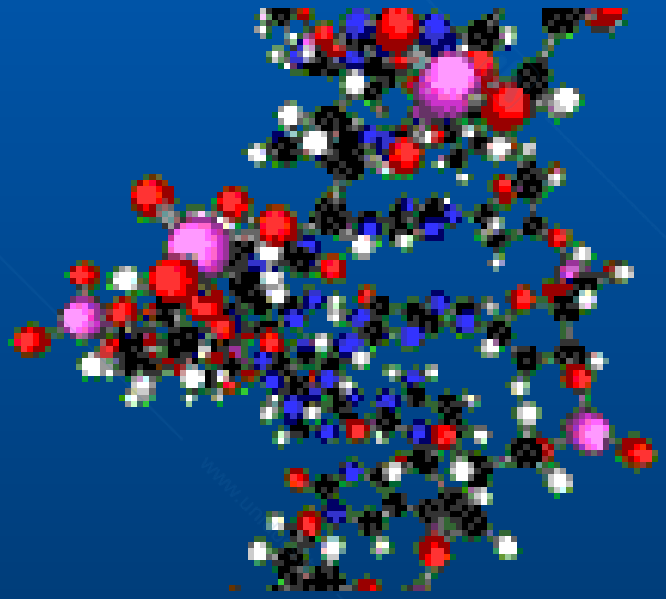
Replication and Maintenance of Genomic DNA

January 29, 2004



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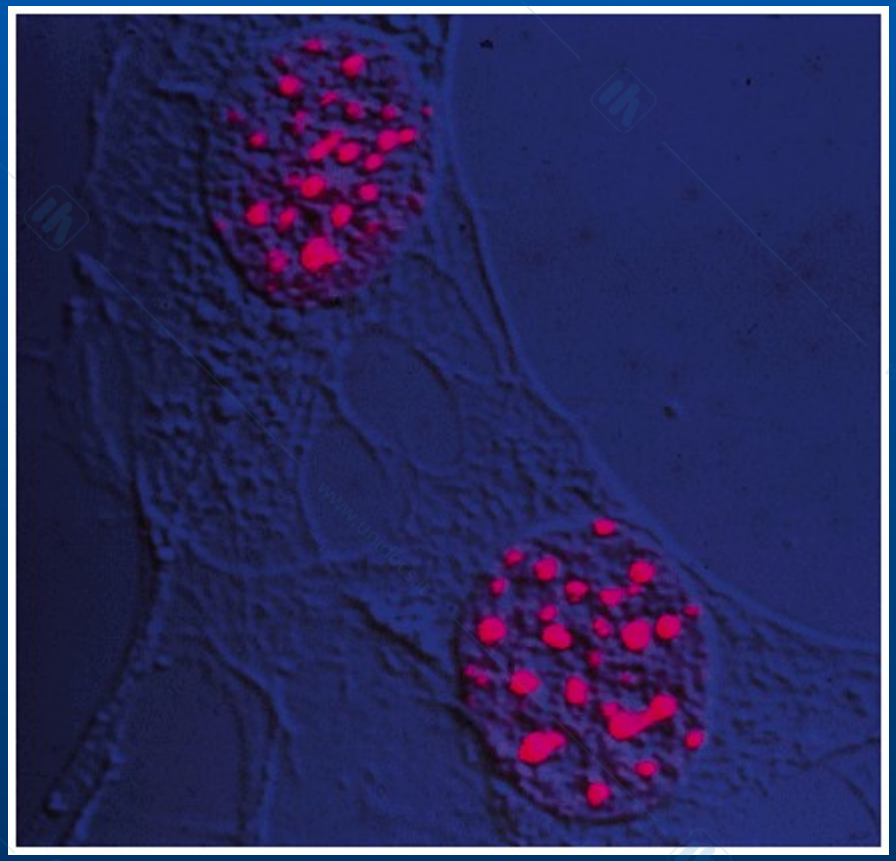
Multiple Sites of DNA Replication



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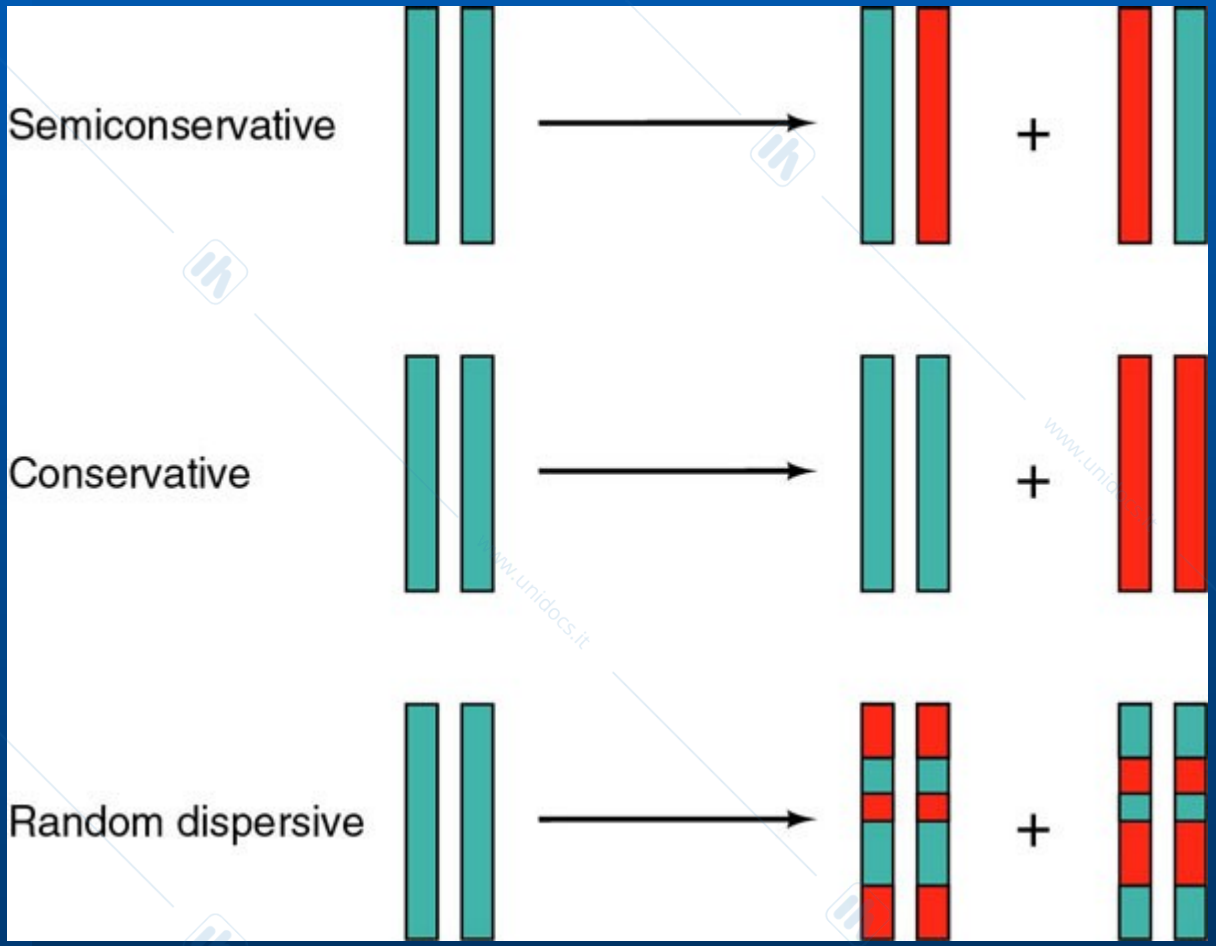
Possible Mechanisms of DNA Replication



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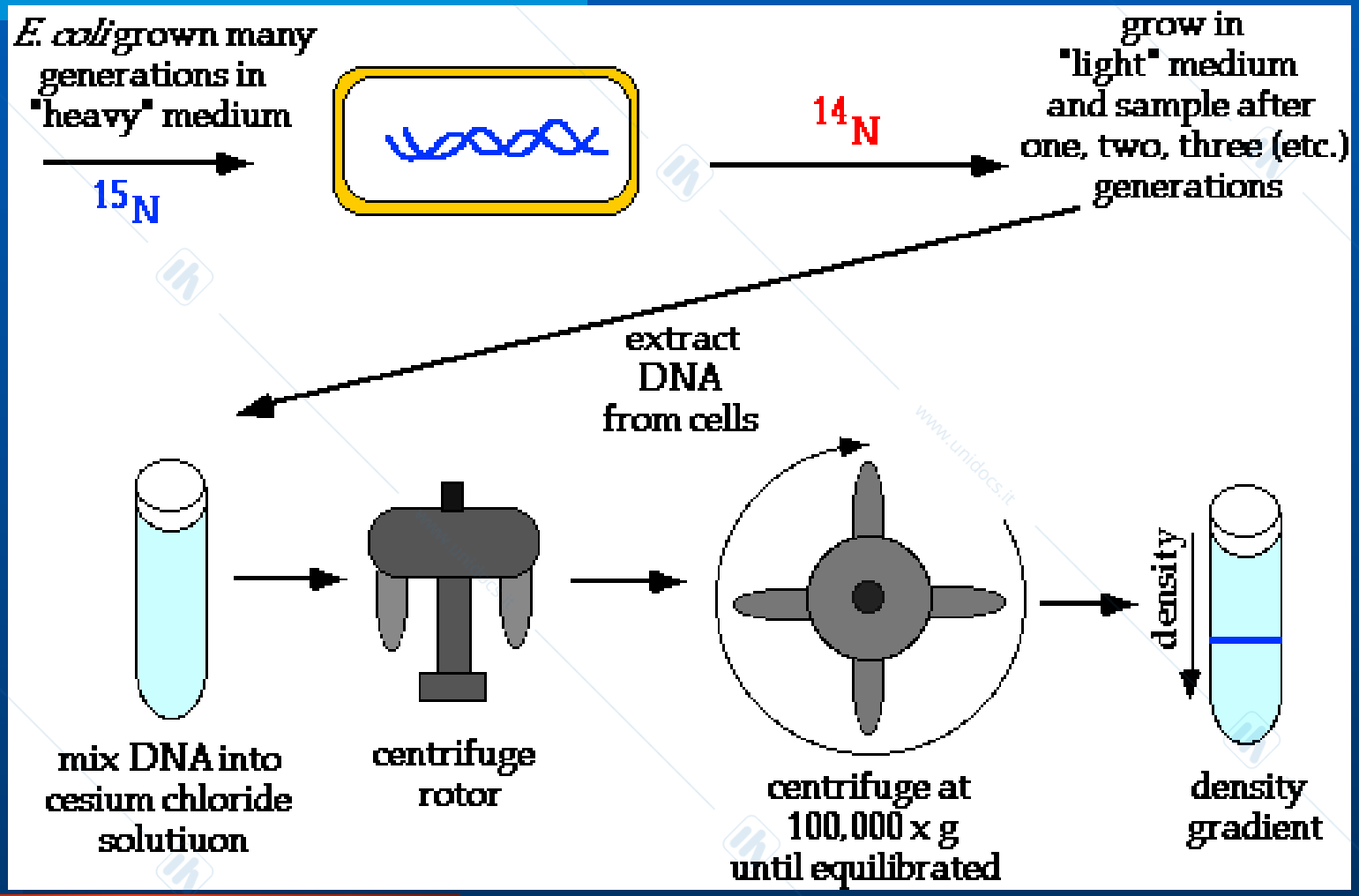
Meselson and Stahl



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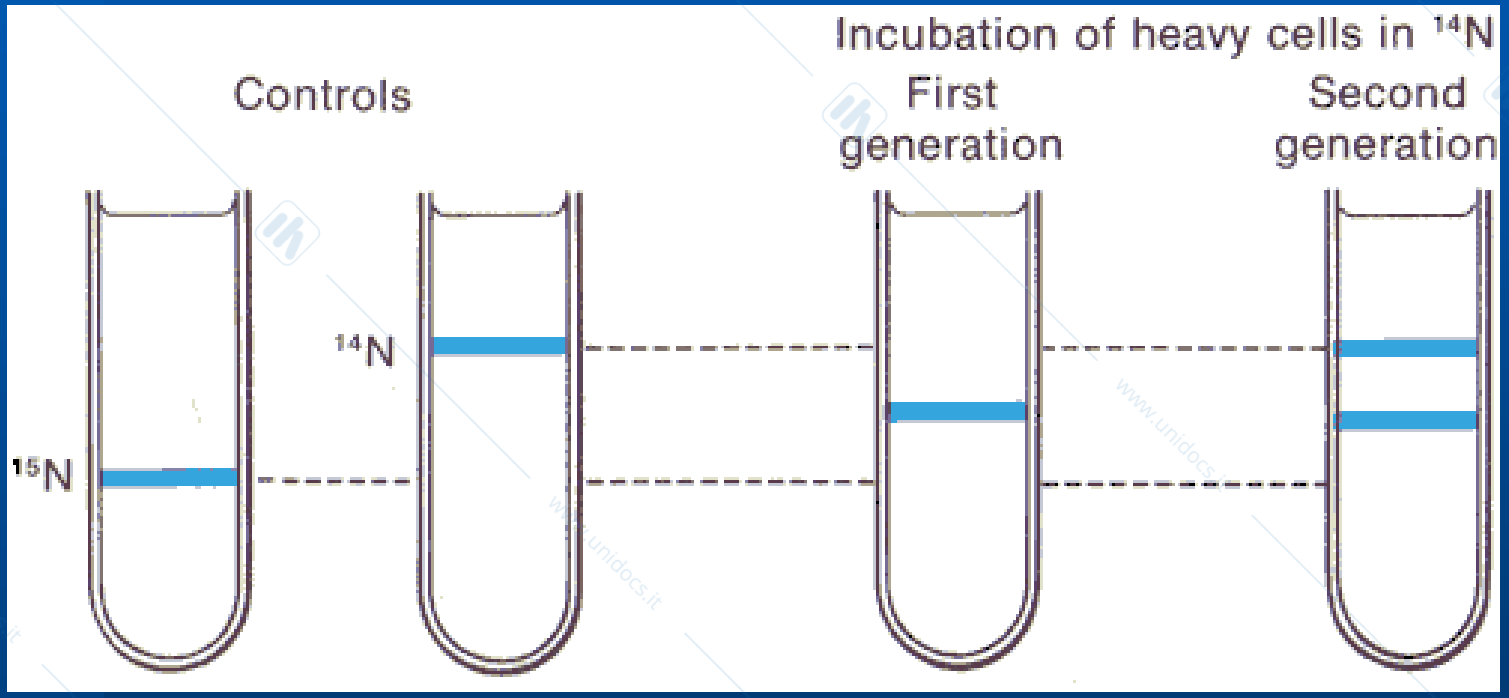
Meselson and Stahl



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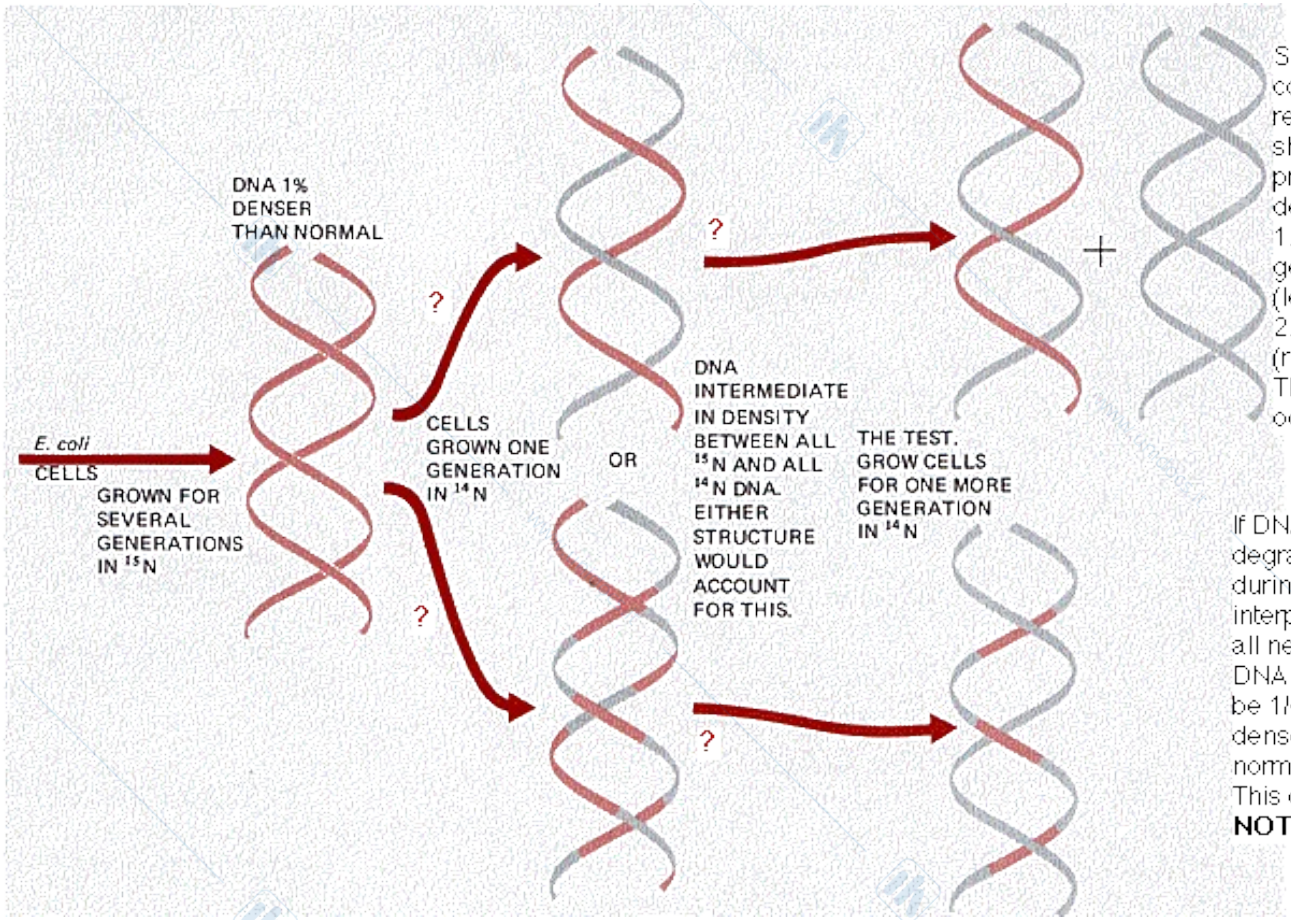

