

Chapter 7: Mechanisms of Mutation

- Definition of mutation
 - Process of mutation
 - Types of mutation
- Mechanisms for correction of mutation



Chapter 13 Opener Principles of Genetics, 4/e

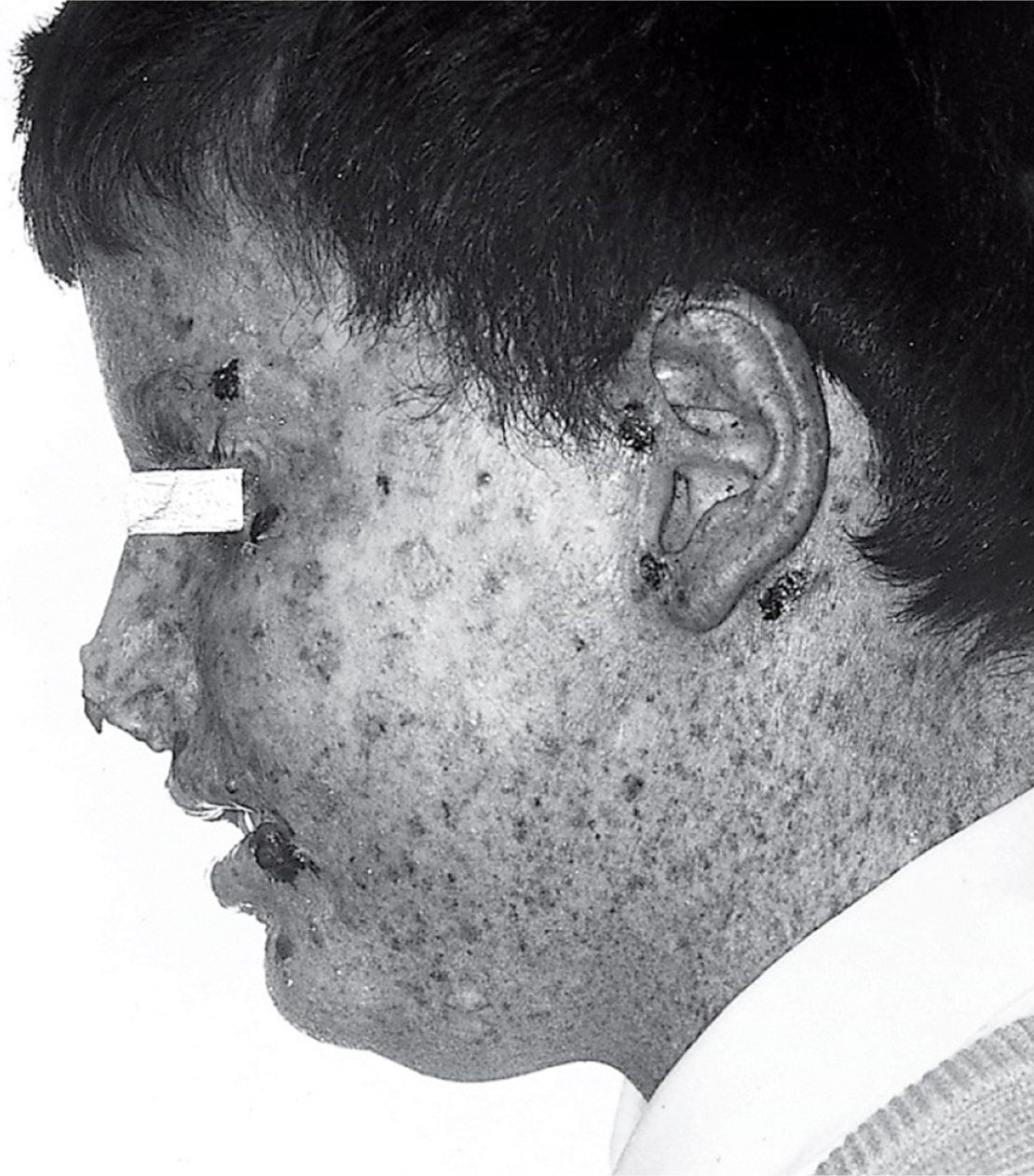


Figure 13-1 Principles of Genetics, 4/e



Figure 13-2a Principles of Genetics, 4/e

Overview of the mutation process and the expression of wild-type and mutant alleles

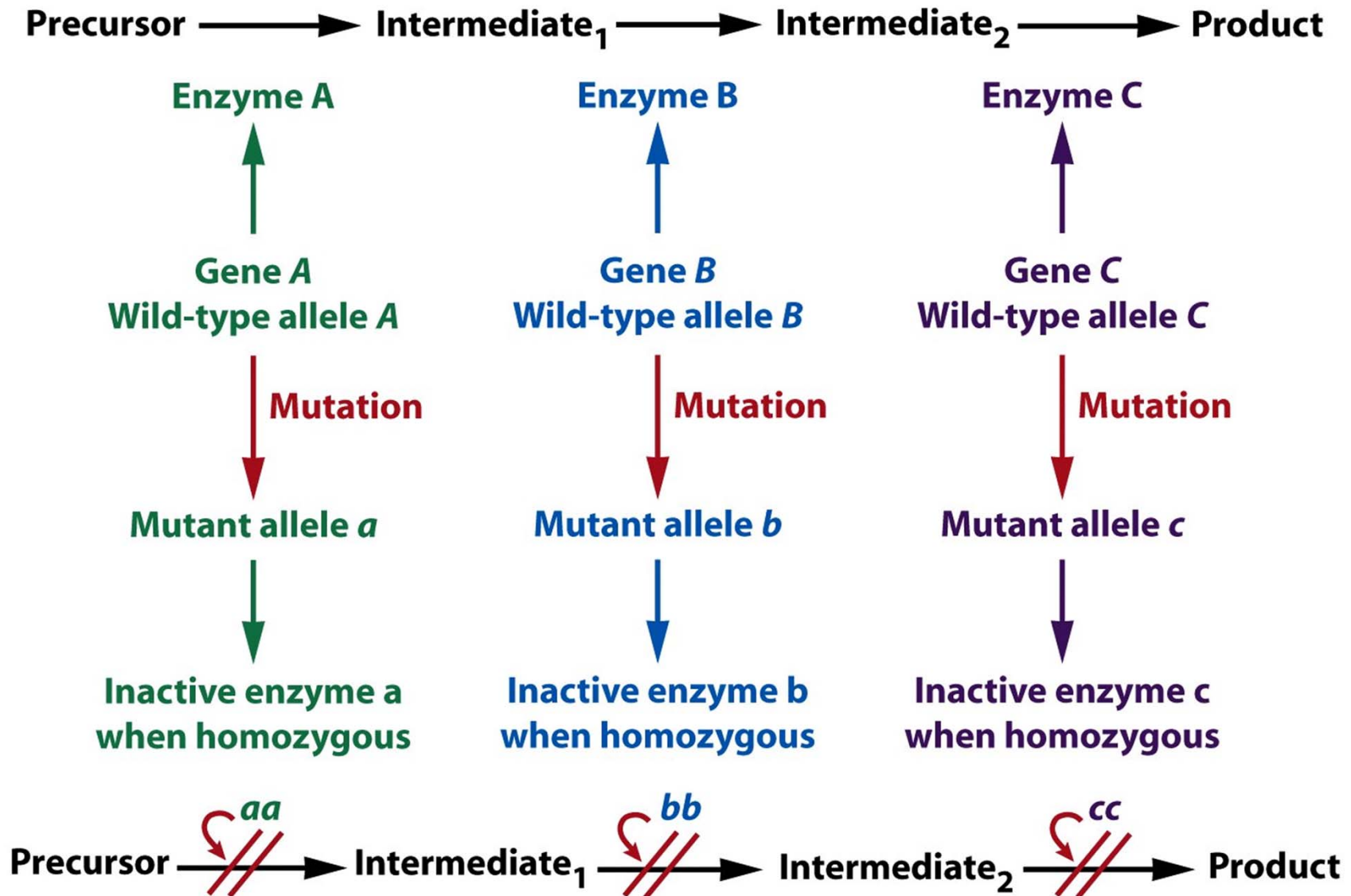


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Overview of the mutation process and the expression of wild-type and mutant alleles

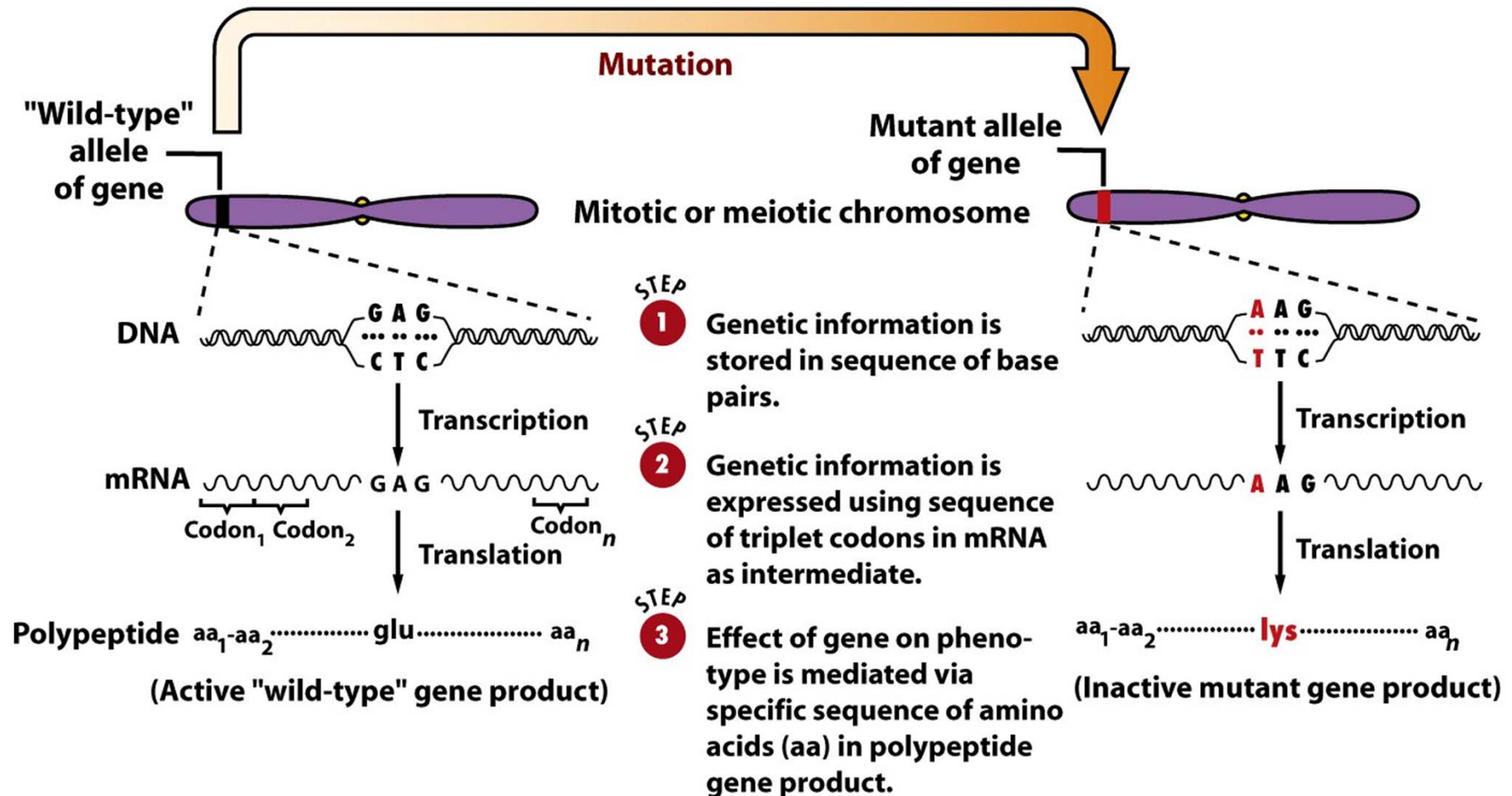


Figure 13-8 Principles of Genetics, 4/e
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Mutations

- Definition of mutation
 - heritable changes in the genetic material of a cell or an organism
 - the process by which the changes occur
 - mutant: an organism that exhibits a novel phenotype resulting from a mutation
- Mutational changes
 - changes in chromosome number and structure
 - changes in the structure of individual genes
 - changes at specific sites in a gene (substitution, insertion, deletion of one or a few nucleotide pairs = narrow sense mutation, point mutation)

Mutations

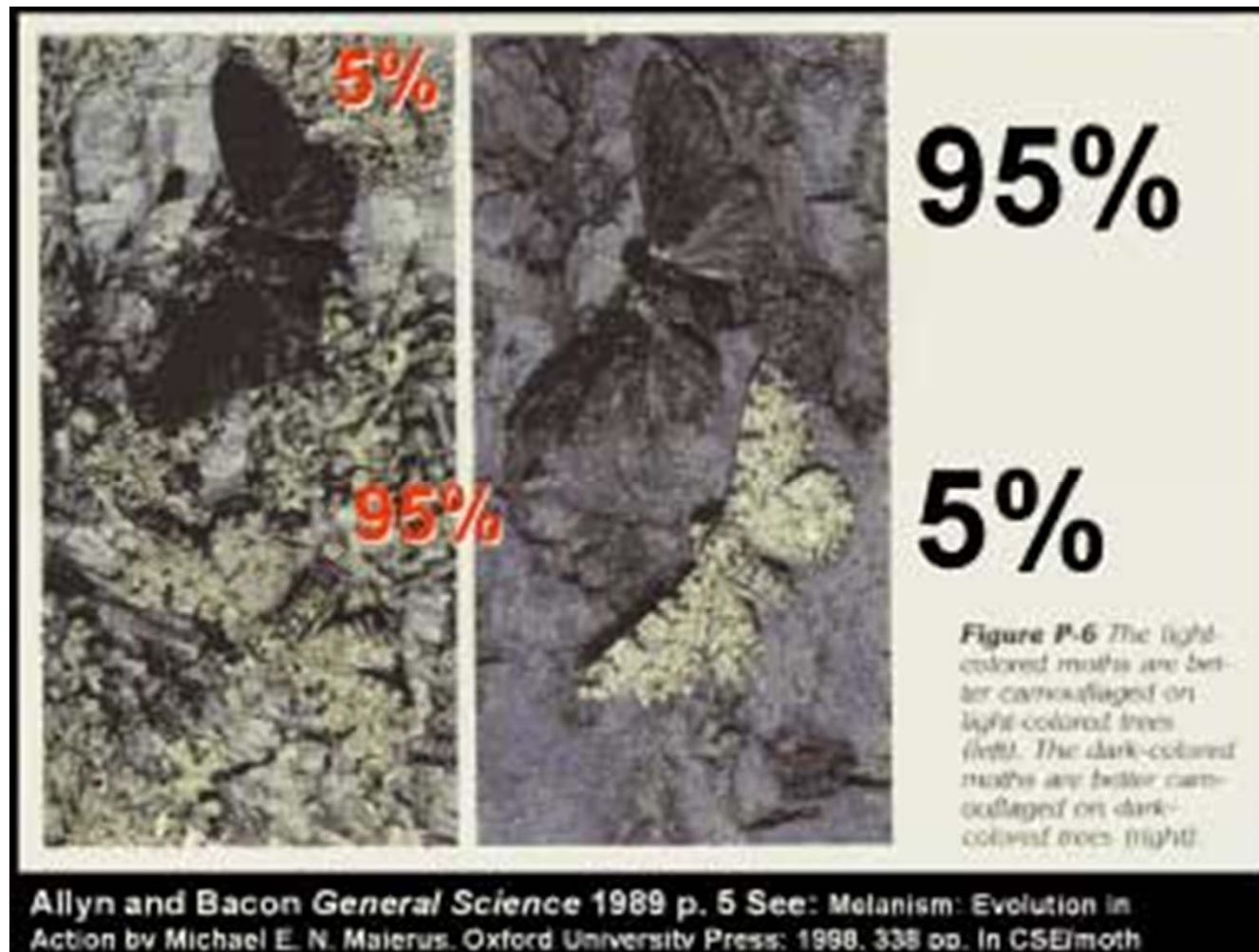
- Role of mutation
 - ultimate source of all **genetic variation**
 - provide the raw material for **evolution**
 - allow organisms to adapt to environmental changes
- Special aspects of mutation
 - most mutations with easily detected phenotypes are **deleterious**
 - the level (frequency) of mutation is **regulated** in order to prevent disruption of faithful transfer of genetic information

