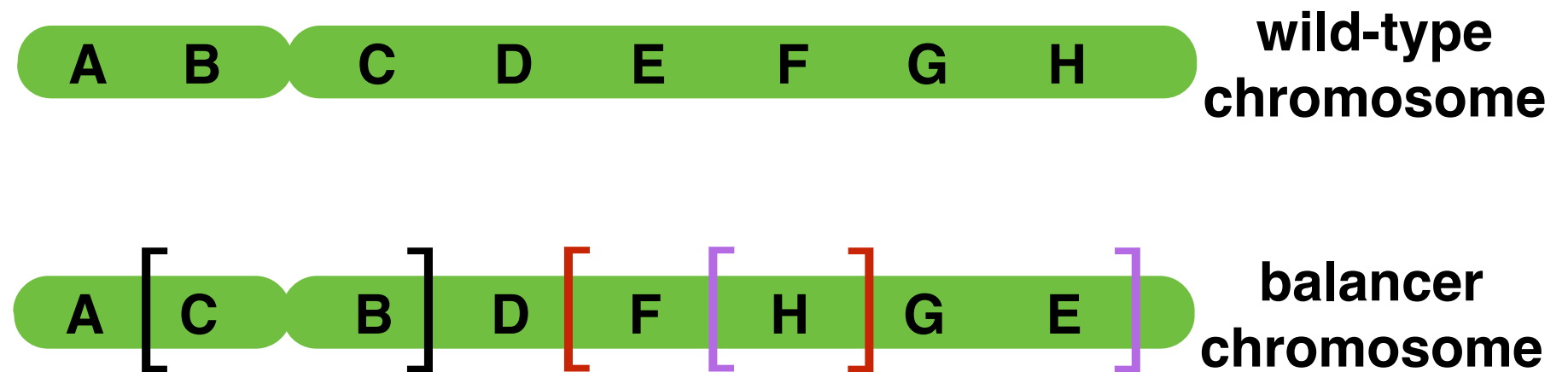
# ***Drosophila* have balancer chromosomes**



Every balancer chromosome:

1. has many inversions to eliminate recombination

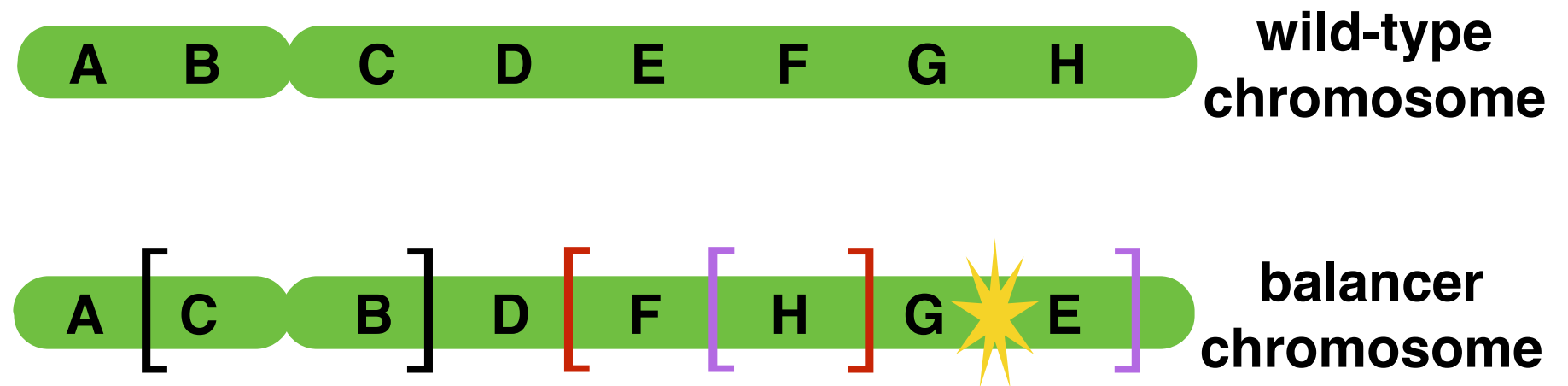
# *Drosophila* have balancer chromosomes



Every balancer chromosome:

1. has many inversions to eliminate recombination
2. confers an easily scored dominant phenotype

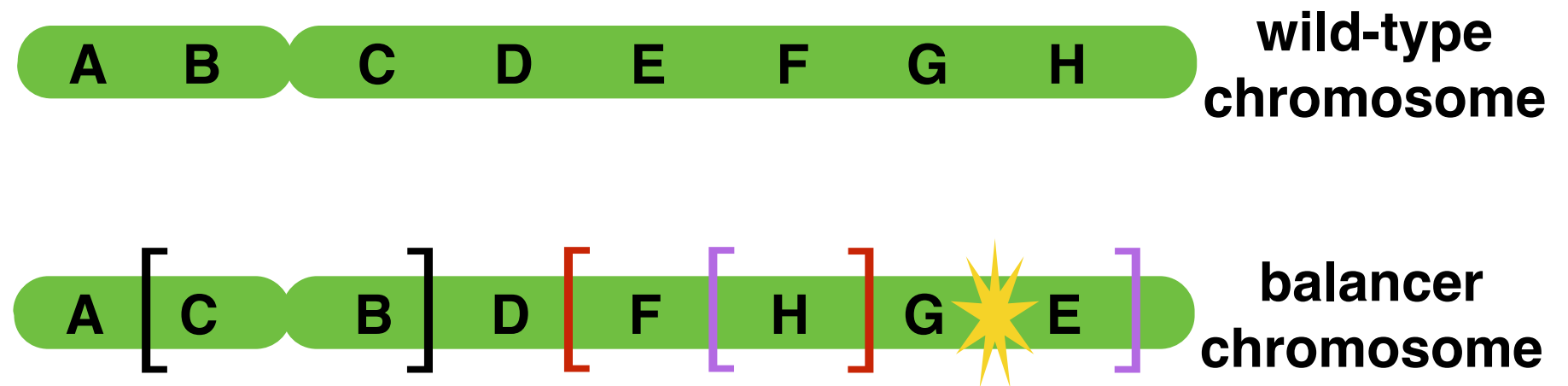
# ***Drosophila* have balancer chromosomes**



Every balancer chromosome:

1. has many inversions to eliminate recombination
2. confers an easily scored dominant phenotype

# *Drosophila* have balancer chromosomes



Every balancer chromosome:

1. has many inversions to eliminate recombination
2. confers an easily scored dominant phenotype
3. is recessive lethal



*Sp*  
*CyO*

# Two ways to isolate mutants: selection or screen

Screen:

EMS

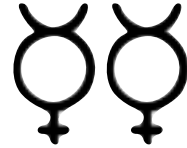


$\frac{+}{+}$



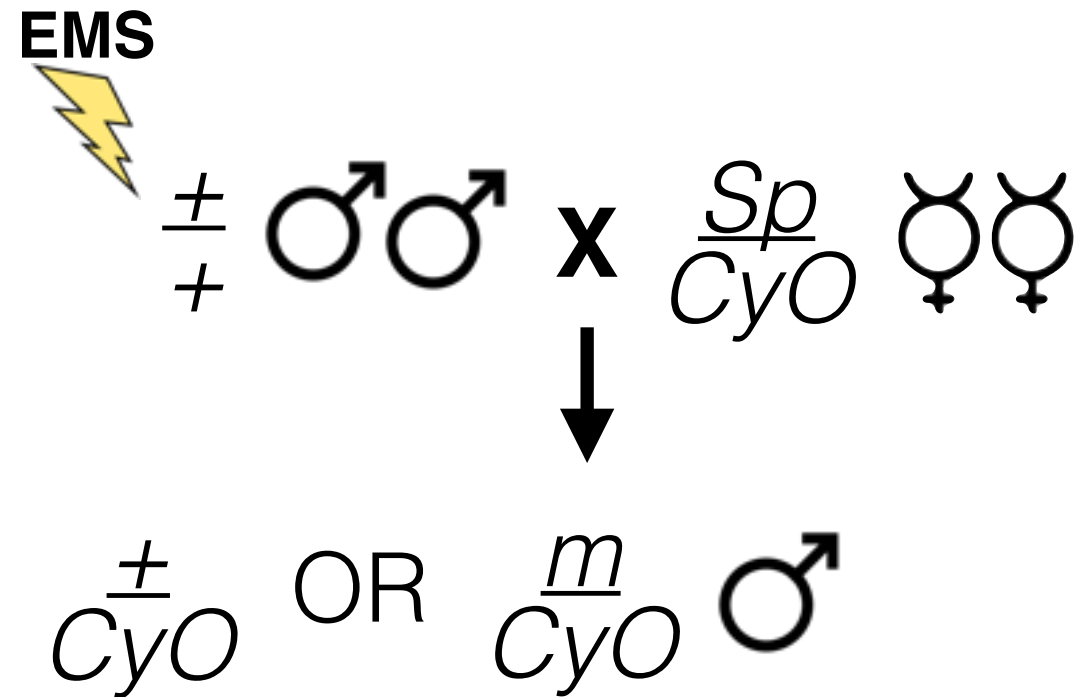
**x**

$\frac{Sp}{CyO}$



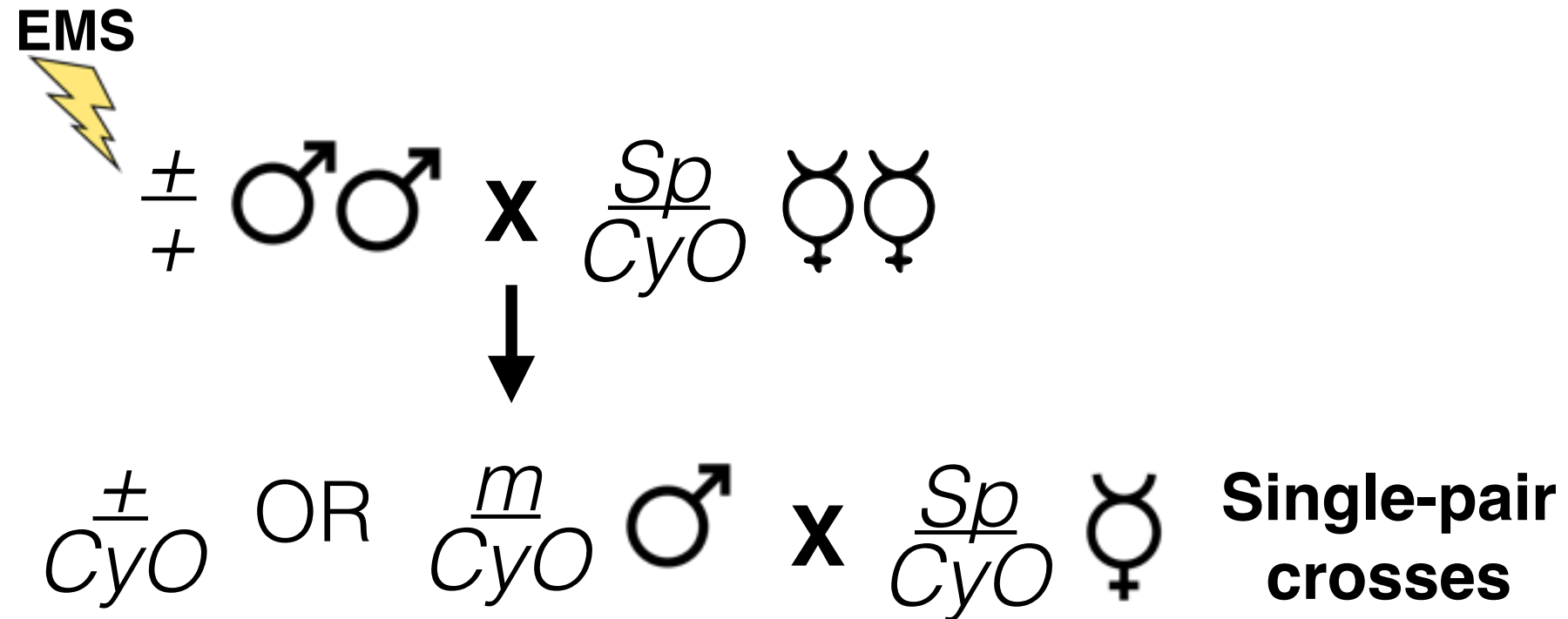
# Two ways to isolate mutants: selection or screen