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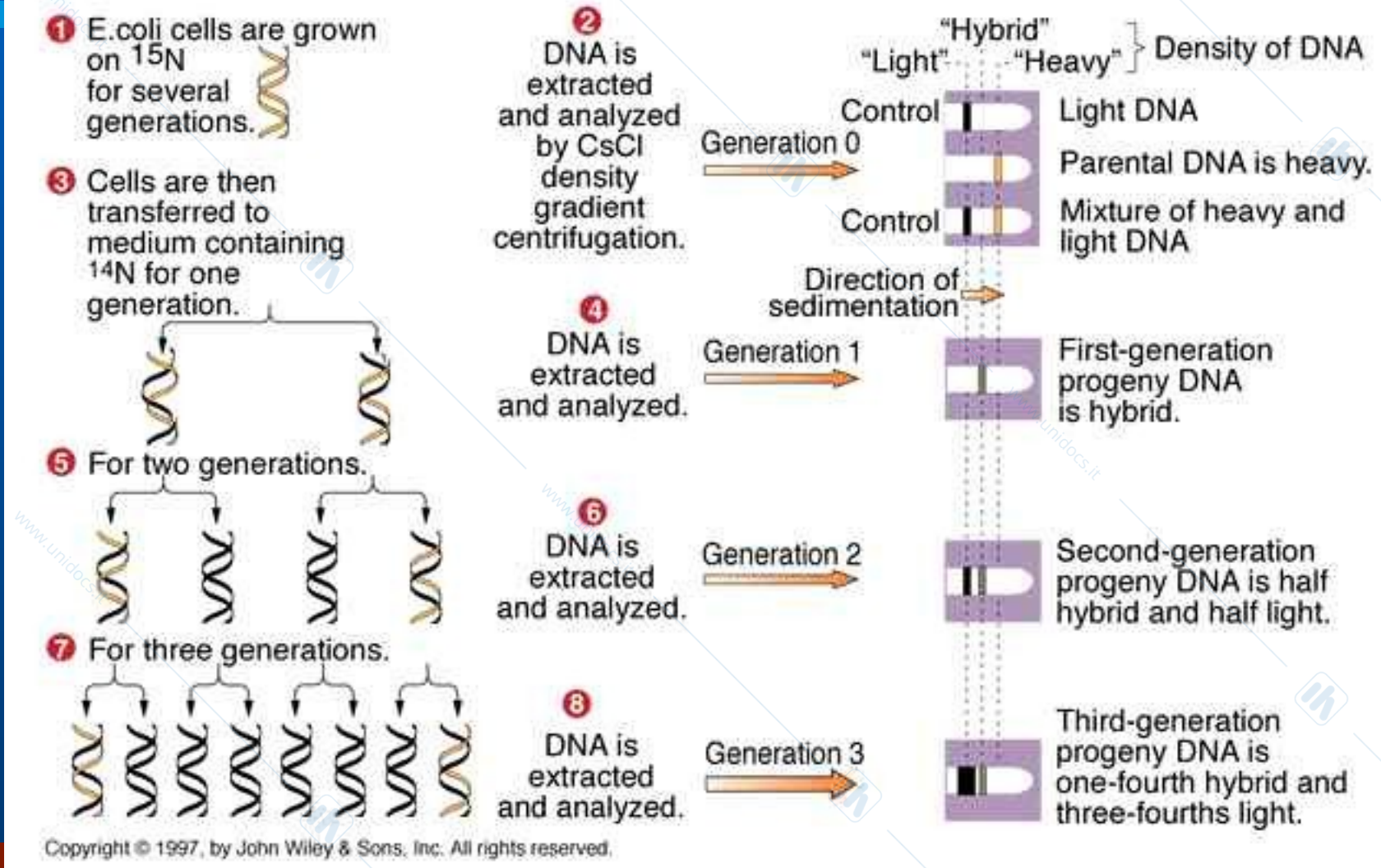

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Fig 6 Meselson and Stahl

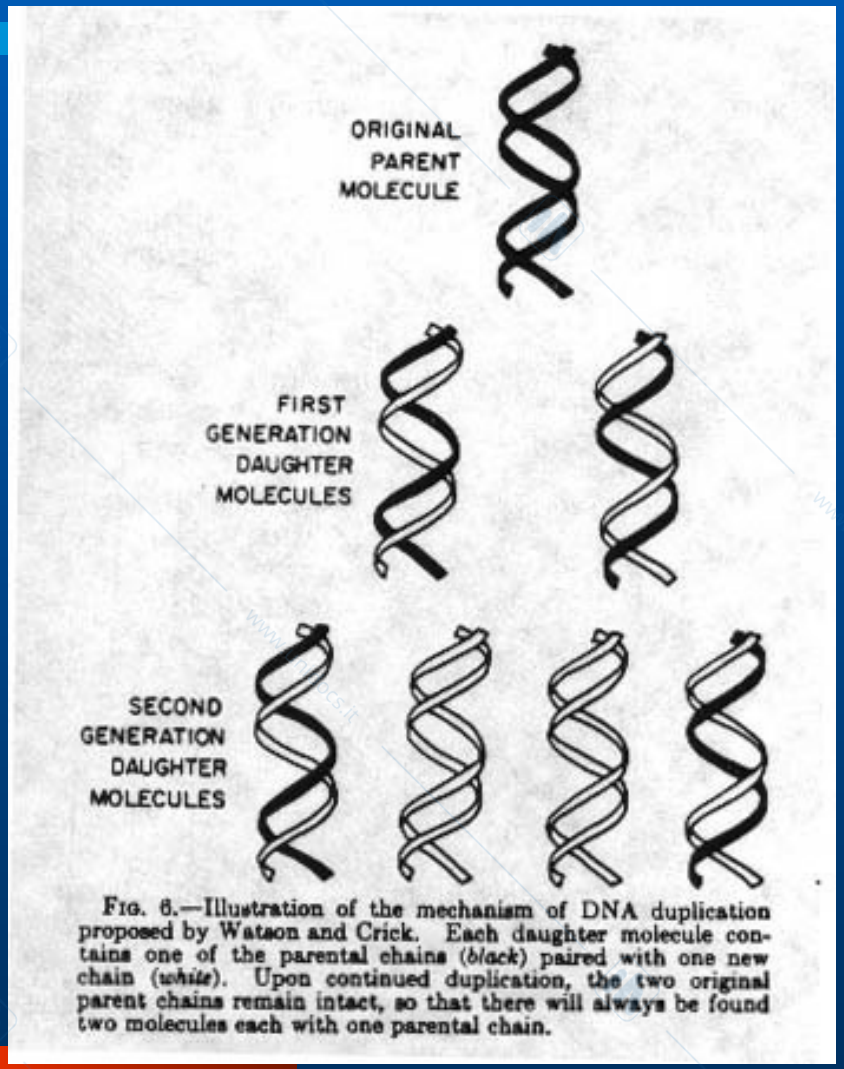

FIG. 6.—Illustration of the mechanism of DNA duplication proposed by Watson and Crick. Each daughter molecule contains one of the parental chains (*black*) paired with one new chain (*white*). Upon continued duplication, the two original parent chains remain intact, so that there will always be found two molecules each with one parental chain.

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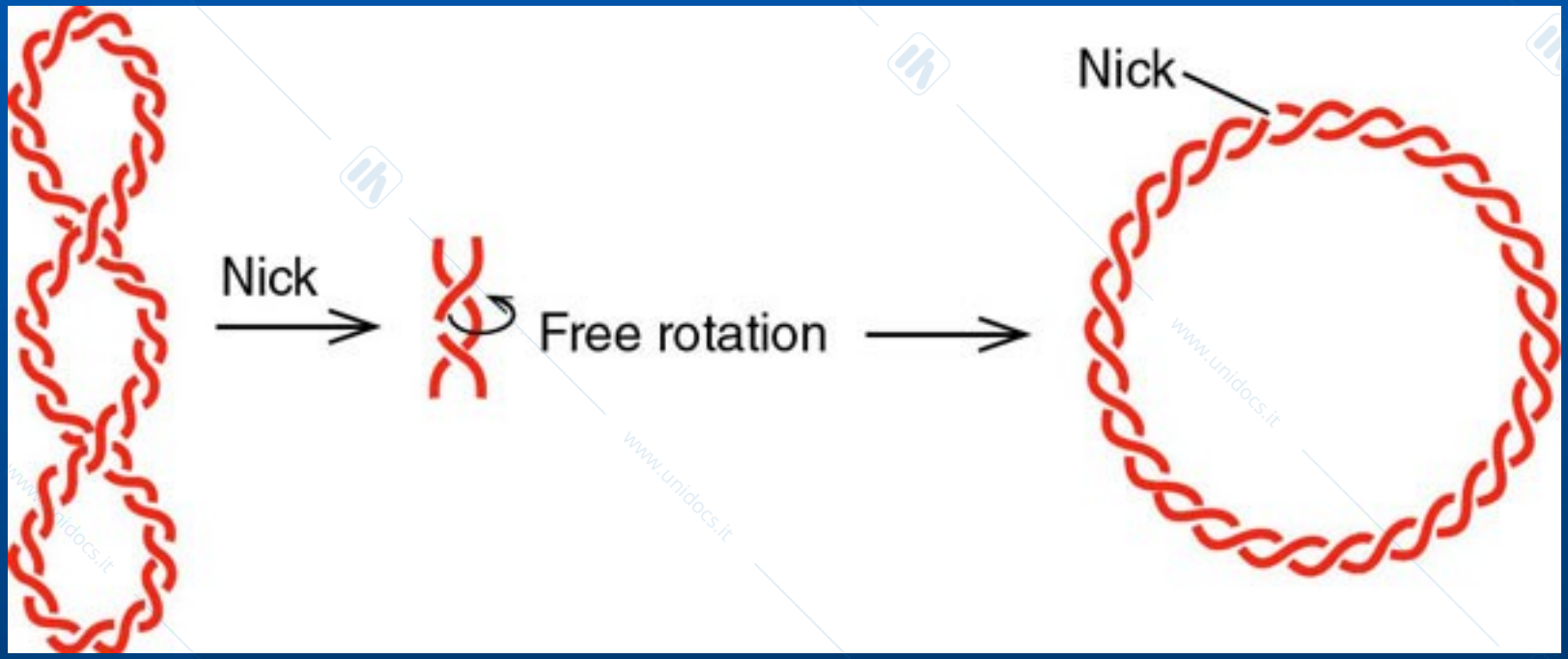
Topoisomerase I



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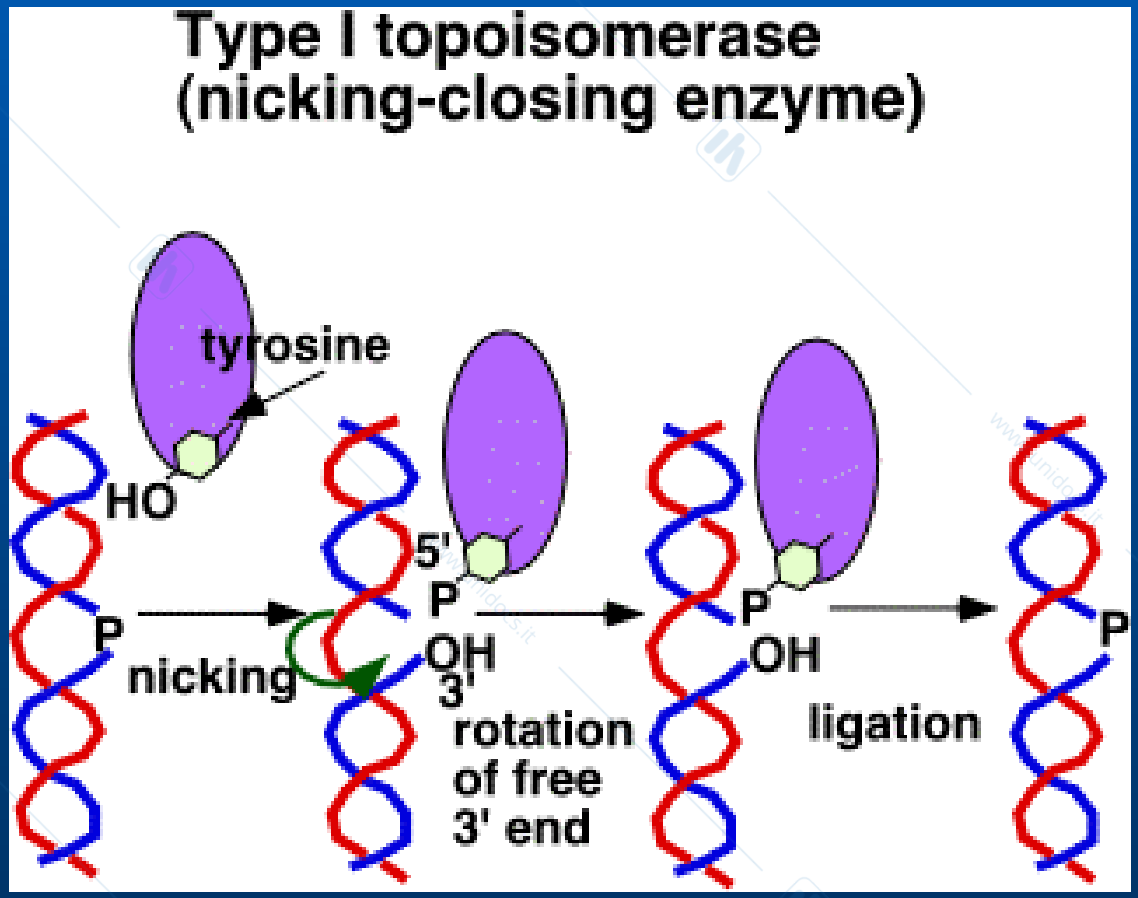

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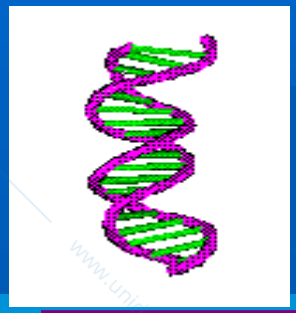

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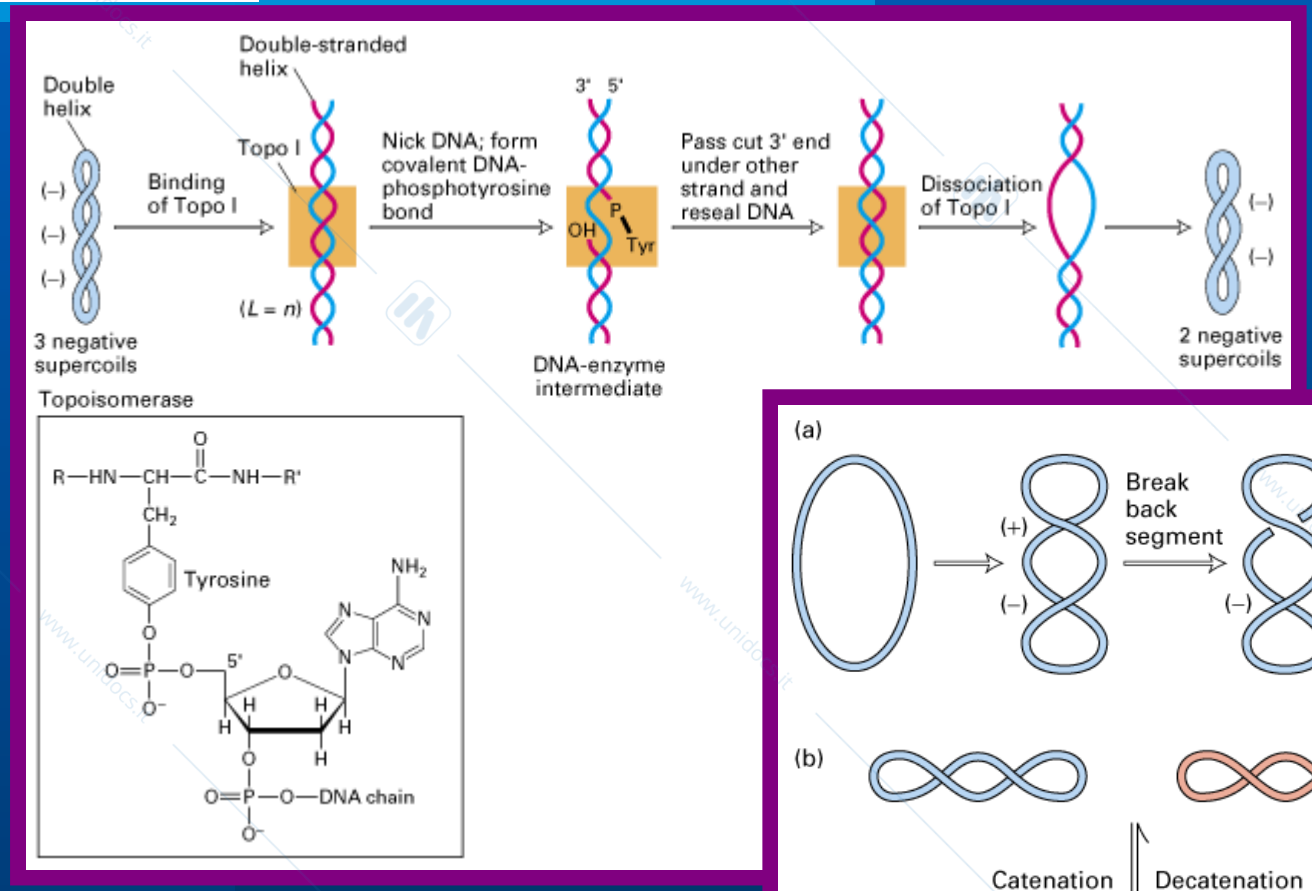

