

## Lecture 5: Genetic interactions and epistasis

- A. Epistasis in a biochemical pathway
- B. Epistasis in a regulatory pathway
- C. Additive interactions
- D. Synergistic interactions
- E.Suppressions

Read 3.14 (p60-61); 7.23 (p232-234)  
8.32 (p290-291); 8.5 (259-260)

*What is epistasis?*

*A gene interaction in which the effects of an allele at one gene hide the effects of alleles at another gene*

# Codominant blood group alleles

(b) Codominant blood group alleles

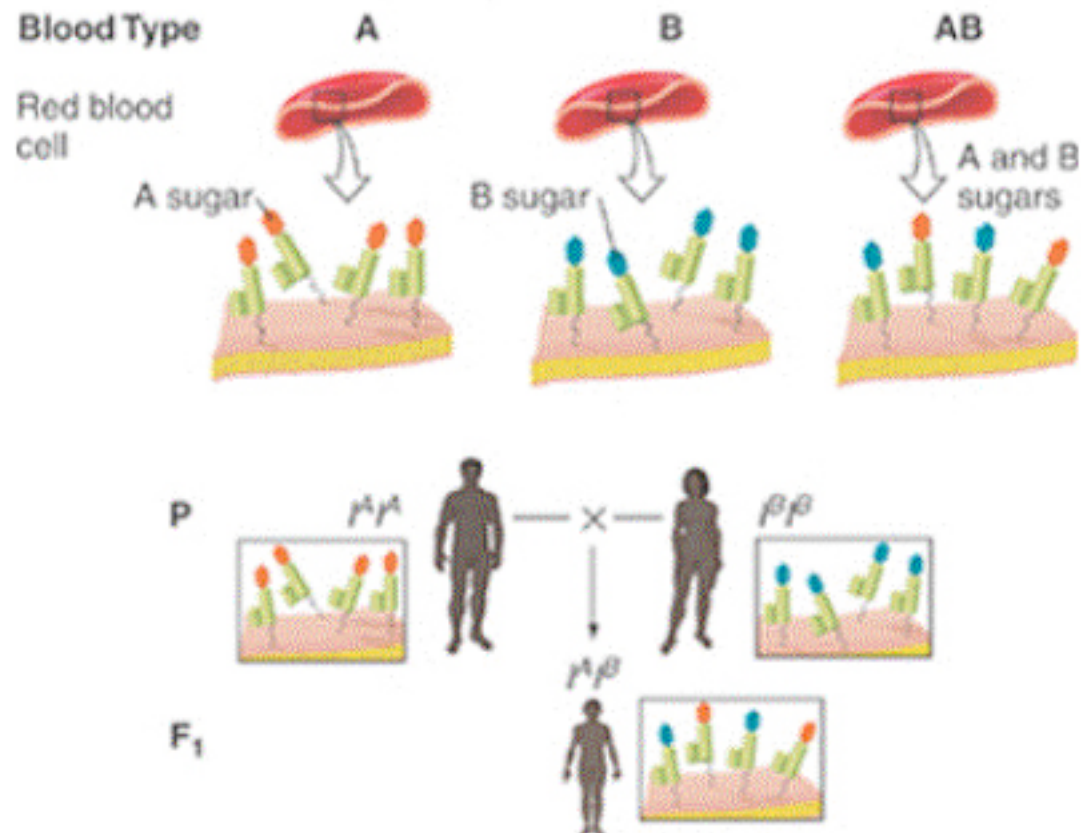


Fig. 3.4b

# Molecular explanation for recessive epistasis in human blood groups

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- Two parents who are apparently type O have offspring that is type A or B on rare occasions.
- Bombay phenotype – mutant recessive allele at second gene (hh) masks phenotype of ABO alleles

