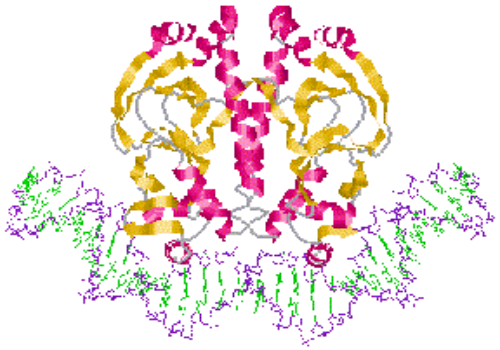
Gene mutation, DNA repair and transposition



Prof. Dr. İsmail AKYOL
Prof. Dr. M. Ali YILDIZ
Prof. Dr. M. Muhip ÖZKAN
Ankara Üniversitesi

Outline of course

- Mutations comprise any change in the nucleotide sequence of an organism’s genome.
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- Mutations are a source of genetic variation and provide the raw material for natural selection.
- Mutations have a wide range of effects on organisms depending on the type of base-pair alteration, the location of the mutation within the chromosome, and the function of the affected gene product.
- Mutations can occur spontaneously as a result of natural biological and chemical processes, or they can be induced by external factors, such as chemicals or radiation.

Outline of course

- Single-gene mutations cause a wide variety of human diseases.
- Organisms rely on a number of DNA repair mechanisms to counteract mutations.
- Mutations in genes whose products control DNA repair lead to genome hypermutability, human DNA repair diseases, and cancers.
- Transposable elements may move into and out of chromosomes, causing chromosome breaks and inducing mutations both within coding regions and in gene-regulatory regions.

Type of Mutations

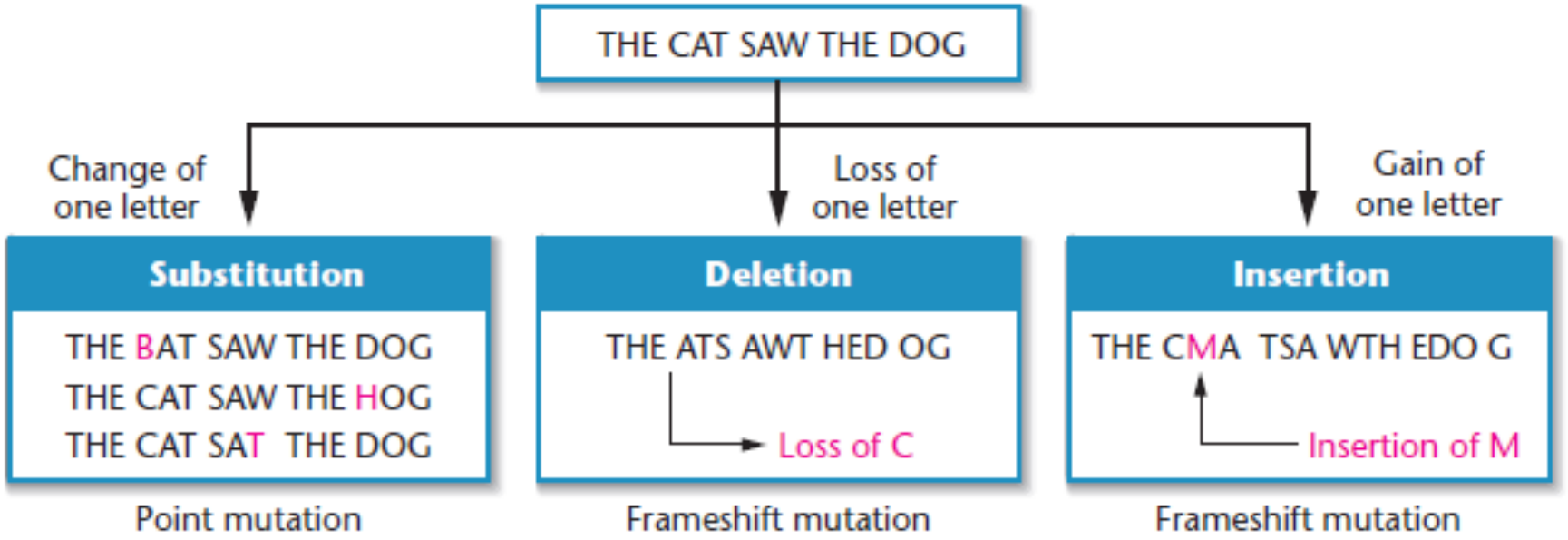


FIGURE 15.1 Analogy showing the effects of substitution, deletion, and insertion of one letter in a sentence composed of three-letter words to demonstrate point and frameshift mutations.