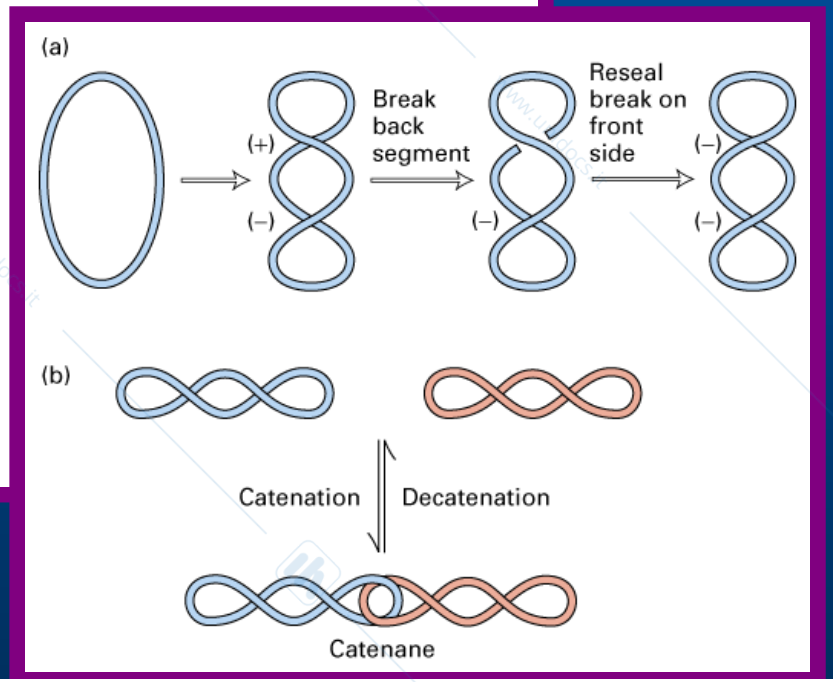

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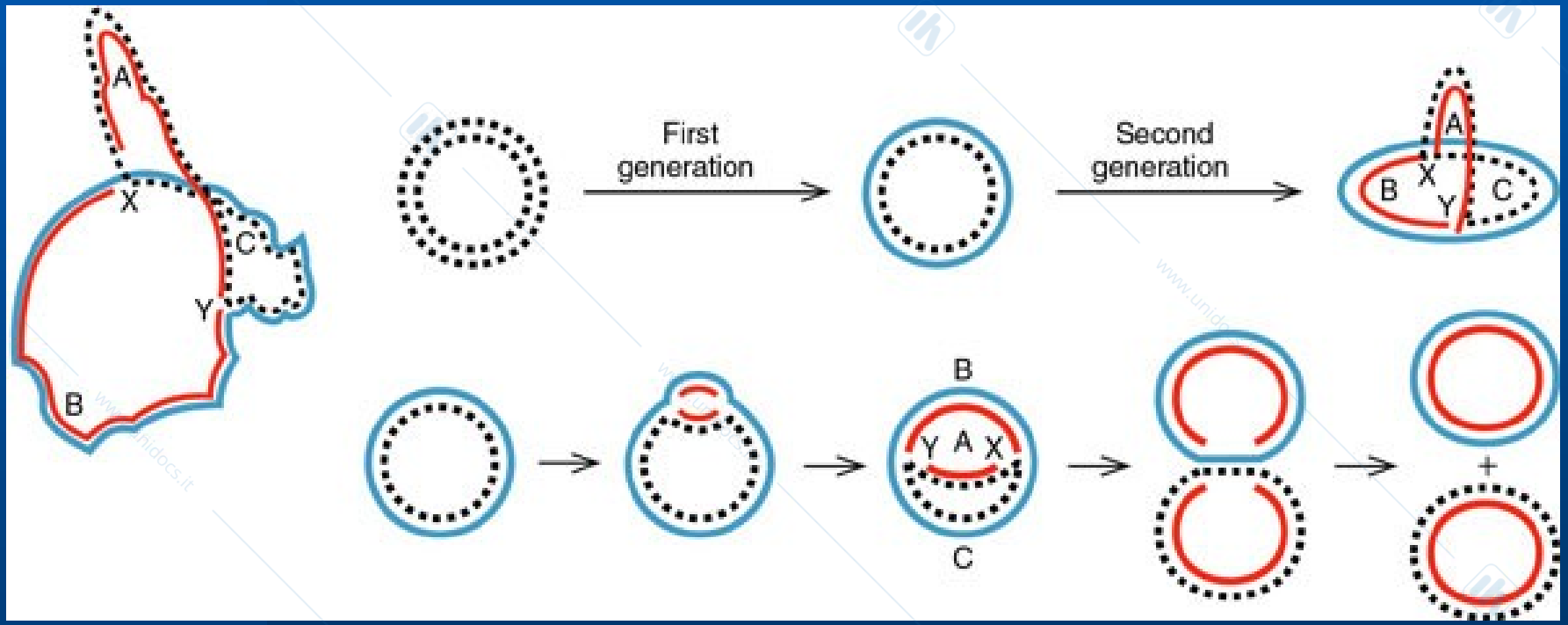
Bidirectional Replication



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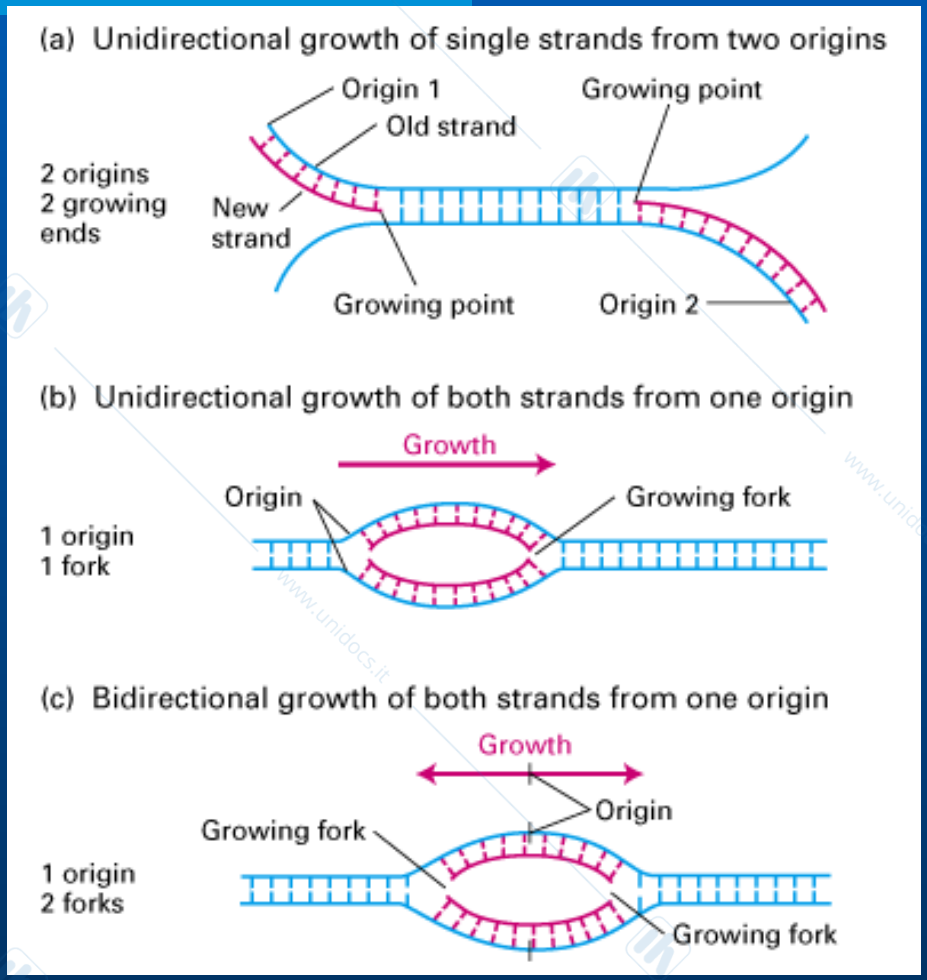
Growth of Linear Replication



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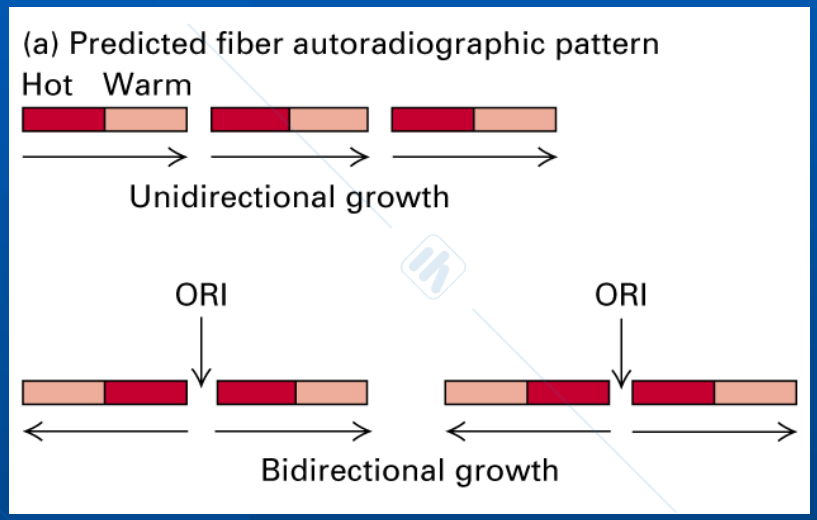
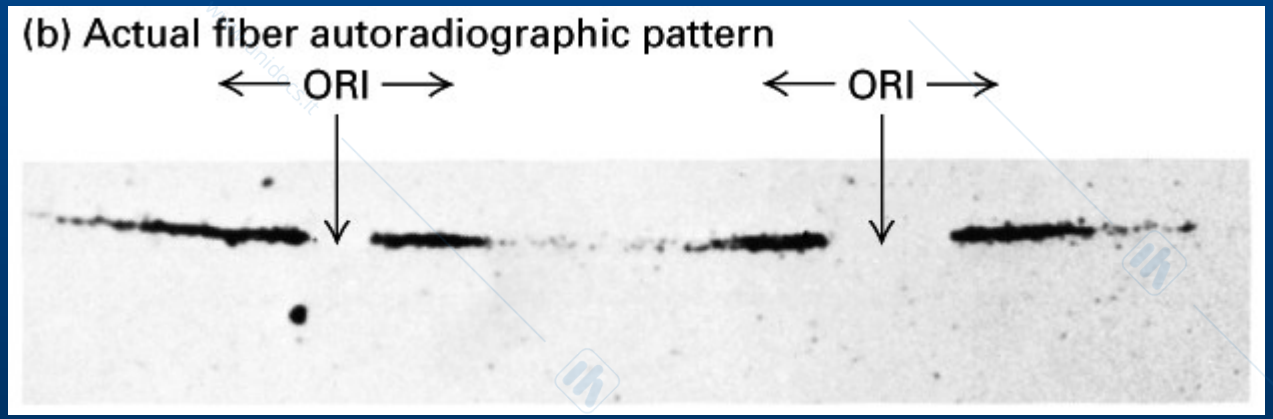
Bidirectional Replication from Origins of Replication





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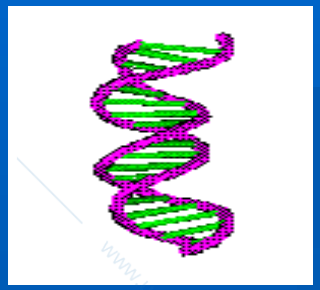

Quantitative Parameters (after Mathews and vanHolde)

Feature	Prokarotic (*E. coli*)	Eukaryotic (Hela cells in culture)
DNA content (nucleotide pairs per cell)	3.9×10^6	$\sim 10^9$
DNA replication rate (nucleotides/sec/rep. fork)	850	60-90
Number of replication origins/cell	1	10^3 - 10^4
Hours for complete genome replication	0.67	8

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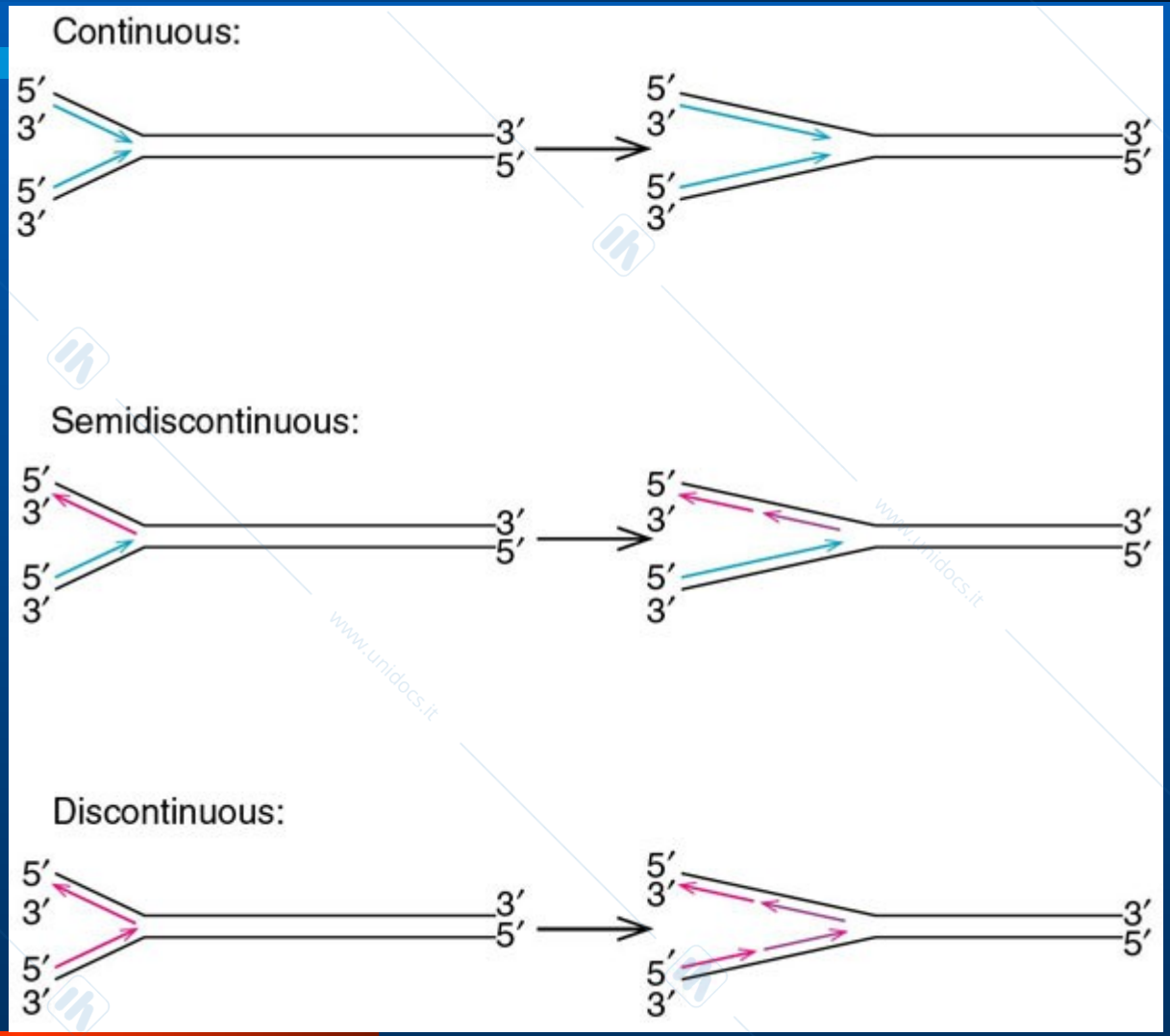
Okazaki's Hypotheses



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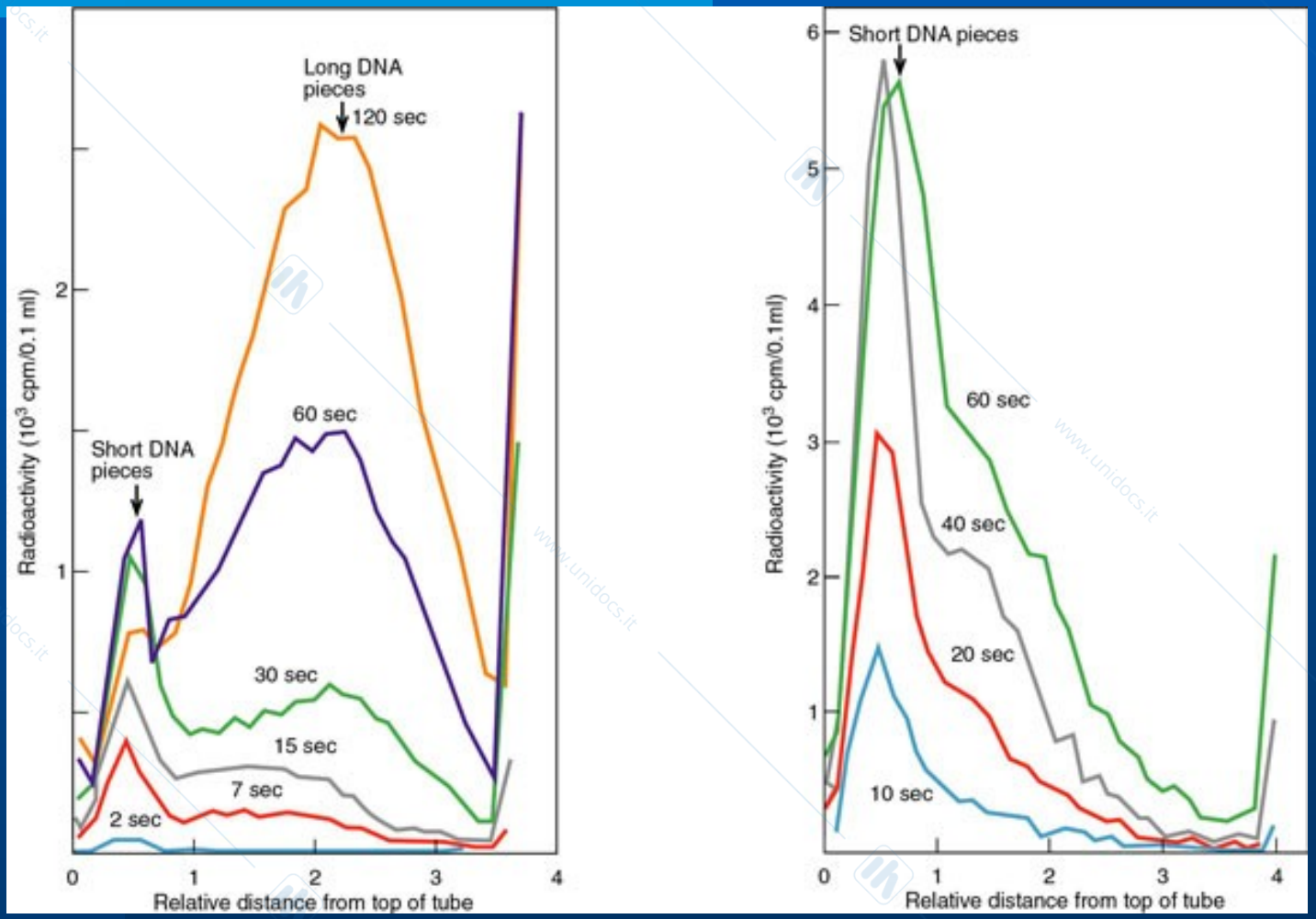
Okazaki's Data