(b) Molecular basis of the Bombay phenotype

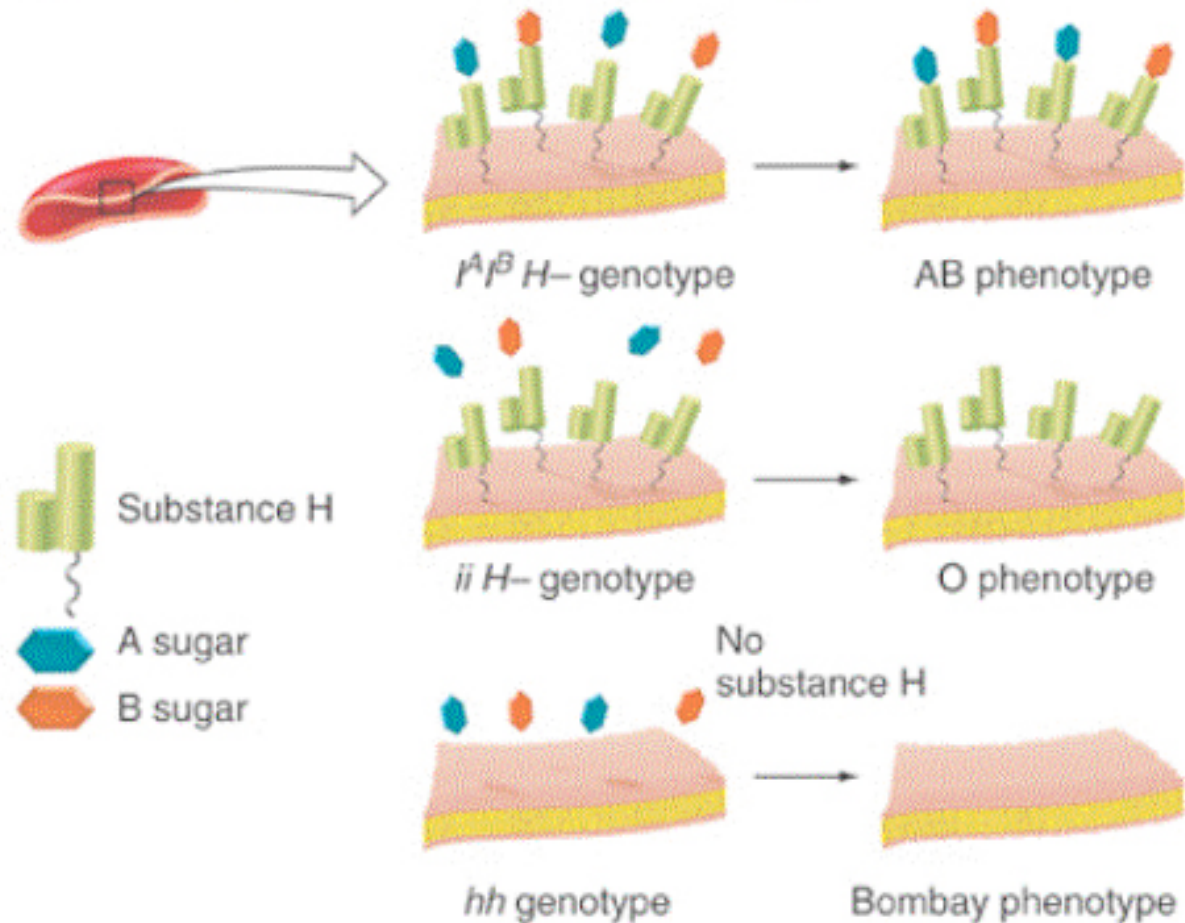
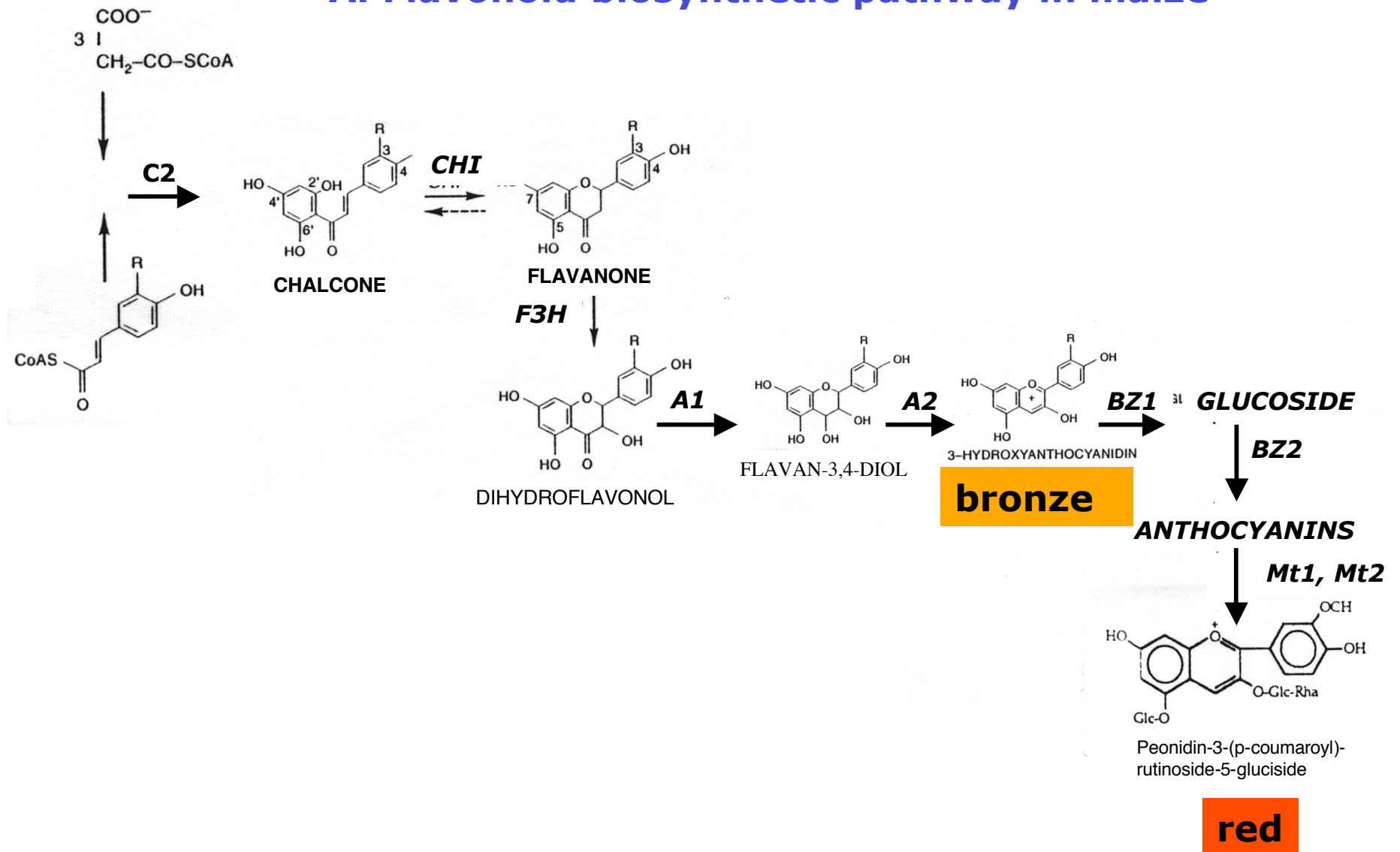