**Screen:**



# Two ways to isolate mutants: selection or screen

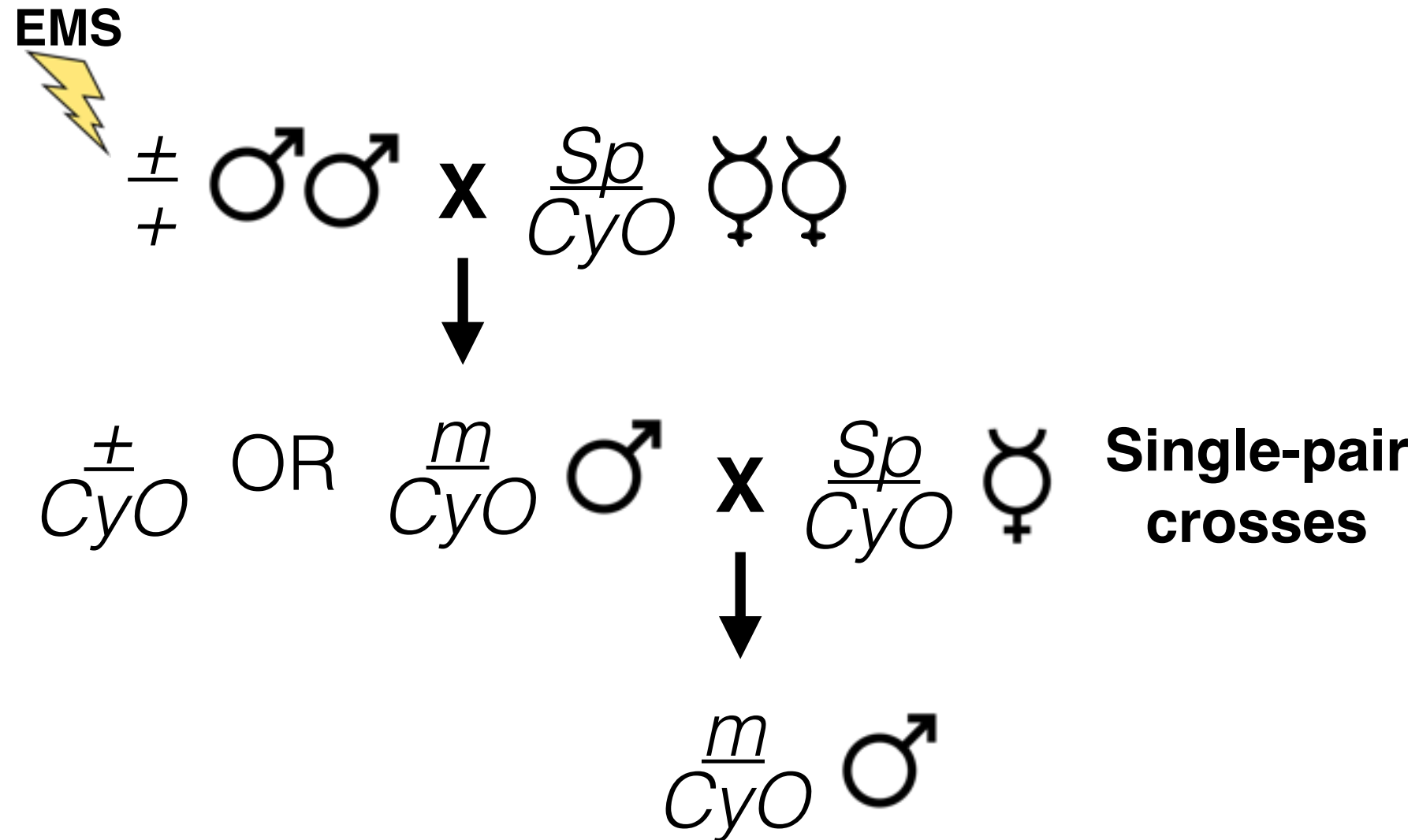