The Process of Mutations

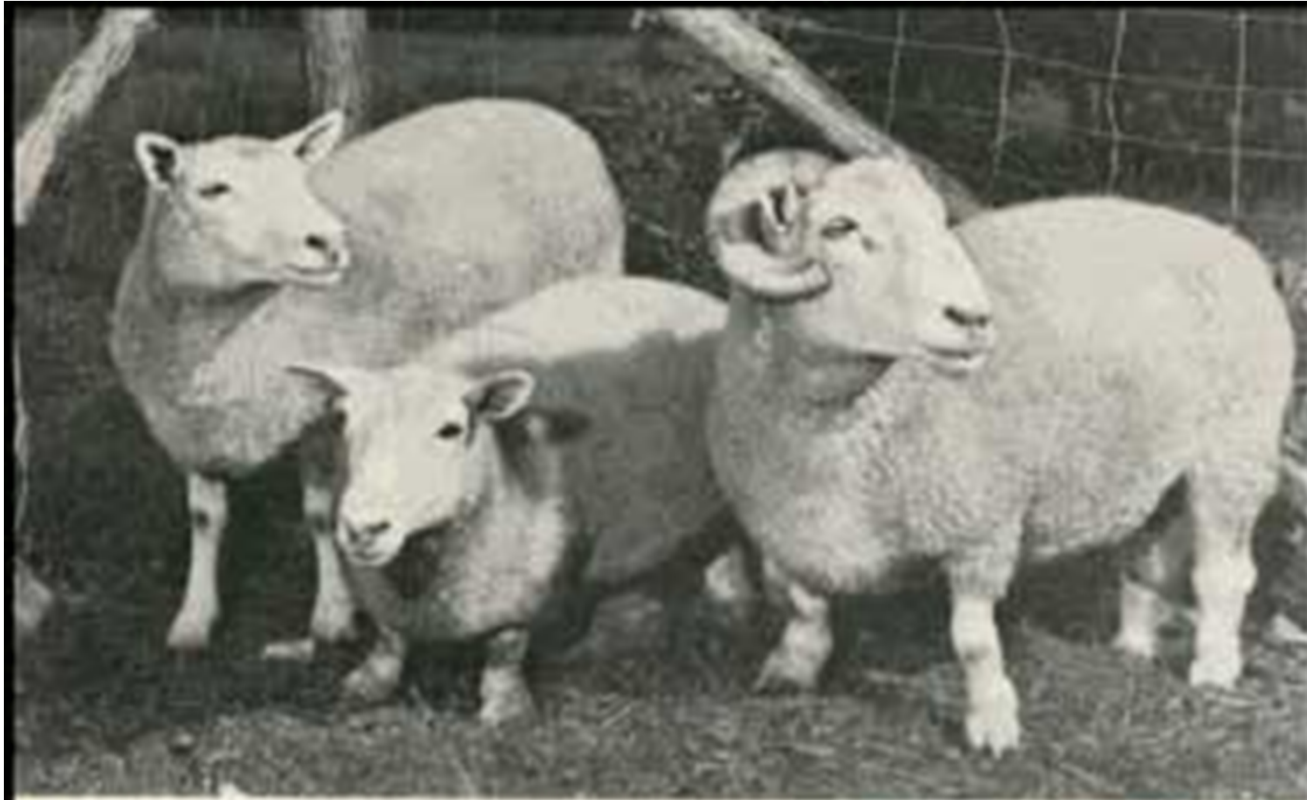
- Effects of mutation and its ability for phenotypic changes determined by
 - 1) dominance vs. recessiveness
 - effects of dominant mutation in germ-line cells expressed immediately in progenies
 - if recessive, the effects are obscured in diploid
 - 2) the type of cell (somatic or germinal)
 - somatic mutation: phenotype occurs only in the descendants of that cell (non-heritable, cultivars of fruit trees)
 - germinal mutation: mutation in a gamete influences only a single member of the progeny. mutation in primordial germ-line cell of the testis or ovary influences several member of the progeny

Mutation & Evolution

"Wow, look at this! Evolution right in front of our eyes!
The white moth evolved into a black moth!"



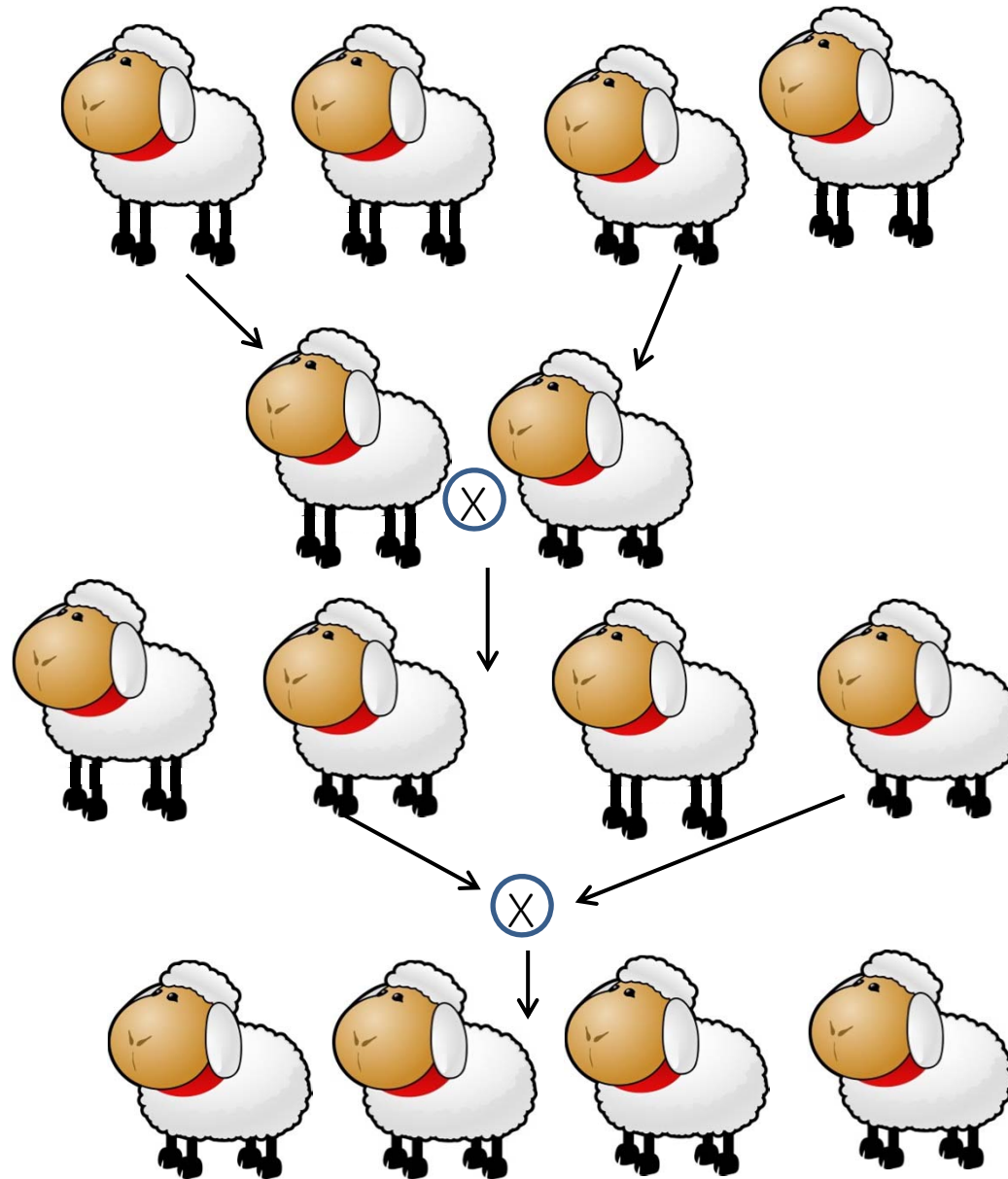
Mutation & Breeding



21-14 Ancon mutant between normal sheep. Useful to colonial farmers, mutation would not last in nature.

Allyn and Bacon *Biology* 1977 p. 364

Mutation & Breeding



Outside of fence?



In general, mutation is **deleterious** and **recessive**!

Type of Mutation

- Mutation: an alteration in the genetic information
- Alteration (base change) in the DNA sequence by **transition, transversion, insertion, deletion, inversion, translocation**)
- **Silent mutation**
 - no observable effect on cell growth or survival
 - Base change in a) non-coding DNA between genes, b) intron in the gene
c) wobble bases (third base redundancy)

Type of Mutation

- Nonsense mutation
 - Changes in base sequence alter a codon and replace with a different amino acid
 - Changes from one amino acid to another amino acid with similar chemical properties = conservative substitution => relatively mild and non-lethal
- Missense mutation
 - Changes from one amino acid to another amino acid with opposite chemical properties = radical substitution => relatively lethal)
 - Replacement of the codon for an amino acid with a stop codon

Twelve different base substitutions can occur in DNA.