Mutations Occur Spontaneously and Randomly

TABLE 15.2 Spontaneous Mutation Rates at Various Loci in Different Organisms

Organism	Character	Locus	Rate*
Bacteriophage T2	Lysis inhibition	$r \rightarrow r^+$	1×10^{-8}
	Host range	$h^+ \rightarrow h$	4×10^{-9}
Escherichia coli	Lactose fermentation	$lac^- \rightarrow lac^+$	2×10^{-7}
	Streptomycin sensitivity	*str-d* → *str-s*	1×10^{-8}
Zea mays	Shrunken seeds	$sh^+ \rightarrow sh^-$	1×10^{-6}
	Purple	$pr^+ \rightarrow pr^-$	1×10^{-5}
Drosophila melanogaster	Yellow body	$y^+ \rightarrow y$	1.2×10^{-6}
	White eye	$w^+ \rightarrow w$	4×10^{-5}
Mus musculus	Piebald coat	$s^+ \rightarrow s$	3×10^{-5}
	Brown coat	$b^+ \rightarrow b$	8.5×10^{-4}

* Rates are expressed per gene replication (T2), per cell division (*Escherichia coli*), or per gamete per generation (*Zea mays*, *Drosophila melanogaster*, and *Mus musculus*).

Depurination and Deamination

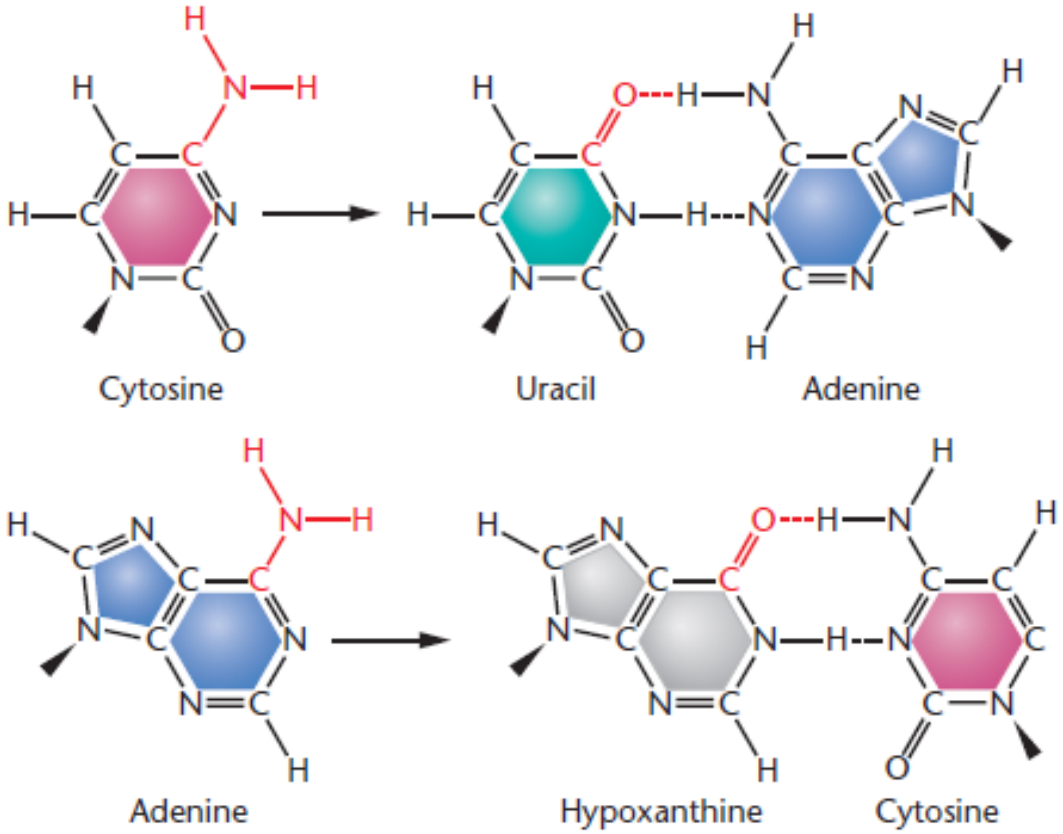


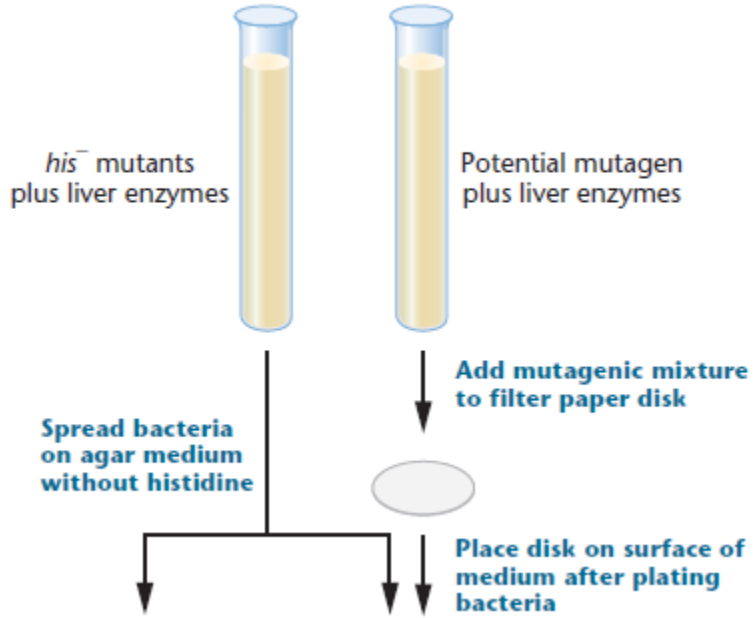