**Screen:**





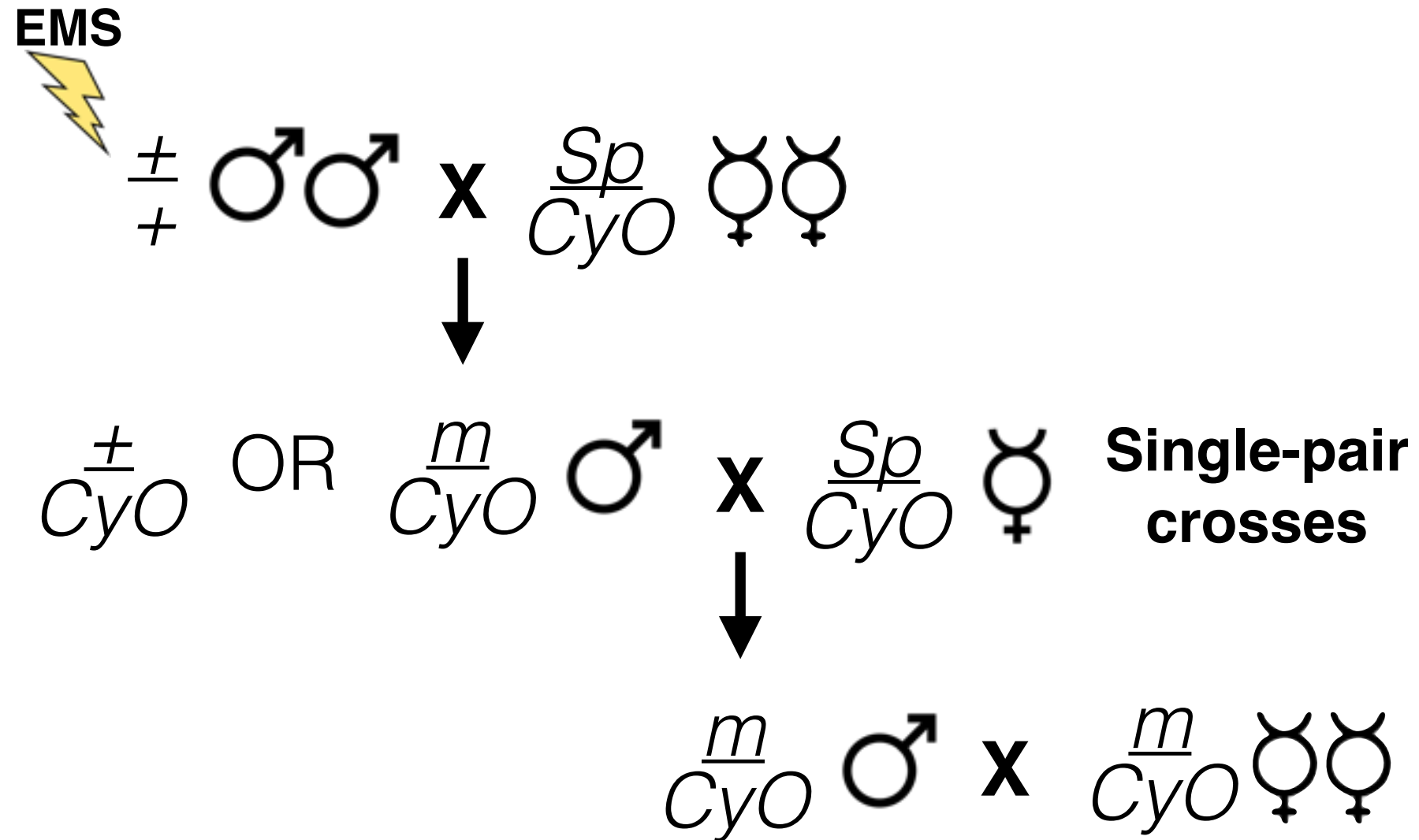
# Two ways to isolate mutants: selection or screen

