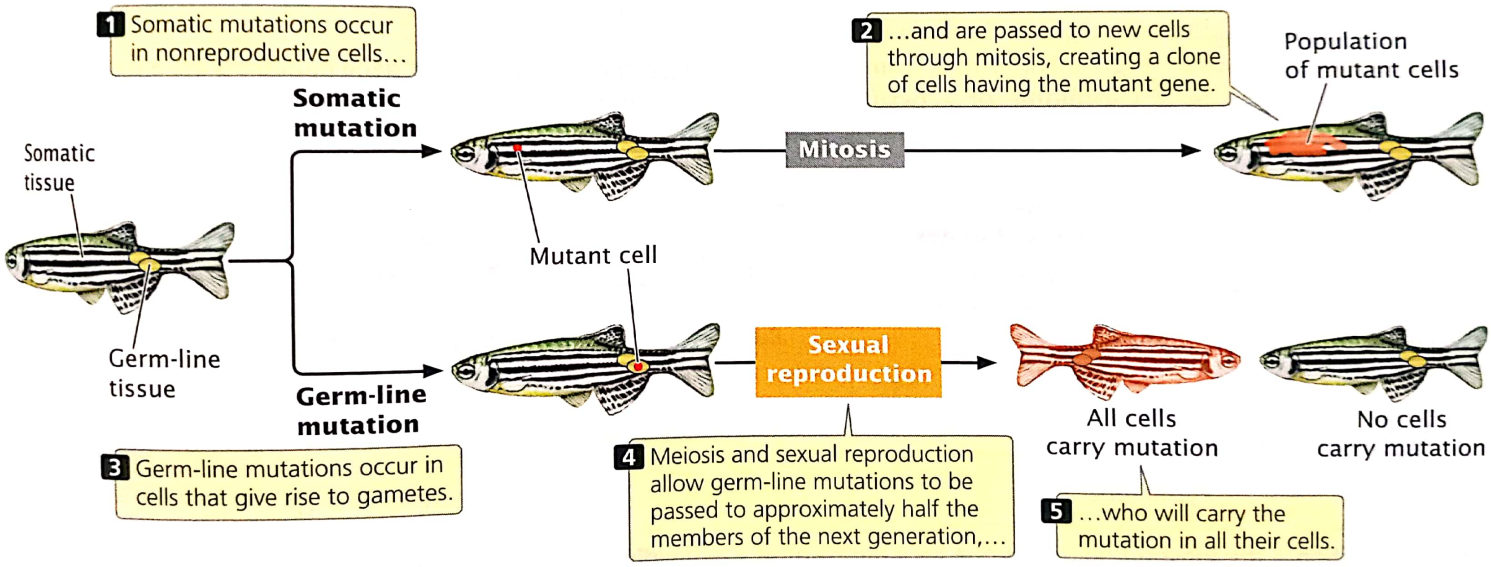
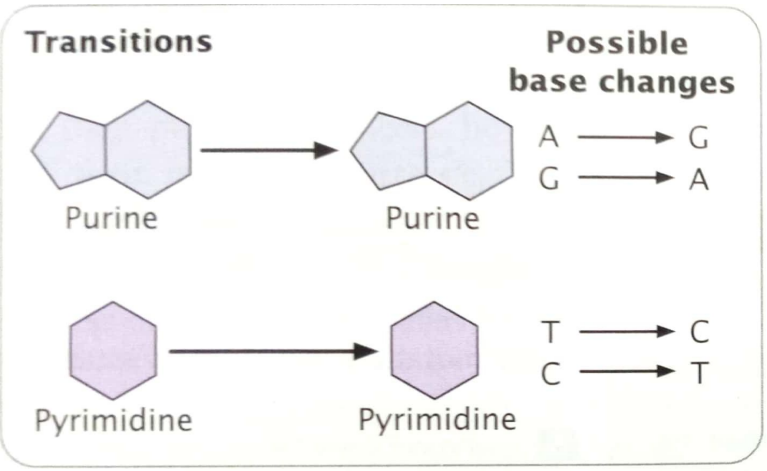
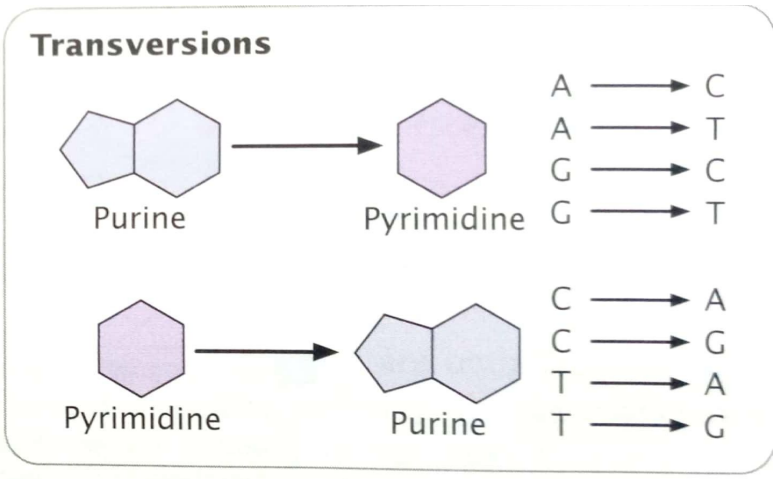
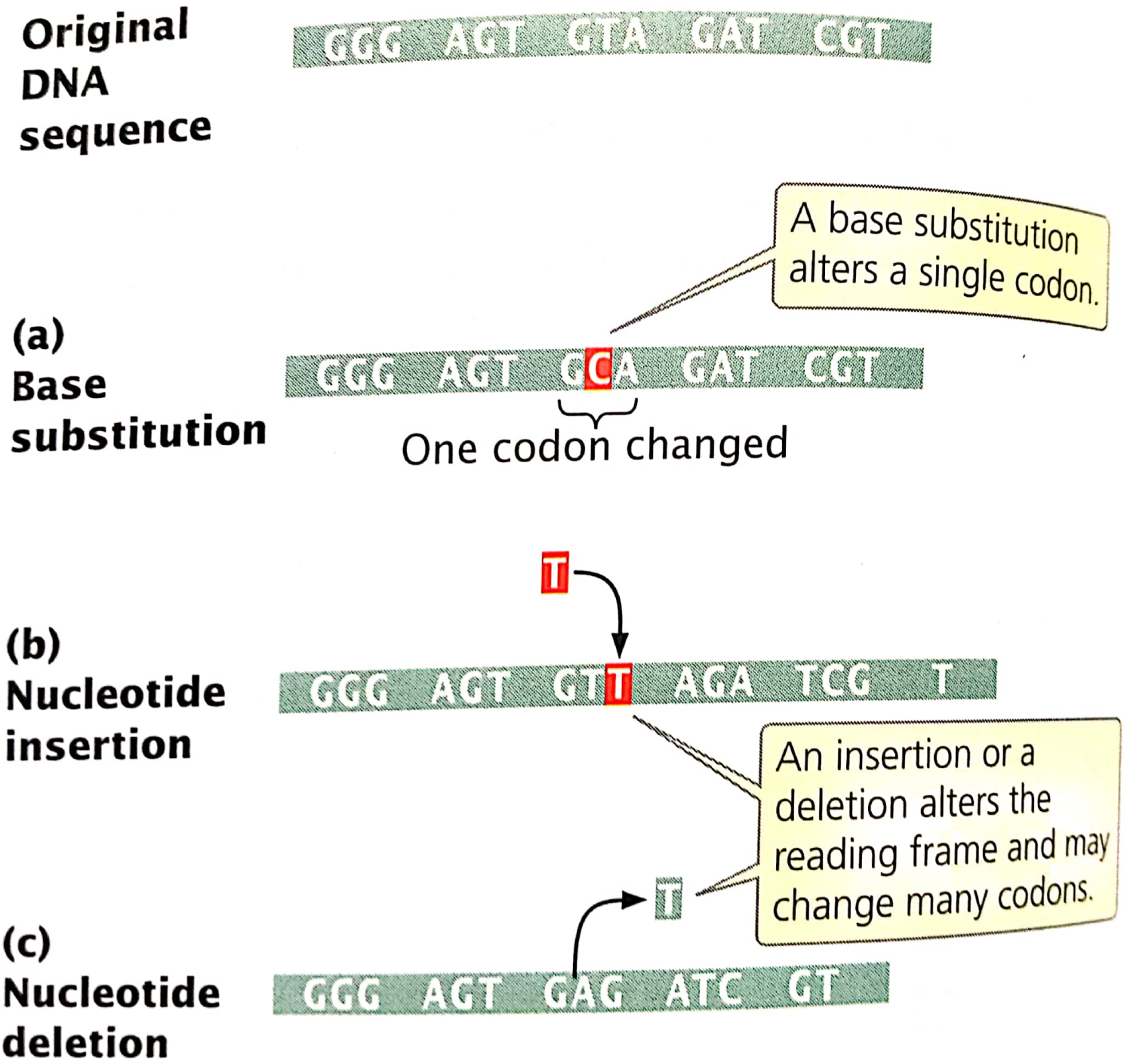