FIGURE 15.4 Deamination of cytosine and adenine, leading to new base pairing and mutation. Cytosine is converted to uracil, which base-pairs with adenine. Adenine is converted to hypoxanthine, which base-pairs with cytosine.

Single-Gene Mutations Cause a Wide Range of Human Diseases

TABLE 15.3 Examples of Human Disorders Caused by Single-Gene Mutations

Type of Mutation	Disorder	Molecular Change
Missense	Achondroplasia	Glycine to arginine at position 380 of *FGFR3* gene
Nonsense	Marfan syndrome	Tyrosine to STOP codon at position 2113 of *fibrillin-1* gene
Insertion	Familial hypercholesterolemia	Various short insertions throughout the *LDLR* gene
Deletion	Cystic fibrosis	Three-base-pair deletion of phenylalanine codon at position 508 of *CFTR* gene
Trinucleotide repeat expansions	Huntington disease	>40 repeats of (CAG) sequence in coding region of *Huntingtin* gene

The Ames Test Is Used to Assess the Mutagenicity of Compounds



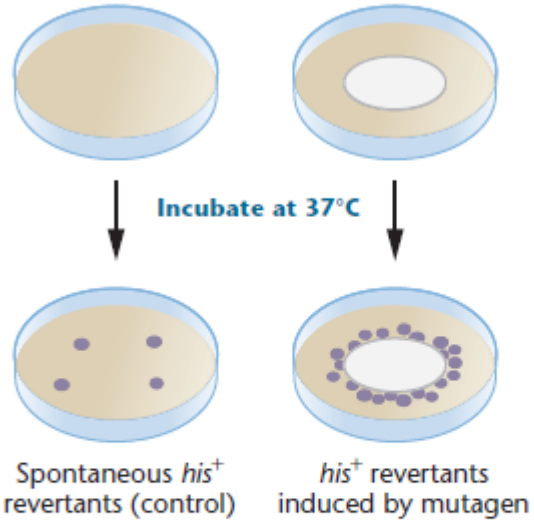


FIGURE 15.17 The Ames test, which screens compounds for potential mutagenicity. The high number of *his*$^+$ revertant colonies on the right side of the figure confirms that the substance being tested was indeed mutagenic.