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Replication Mechanisms

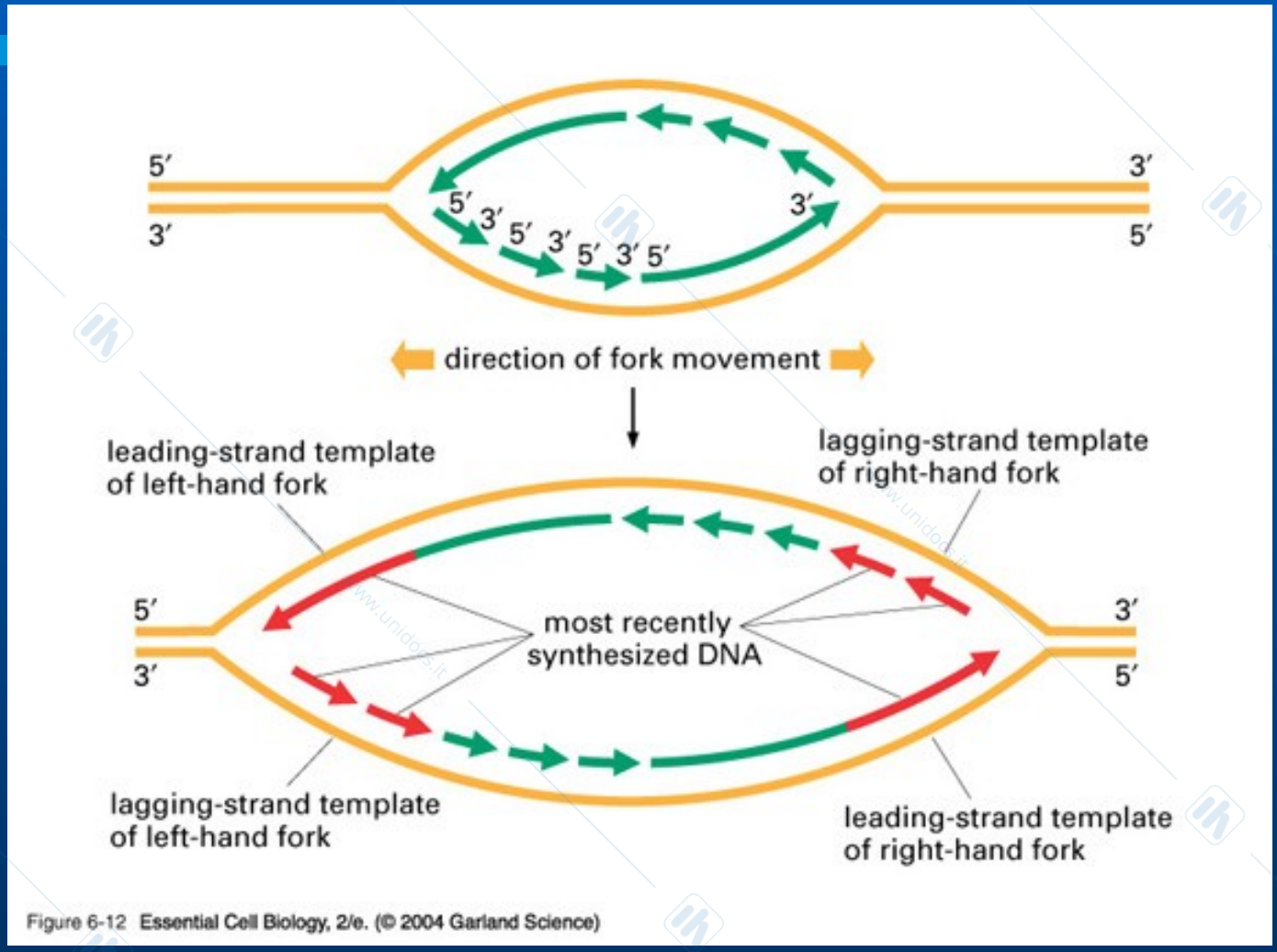

Figure 6-12 Essential Cell Biology, 2/e. (© 2004 Garland Science)

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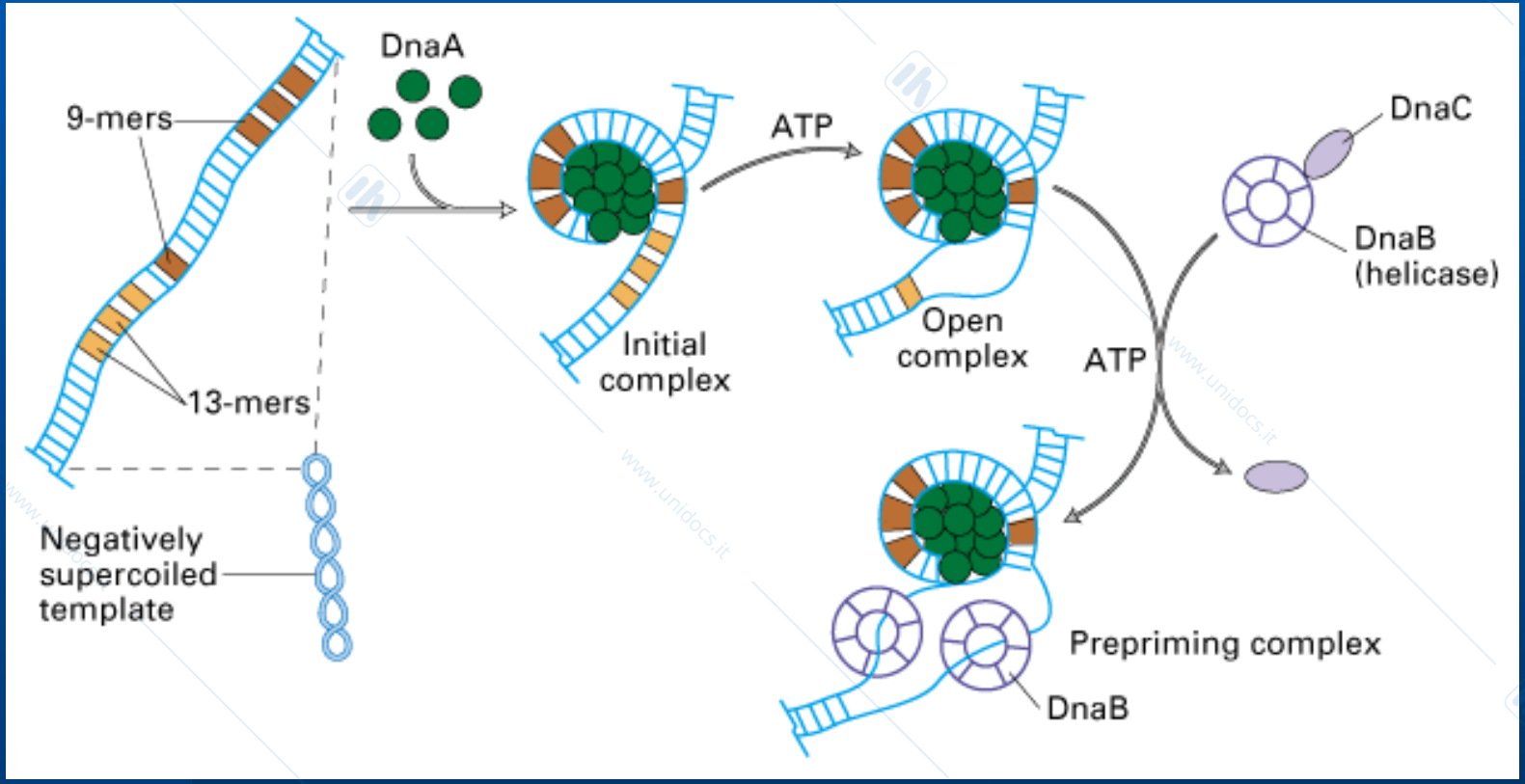
Helicase - Initiation



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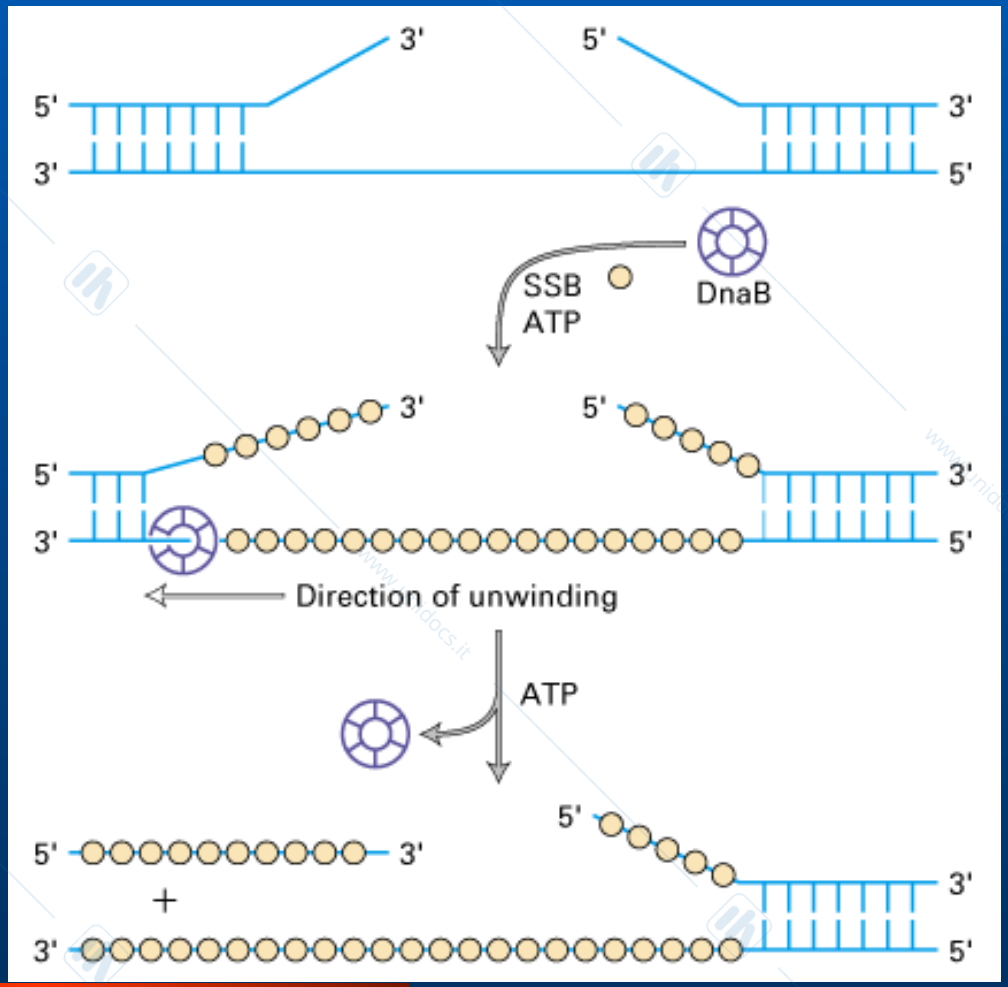
Helicase



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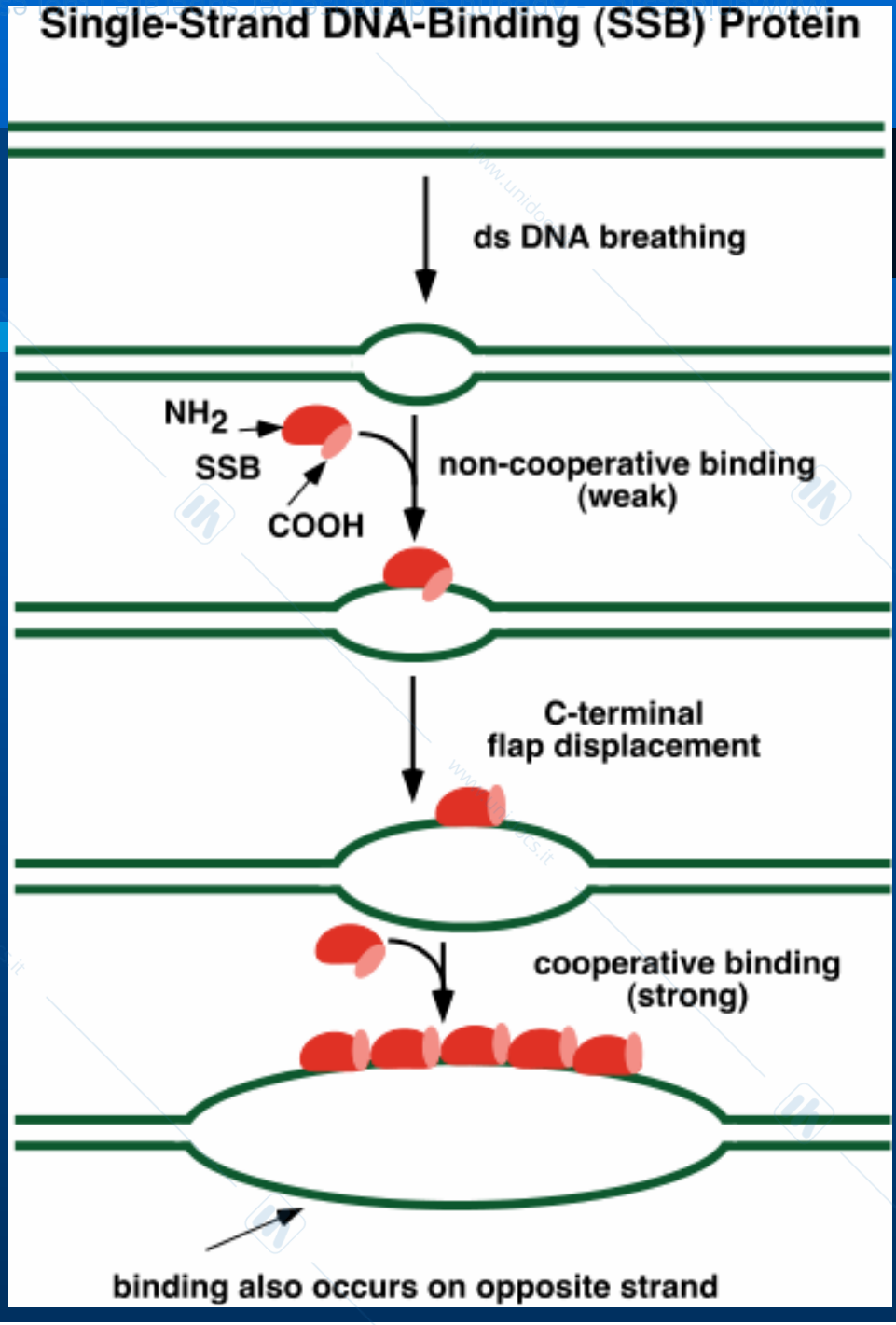
Single-strand Binding Protein



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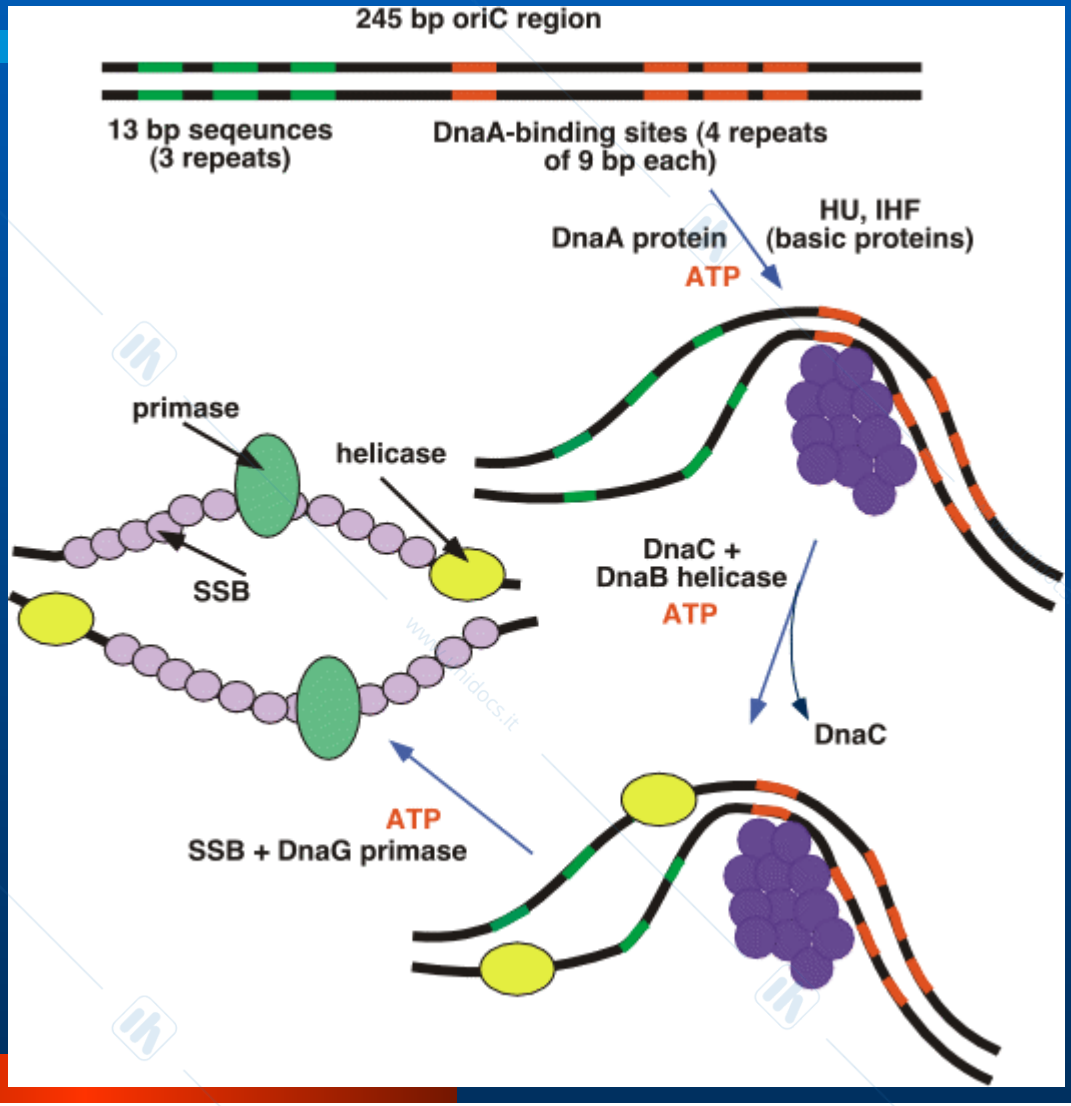
Initiation of Replication



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Replication Machinery

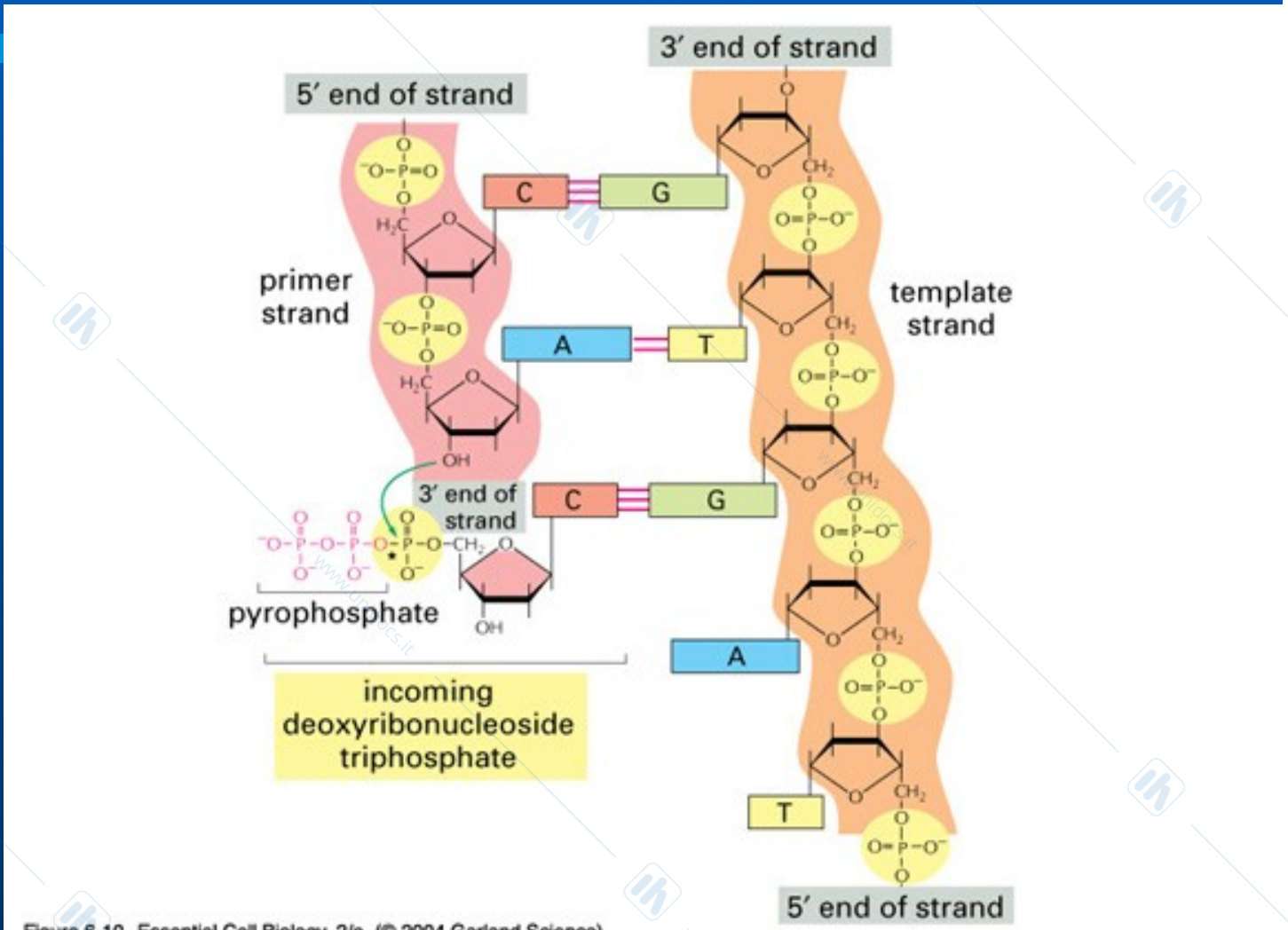

Figure 6-10 Essential Cell Biology, 2/e. (© 2004 Garland Science)