18.1 **The two basic classes of mutations are somatic mutations and germ-line mutations.**





18.3 A transition is the substitution of a purine for a purine or of a pyrimidine for a pyrimidine; a transversion is the substitution of a pyrimidine for a purine or of a purine for a pyrimidine.



18.2 Three basic types of gene mutations are base substitutions, insertions, and deletions.

TABLE 18.1 Examples of human genetic diseases caused by expanding nucleotide repeats

Disease	Repeated Sequence	Number of Copies of Repeat	
		Normal Range	Disease Range
Spinal and bulbar muscular atrophy	CAG	11–33	40–62
Fragile-X syndrome	CGG	6–54	50–1500
Jacobsen syndrome	CGG	11	100–1000
Spinocerebellar ataxia (several types)	CAG	4–44	21–130
Autosomal dominant cerebellar ataxia	CAG	7–19	37–220
Myotonic dystrophy	CTG	5–37	44–3000
Huntington disease	CAG	9–37	37–121
Friedreich ataxia	GAA	6–29	200–900
Dentatorubral-pallidoluysian atrophy	CAG	7–25	49–75
Myoclonus epilepsy of the Unverricht–Lundborg type	CCCCGCCCCGCG	2–3	12–13
Amyotrophic lateral sclerosis	GGGGCC	2–23	700–1600

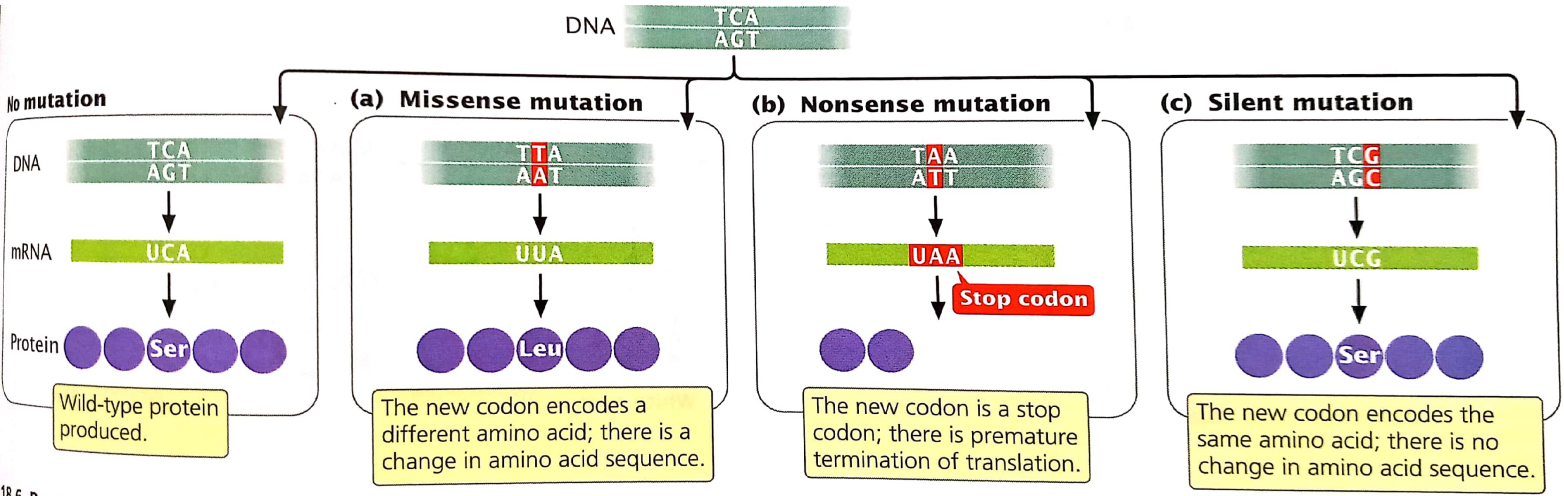
CONCEPTS

Gene mutations are changes in a single gene. They can be base substitutions (in which a single pair of nucleotides is altered) or insertions or deletions (in which nucleotides are added or removed). A base substitution can be a transition (substitution of like bases) or a transversion (substitution of unlike bases). Insertions and deletions often lead to a change in the reading frame of a gene.

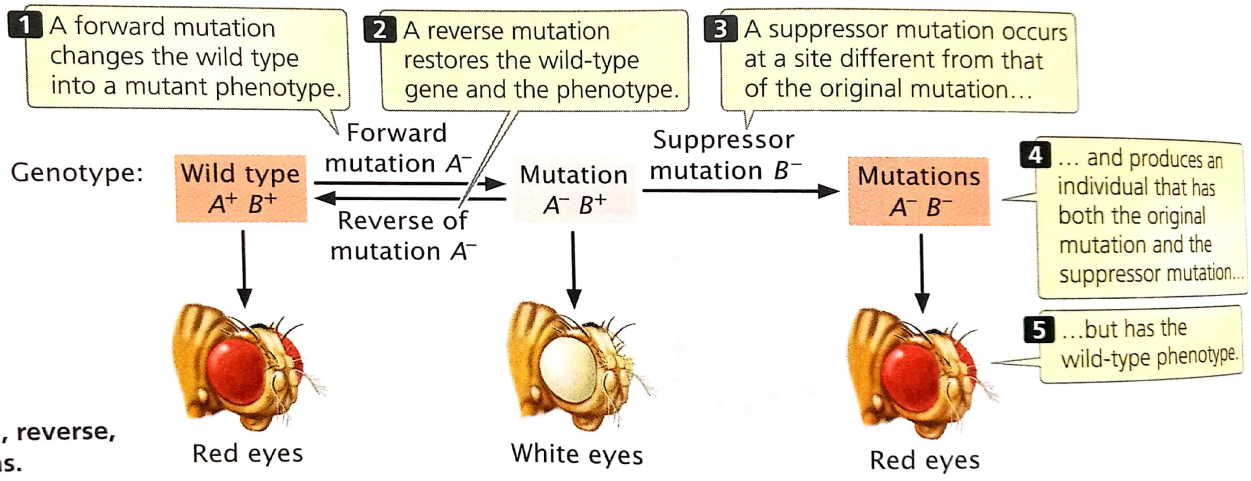
✓ CONCEPT CHECK 1

Which of the following changes is a transition base substitution?