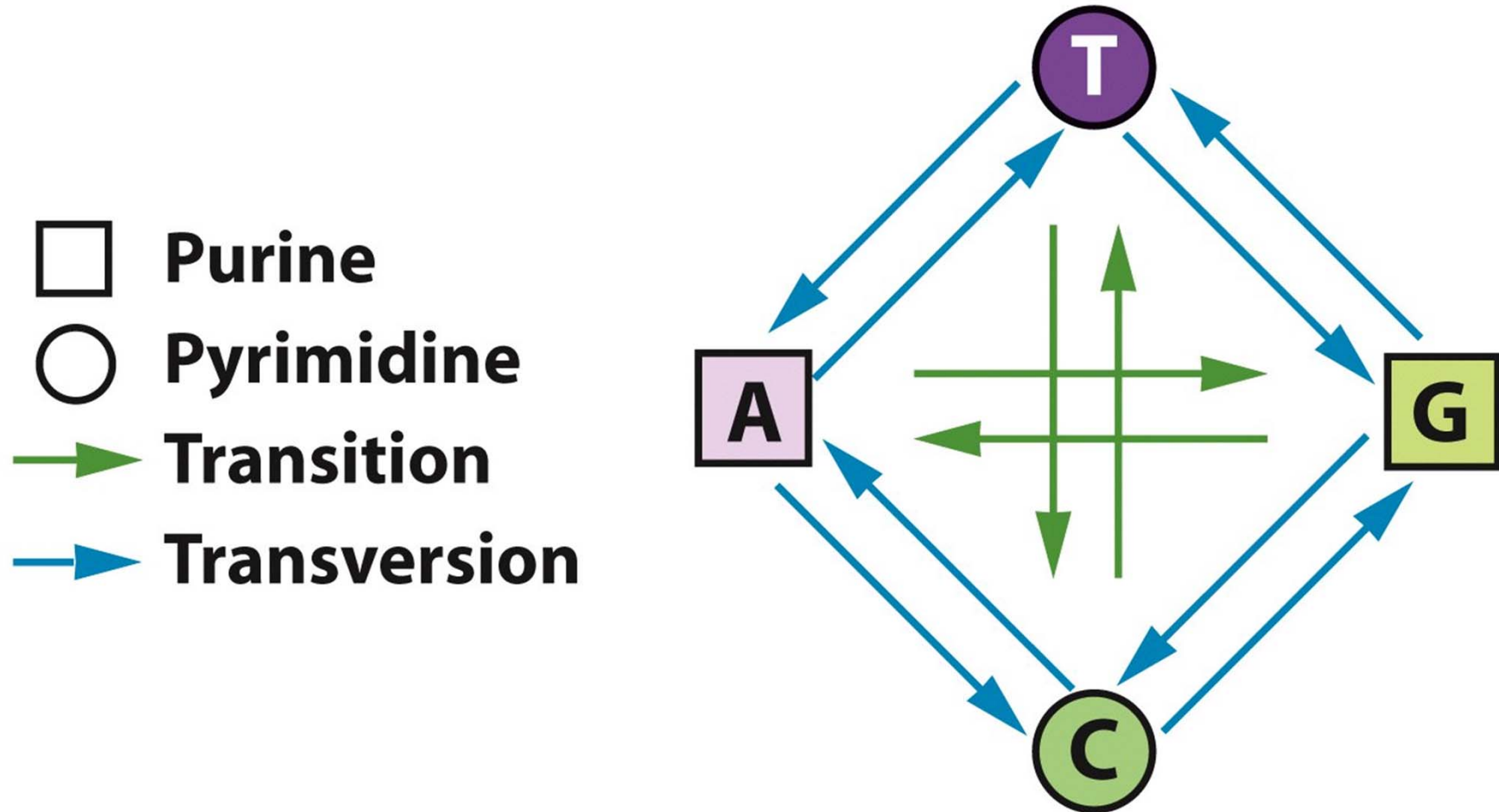


Figure 13-15a Principles of Genetics, 4/e
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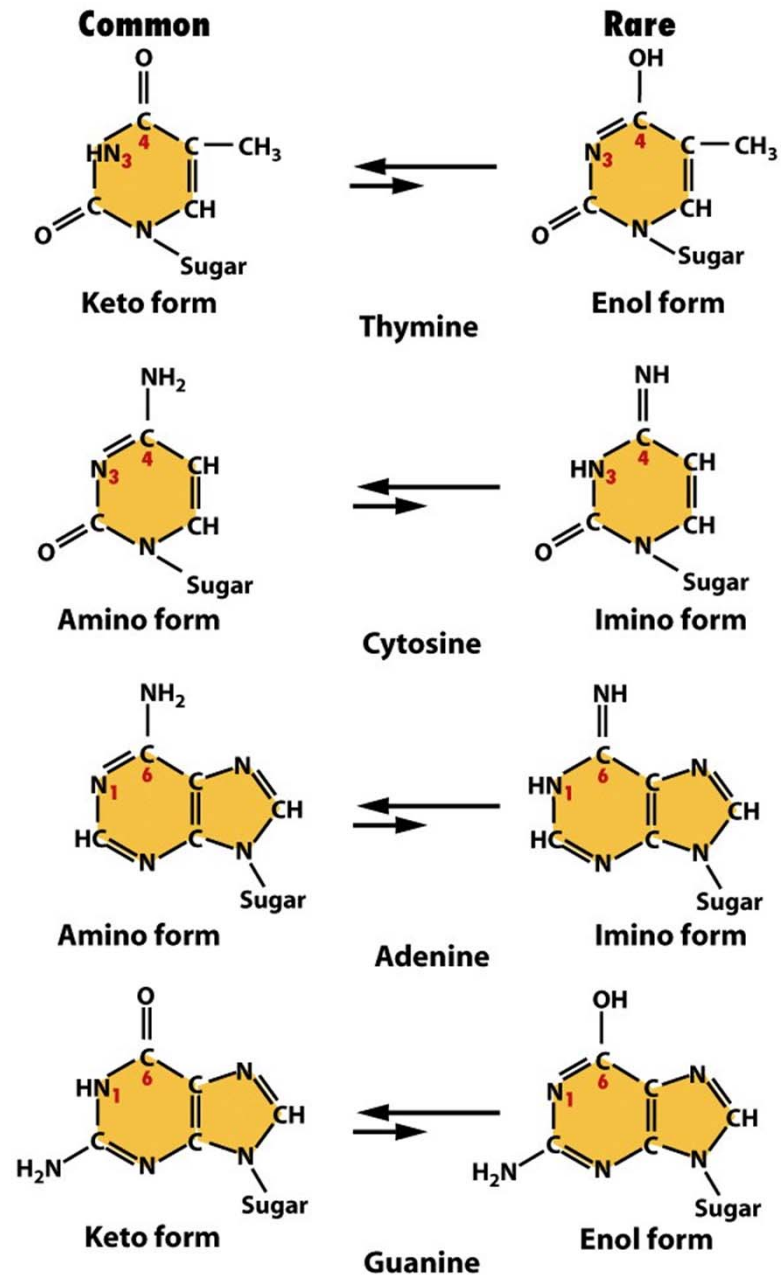
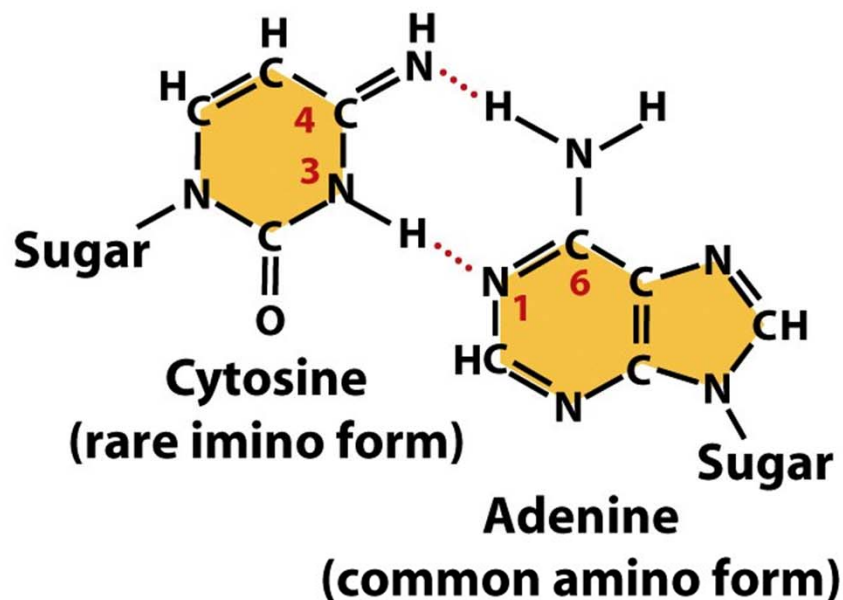
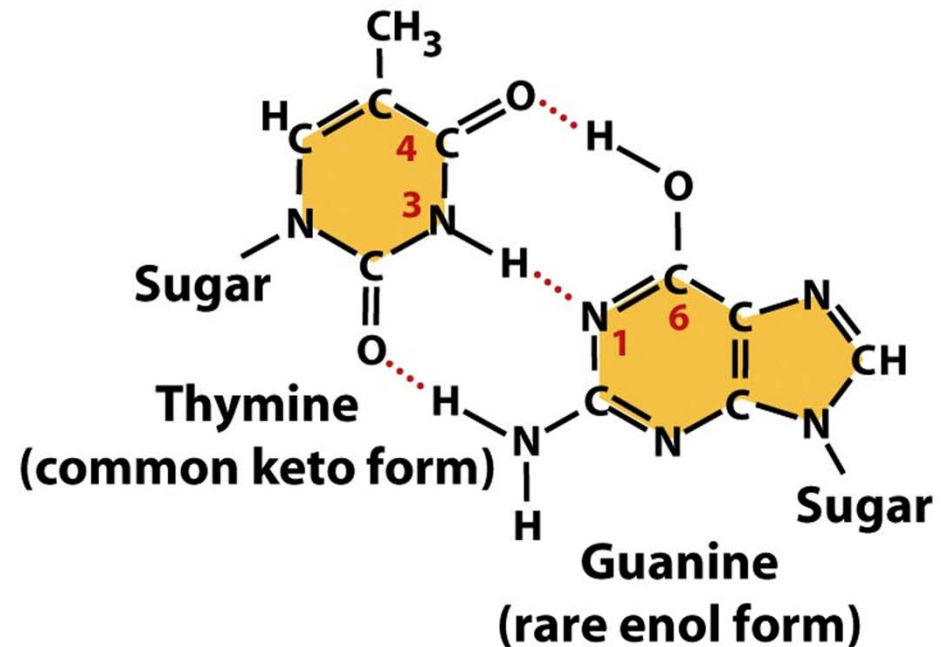


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Rare A:C base pair



Rare G:T base pair



Hydrogen-bonded A:C and G:T base pairs that form when cytosine and guanine are in their rare imino and enol tautomeric forms.

Mechanism by which tautomeric shifts in the bases in DNA cause mutations.

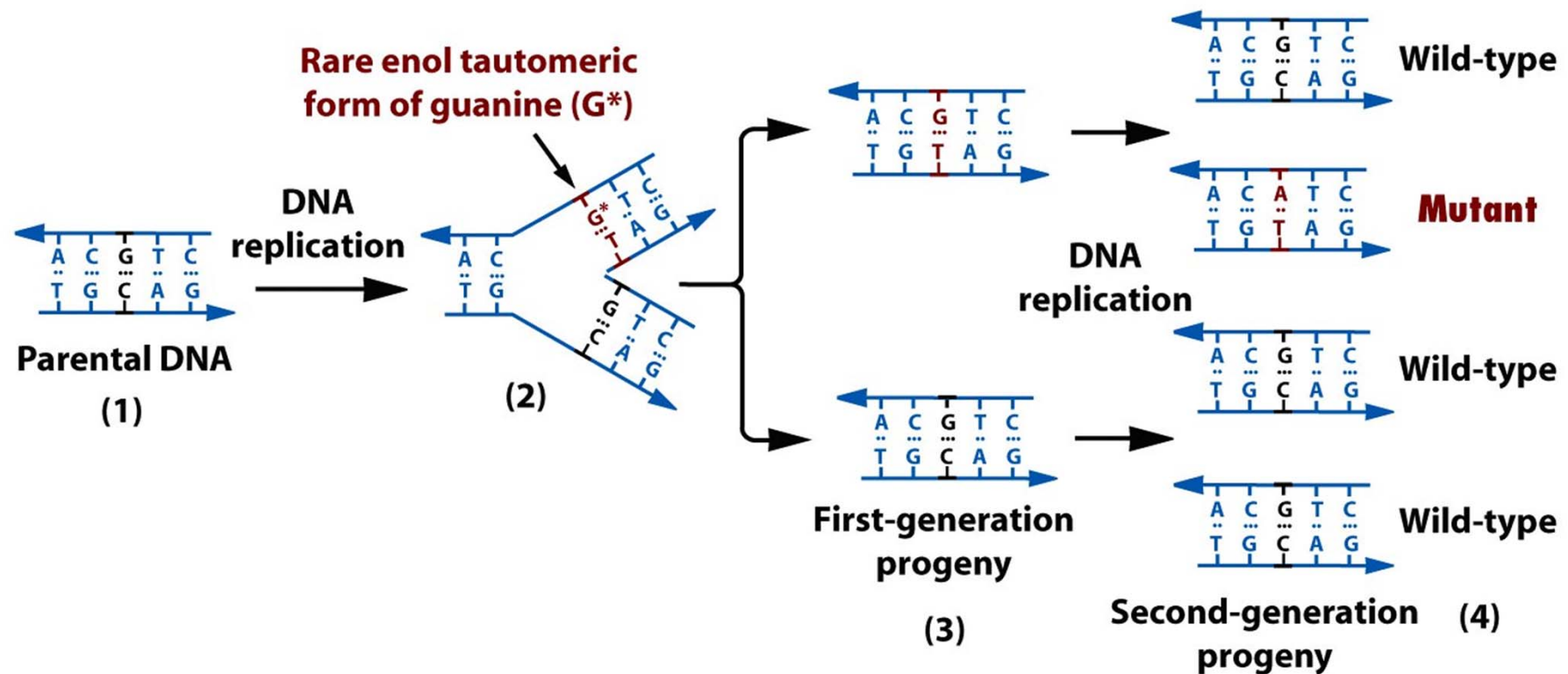
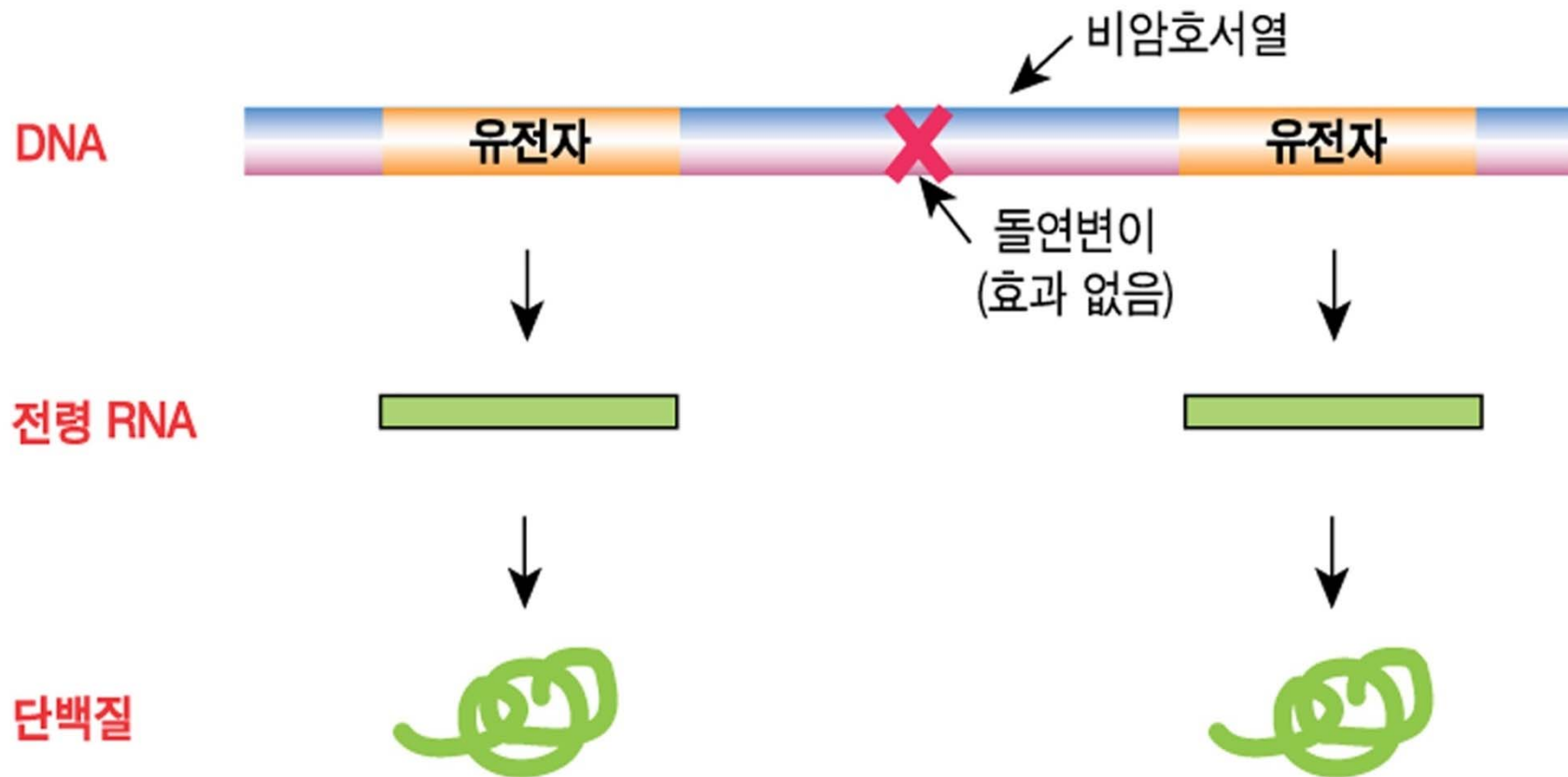
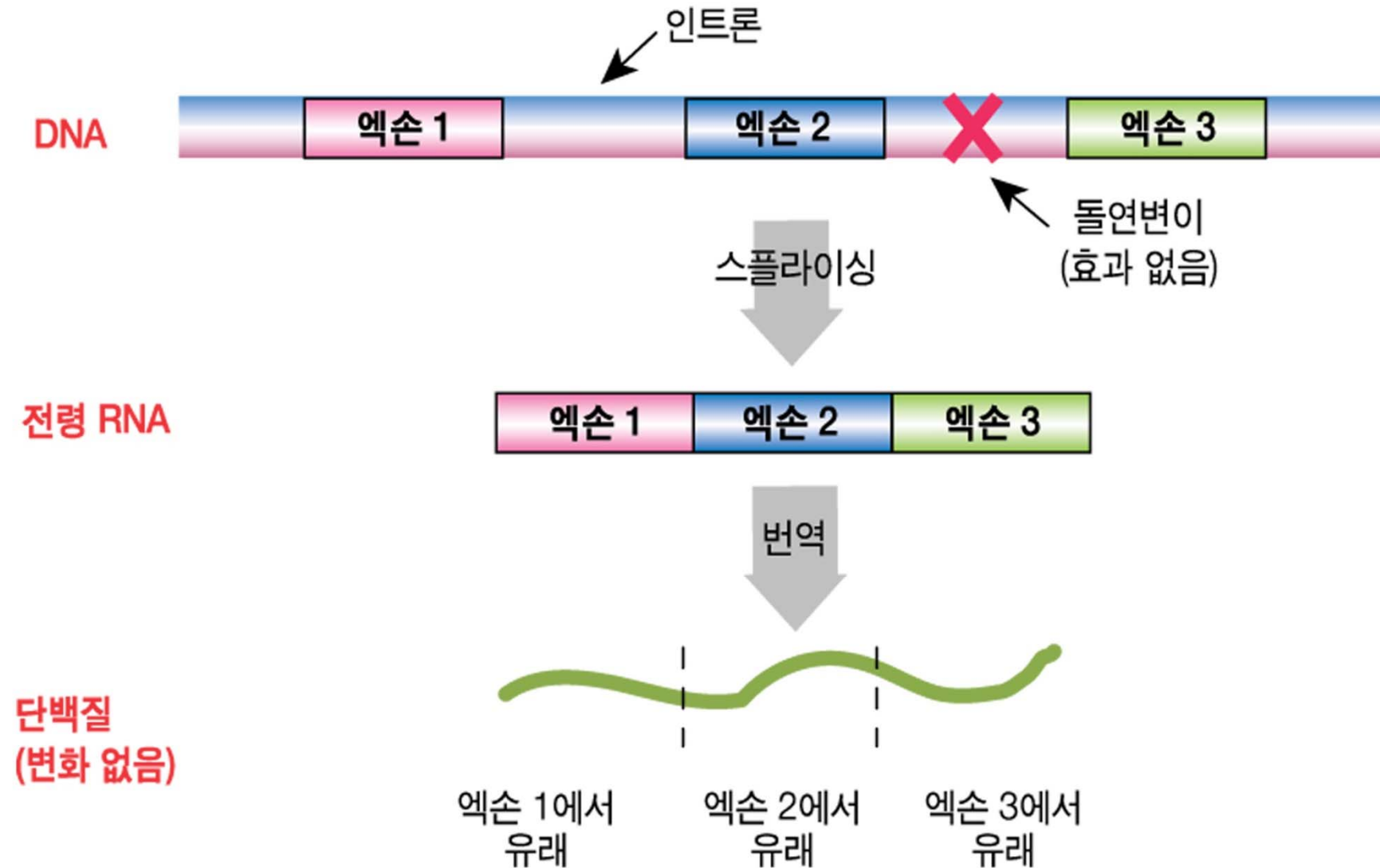