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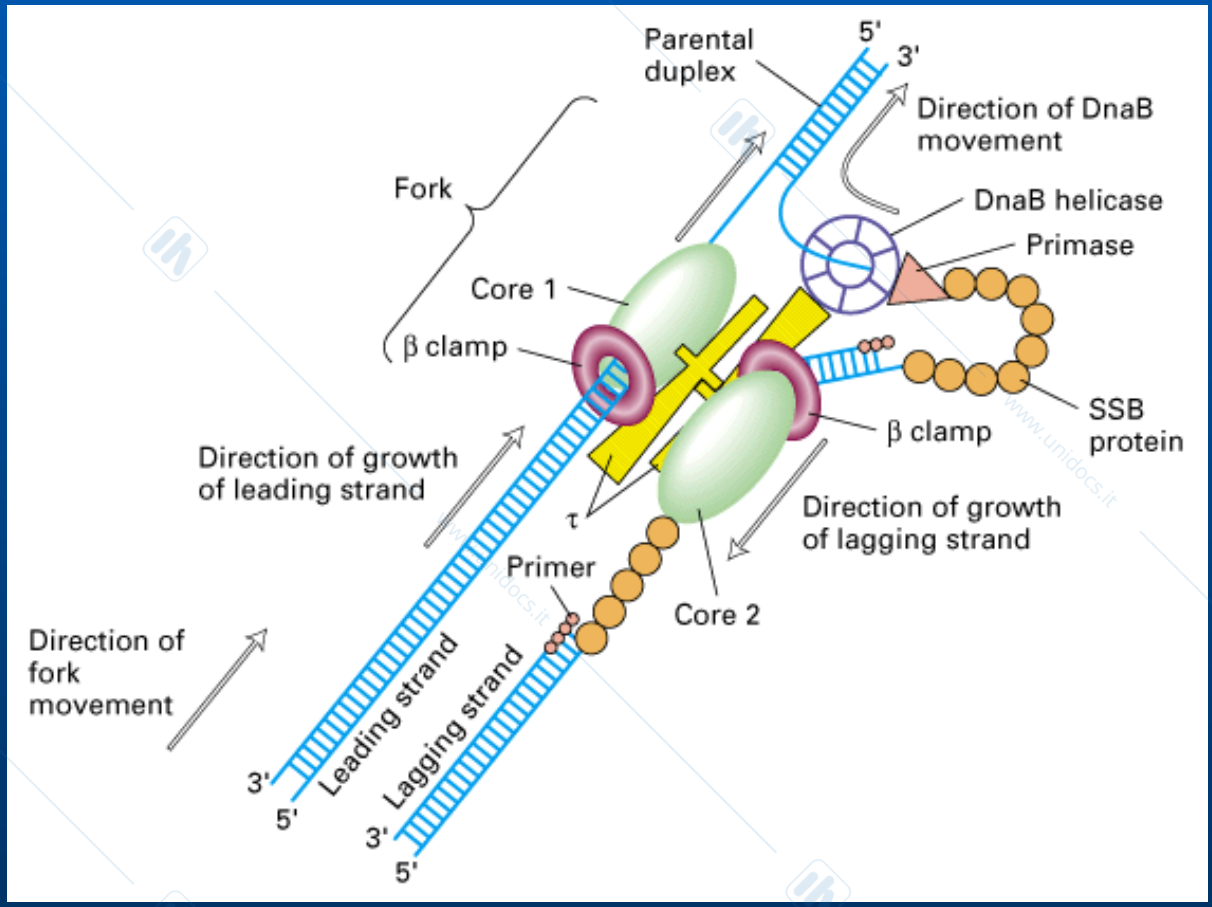
Replication Machinery



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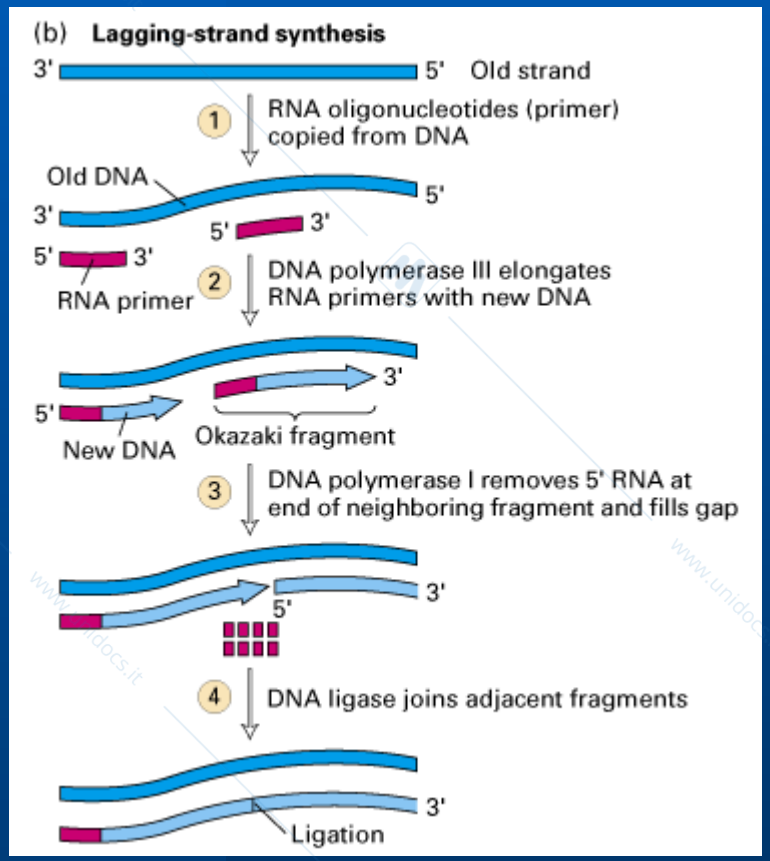
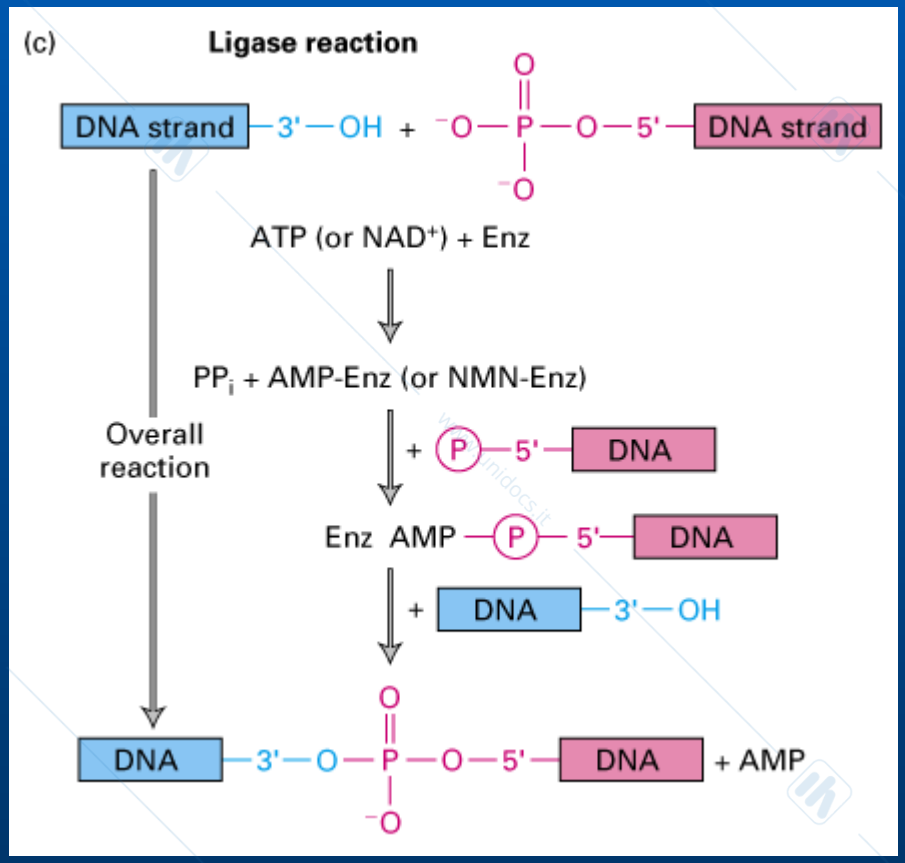
Lagging Strand Synthesis





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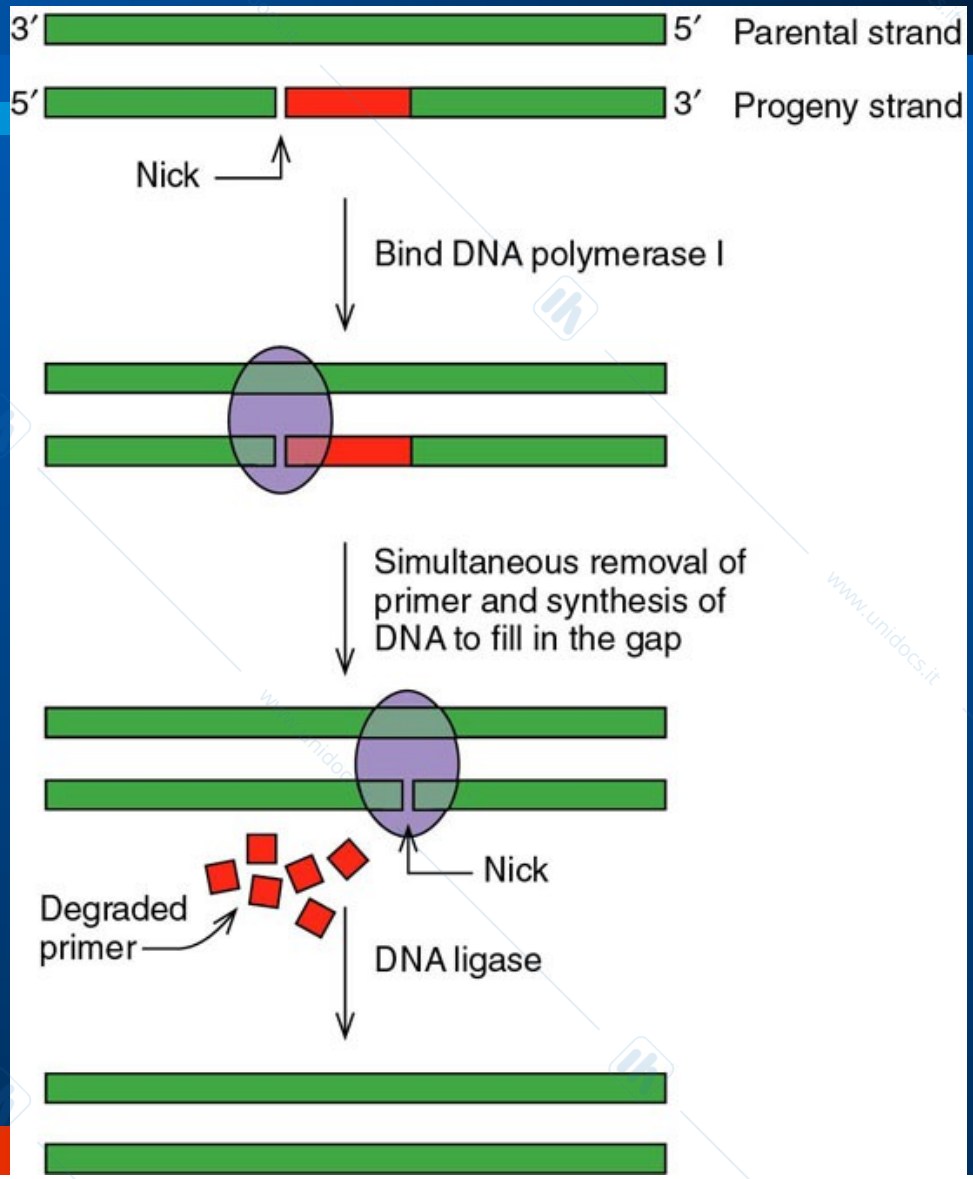
Replacement of RNA Primers



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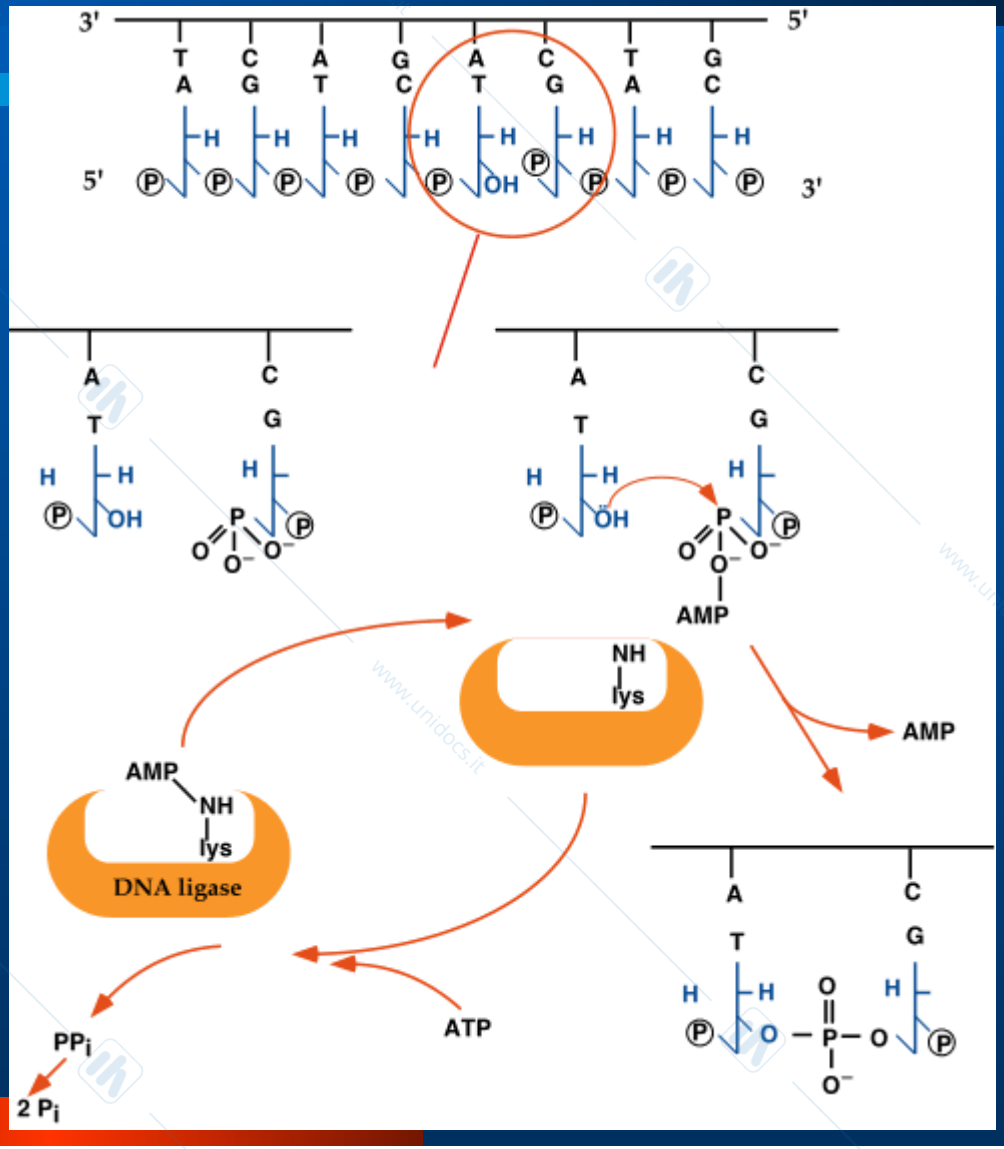
DNA Ligase