Fig. 3.14b

## epistasis analyses (genetic interactions among different mutations)

### A. Flavonoid biosynthetic pathway in maize



<b>WT:</b>	<b>Red</b>
<b>Mutations in c2, a1, a2:</b>	<b>Colorless</b>
<b>Mutations in bz1, bz2:</b>	<b>bronze</b>

### Double mutants

**C2/a1: colourless-but uninformative**

**bz1/a1: colorless-a1 comes before bz1**

**bz2/a1: colorless-a1 comes before bz2**

**For biosynthetic pathways, the phenotype of the earlier gene in the pathway shows in the double mutant.  
ie. the earlier-step mutant is epistatic to the late-step mutant**

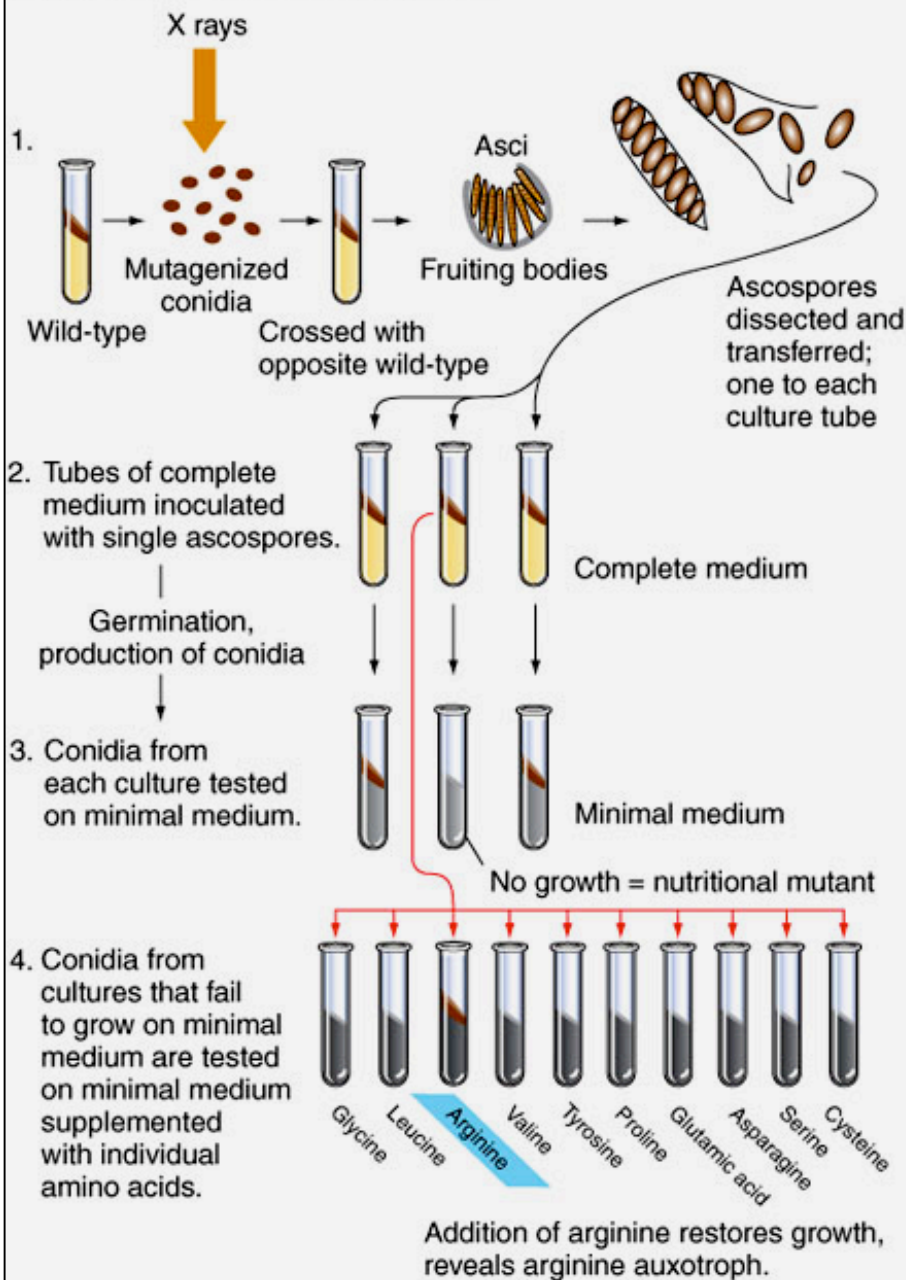
**Determine relationship between a1 and c2 by feeding experiment:  
add flavanone (naringenin): c2+naringenin = red  
a1+naringenin = colorless**

**Fig. 7.23**

# Biochemical Pathways

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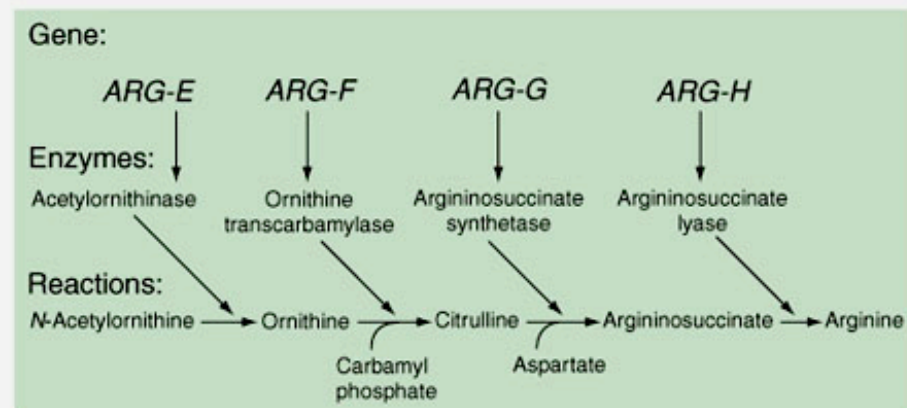
**(a) Isolation of arginine auxotrophs**