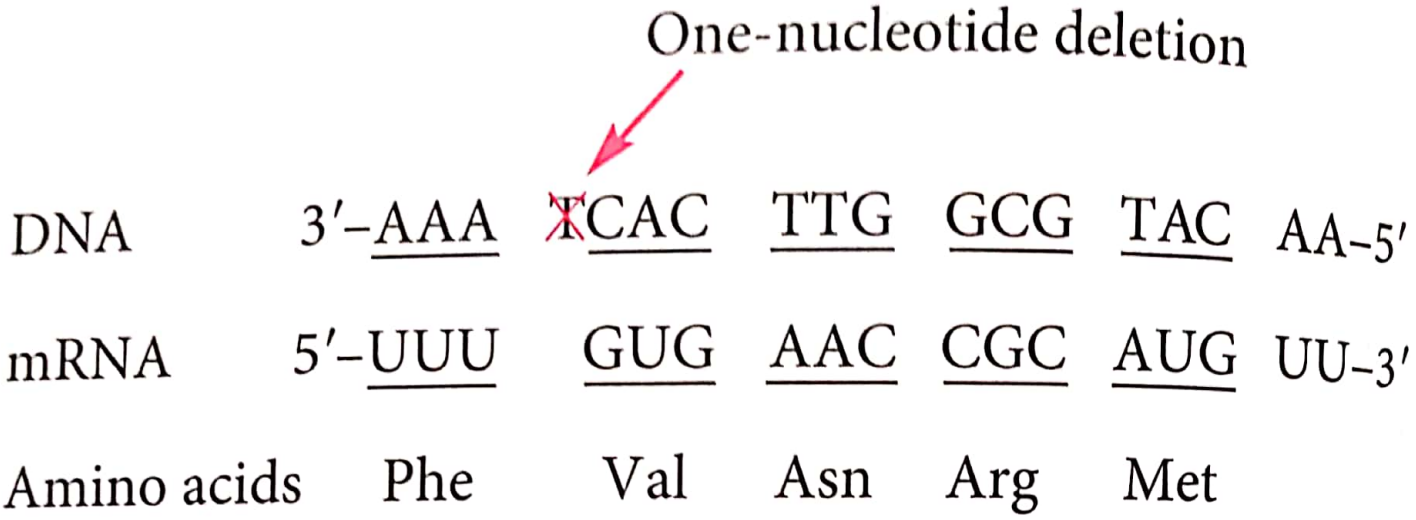
a. Adenine is replaced by thymine.
b. Cytosine is replaced by adenine.
c. Guanine is replaced by adenine.
d. Three nucleotide pairs are inserted into DNA.



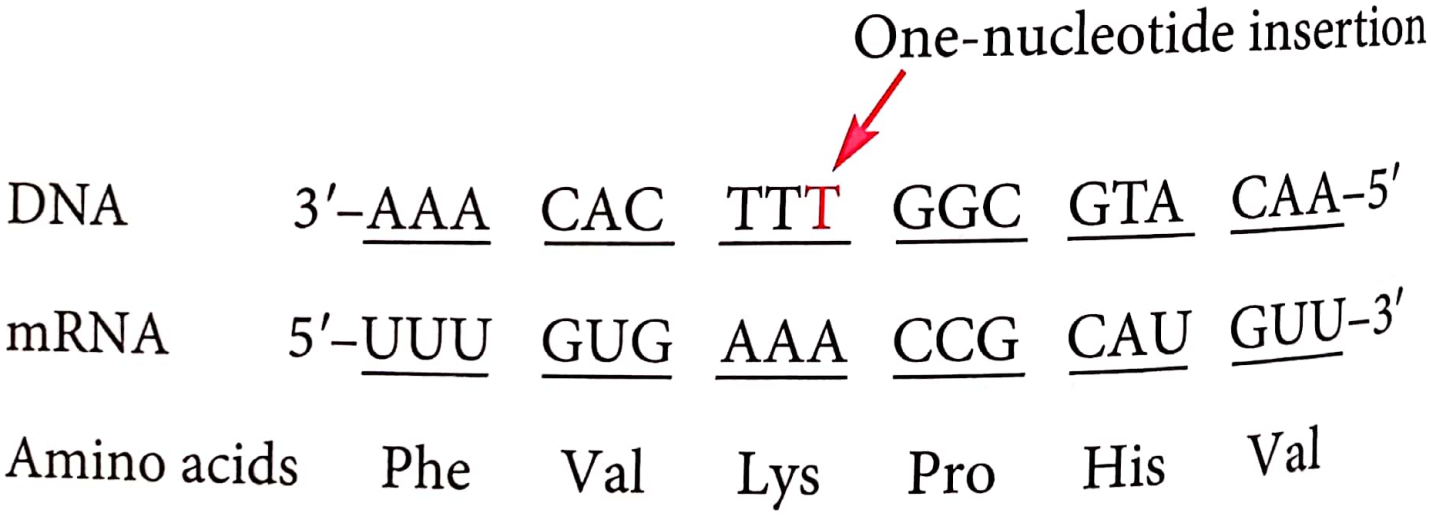
18.6 **Base substitutions can cause (a) missense, (b) nonsense, or (c) silent mutations.**