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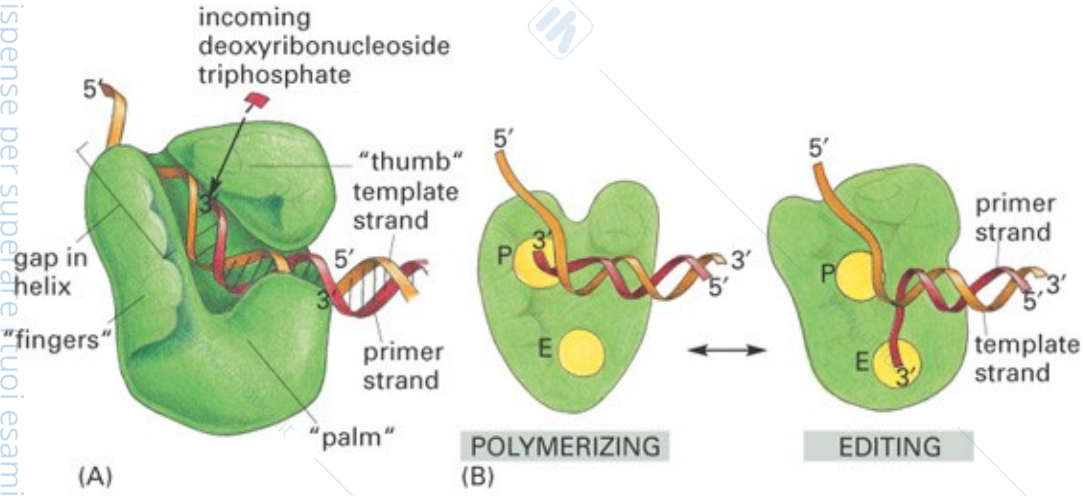
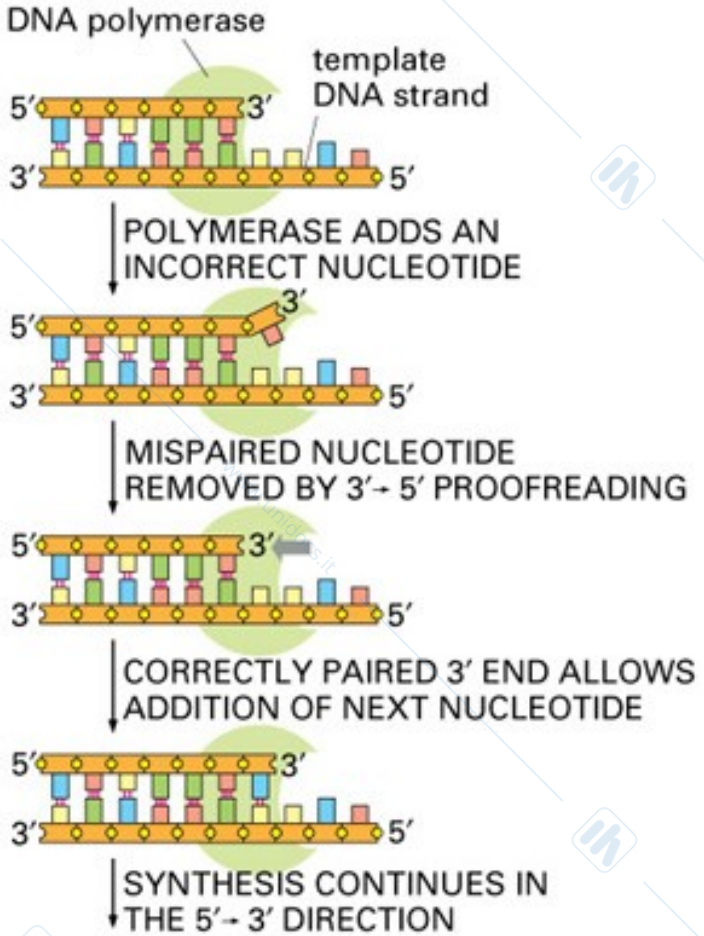


Figure 6-14 Essential Cell Biology, 2/e. (© 2004 Garland Science)



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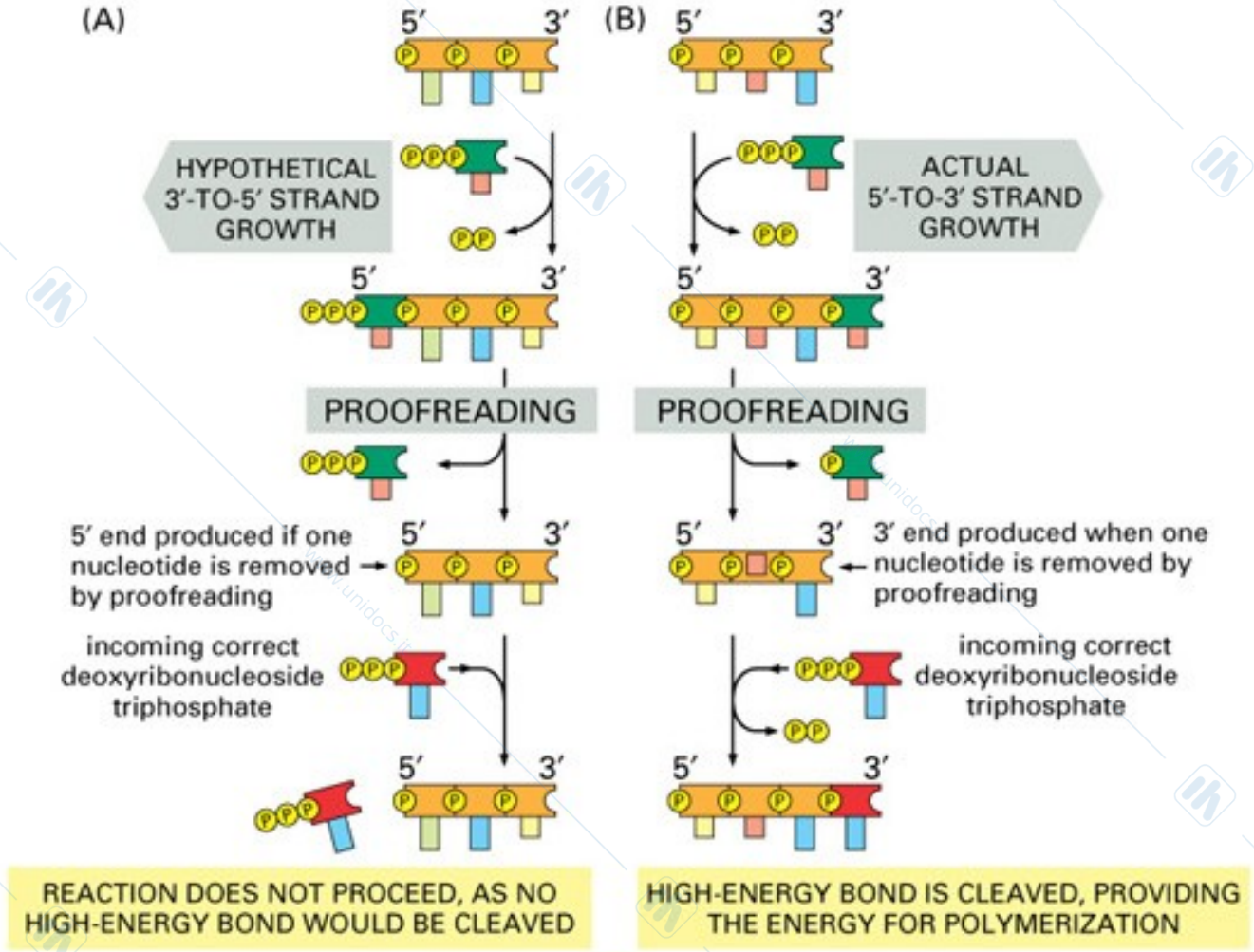

Figure 6-15 Essential Cell Biology, 2/e. (© 2004 Garland Science)

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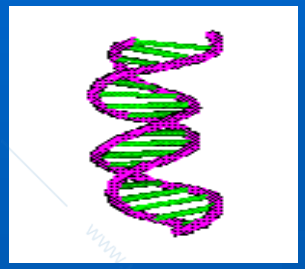

DNA Damage

TABLE 12-2 DNA Lesions That Require Repair

DNA Lesion	Example/Cause
Missing base	Removal of purines by acid and heat (under physiological conditions $\approx 10^4$ purines/day/cell in a mammalian genome); removal of altered bases (e.g., uracil) by DNA glycosylases
Altered base	Ionizing radiation; alkylating agents (e.g., ethylmethane sulfonate)
Incorrect base	Mutations affecting 3′ → 5′ exonuclease proofreading of incorrectly incorporated bases
Bulge due to deletion or insertion of a nucleotide	Intercalating agents (e.g., acridines) that cause addition or loss of a nucleotide during recombination or replication
Linked pyrimidines	Cyclotubyl dimers (usually thymine dimers) resulting from UV irradiation
Single- or double-strand breaks	Breakage of phosphodiester bonds by ionizing radiation or chemical agents (e.g., bleomycin)
Cross-linked strands	Covalent linkage of two strands by bifunctional alkylating agents (e.g., mitomycin C)
3′-deoxyribose fragments	Disruption of deoxyribose structure by free radicals leading to strand breaks

SOURCE: Adapted from A. Kornberg and T. Baker, 1992, *DNA Replication*, 2d ed., W. H. Freeman and Company, pp. 771 – 773.

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DNA Damage

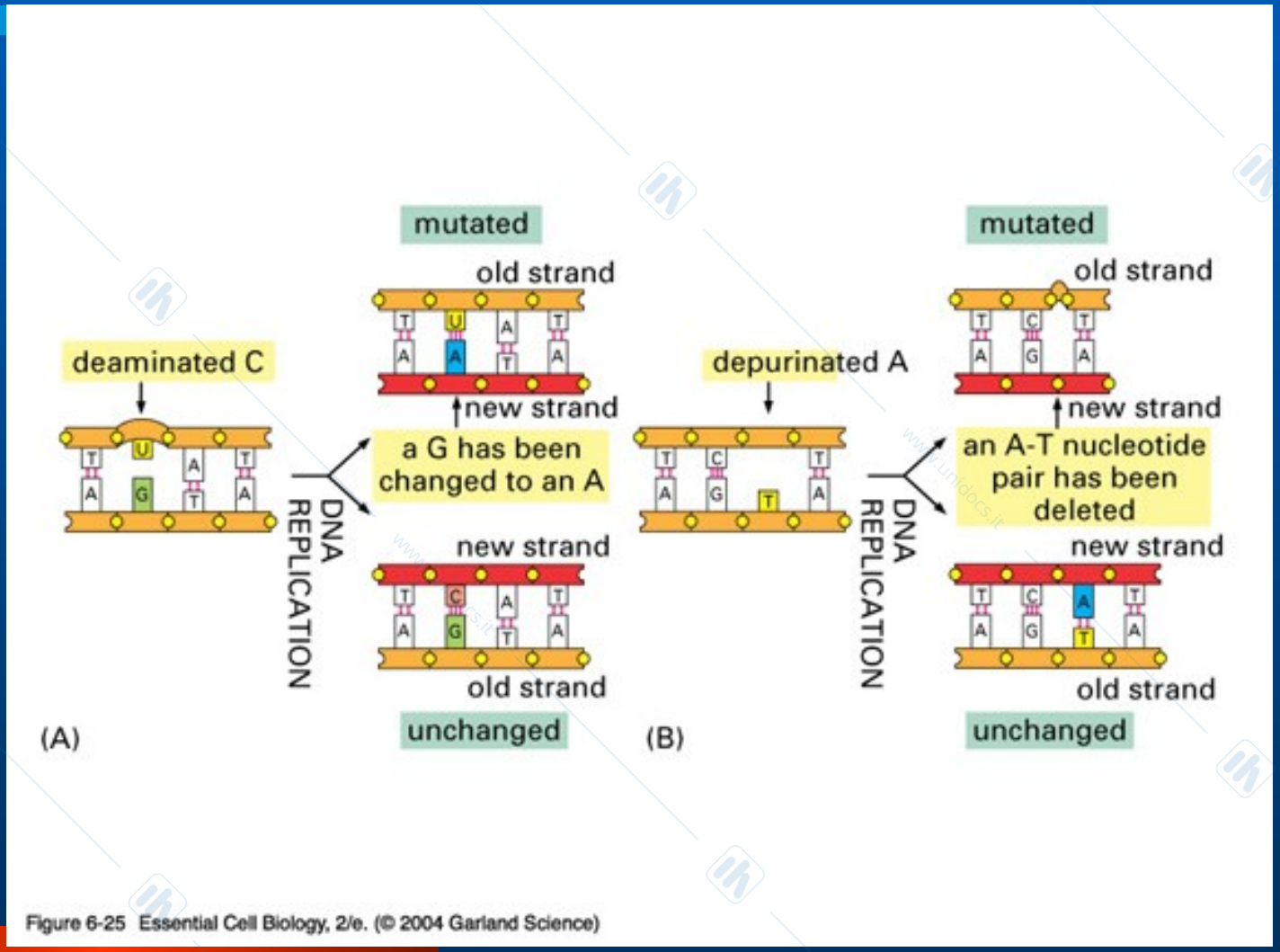

Figure 6-25 Essential Cell Biology, 2/e. (© 2004 Garland Science)

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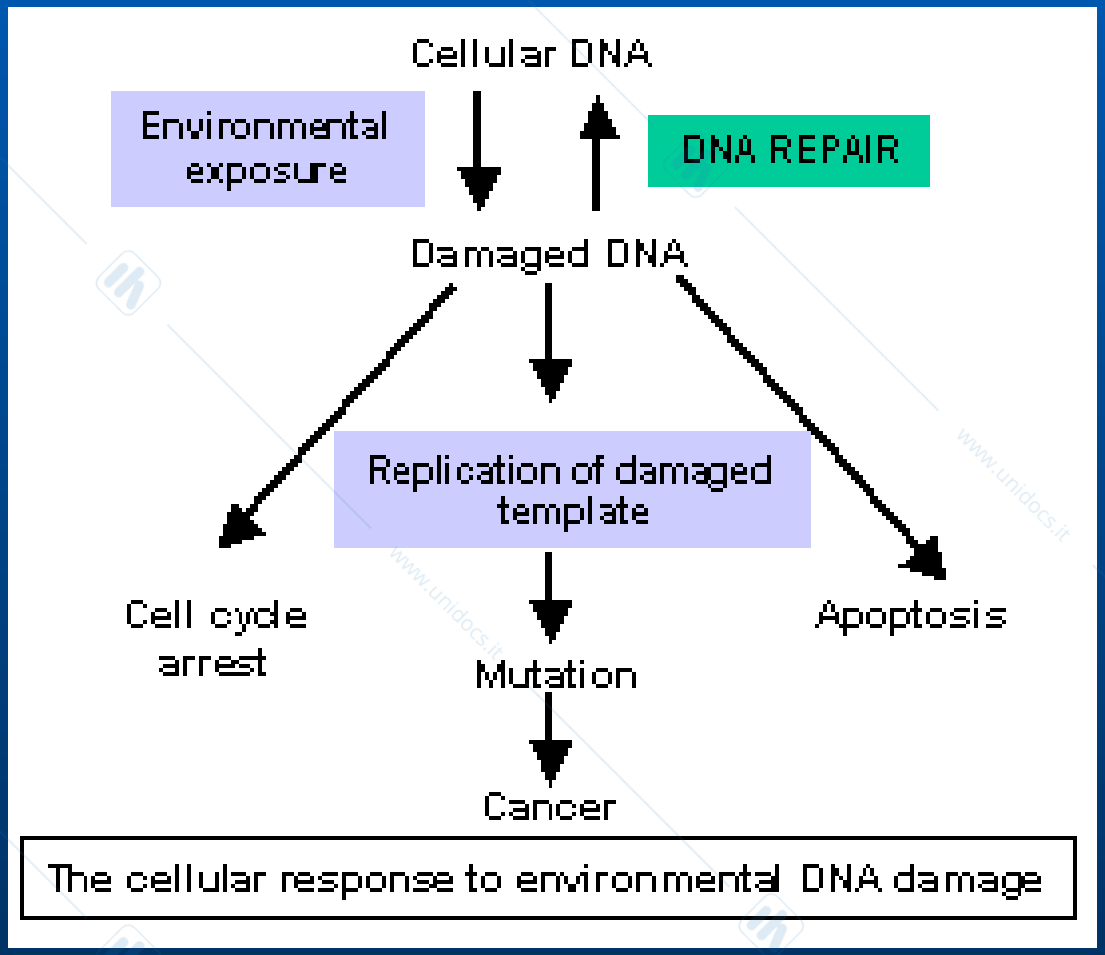
Responses To DNA Damage



The cellular response to environmental DNA damage

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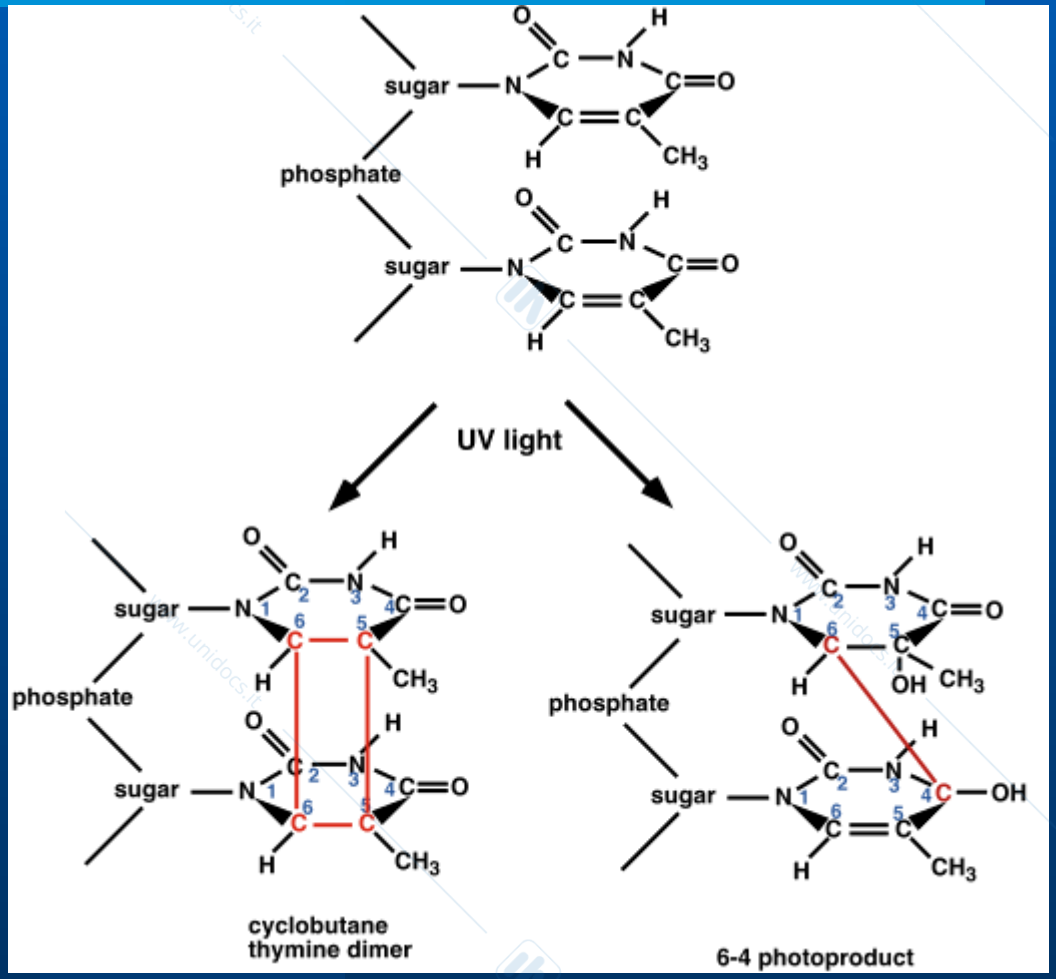
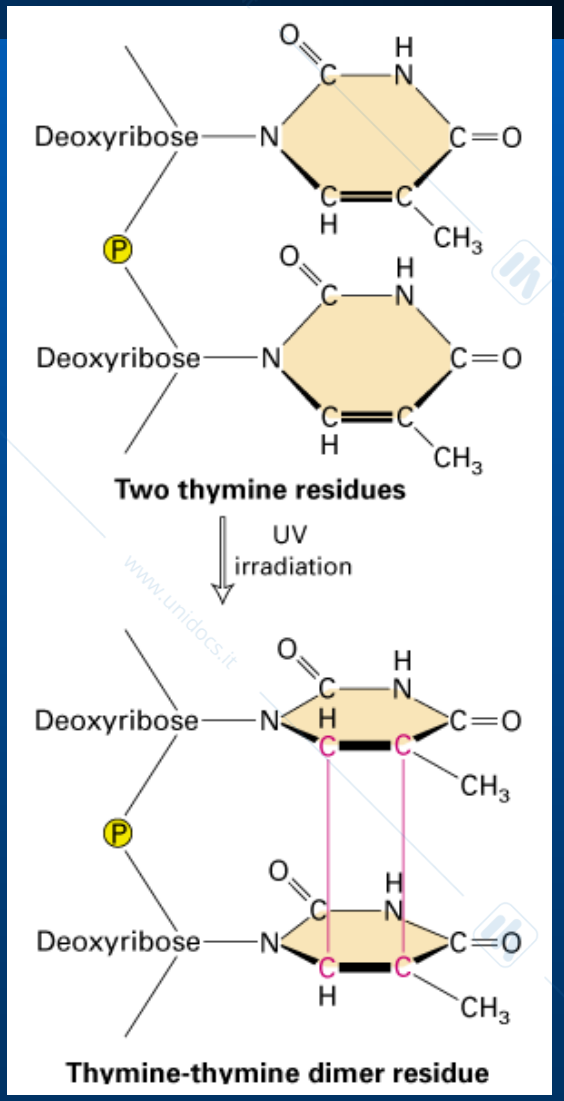
DNA Damage – Thymine Dimers