**(b) Growth response if nutrient is added to minimal medium**

Mutant strain	Supplements				
	Nothing	Ornithine	Citrulline	Arginino-succinate	Arginine
Wildtype: <i>Arg</i> <sup>+</sup>	+	+	+	+	+
<i>Arg-E</i> <sup>-</sup>	-	+	+	+	+
<i>Arg-F</i> <sup>-</sup>	-	-	+	+	+
<i>Arg-G</i> <sup>-</sup>	-	-	-	+	+
<i>Arg-H</i> <sup>-</sup>	-	-	-	-	+

**(c) Inferred biochemical pathway**



## B. Regulatory pathways

Signal  $\rightarrow$  A  $\rightarrow$  B  $\rightarrow$  C  $\text{---|}$  D  $\text{---|}$  gene expression

$\rightarrow$  Positive action-stimulate next step.  
Null mutation makes insensitive to signal

$\text{---|}$  Negative action-represses next step.  
Null mutation makes the gene turned on at all time (constitutively)

$b^-$ : gene expression never turned on  
even in the presence of the signal

$d^-$ : gene expression constitutively on  
even in the absence of signal

$b^-d^- = d^-$  : constitutively on

For regulatory pathways, the phenotype of the later-acting genes shows in the double mutant.

ie. the later-acting mutant is epistatic to the earlier-acting mutant



<i>wt</i>	<i>wt</i>	<i>ctr1</i>	<i>ein2</i>
ethylene	air	air	ethylene



*ctr ein2* :?



Ethylene —| CTR1 (Kinase) —| EIN2 → triple response

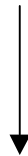
For regulatory pathways, the phenotype of the later-acting genes shows in the double mutant.  
ie. the later-acting mutant is epistatic to the earlier-acting mutant

## C. Additive pathways

**Double mutants of dissimilar phenotypes produce a combination of both phenotypes**

**Indicate that the two mutations are in genes acting in separate pathways**

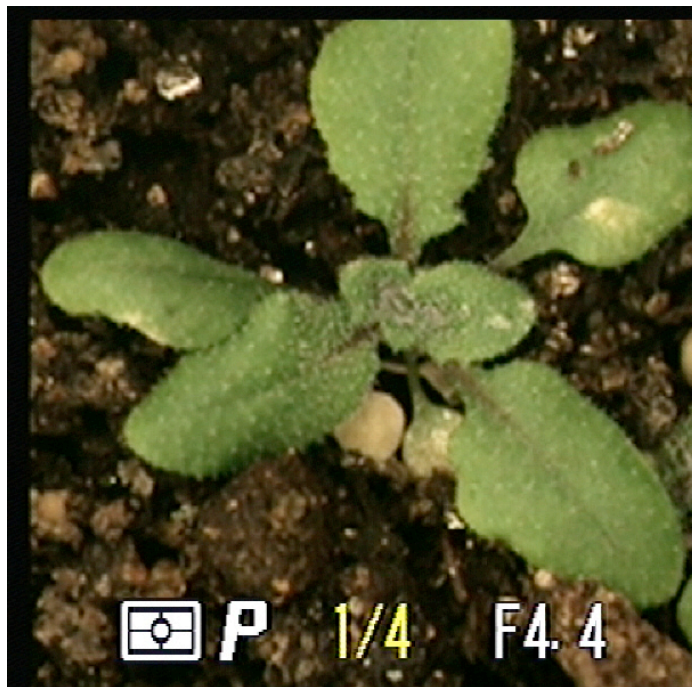
*ap2-2* (flower abnormal) X *gl* (no trichome)



*ap2-2 gl* double mutant  
abnormal flower and no trichome



*ap2-2*



*gl1*



## **D. Synergistic interactions (enhancement)**

Two genes may act at the same step of a pathway  
Or in parallel or (redundant) pathways



*ap1-1 cal-1*



*ap1-1*

## E. Suppression

Intragenic suppressors

Extragenic suppressors

Allele-specific suppression

Suppressors are defined classically as mutations that correct the phenotypic defects of another mutation without restoring its wild-type sequence. Suppressors may be intragenic (affecting the same gene) or they may be extragenic (affecting a different gene).