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Silent mutation by changes in non-coding DNA between genes



Silent mutation by changes in intron in the gene

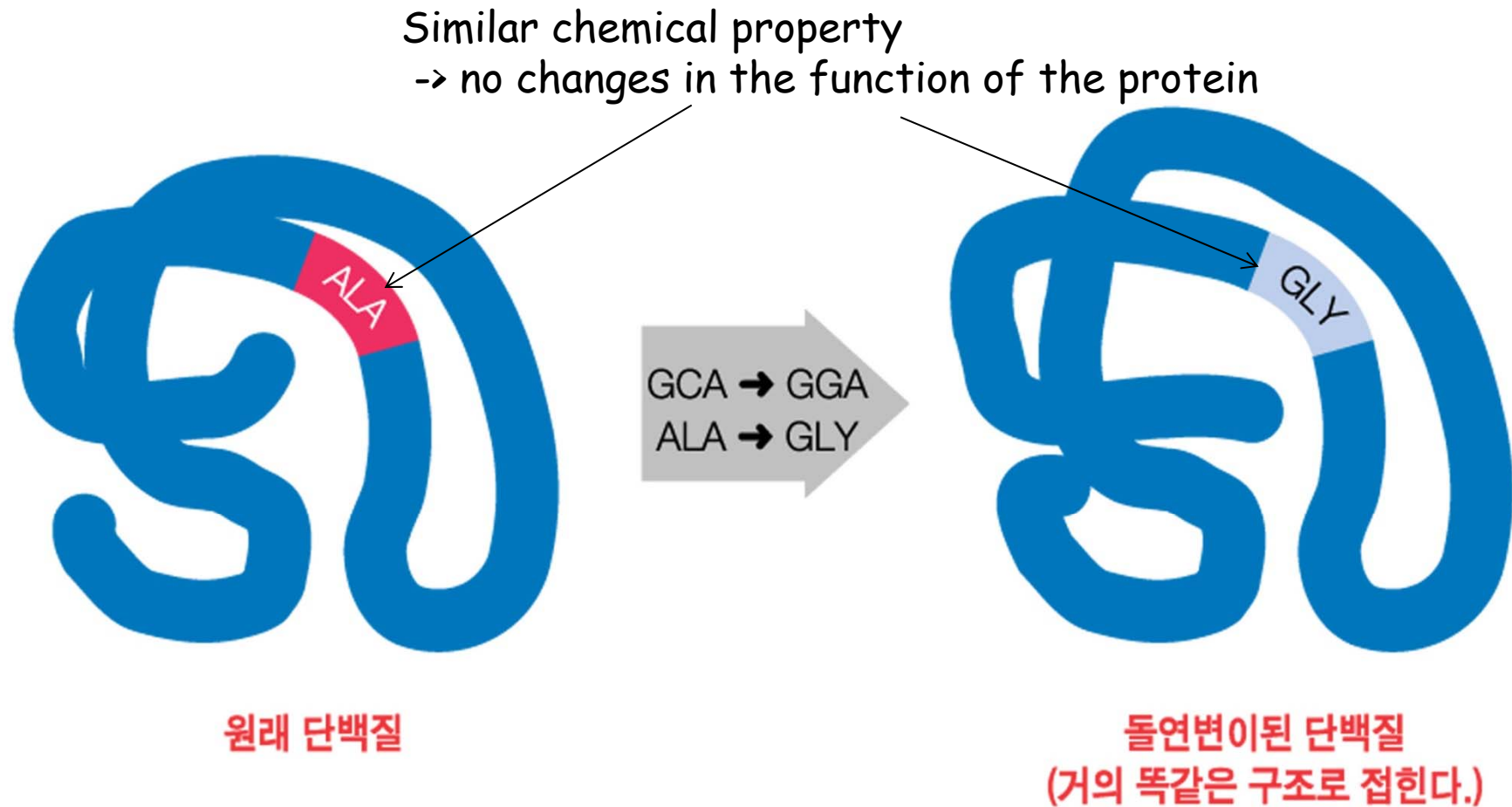


Silent mutation by changes in wobble bases

두 번째 (중간) 염기

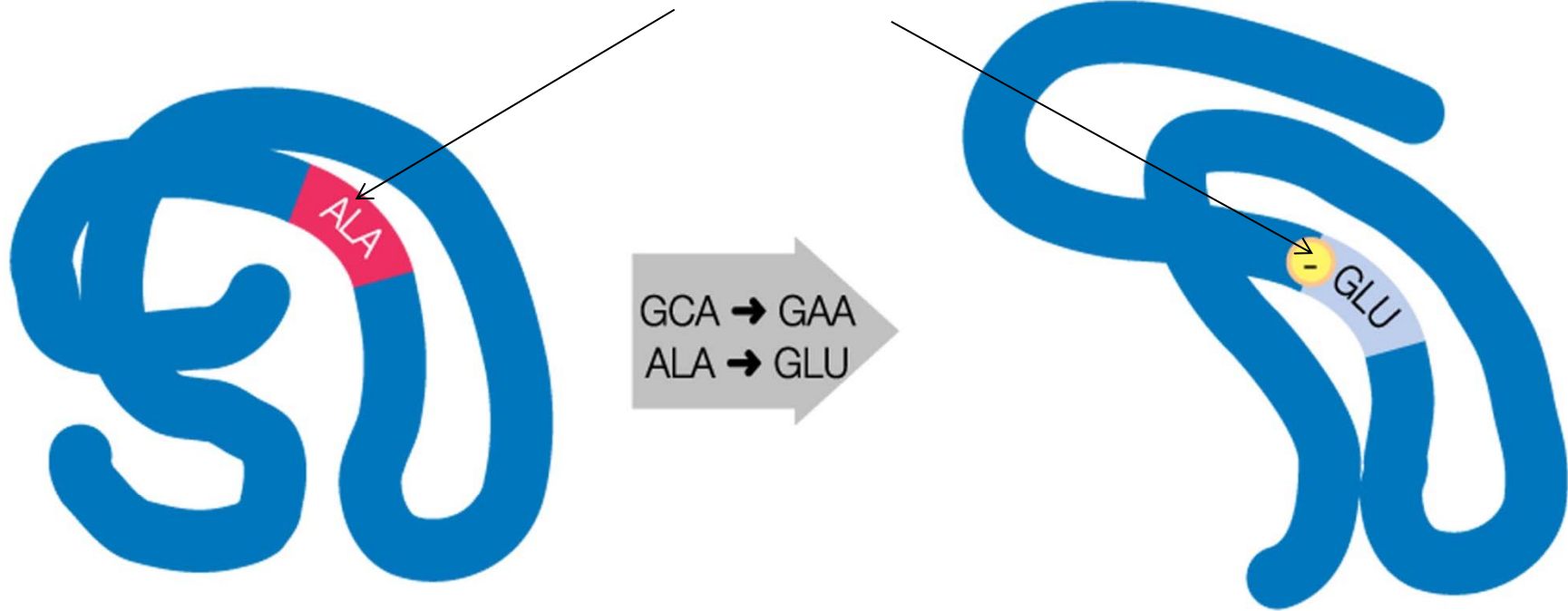
첫 번째 염기	U	C	A	G	세 번째 염기
U	UUU Phe UUC Phe UUA Leu UUG Leu	UCU Ser UCC Ser UCA Ser UCG Ser	UAU Tyr UAC Tyr UAA STOP UAG STOP	UGU Cys UGC Cys UGA STOP UGG Trp	U C A G
C	CUU Leu CUC Leu CUA Leu CUG Leu	CCU Pro CCC Pro CCA Pro CCG Pro	CAU His CAC His CAA Gln CAG Gln	CGU Arg CGC Arg CGA Arg CGG Arg	U C A G
A	AUU Ile AUC Ile AUA Ile AUG Met	ACU Thr ACC Thr ACA Thr ACG Thr	AAU Asn AAC Asn AAA Lys AAG Lys	AGU Ser AGC Ser AGA Arg AGG Arg	U C A G
G	GUU Val GUC Val GUA Val GUG Val	GCU Ala GCC Ala GCA Ala GCG Ala	GAU Asp GAC Asp GAA Glu GAG Glu	GGU Gly GGC Gly GGA Gly GGG Gly	U C A G

Nonsense mutation by conservative substitution



Missense mutation by radical substitution

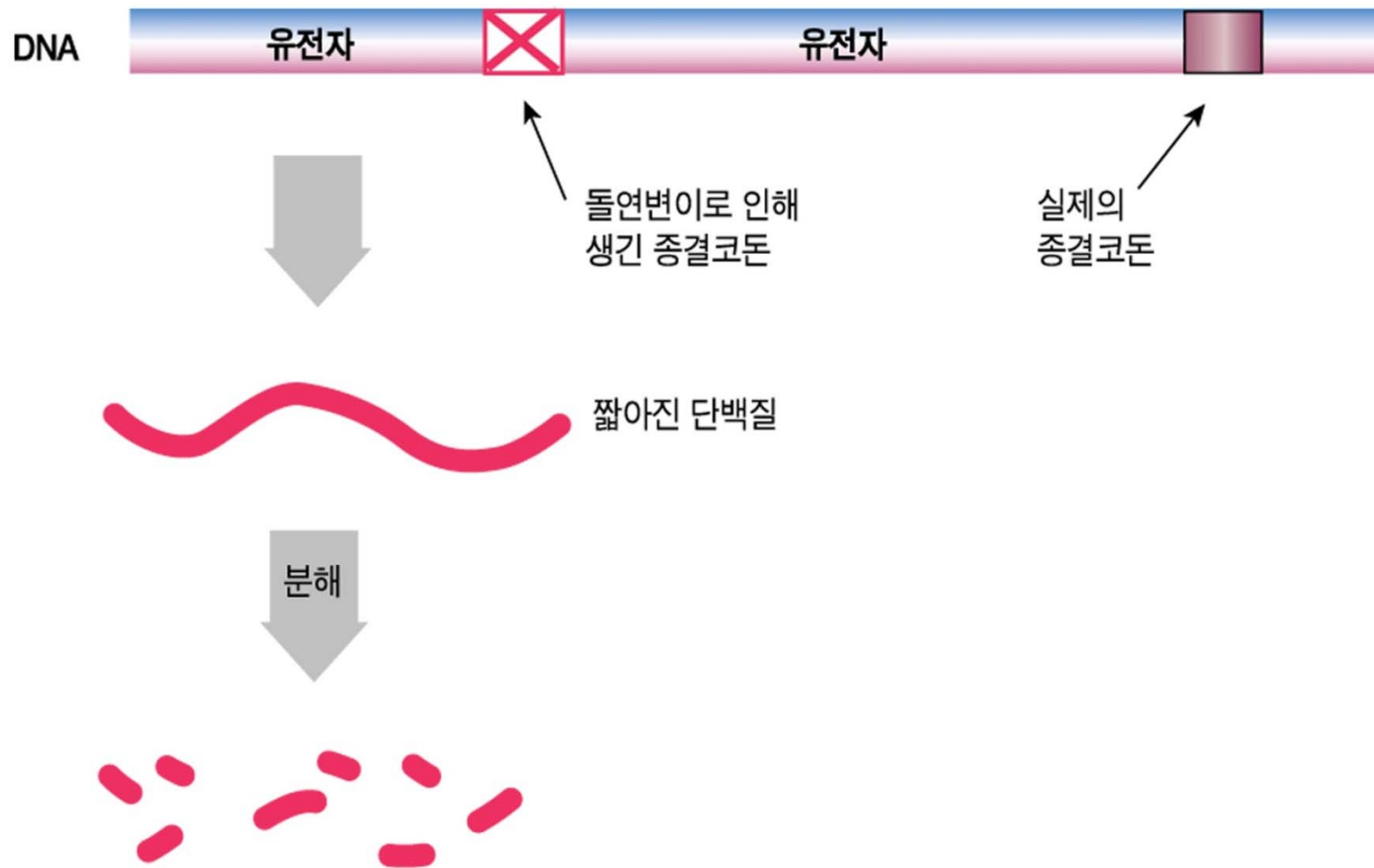
Opposite chemical property
-> changes in the function of the protein



원래 단백질

돌연변이된 단백질
(여분의 음성전하를 가지게
되어 부정확하게 접힌다.)

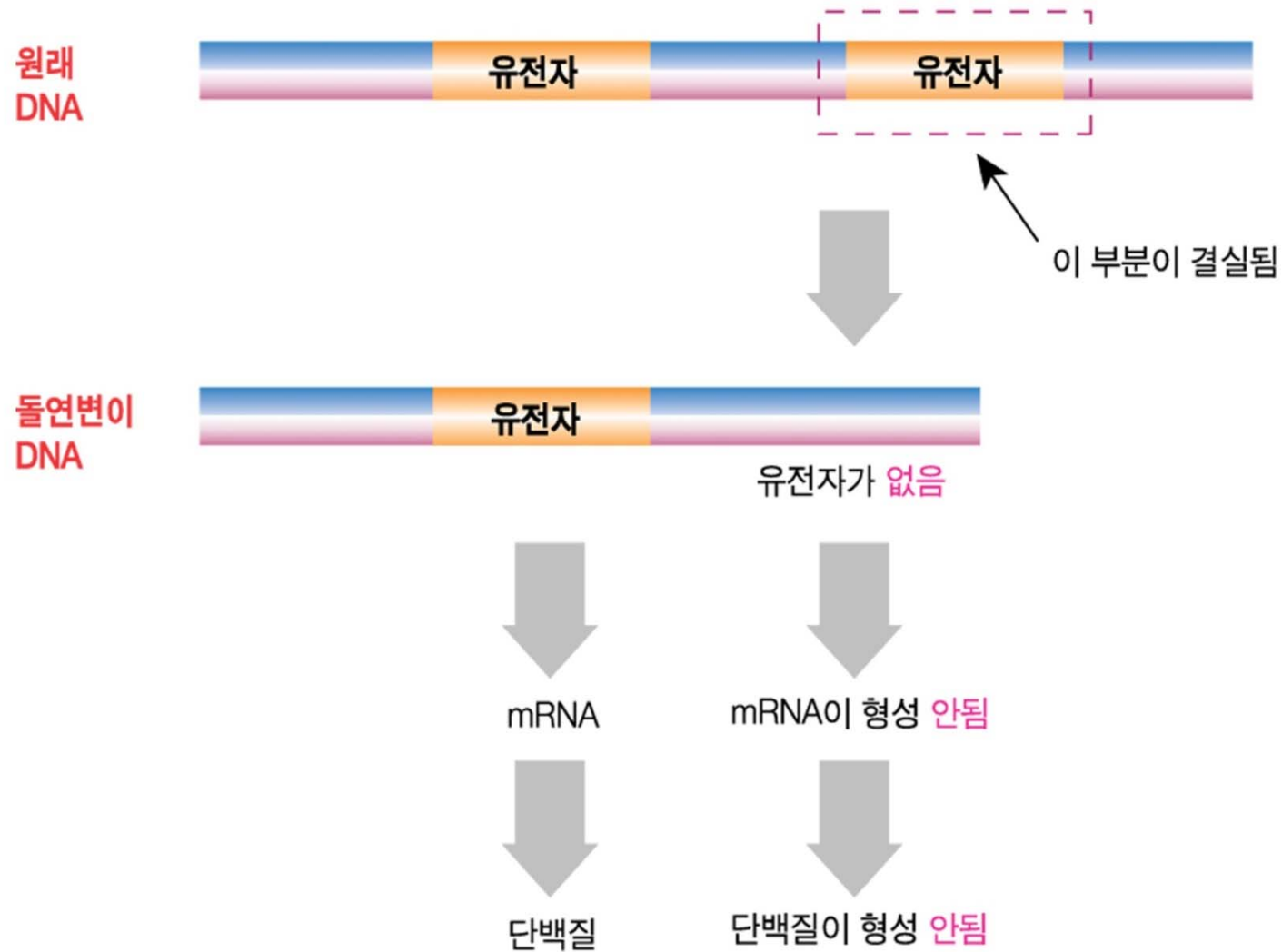
Missense mutation by replacement with stop codon