**Screen:**



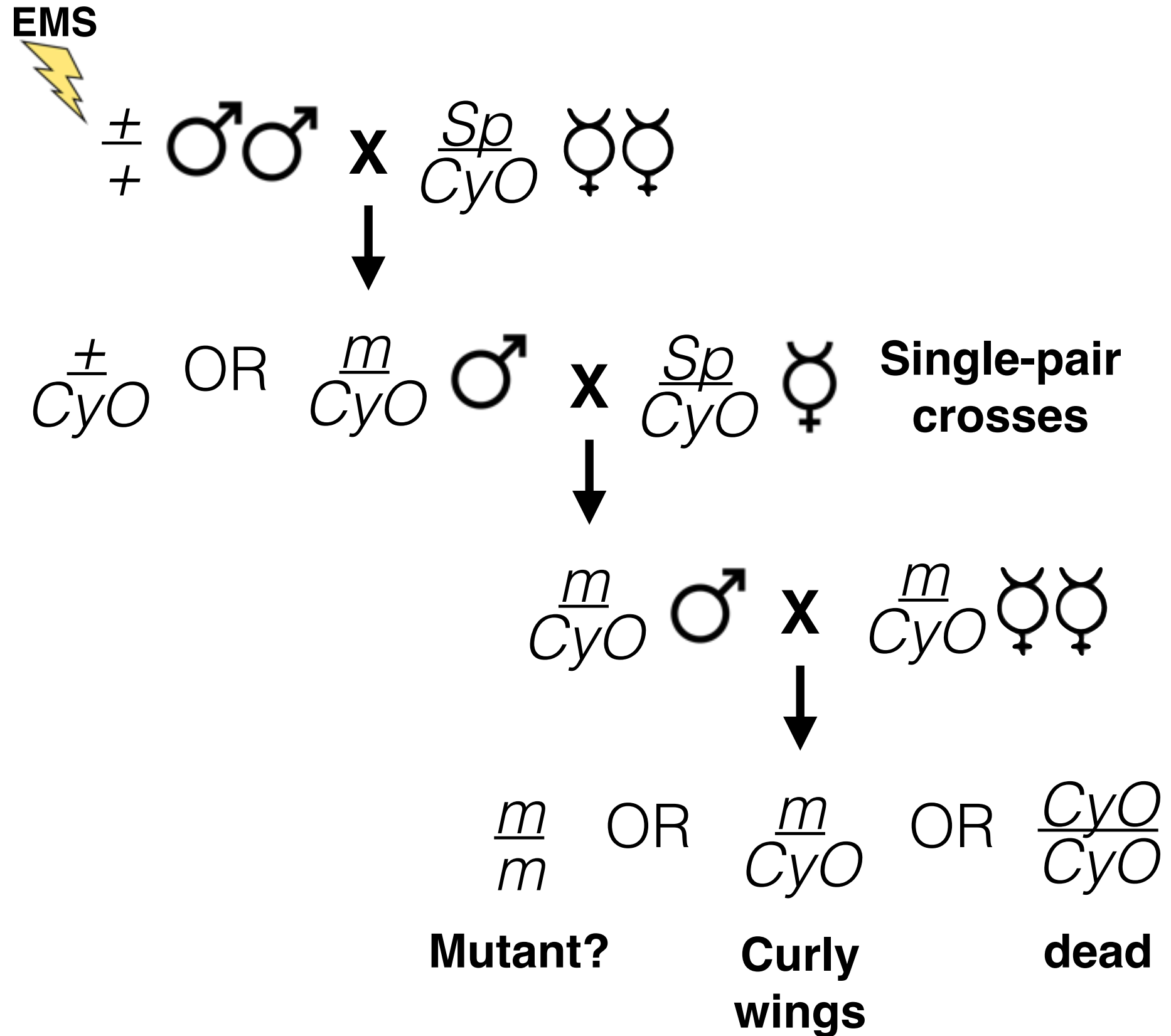
# Two ways to isolate mutants: selection or screen

**Screen:**



# Two ways to isolate mutants: selection or screen

**Screen:**



**How would you screen or select for mutants that cause a dominant or recessive phenotype in yeast, *C. elegans*, *Drosophila*, and mice?**