## ***Intragenic suppressor***

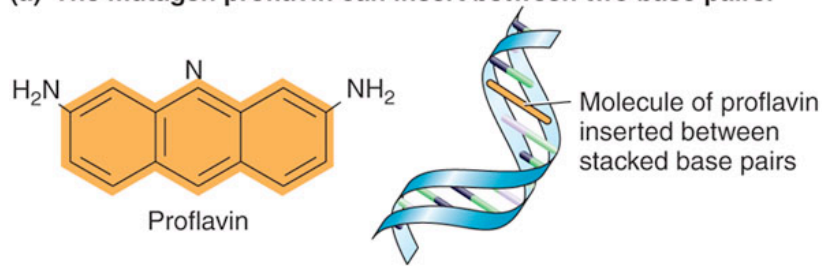
*Frameshift mutation caused by a single base insertion can be suppressed by a second mutation that cause a single base deletion downstream from the first mutation.  
See Fig. 8.5 and p259-260.*



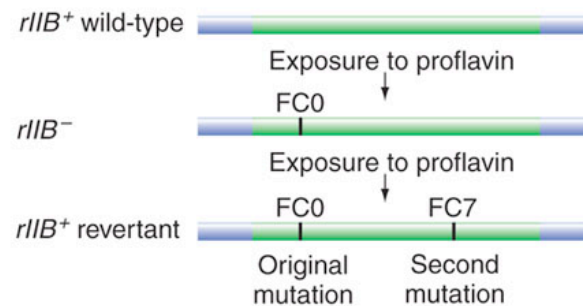
# Studies of frameshift mutations in bacteriophage T4 rIIB gene

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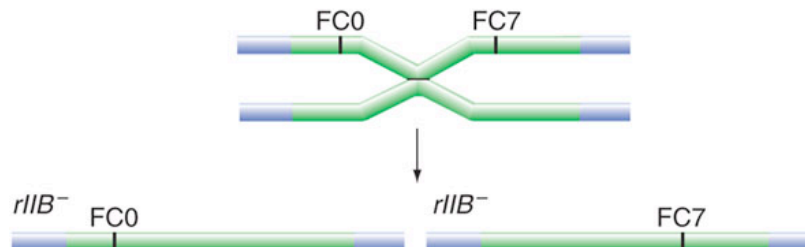
(a) The mutagen proflavin can insert between two base pairs.



(b) Consequences of exposure to proflavin



(c) *rIIB*<sup>+</sup> revertant X wild type yields *rIIB*<sup>-</sup> recombinants.



(d) Different sets of mutations generate either a mutant or a normal phenotype.

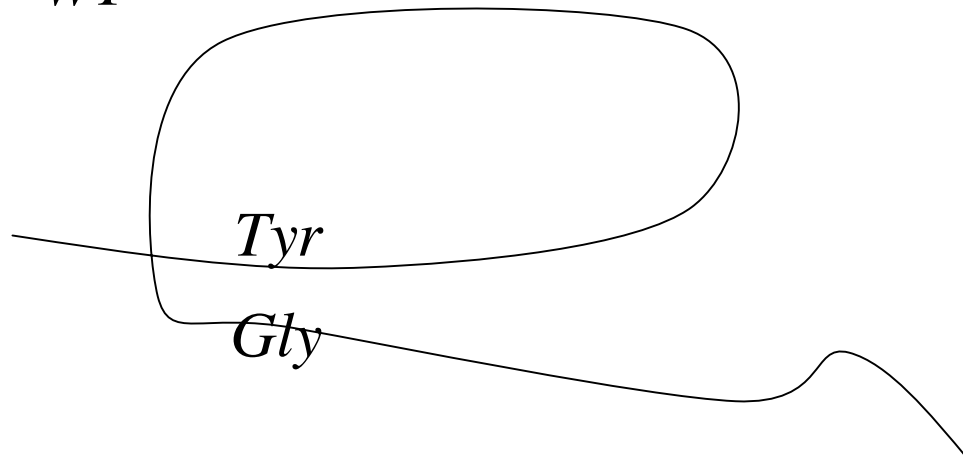
Proflavin-induced mutations (+) insertion (-) deletion	Phenotype
- or +	Mutant
-- or ++	Mutant
----- or ----- or ++++ or +++++	Mutant
- +	Wild type
--- or ----- or +++ or +++++	Wild type