Type of Mutation

- Deletion/Insertion
 - removal or addition of one or many nucleotides from DNA
- Frameshift mutation
 - changes the reading frame of the protein encoded by a gene
- In frame deletion mutation
 - deletion of three bases of a complete codon
- DNA rearrangement
 - Inversion: a segment of DNA is removed, flipped, and reinserted, facing the opposite direction
 - Translocation: a segment of DNA is removed and reinserted in a different place

Deletion of a whole gene



Frameshift mutation by deletion of a nucleotide in coding sequence

RNA 코드: GAG - GCC - GUA - AUC - GAA - UGU - UUG - GCA - AGG - AAA

단백질: Glu - Ala - Val - Ile - Glu - Cys - Leu - Ala - Arg - Lys

야생형

GAG - GCC - GUA - AUC - GAA - UGU - UUG - GCA - AGG - AAA

돌연변이형

GAG - GCC - G●A - AUC - GAA - UGU - UUG - GCA - AGG - AAA

Frameshift mutation by deletion of a nucleotide in coding sequence

야생형

RNA 코드: GAG - GCC - GUA - AUC - GAA - UGU - UUG - GCA - AGG - AAA

단백질: Glu - Ala - Val - Ile - Glu - Cys - Leu - Ala - Arg - Lys

돌연변이형

RNA 코드: GAG - GCC - GAA - UCG - AAU - GUU - UGG - CAA - GGA - AA

단백질: Glu - Ala - Glu - Leu - Asn - Val - Trp - Gln - Gly---

In-frame deletion mutation by deletion of a complete codon

야생형

RNA 코드: GAG - GCC - GUA - AUC - GAA - UGU - UUG - GCA - AGG - AAA

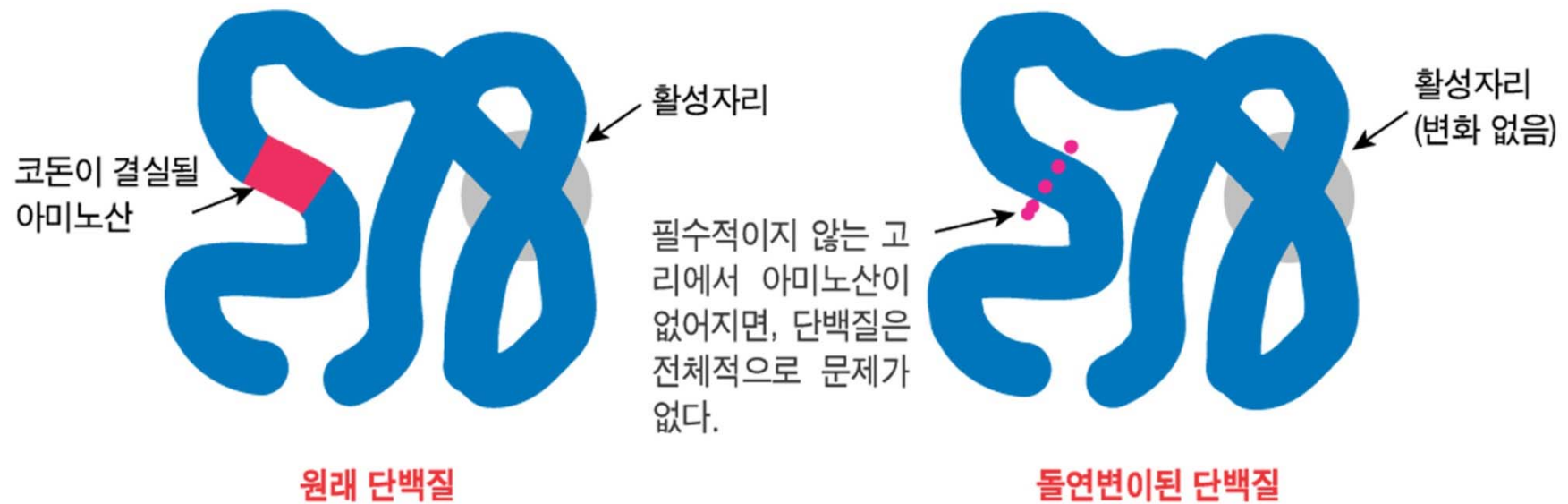
단백질: Glu - Ala - Val - Ile - Glu - Cys - Leu - Ala - Arg - Lys

돌연변이형

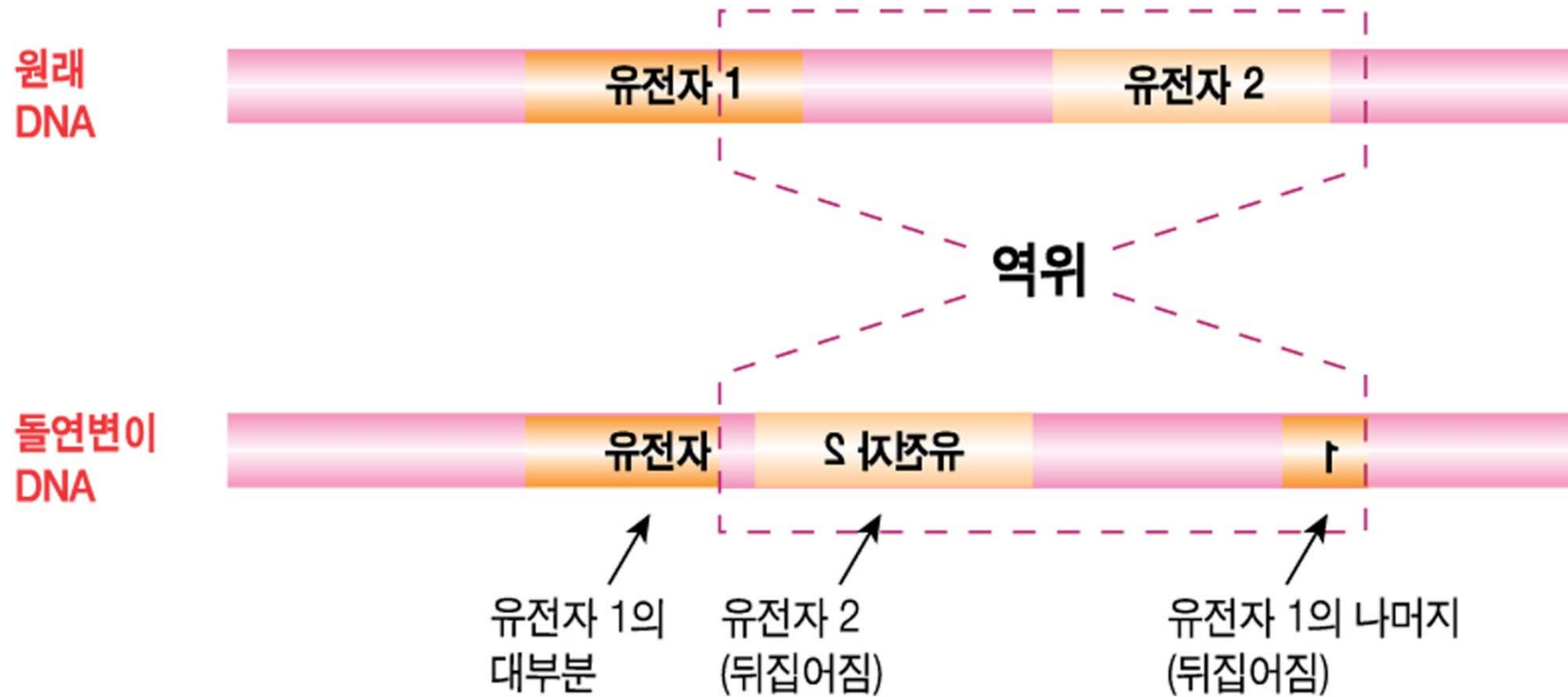
RNA 코드: GAG - ●●● - GUA - AUC - GAA - UGU - UUG - GCA - AGG - AAA

단백질: Glu - ●●● - Val - Ile - Glu - Cys - Leu - Ala - Arg - Lys

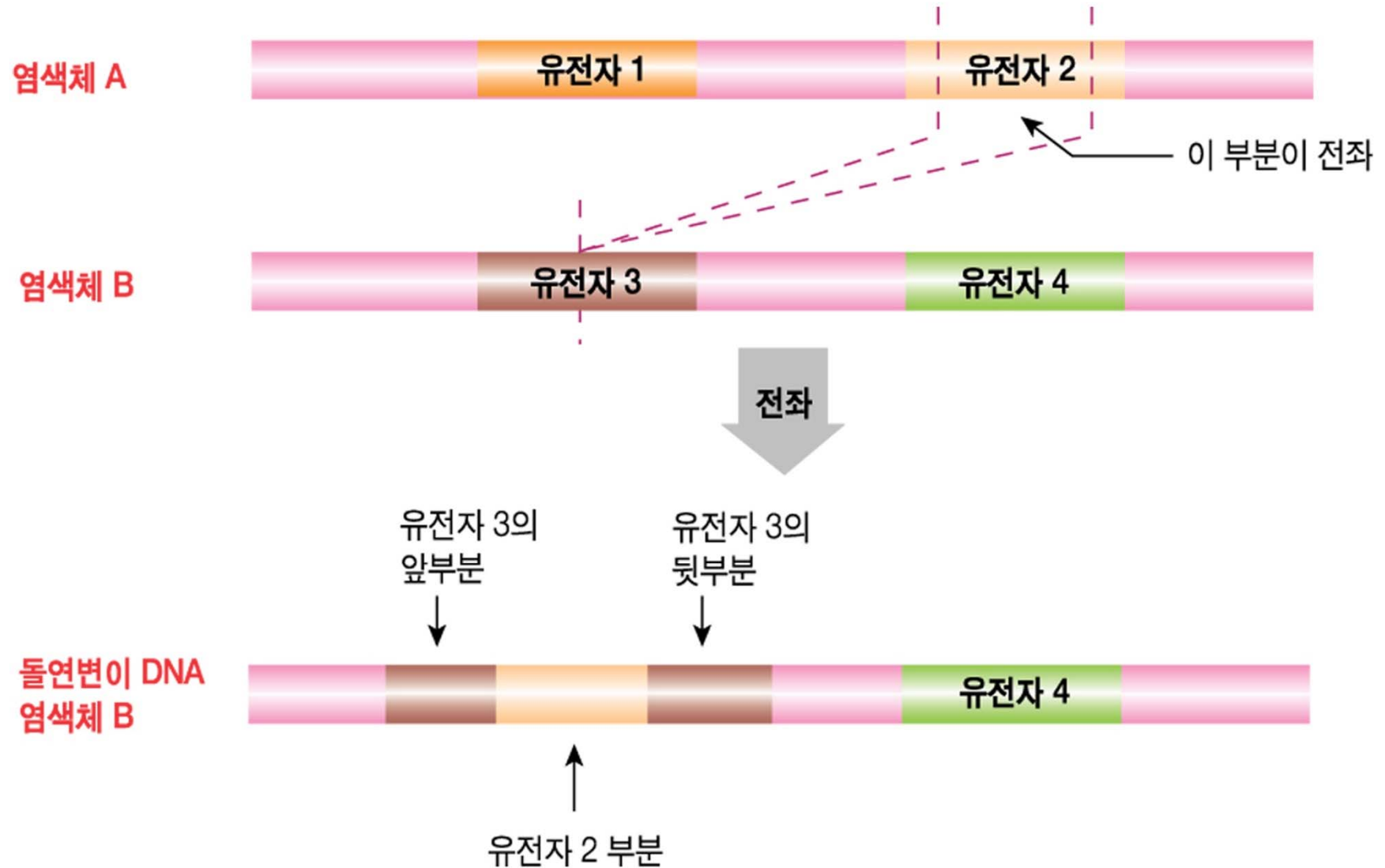
In-frame deletion mutation by deletion of a complete codon



DNA rearrangement by inversion



DNA rearrangement by translocation



Causes of Mutation

- **Induced mutation**: mutation caused by mutagens (toxic chemical or radiation)
 - **EMS** (ethyl methane sulfonate):
adds methyl group to bases in DNA and changes their shape
 - **Nitrite**:
replaces amino groups with hydroxyl groups and converts the base cytosine to uracil
 - **Base analogs** (bromouracil):
chemical that resembles a base of a nucleic acid (bromouridine triphosphate) and inserted by mistake
 - **Ultraviolet (UV) light**:
two neighboring thymine bases react with each other to give thymine dimer
 - **X-ray**:
produces multiple mutations and DNA rearrangement (deletion inversion, translocations)

Causes of Mutation

- Spontaneous mutation: mutation caused by errors in DNA replication
- Mutation caused by insertion of Transposons (jumping gene)
- Mutation caused by Genetically engineered gene disruption (gene cassette)