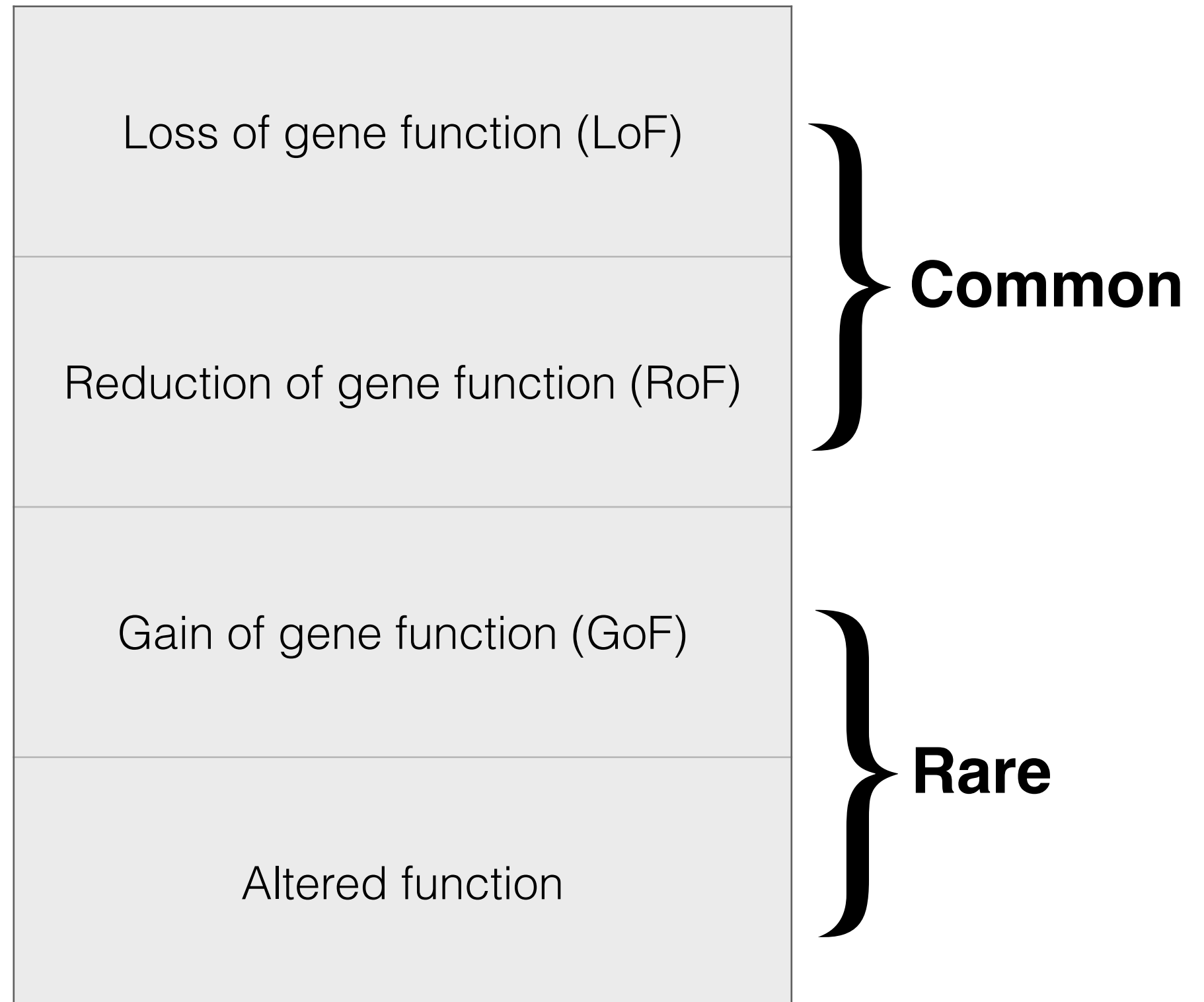
**What does a mutation do to gene function?**