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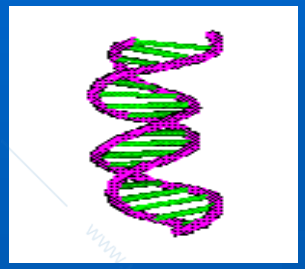
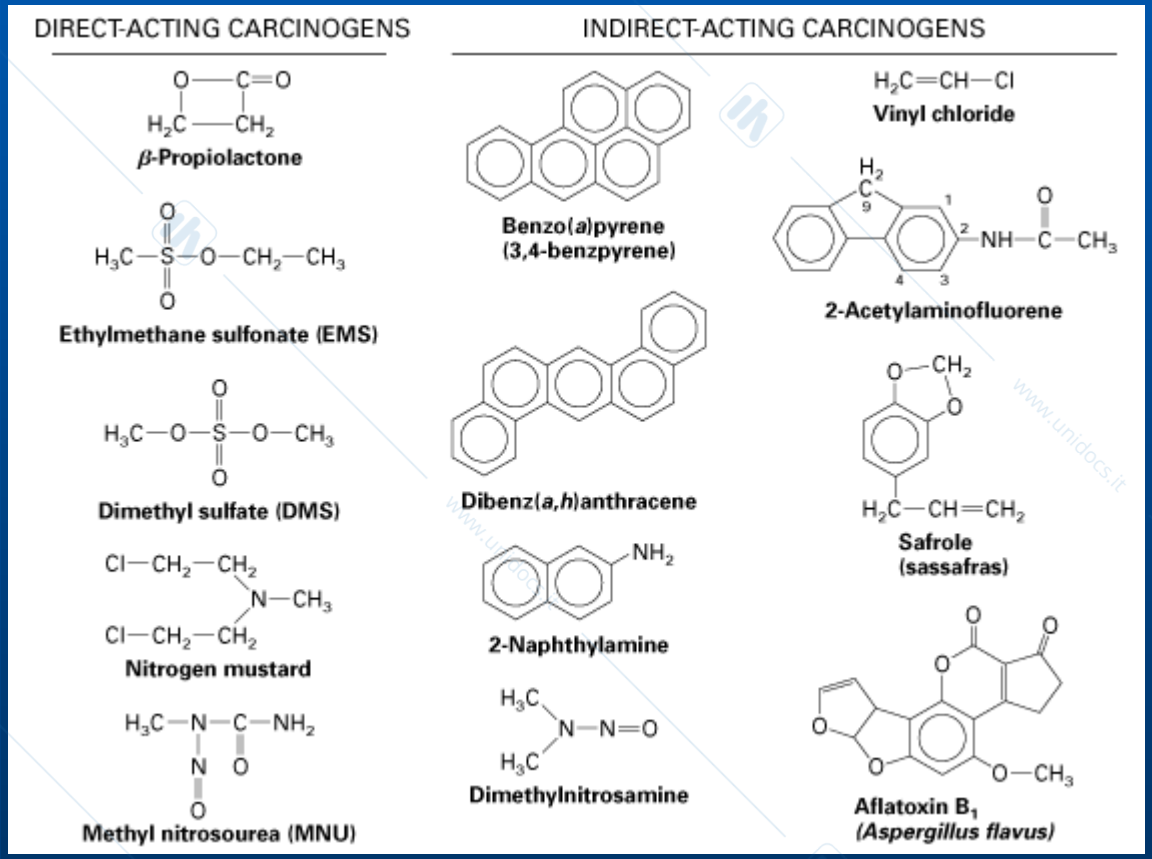


Chemicals Affecting DNA



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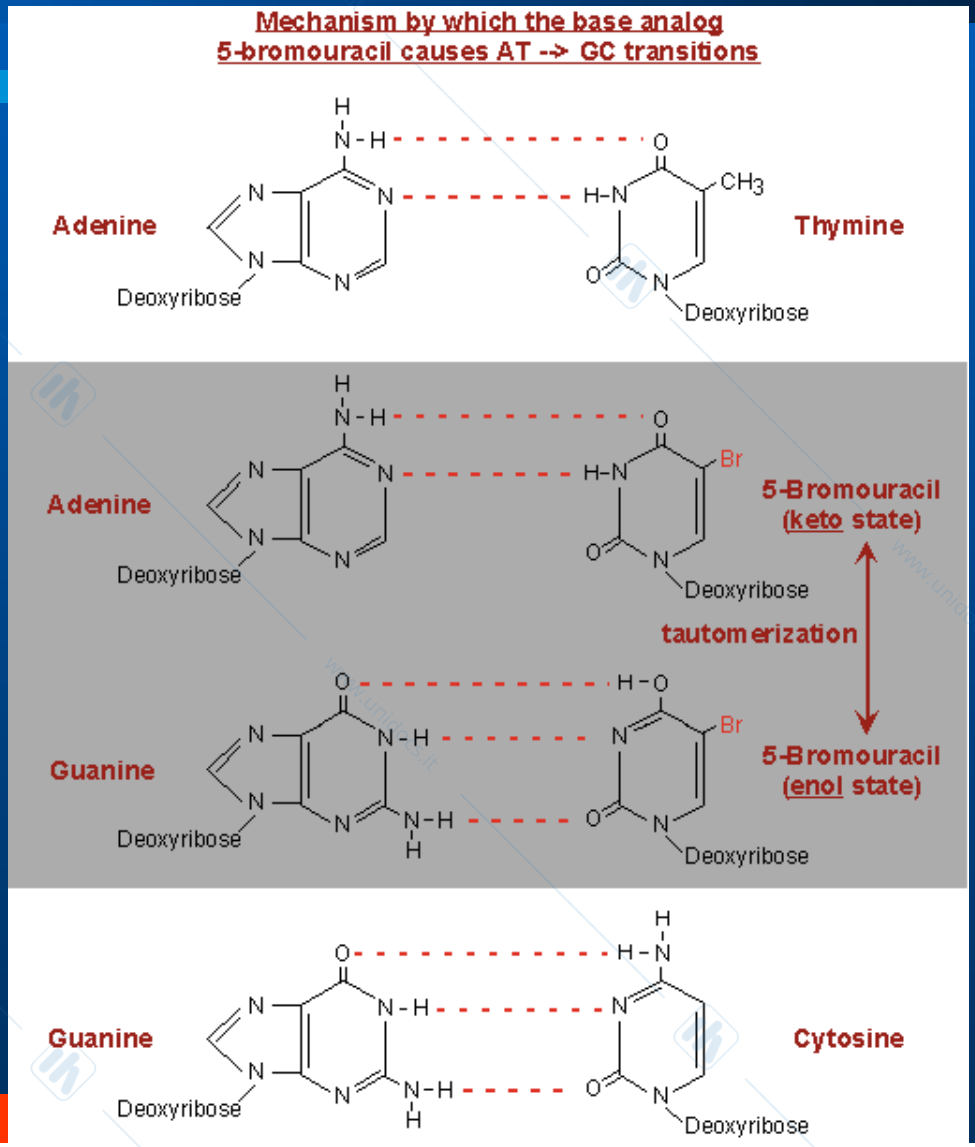
DNA Damage – Base Analogs



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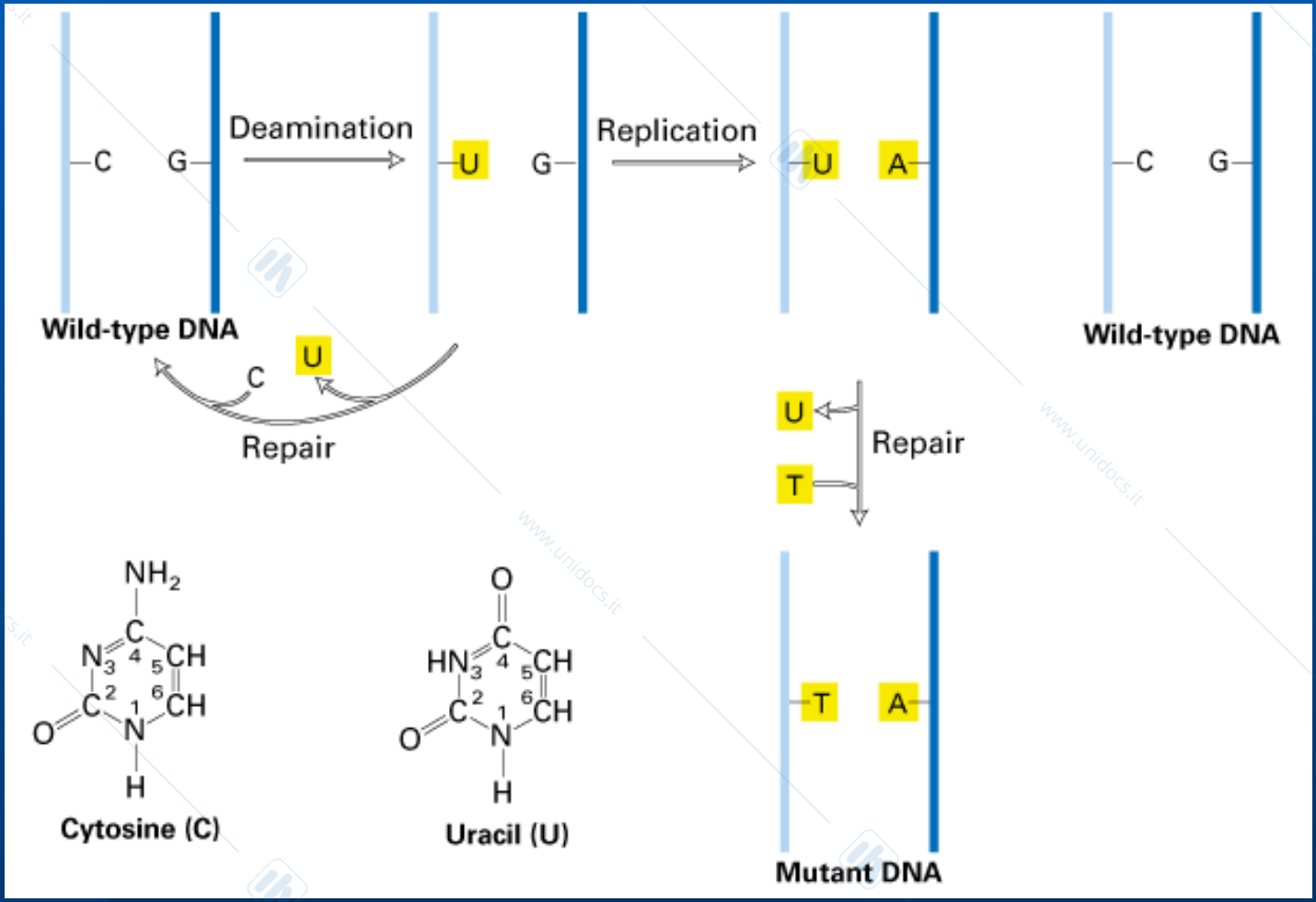
DNA Damage – Point Mutations



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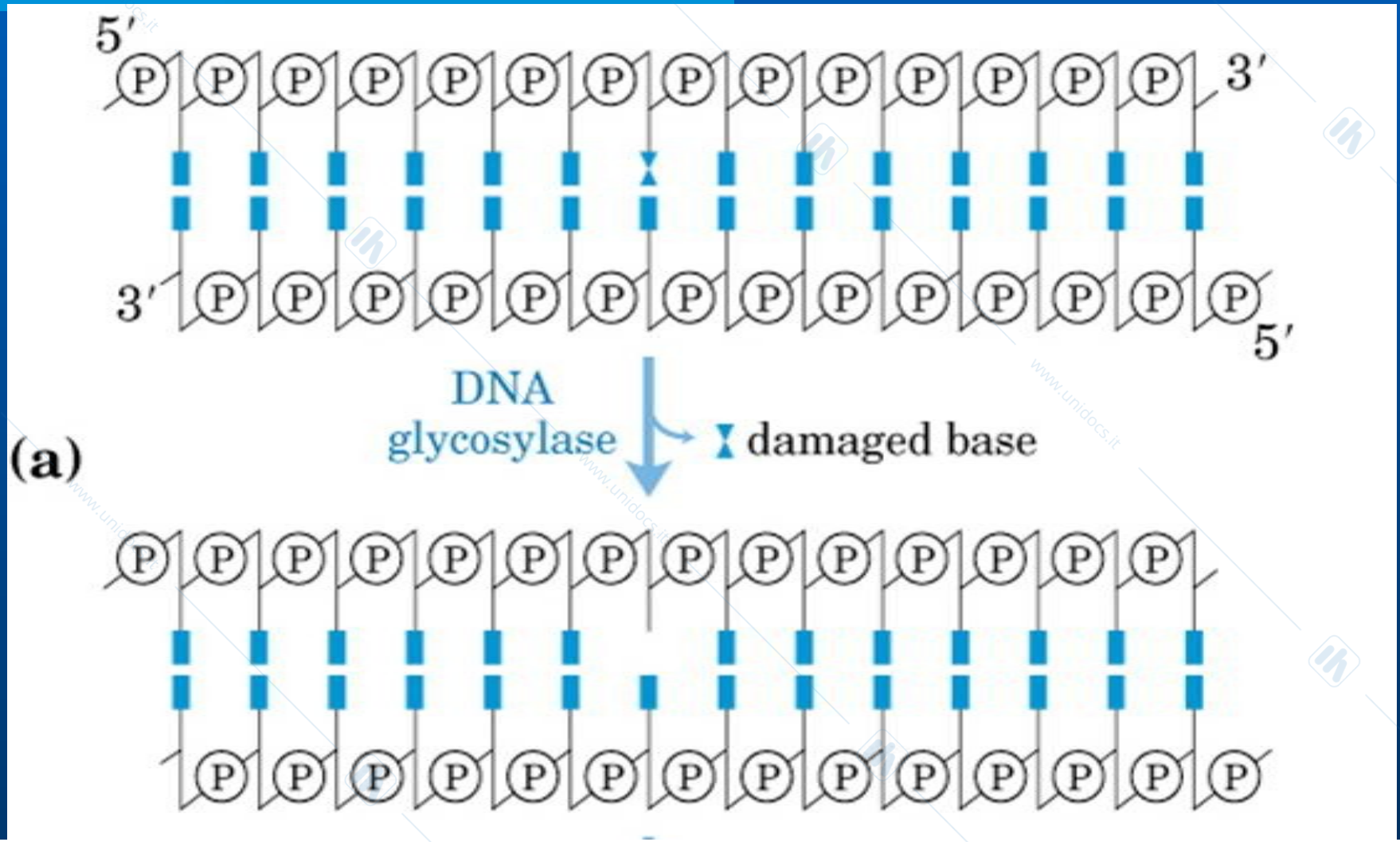
Base Excision Repair 1



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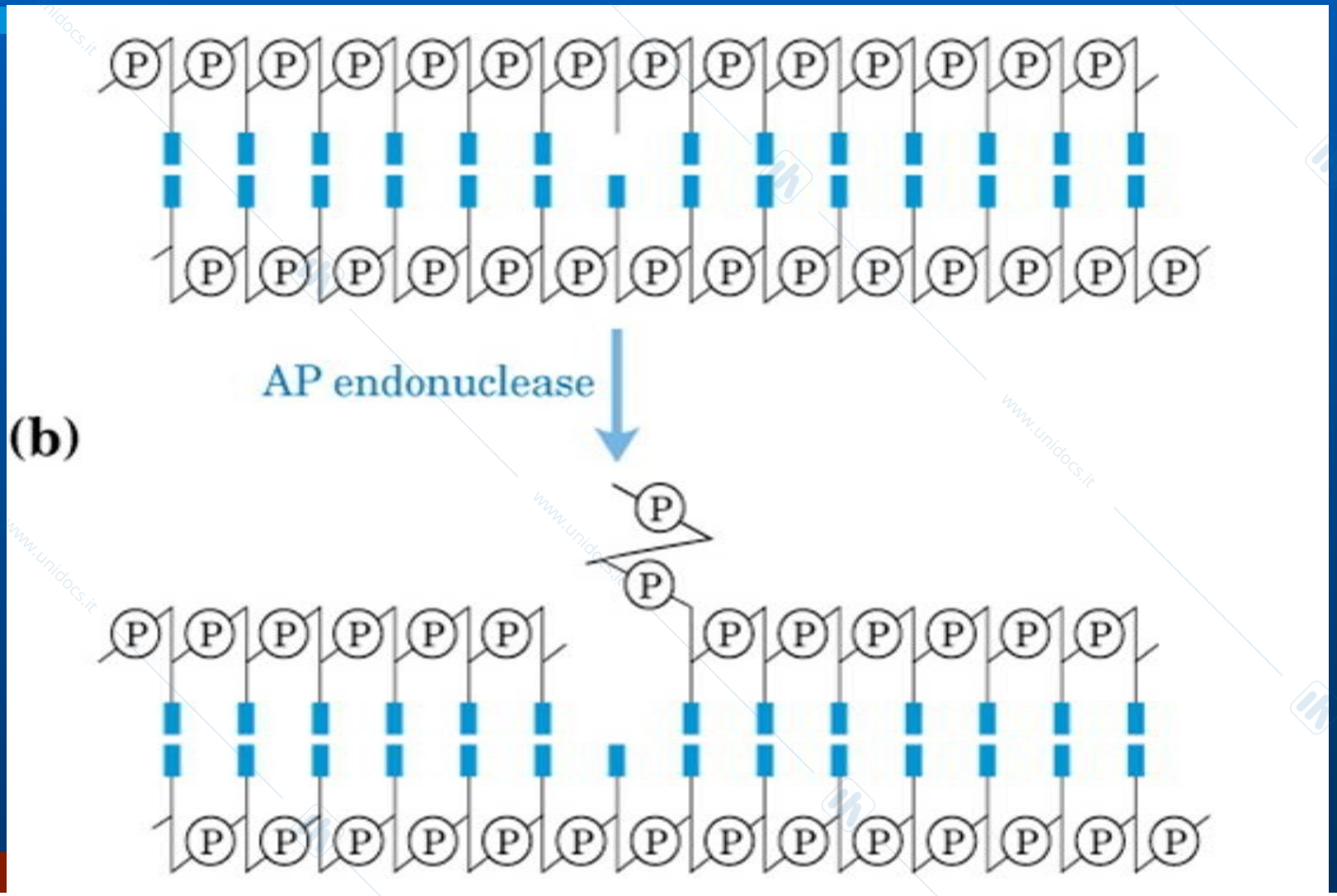
Base Excision Repair II