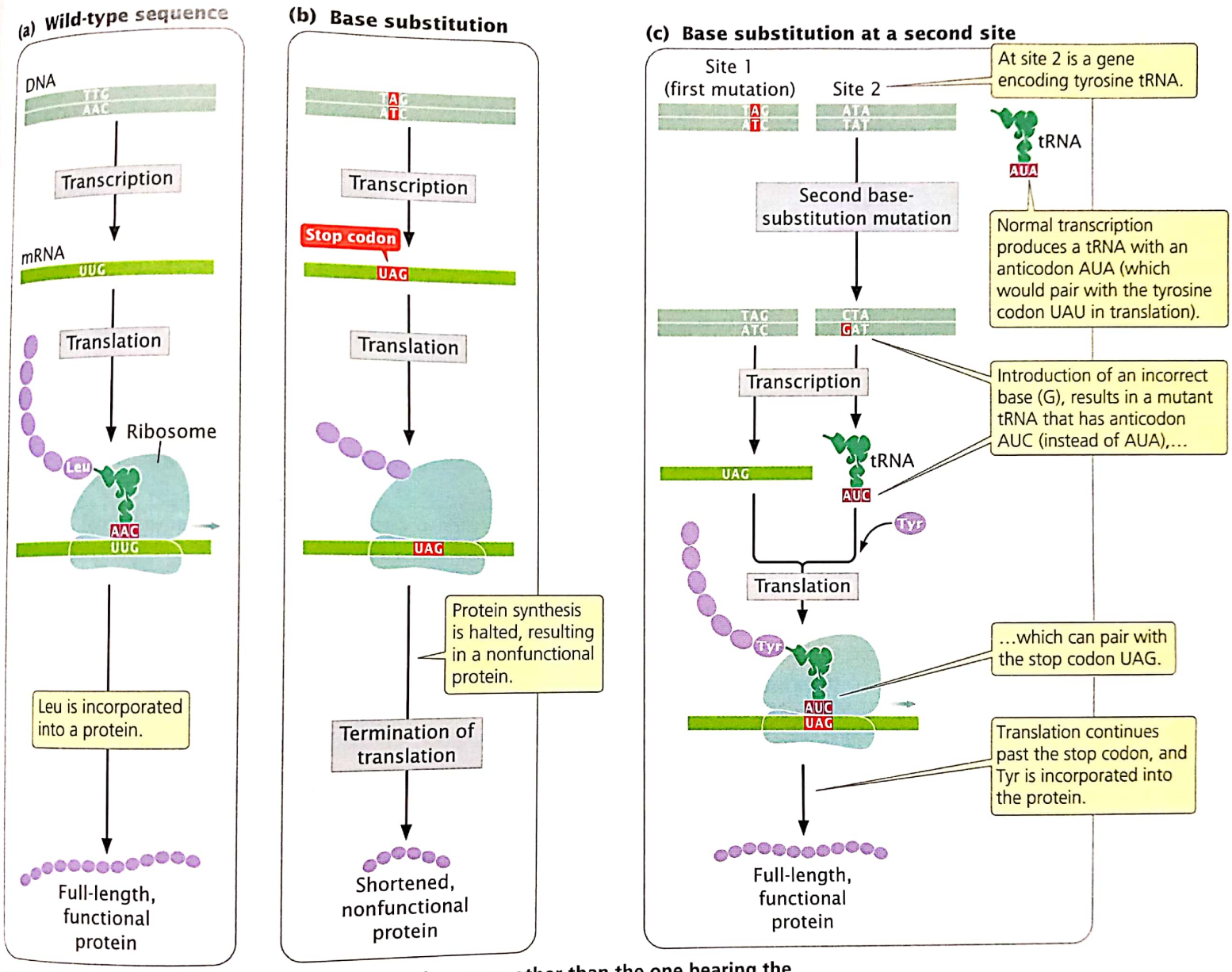
18.7 Relation of forward, reverse, and suppressor mutations.



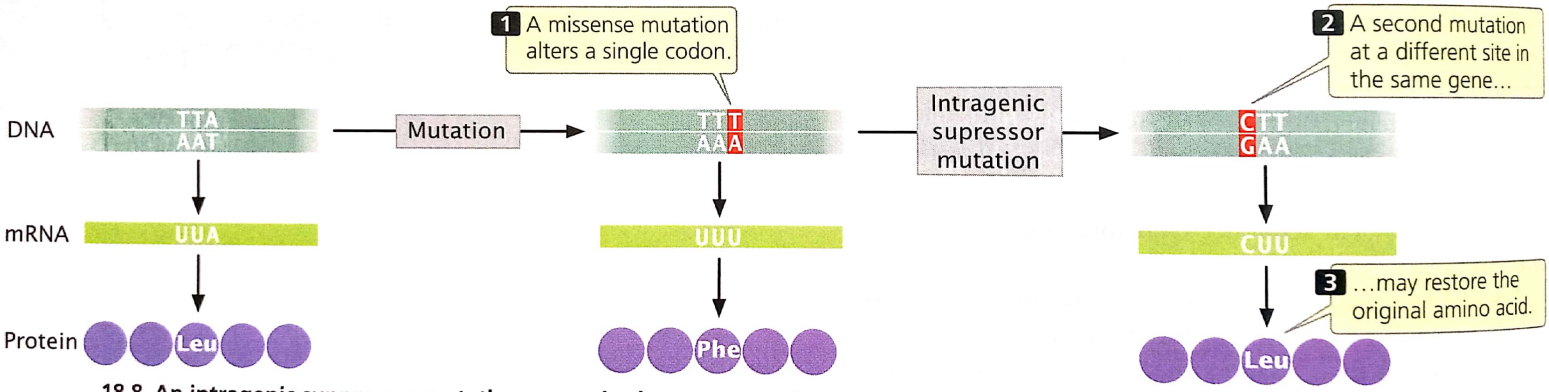
If a single nucleotide is added to the third codon (the suppressor mutation), the reading frame is restored, although two of the amino acids differ from those specified by the original sequence:



Similarly, a mutation due to an insertion may be suppressed by a subsequent deletion in the same gene.



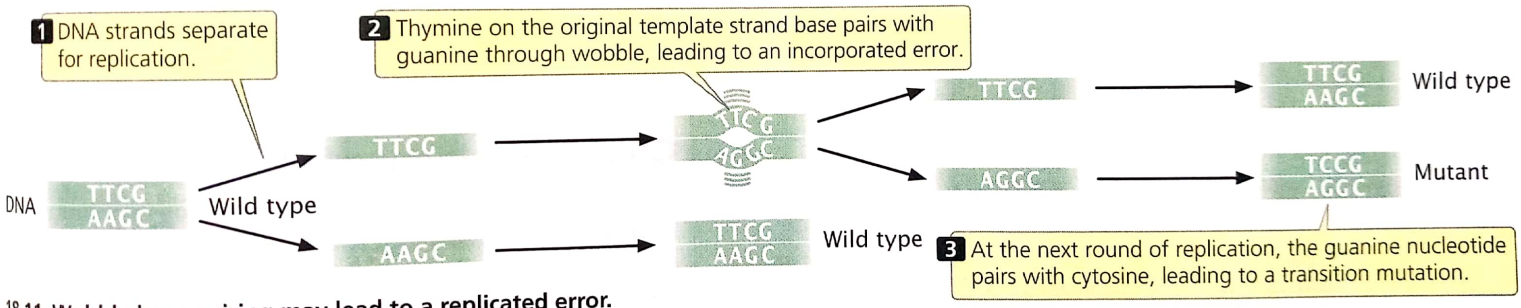
18.9 An intergenic suppressor mutation occurs in a gene other than the one bearing the original mutation that it suppresses. (a) A wild-type sequence produces a full-length, functional protein. (b) A base substitution at a site in that gene produces a premature stop codon, resulting in a truncated, nonfunctional protein. (c) A base substitution at a site in another gene, which in this case encodes tRNA, alters the anticodon of $tRNA^{Tyr}$; $tRNA^{Tyr}$ can then pair with the stop codon produced by the original mutation, allowing tyrosine to be incorporated into the protein and translation to continue.