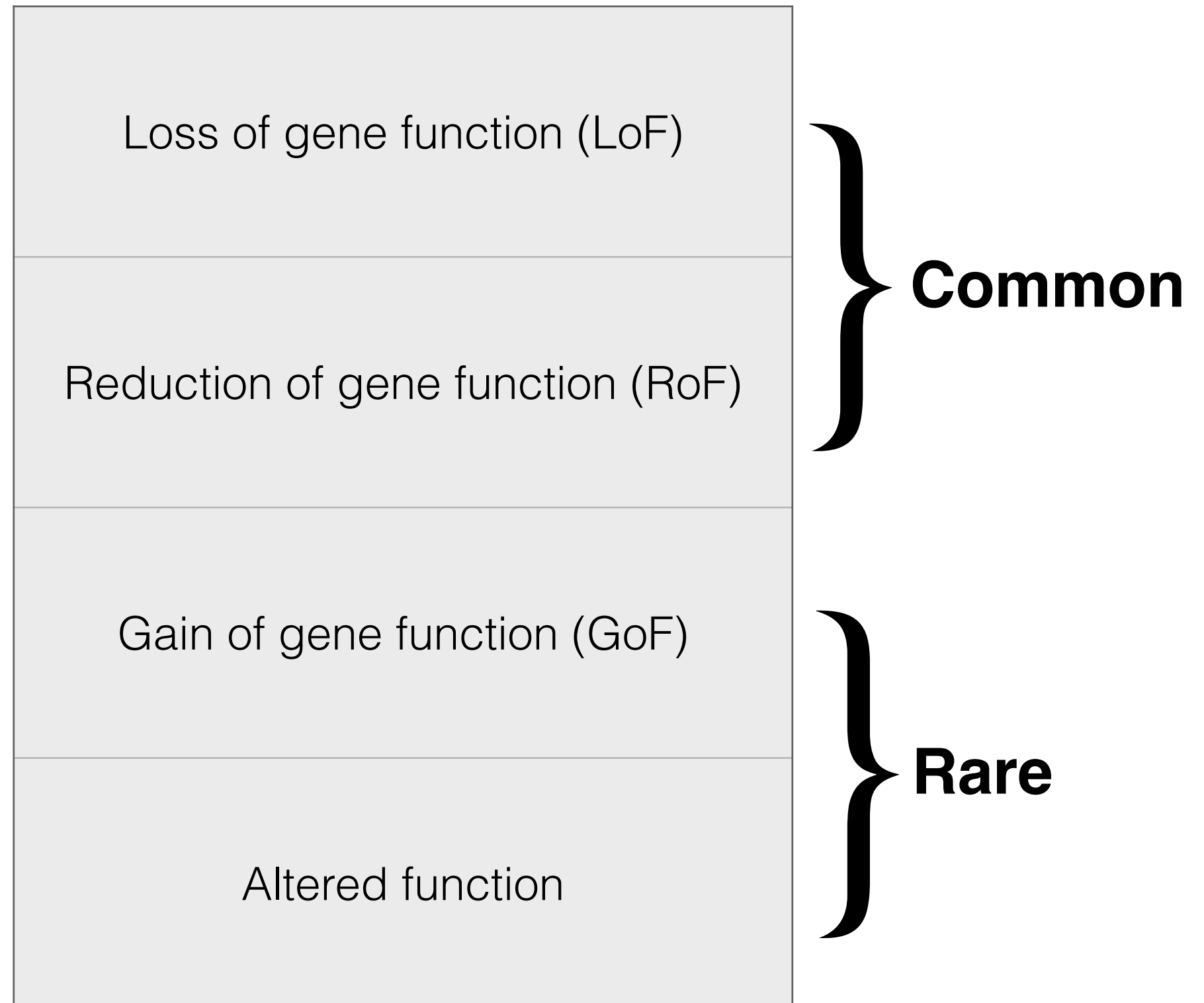
Loss of gene function (LoF)

Reduction of gene function (RoF)

Gain of gene function (GoF)

Altered function





**Dominant or recessive  
correlates with mutation type most times**





**Hermann Muller**



# Muller's morphs - gene dosage tests

|                                  |                     |
|----------------------------------|---------------------|
| Loss of gene function (LoF)      | amorph, nullomorph  |
| Reduction of gene function (RoF) | hypomorph           |
| Gain of gene function (GoF)      | hypermorph          |
| Altered function                 | neomorph, antimorph |

m = mutation of gene

$\Delta$  = deletion of gene

+

= normal copy of gene

= = Phenotype is equivalent

> = Phenotype is more mutant than

< = Phenotype is less mutant than