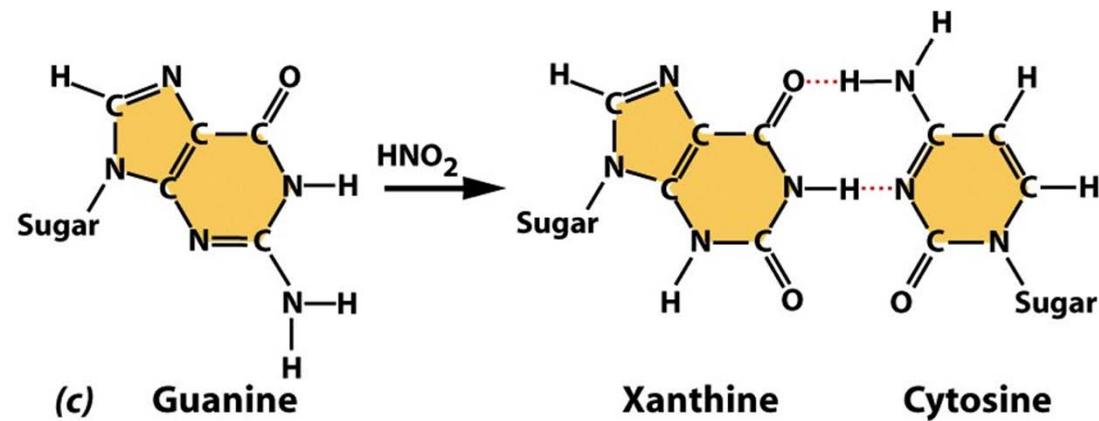
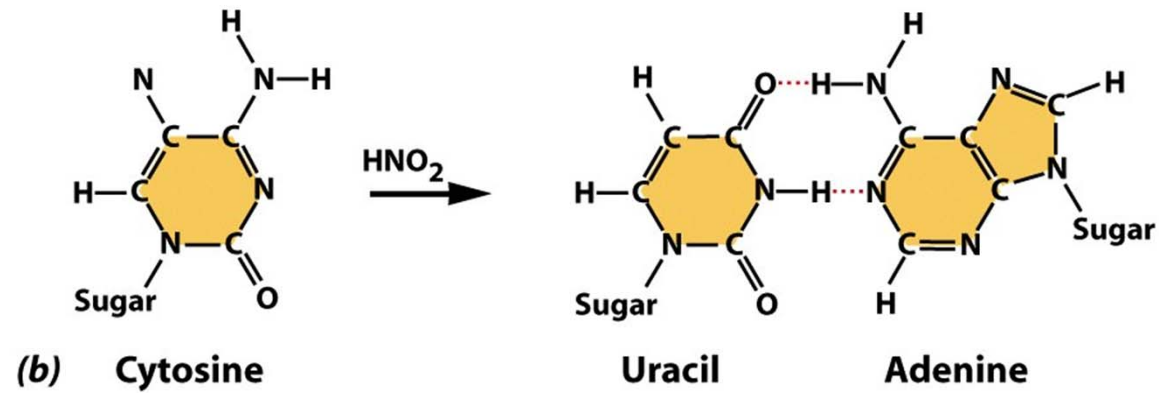
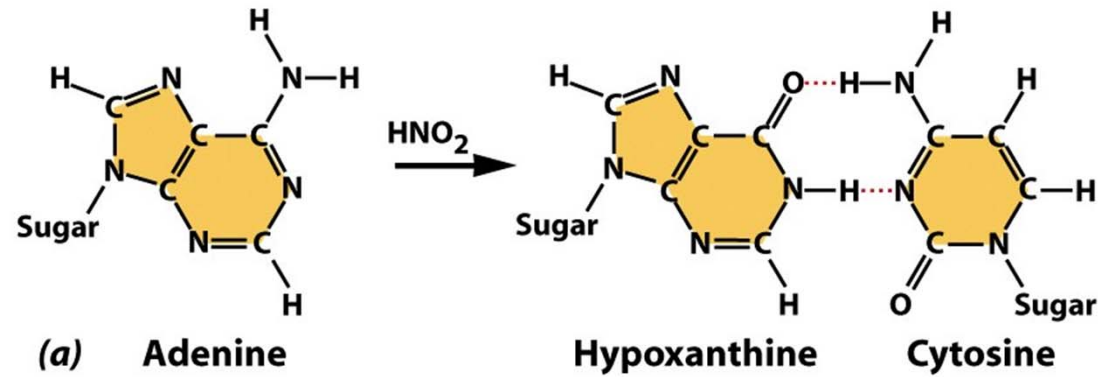
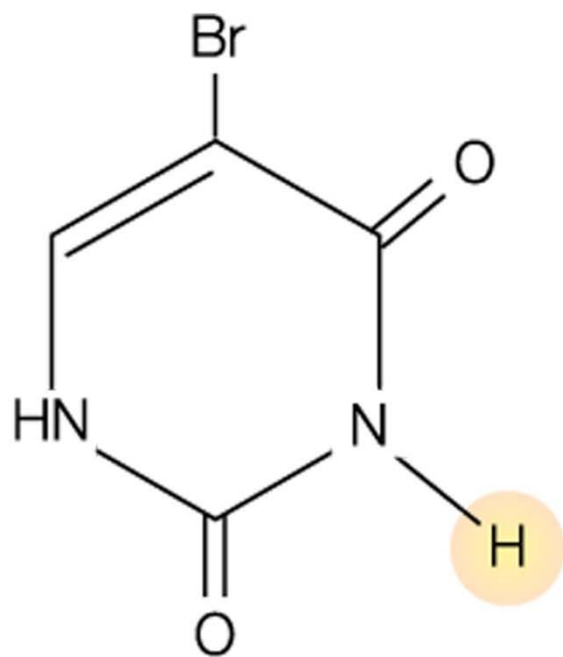
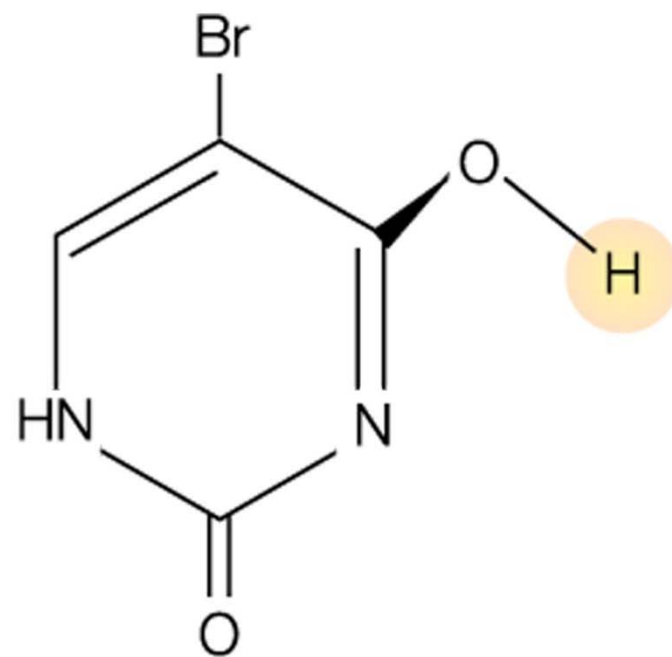


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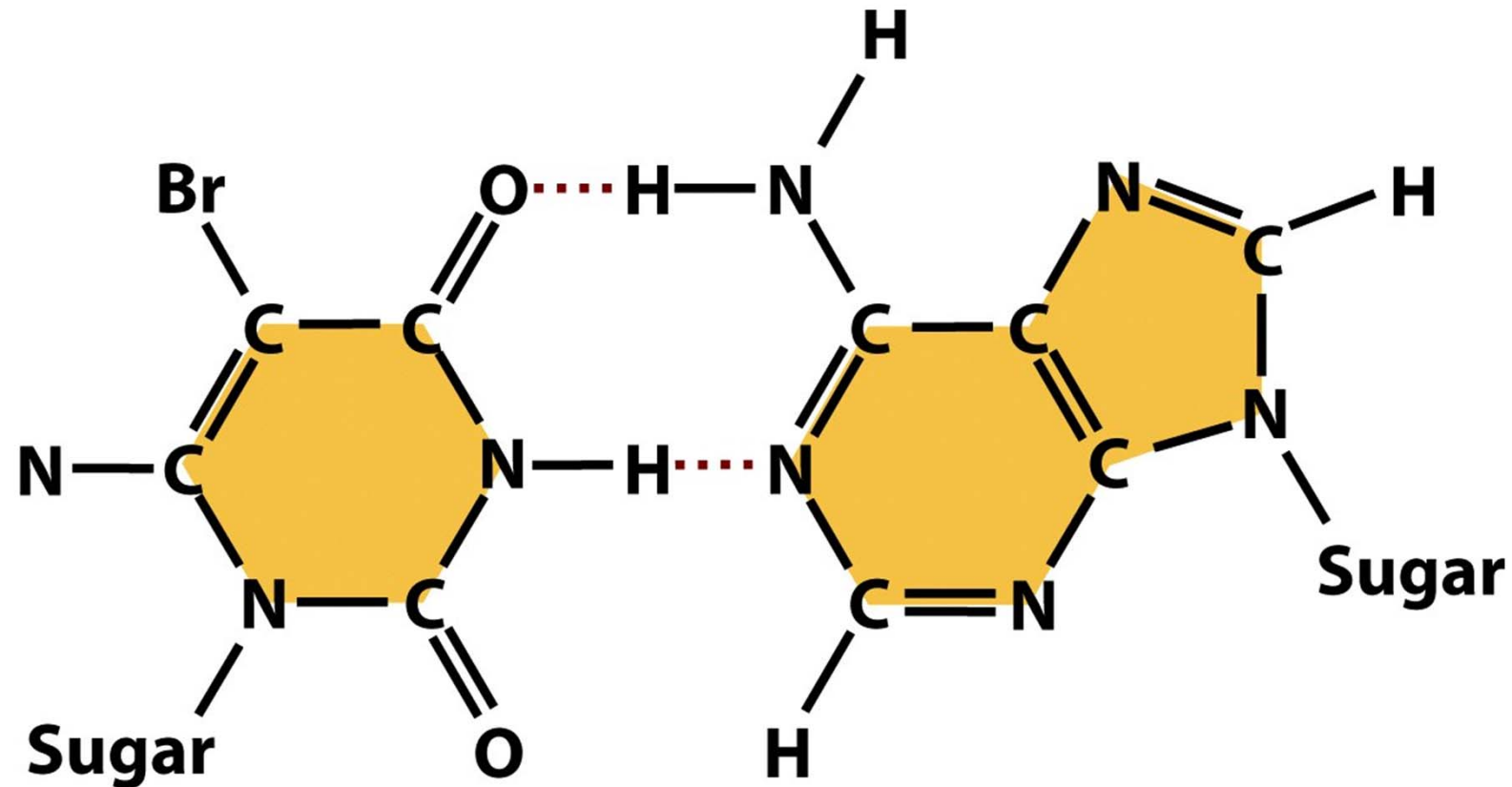


A와 짝을 이루는
T처럼 보인다.



G와 짝을 이루는
C처럼 보인다.

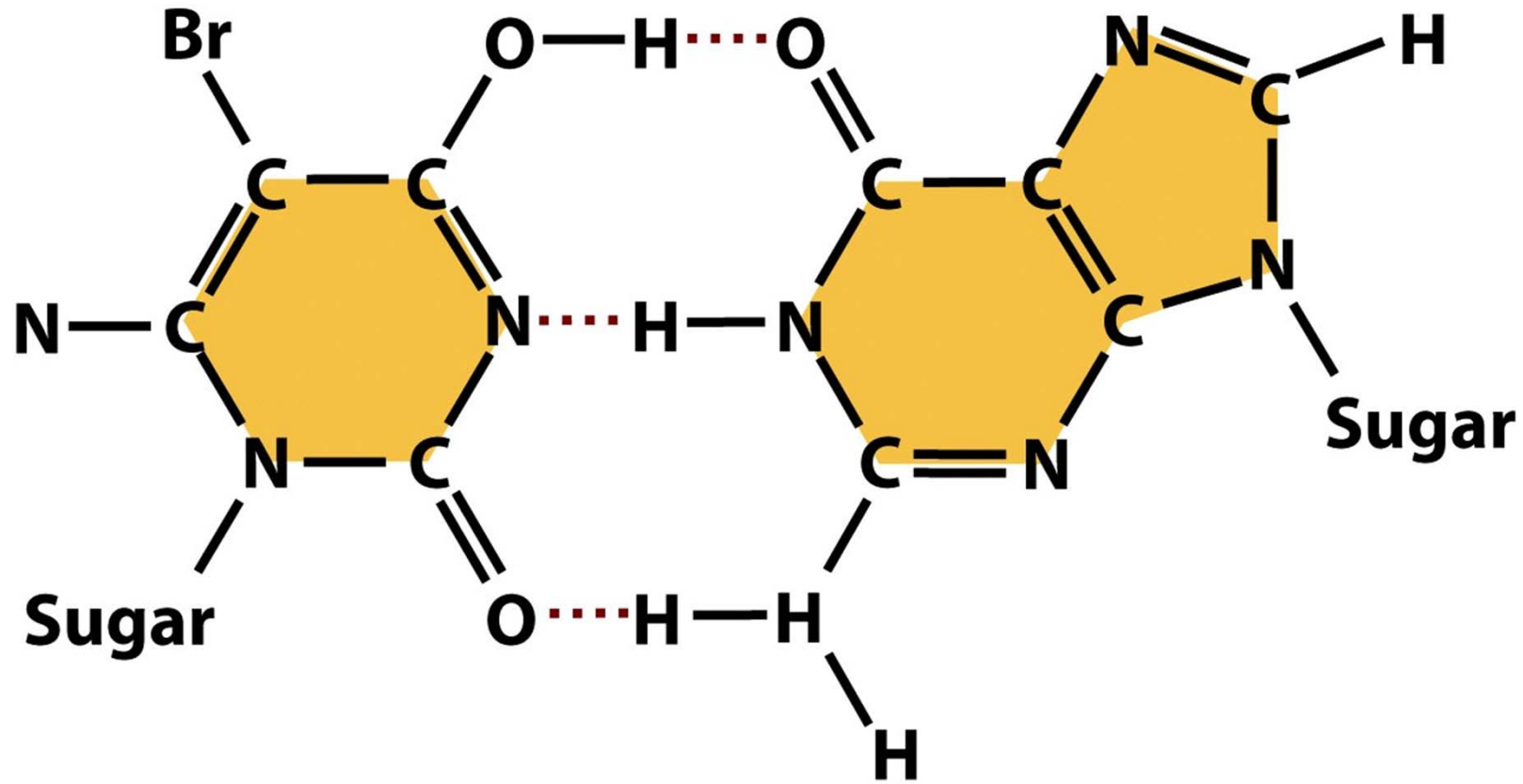
Keto or enol form of 5-Bromouracil



**5-Bromouracil
(keto form)**

Adenine

5-Bromouracil: adenine base pair.



**5-Bromouracil
(enol form)**

Guanine

5-Bromouracil: guanine base pair.

Effect of enol form of 5-bromouracil during:

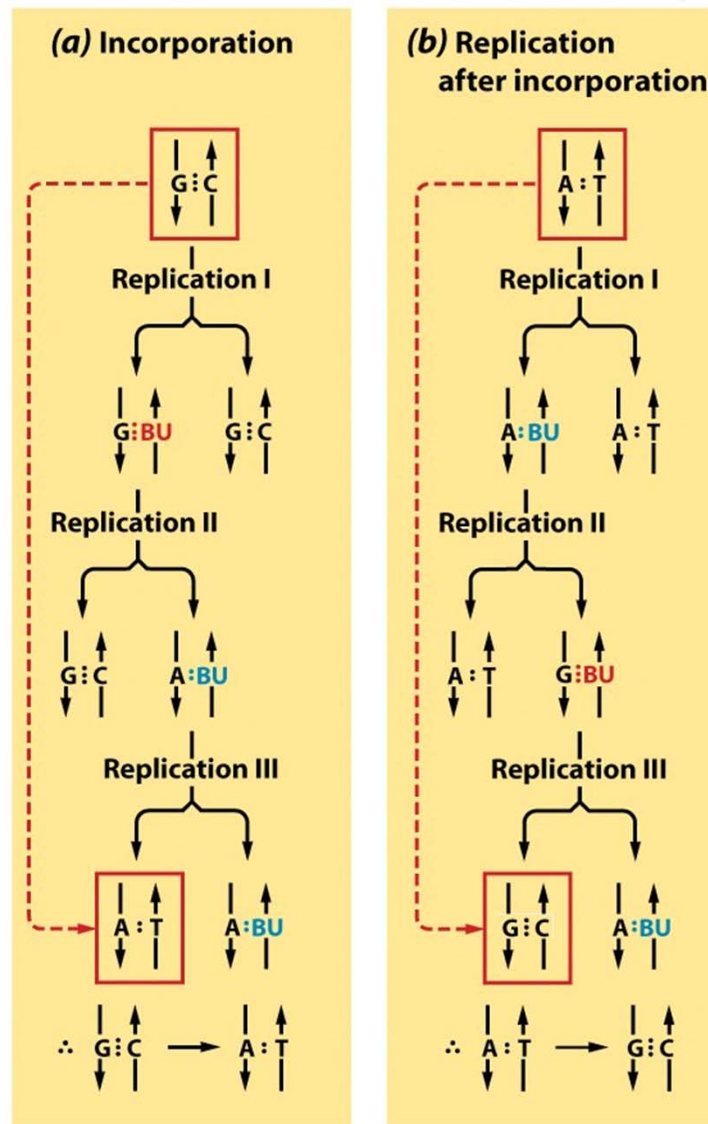
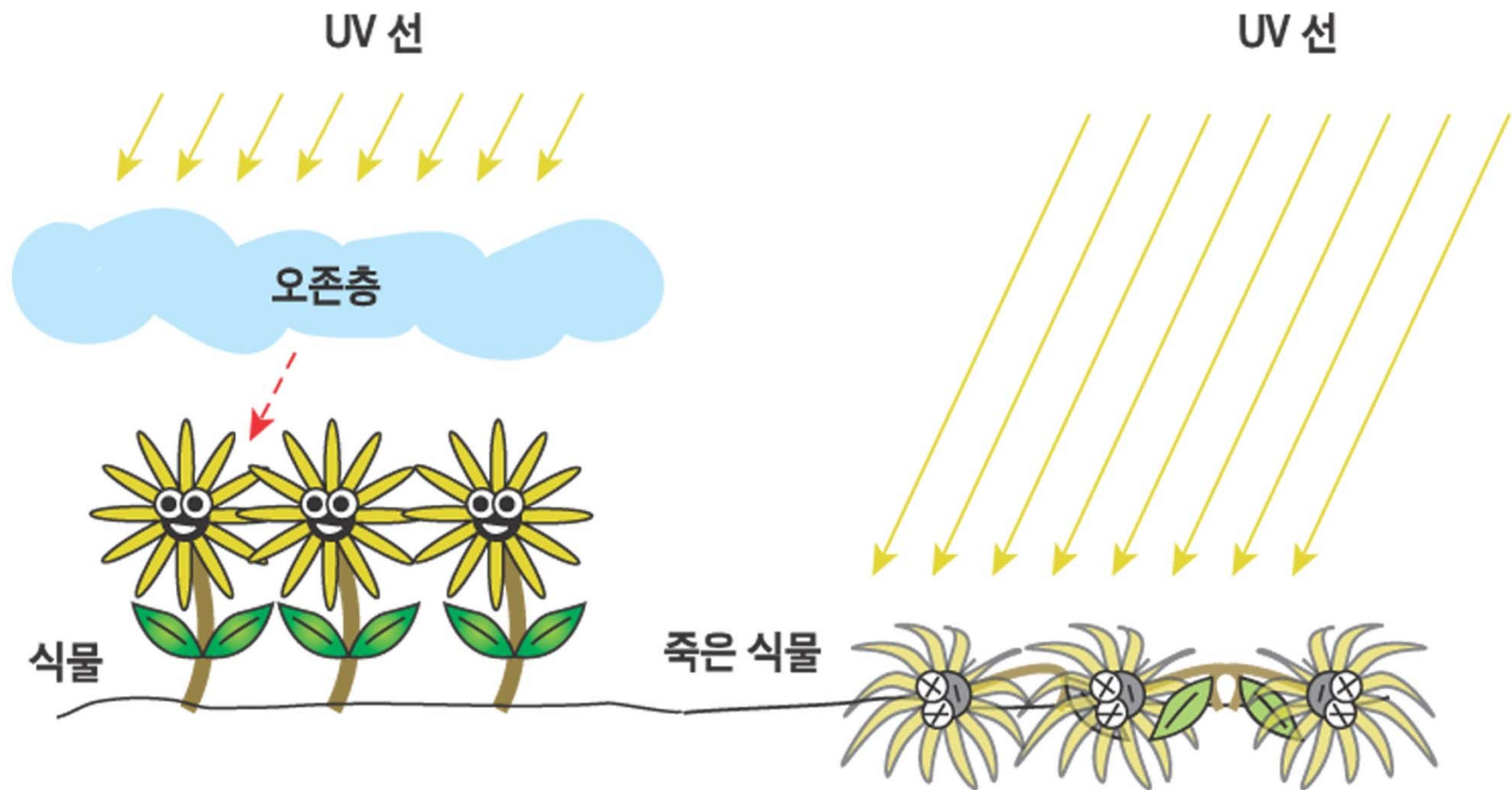
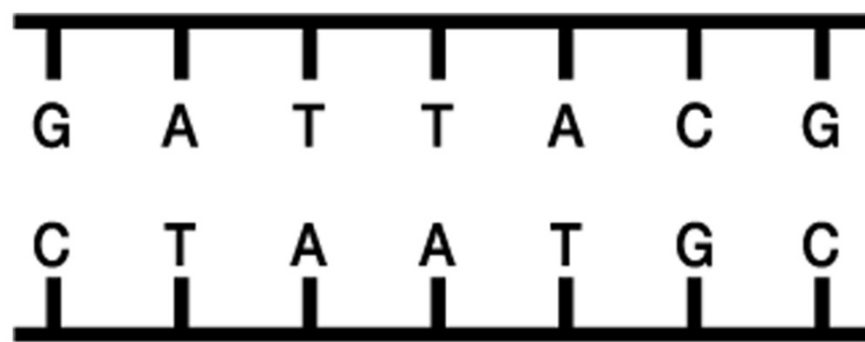


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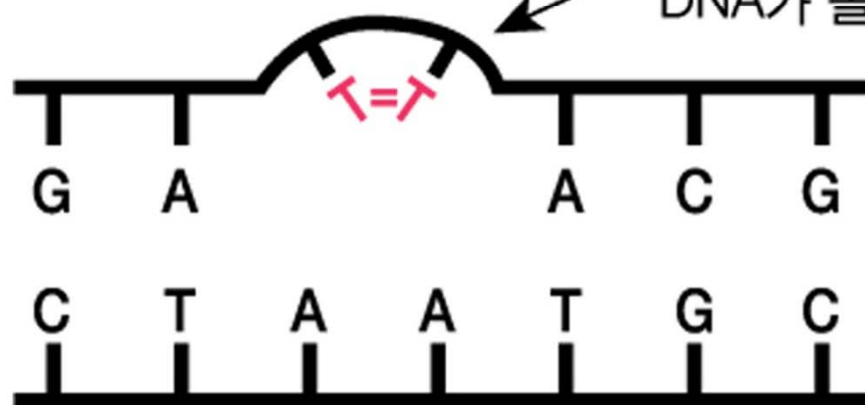




UV 선



T 이량체 부분에서
DNA가 볼록 튀어나온다.



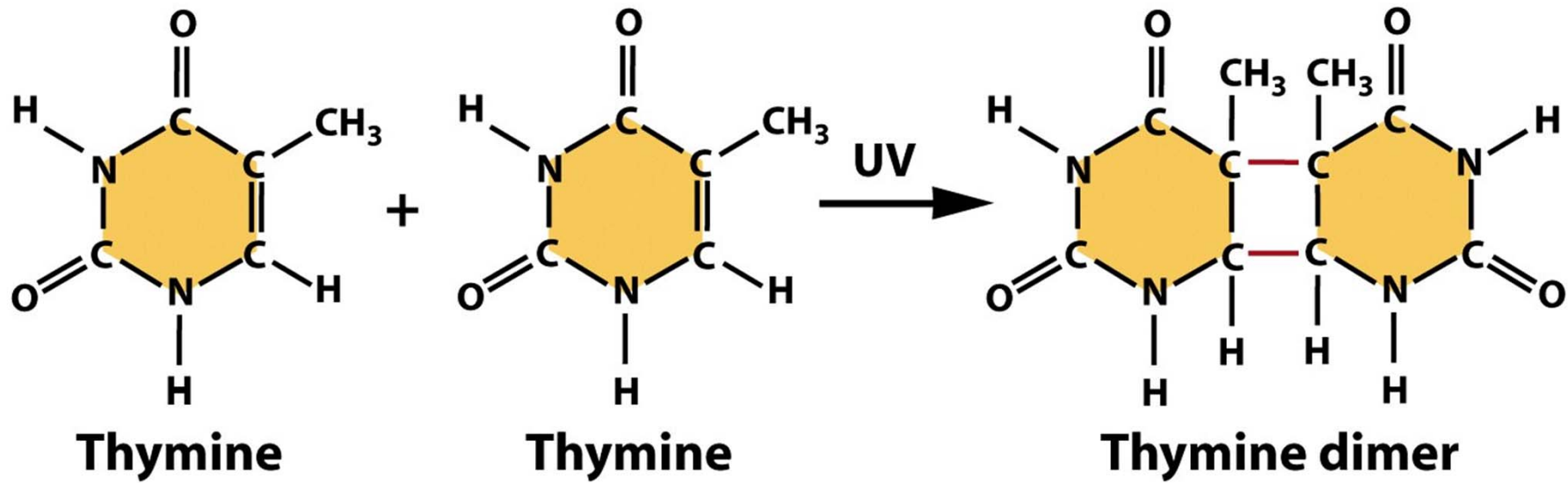
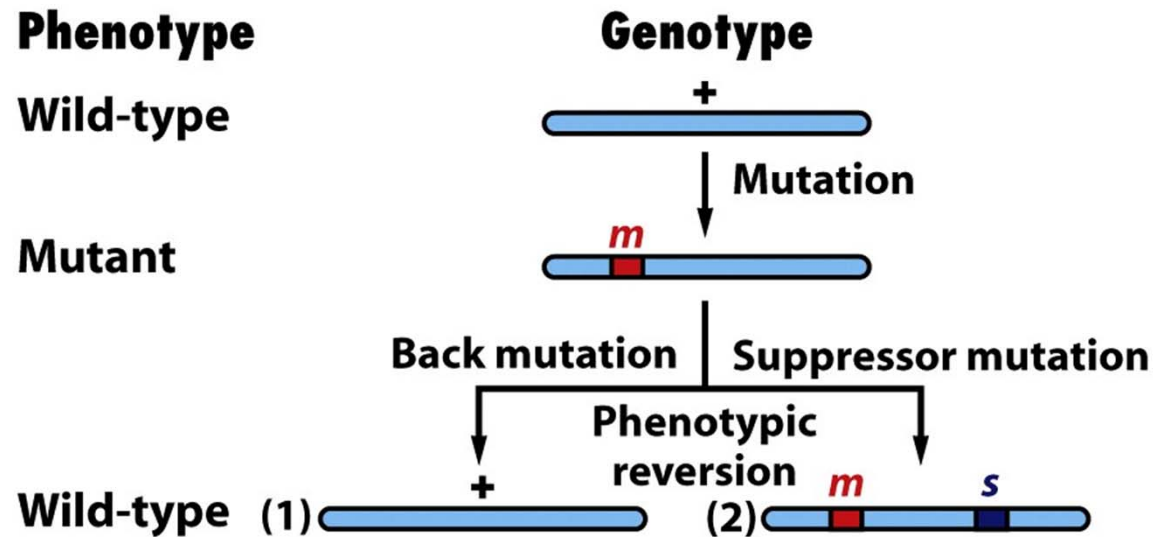


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Mechanisms for Correction of Mutation

- **Reversion**: a second mutation restores original characteristics
 - **True revertant**: the original DNA base sequence is exactly restored
 - **Second-site revertant**: a second change in DNA base sequence cancels out the effects of the first
- **DNA repair** (damage control system): mismatch repair system
 - **Excision repair** is the most wide distributed system: damaged bases (ex. deaminated bases) are recognized (glycosylase), excised (endonuclease) and patched (filling the gap by DNA polymerase I and seal the nick by ligase)
 - **Mismatch repair**: GATC tagging with methyl groups allows mutant strand (error-carrying daughter strand) identification and GATC specific endonuclease cleaves the unmethylated strand



Backcross to wild-type:

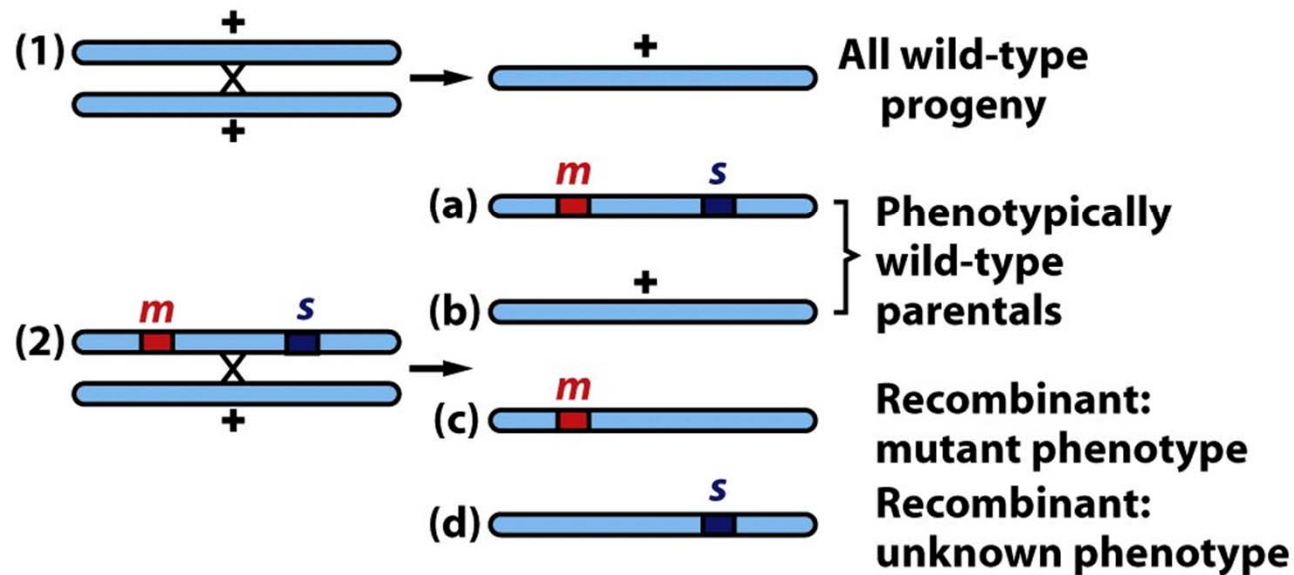


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Correction of mutation by reversion (second-site revertant)

야생형

GAG - GCC - ATC - GAA - TGT - TTG - GCA - AGG - AAA

단백질: Glu - Ala - Ile - Glu - Cys - Leu - Ala - Arg - Lys

원래의 결실돌연변이체

DNA: GAG - G●C - ATC - GAA - TGT - TTG - GCA - AGG - AAA

코돈 묶음: GAG - GCA - TCG - AAT - GTT - TGG - CAA - GGA - AA

단백질: Glu - Ala - Ser - Asn - Val - Trp - Gln - Ala - ----

Correction of mutation by reversion (second-site revertant)