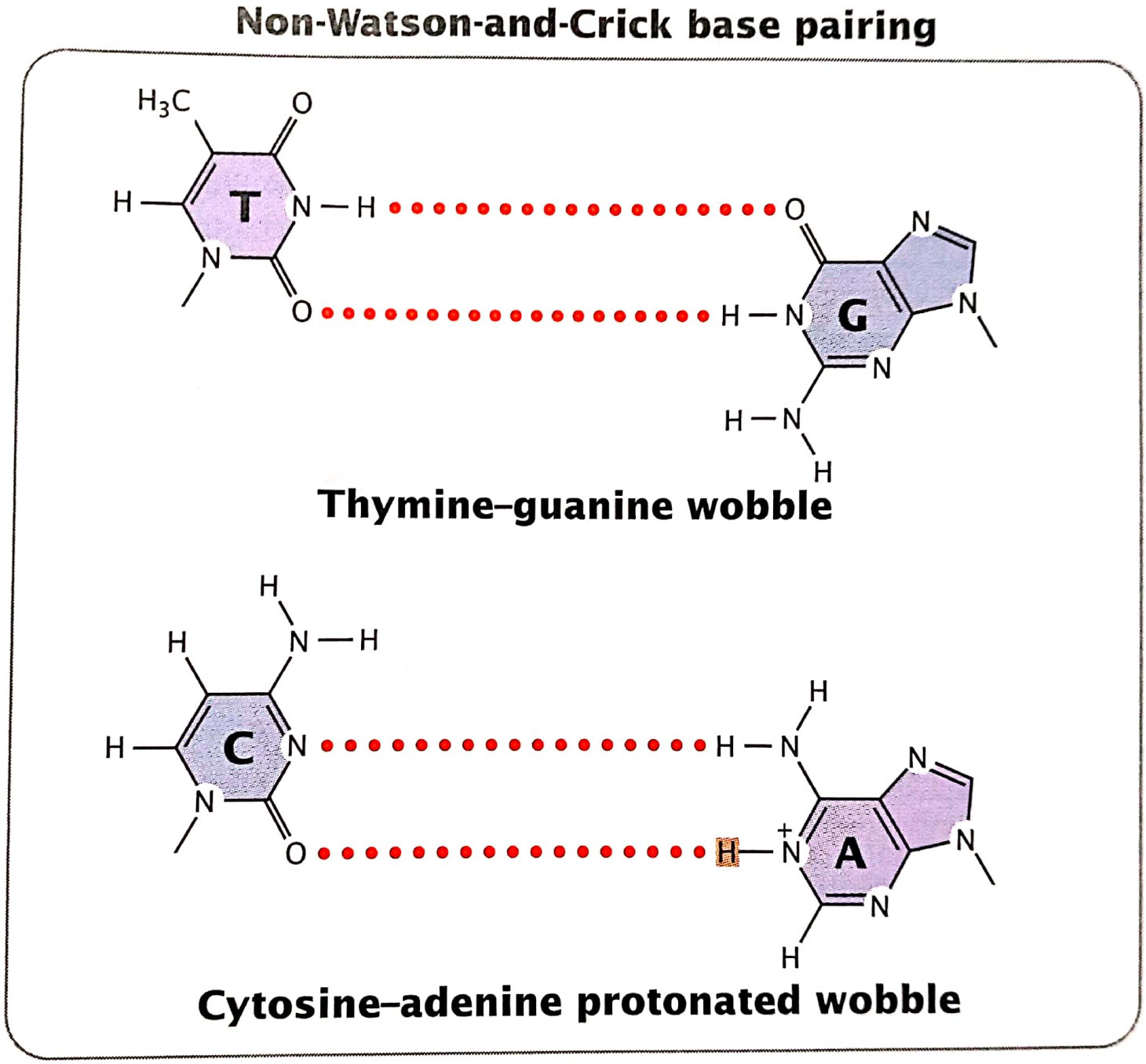
18.8 An intragenic suppressor mutation occurs in the gene containing the mutation being suppressed.

TABLE 18.2 Characteristics of different types of mutations

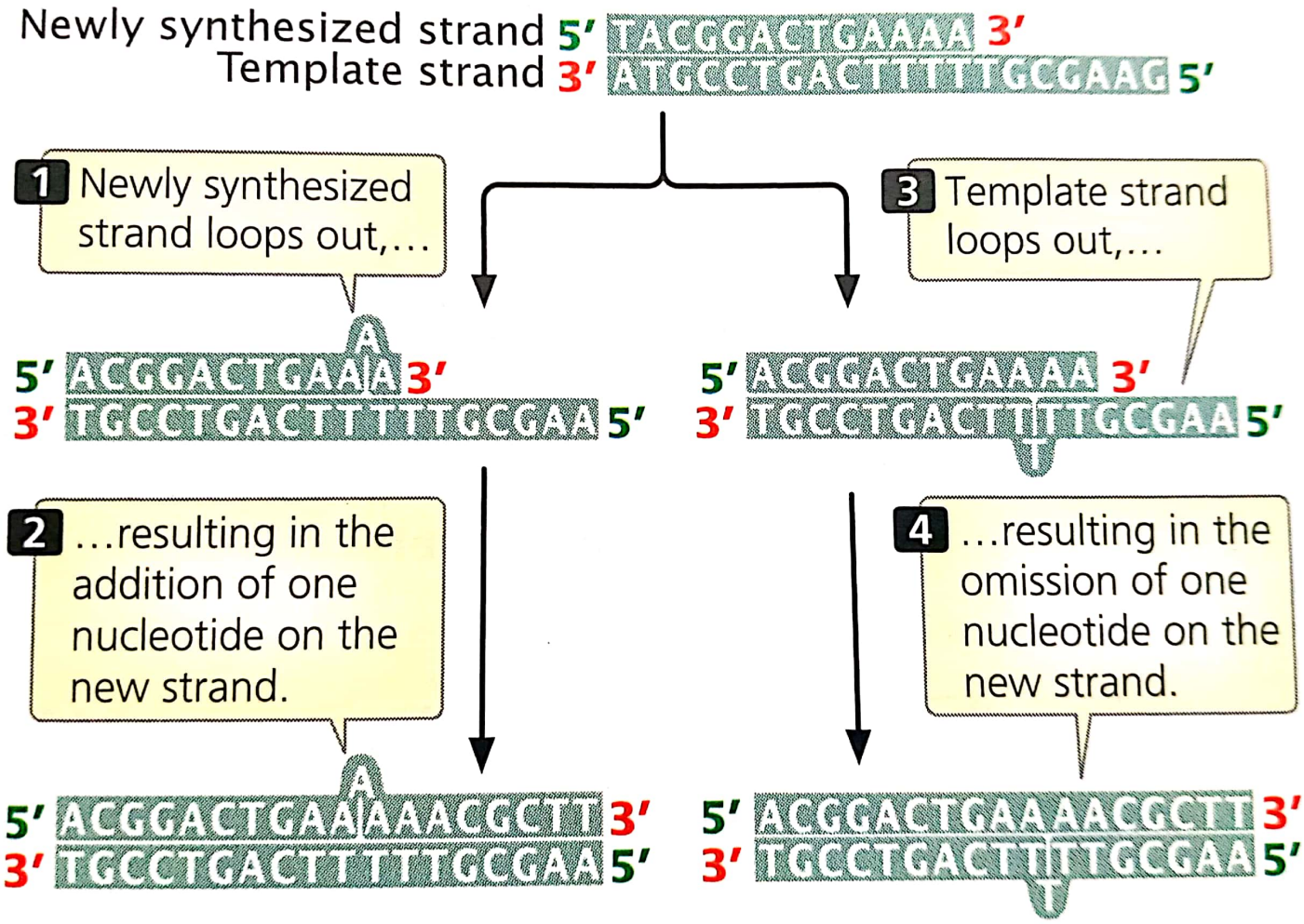
Type of Mutation	Definition
Base substitution	Changes the base of a single DNA nucleotide
Transition	Base substitution in which a purine replaces a purine or a pyrimidine replaces a pyrimidine
Transversion	Base substitution in which a purine replaces a pyrimidine or a pyrimidine replaces a purine
Insertion	Addition of one or more nucleotides
Deletion	Deletion of one or more nucleotides
Frameshift mutation	Insertion or deletion that alters the reading frame of a gene
In-frame deletion or insertion	Deletion or insertion of a multiple of three nucleotides that does not alter the reading frame
Expanding nucleotide repeats	Increases the number of copies of a set of nucleotides
Forward mutation	Changes the wild-type phenotype to a mutant phenotype
Reverse mutation	Changes a mutant phenotype back to the wild-type phenotype
Missense mutation	Changes a sense codon into a different sense codon, resulting in the incorporation of a different amino acid in the protein
Nonsense mutation	Changes a sense codon into a nonsense (stop) codon, causing premature termination of translation
Silent mutation	Changes a sense codon into a synonymous codon, leaving the amino acid sequence of the protein unchanged
Neutral mutation	Changes the amino acid sequence of a protein without altering its ability to function
Loss-of-function mutation	Causes a complete or partial loss of function
Gain-of-function mutation	Causes the appearance of a new trait or function or causes the appearance of a trait in inappropriate tissue or at an inappropriate time
Lethal mutation	Causes premature death
Suppressor mutation	Suppresses the effect of an earlier mutation at a different site
Intragenic suppressor mutation	Suppresses the effect of an earlier mutation within the same gene
Intergenic suppressor mutation	Suppresses the effect of an earlier mutation in another gene