Fig. 8.5



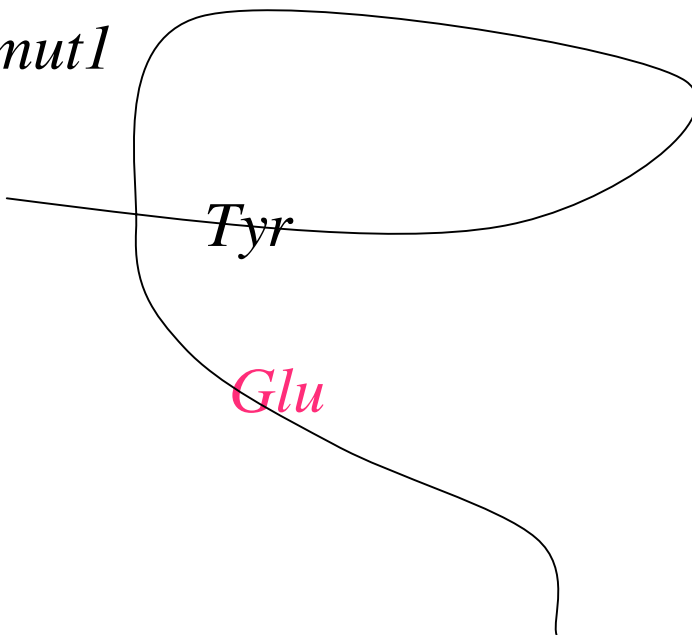
# *Intragenic suppressors*

*WT*

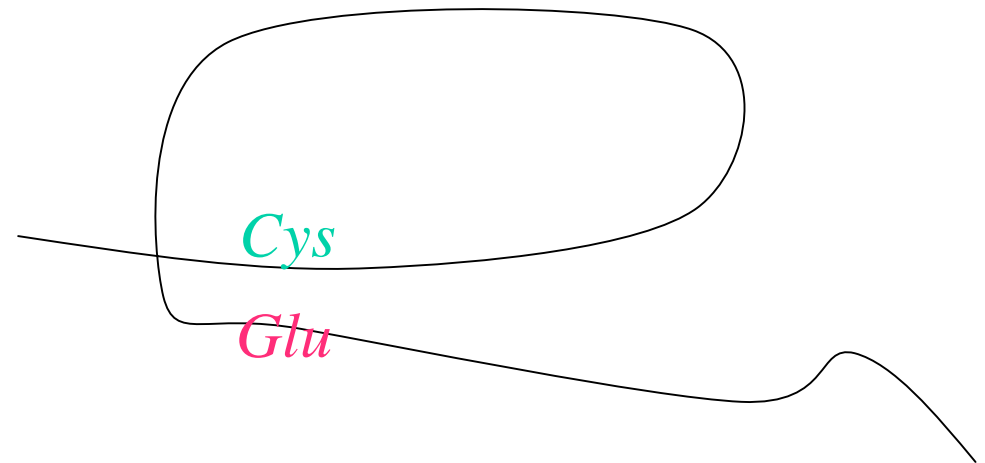


*E. coli*  
*tryptophan*  
*synthase*

*mut1*



*mut1 mut2*



## *Extragenic suppressors*

*Mutation in one gene could correct the effect of a mutation in another gene*

*Nonsense (information) suppressor*

*Mutations in genes whose protein products interact*

- Nonsense suppression
  - (a) Nonsense mutation that causes incomplete nonfunctional polypeptide
  - (b) Nonsense-suppressing mutation causes addition of amino acid at stop codon allowing production of full length polypeptide.