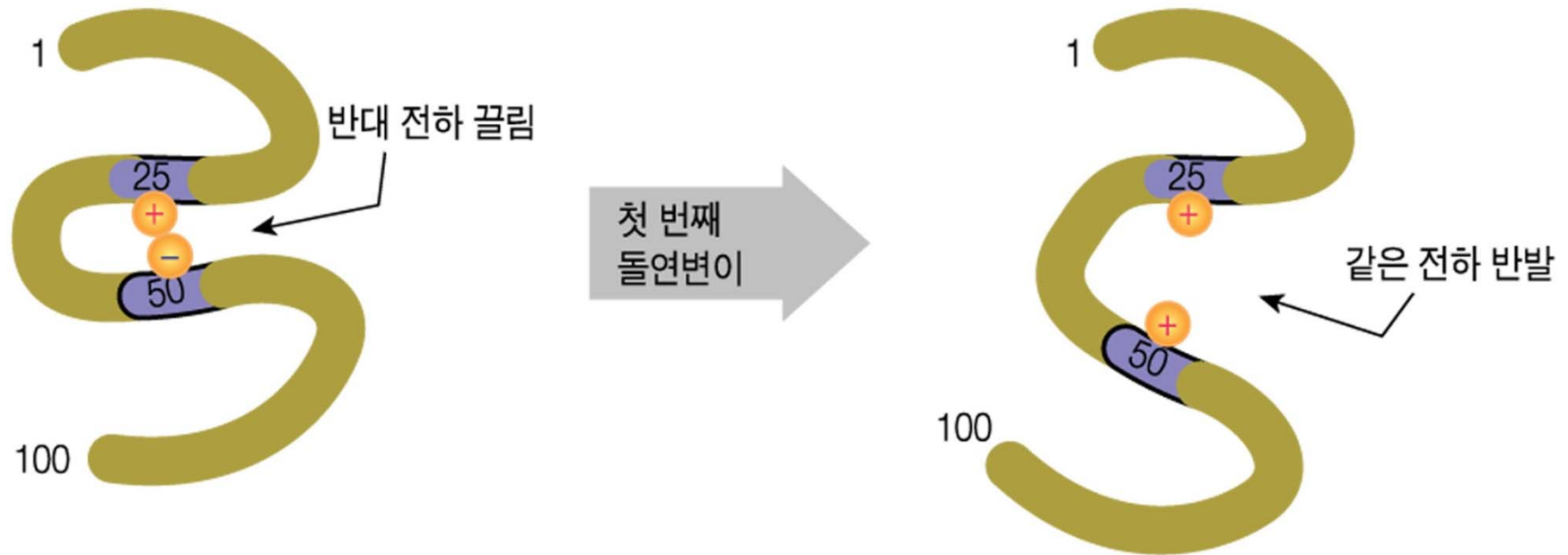
복귀돌연변이

DNA: GAG - G●C - AATC - GAA - TGT - TTG - GCA - AGG - AAA

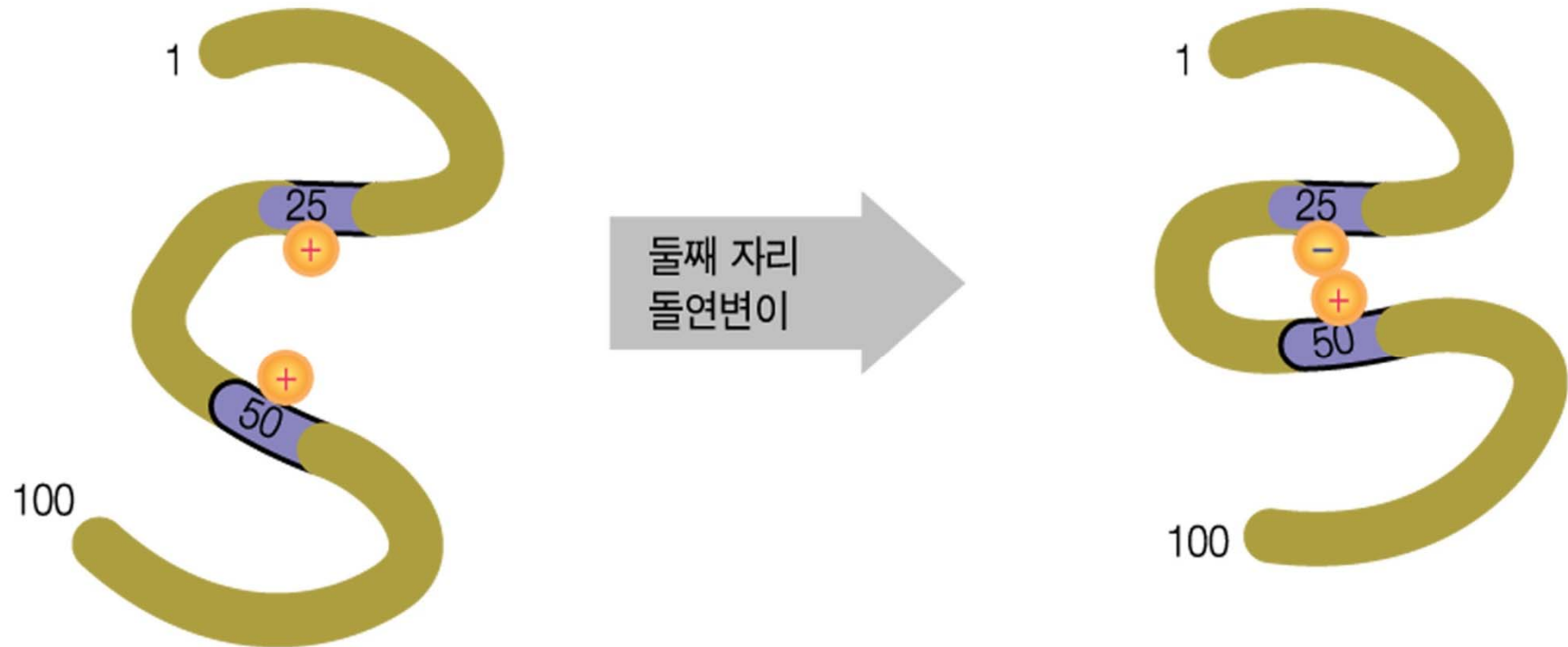
코돈 묶음: GAG - GCA - ATC - GAA - TGT - TTG - GCA - AGG - AAA

단백질: Glu - Ala - Ile - Glu - Cys - Leu - Ala - Arg - Lys

Correction of mutation by reversion (second-site revertant)

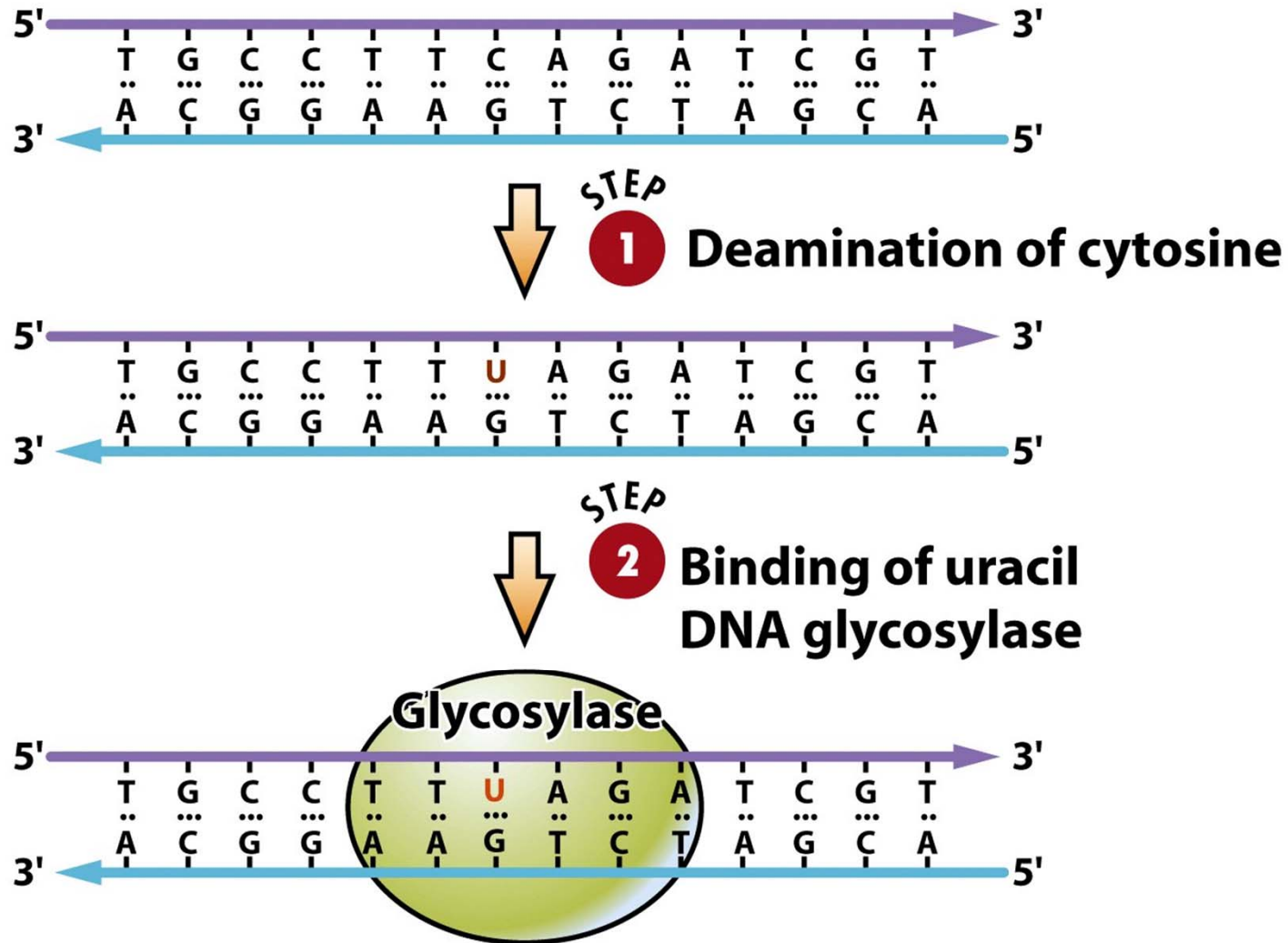


Correction of mutation by reversion (second-site revertant)



Correction of mutation by DNA repair

- Excision repair



Correction of mutation by DNA repairment

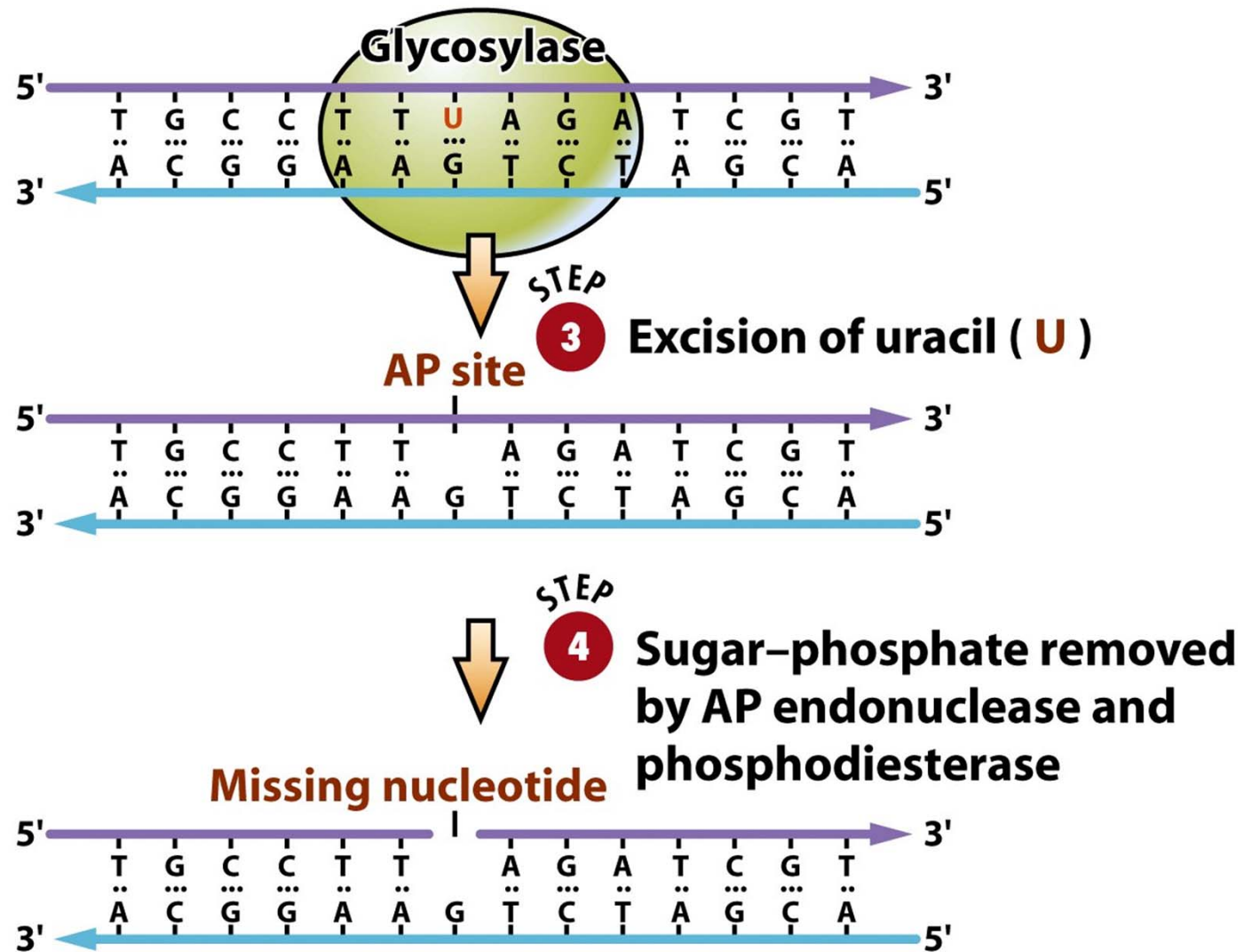


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Correction of mutation by DNA repairment

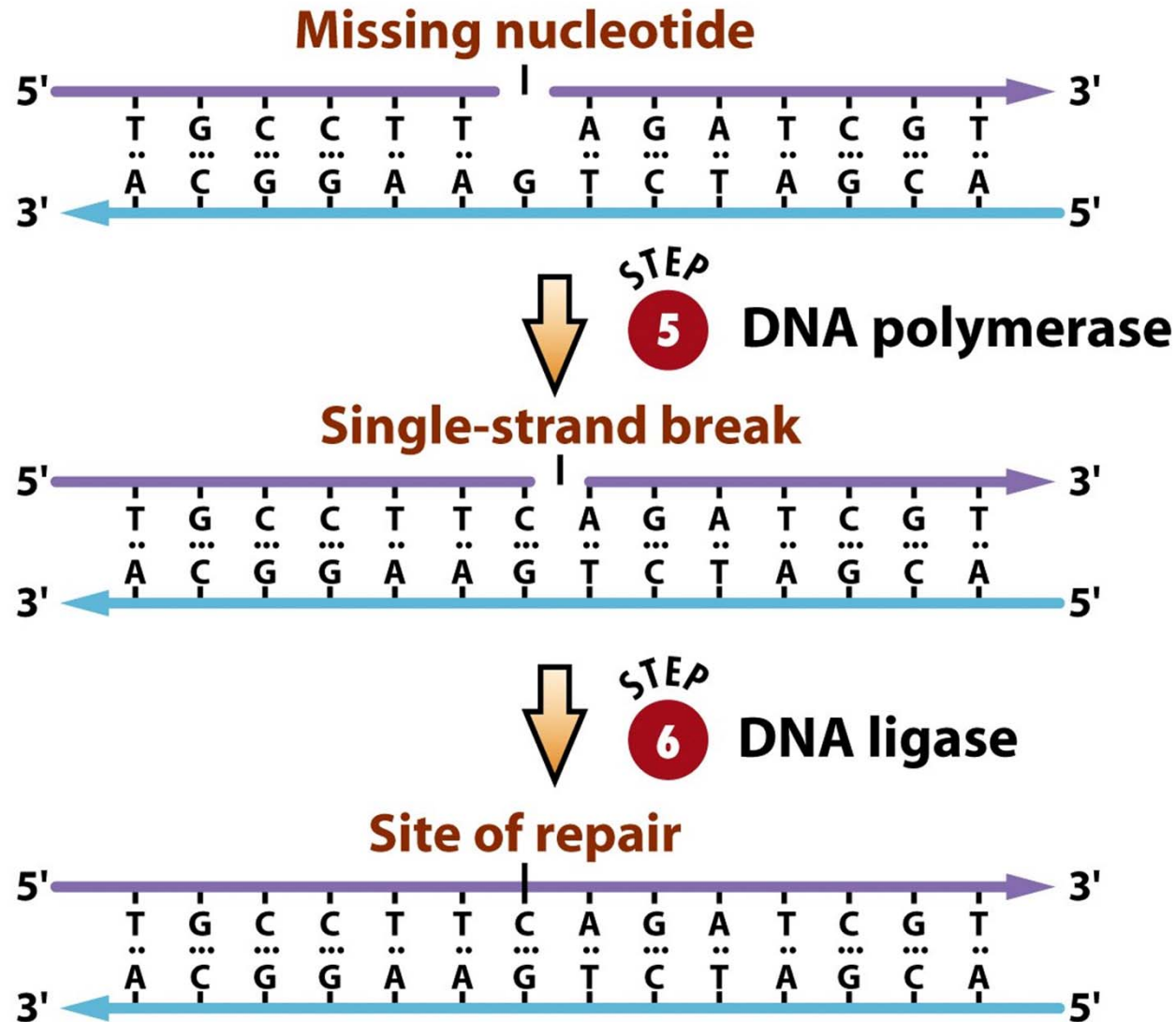


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Correction of mutation by DNA repair

-Mismatch repair by *GATC*-specific endonuclease