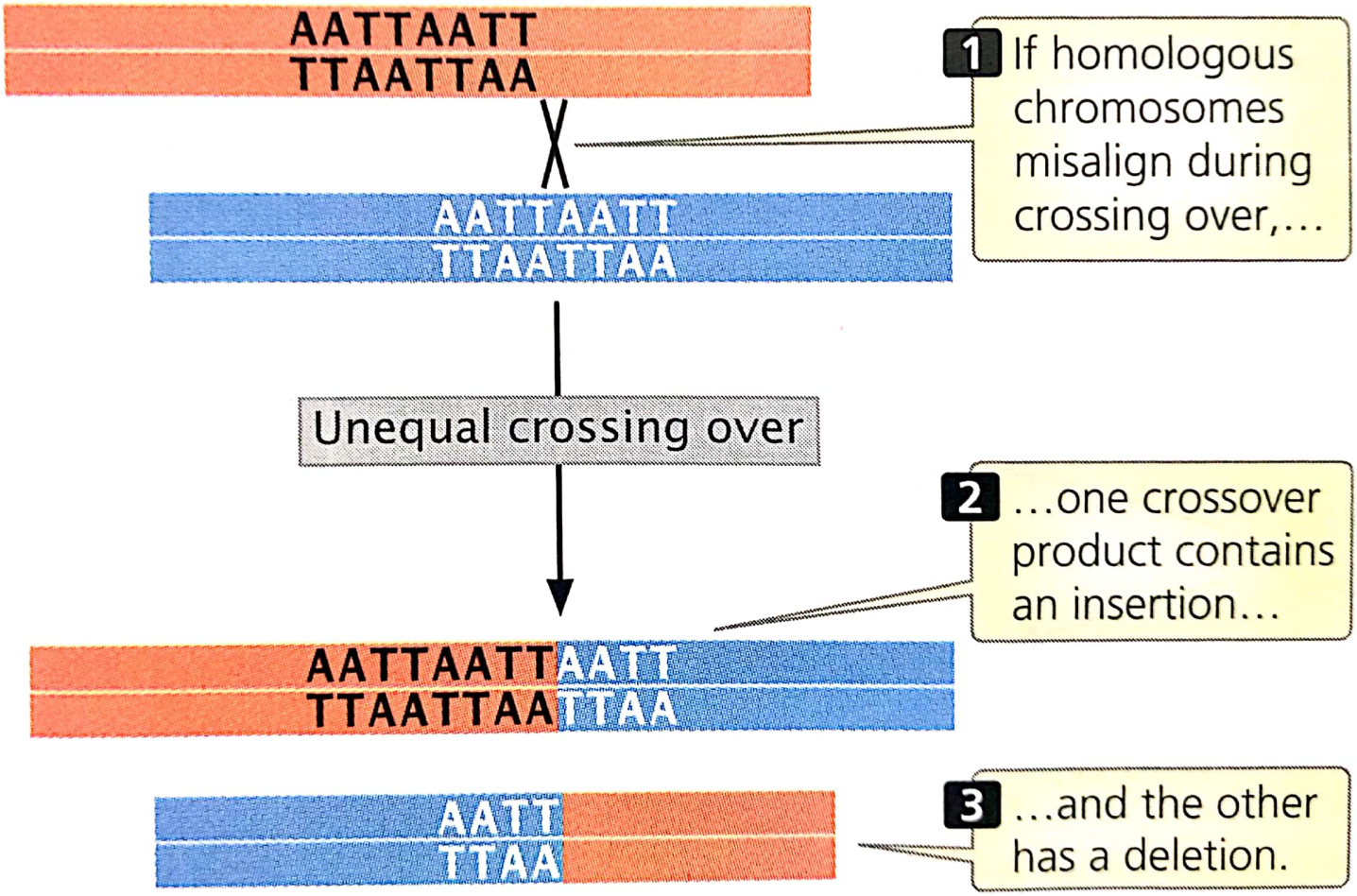
18.11 Wobble base pairing may lead to a replicated error.



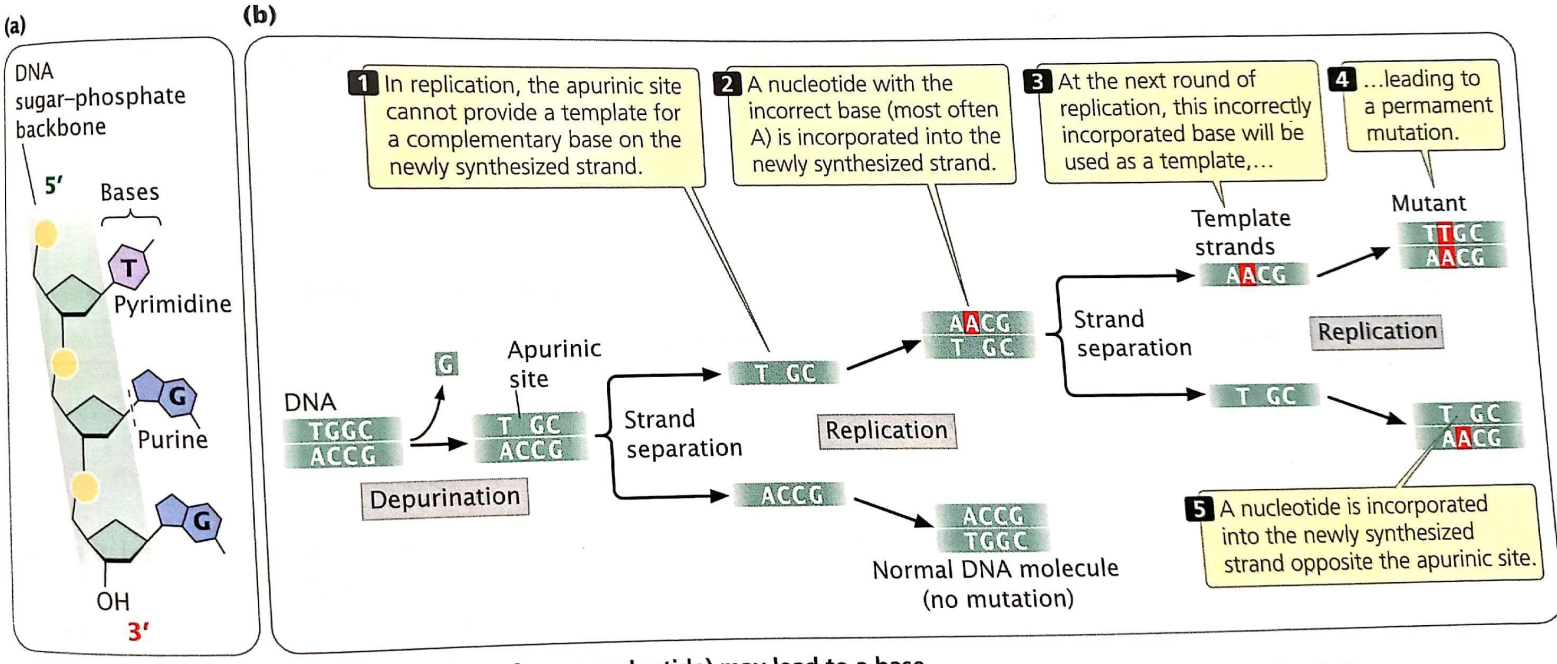
18.10 Nonstandard base pairings can occur as a result of the flexibility in DNA structure. Thymine and guanine in their normal forms can pair through wobble. Cytosine and adenine can pair through wobble when adenine is protonated (has an extra hydrogen atom).