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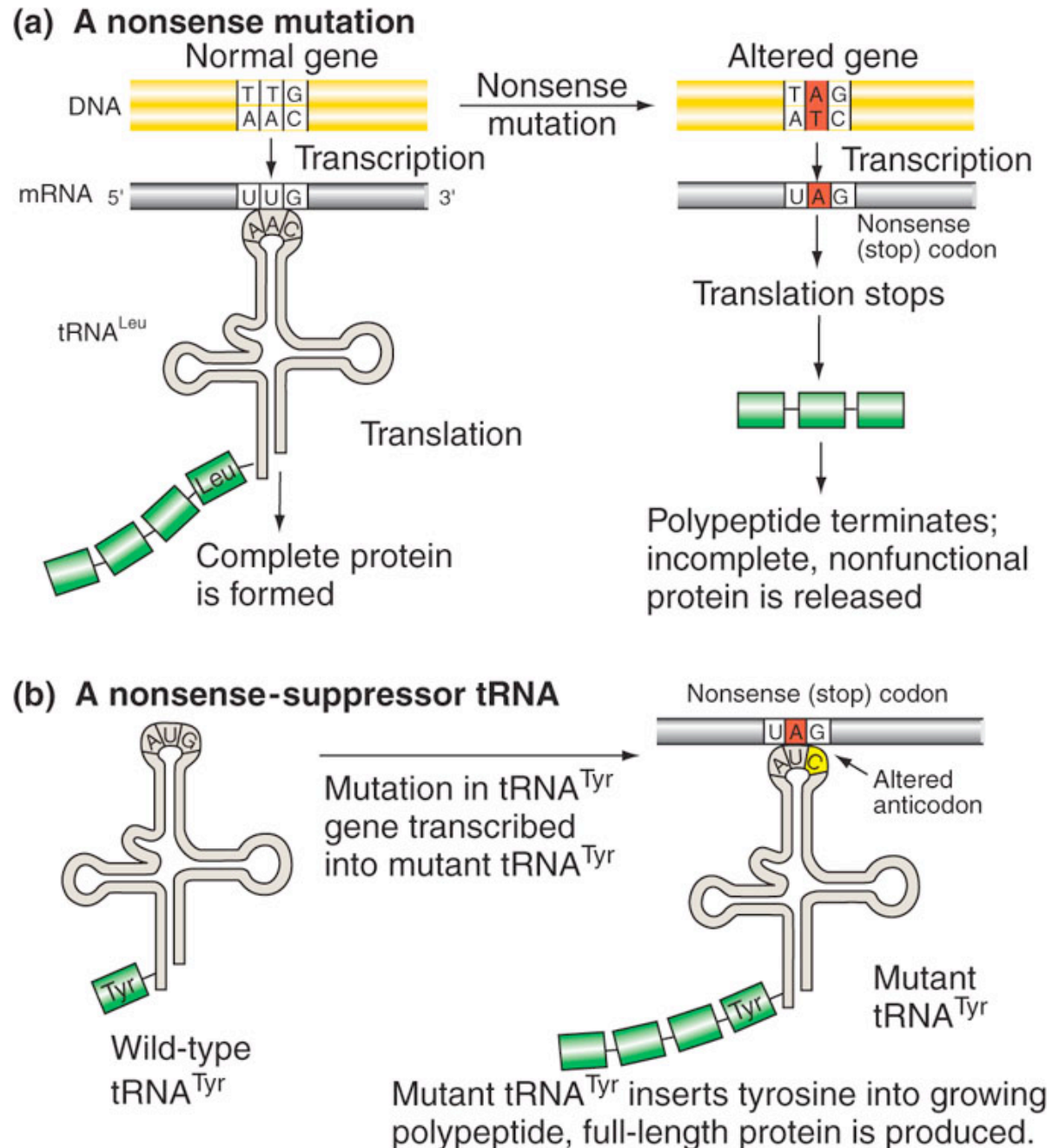


Fig. 8.32

## Extragenic suppressors

Particularly useful during genetic analyses, because they often identify additional components of a biological system or process.