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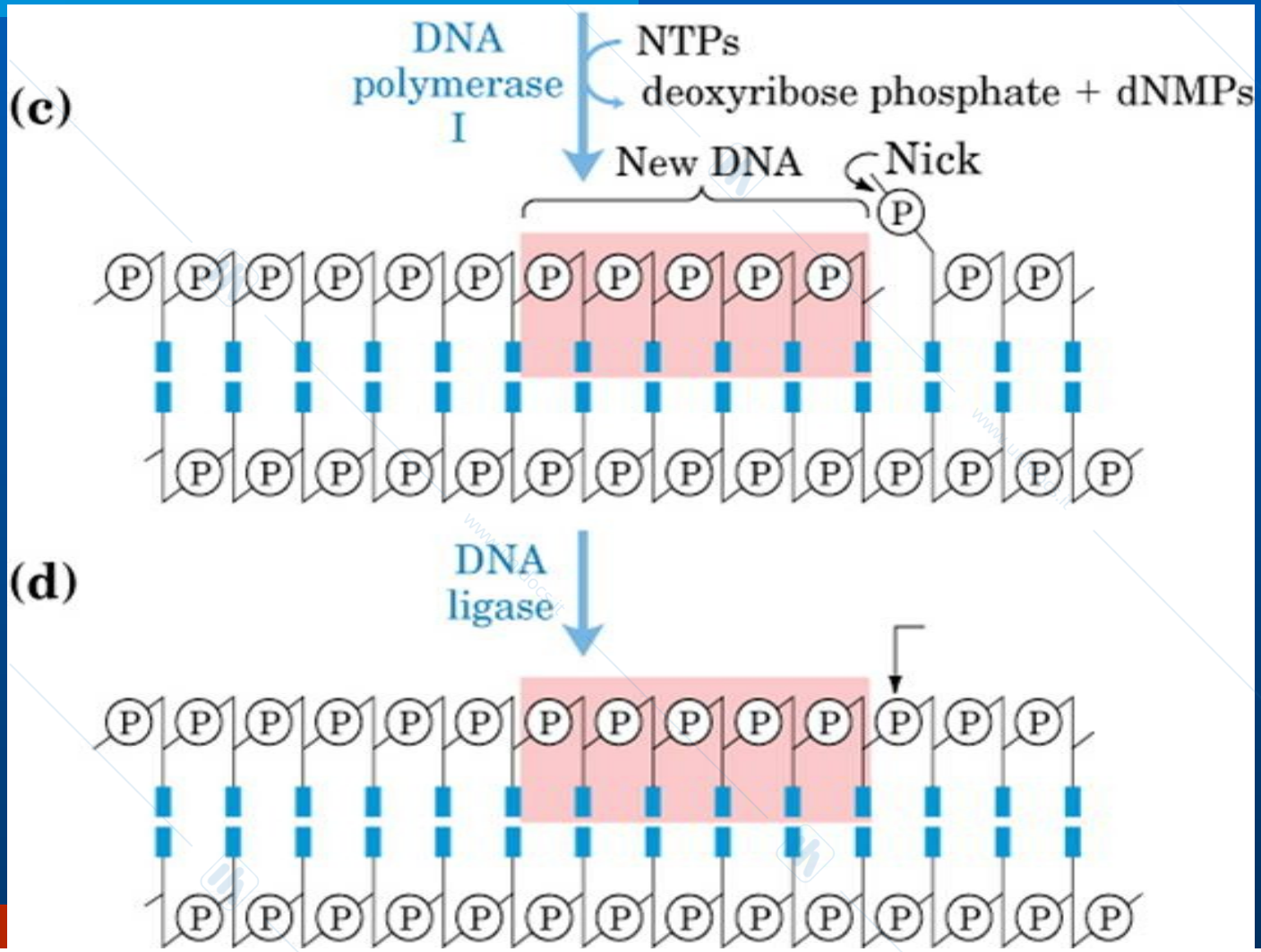
Base Excision Repair III



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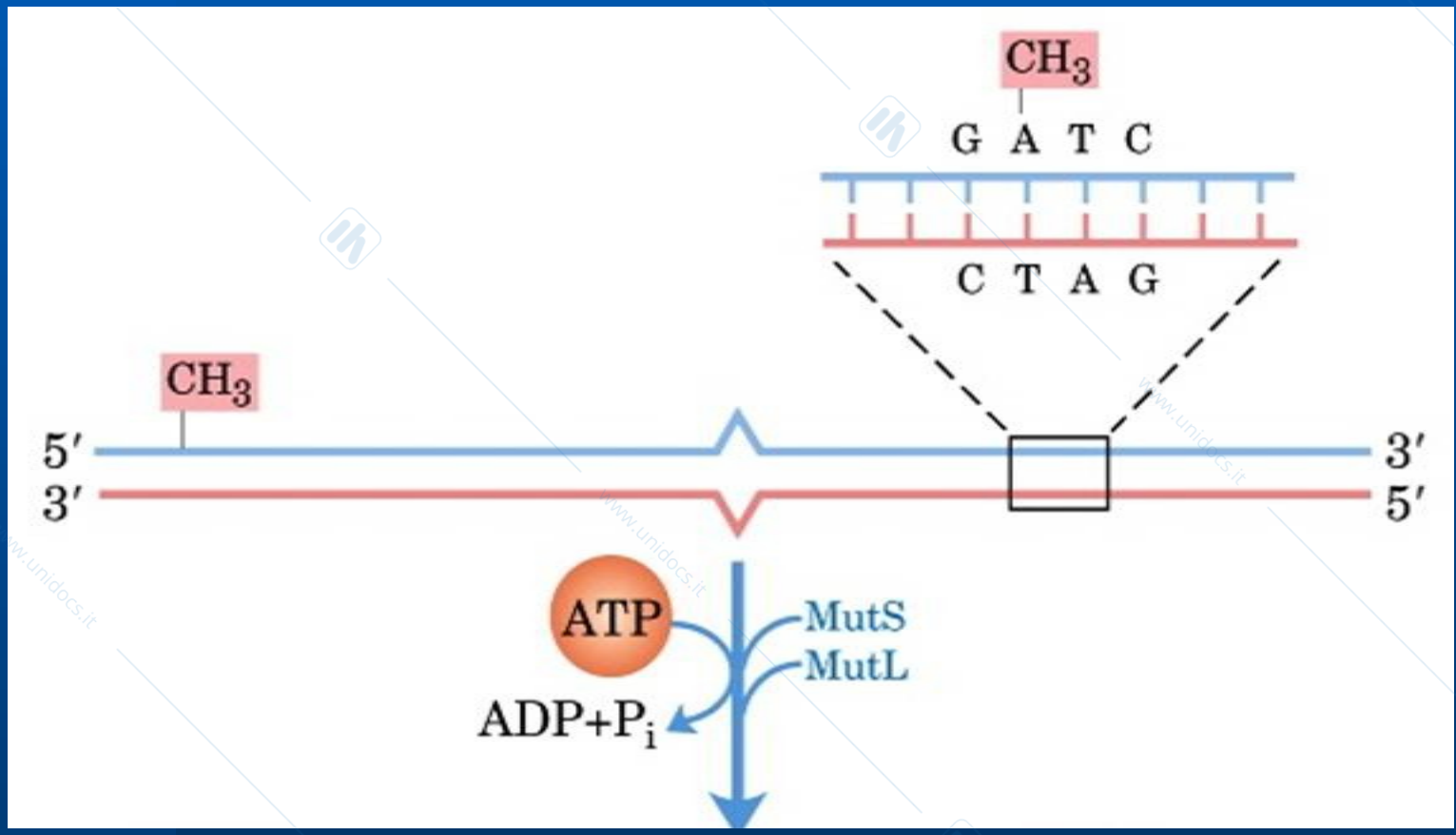
Repair Reference



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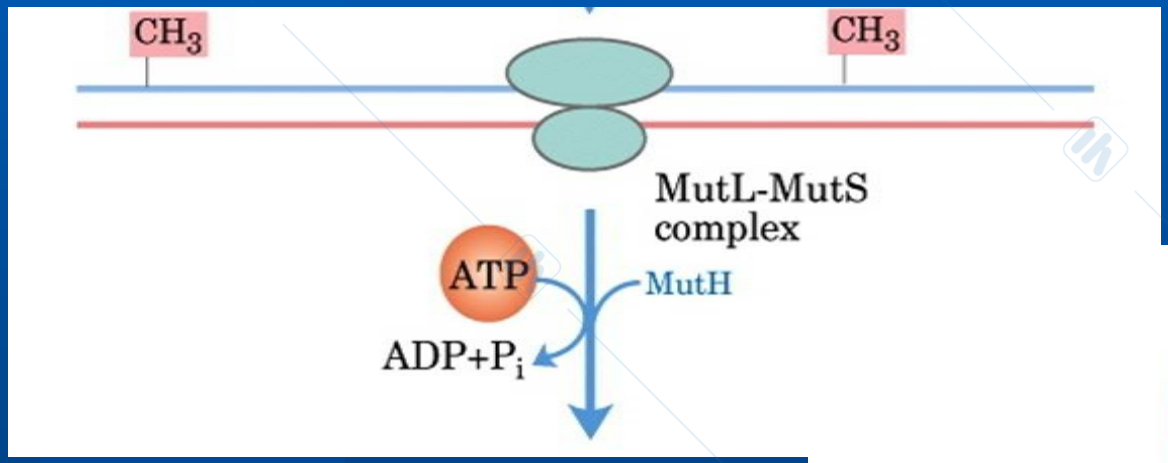
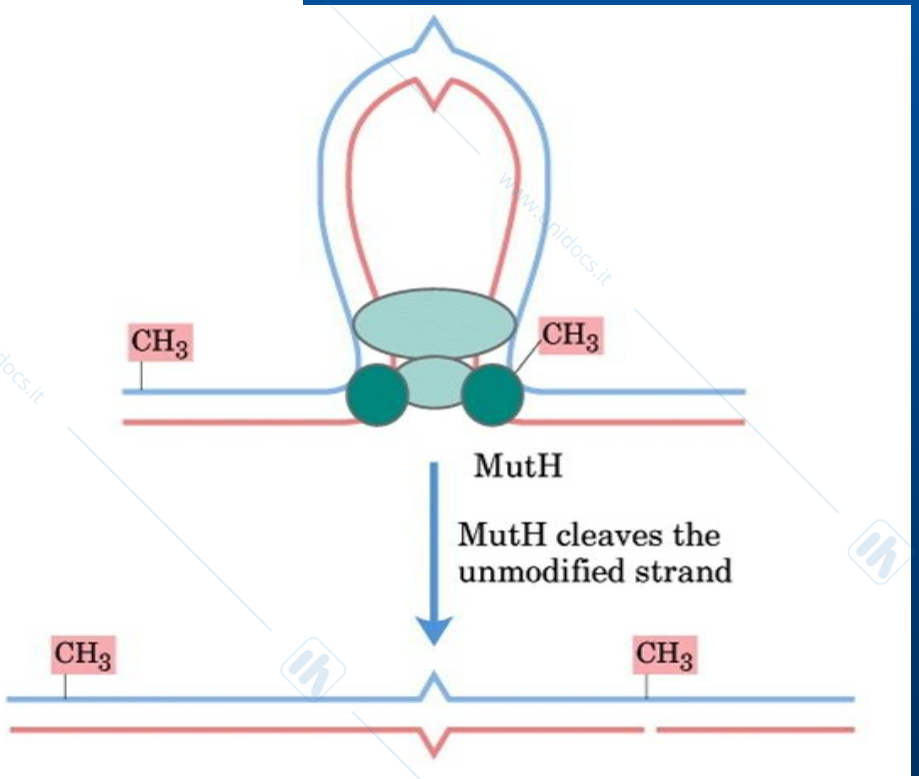
Base Excision Repair





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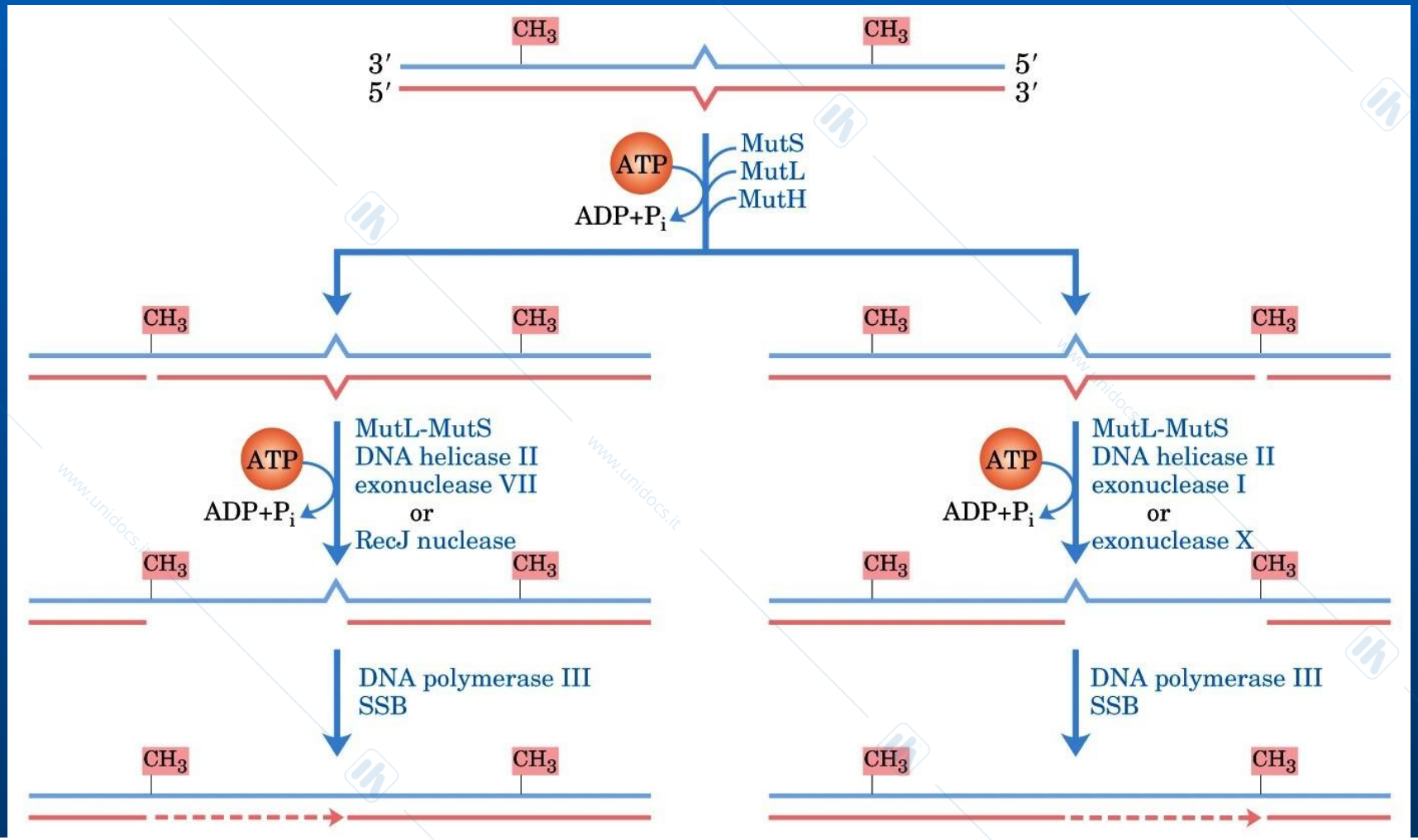
Repair



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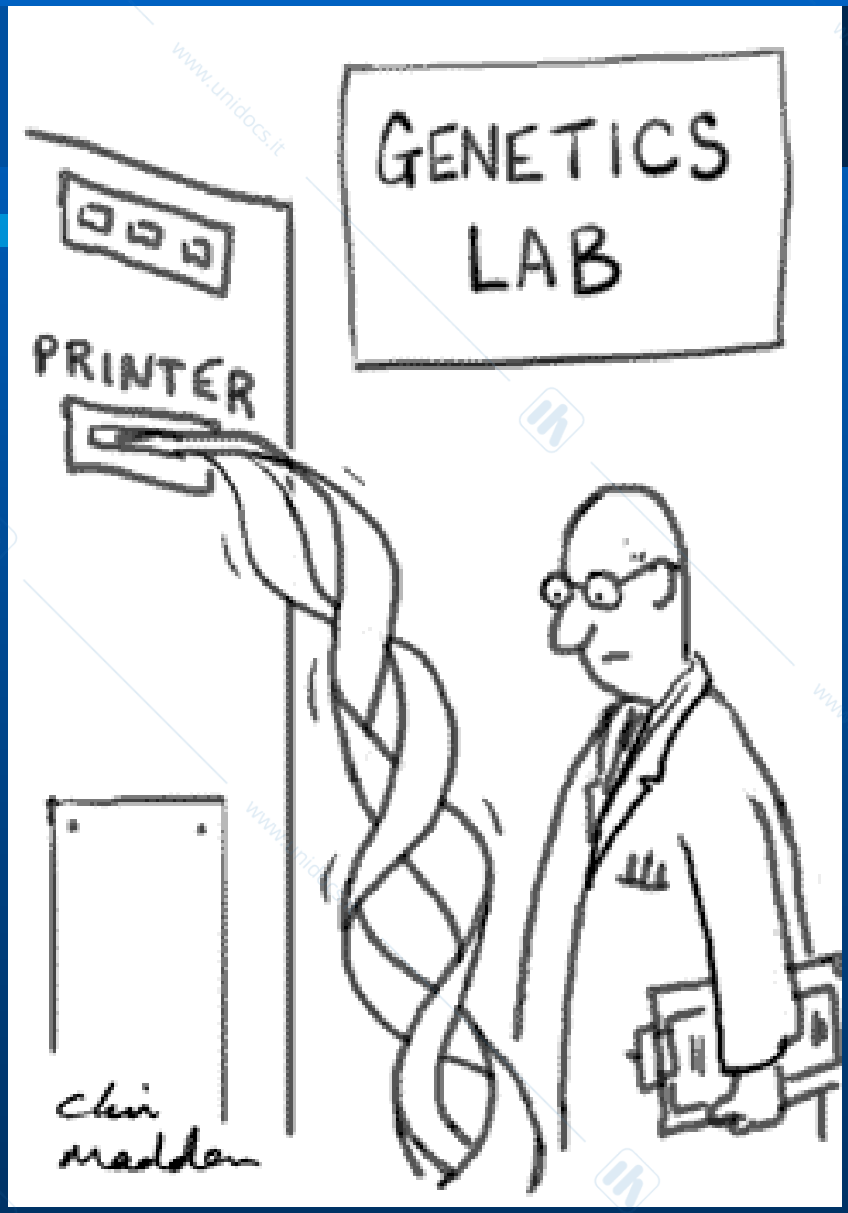

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