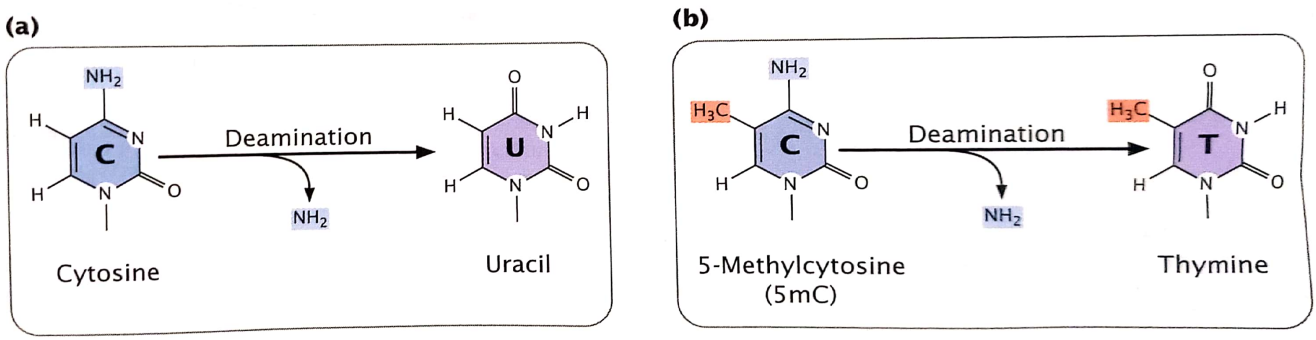
18.12 Insertions and deletions may result from strand slippage.



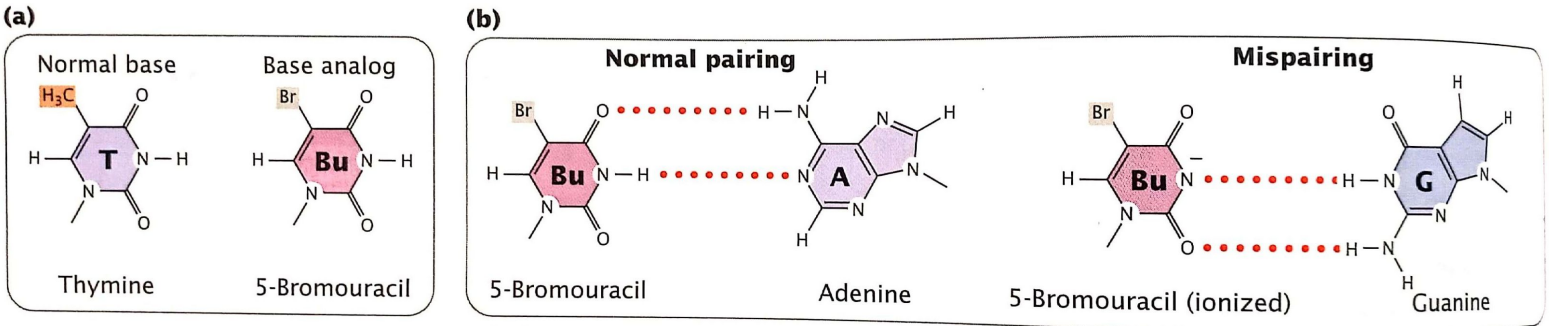
18.13 Unequal crossing over produces insertions and deletions.



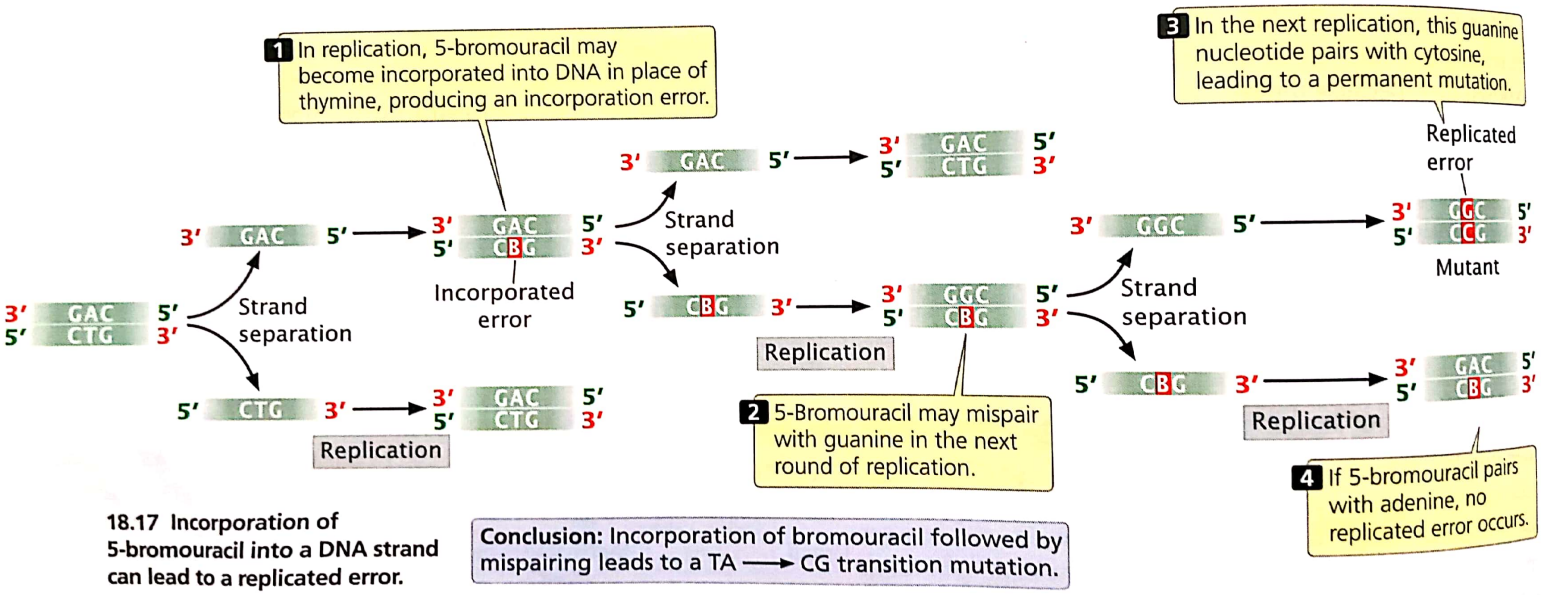
18.14 Depurination (the loss of a purine base from a nucleotide) may lead to a base substitution. (a) Depurination occurs when the covalent bond connecting a purine to the 1′ carbon of the sugar is broken (indicated by dotted red line). (b) Replication of a template strand with an apurinic site may lead to an incorporated error.



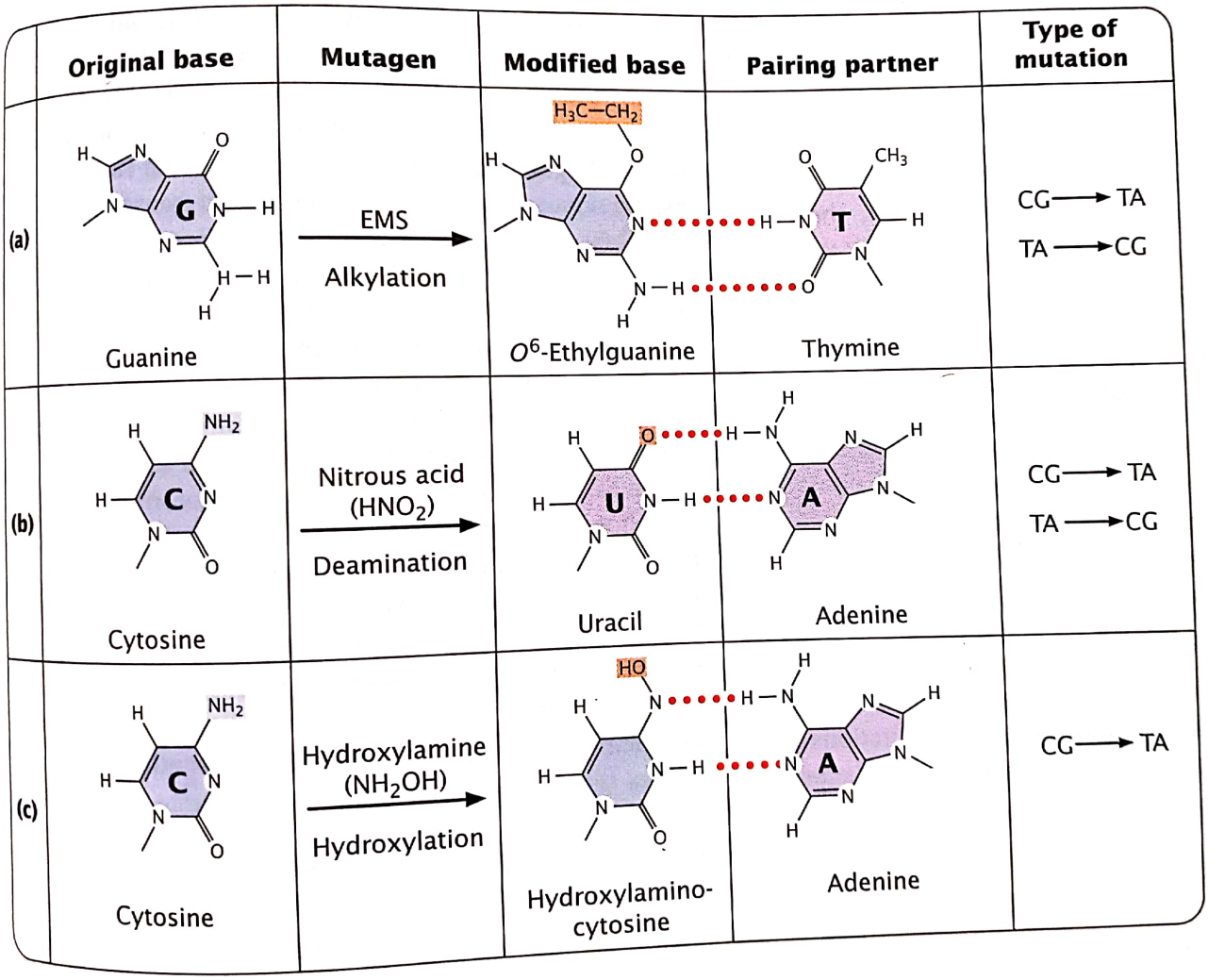
18.15 **Deamination alters DNA bases.**



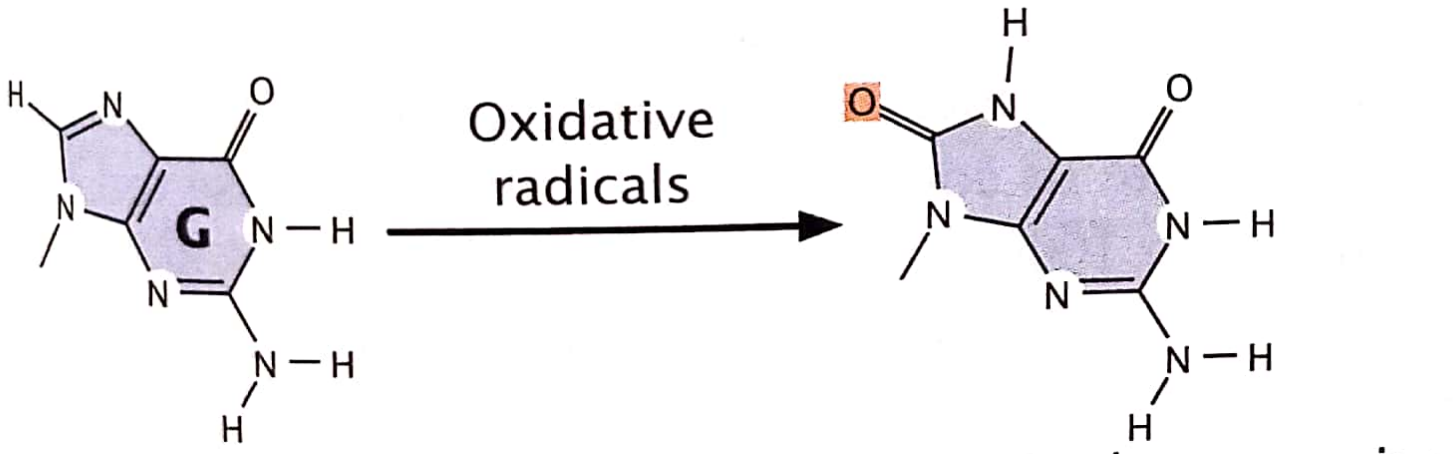
18.16 5-Bromouracil (a base analog) resembles thymine, except that it has a bromine atom in place of a methyl group on the 5-carbon atom. Because of the similarity in their structures, 5-bromouracil may be incorporated into DNA in place of thymine. Like thymine, 5-bromouracil normally pairs with adenine, but when ionized, it may pair with guanine through wobble.



18.17 Incorporation of 5-bromouracil into a DNA strand can lead to a replicated error.



18.18 Chemicals may alter DNA bases. Shown here are some examples of mutations produced by chemical agents.



18.19 Oxidative radicals convert guanine into 8-oxy-7,8-dihydrodeoxyguanine.