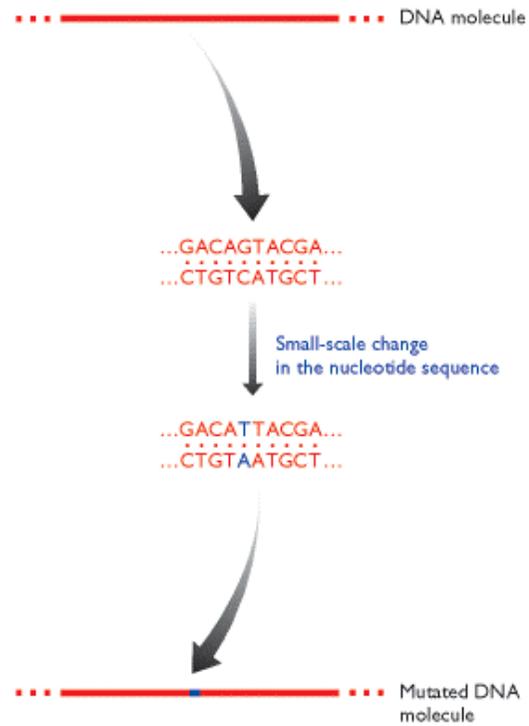


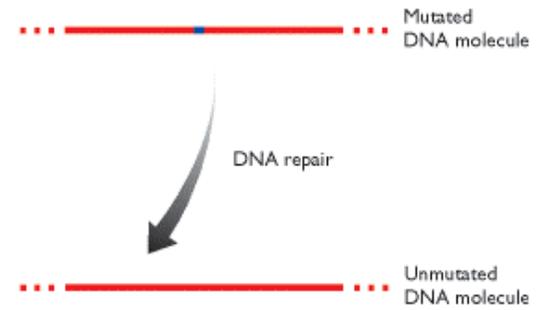
Mutazioni

Una alterazione nella sequenza nucleotidica di una molecola di DNA

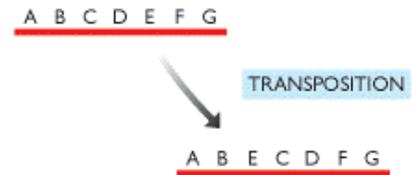
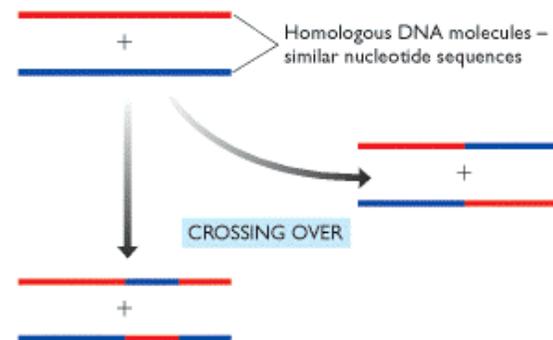
(A) A mutation



(B) DNA repair



(C) Recombination events

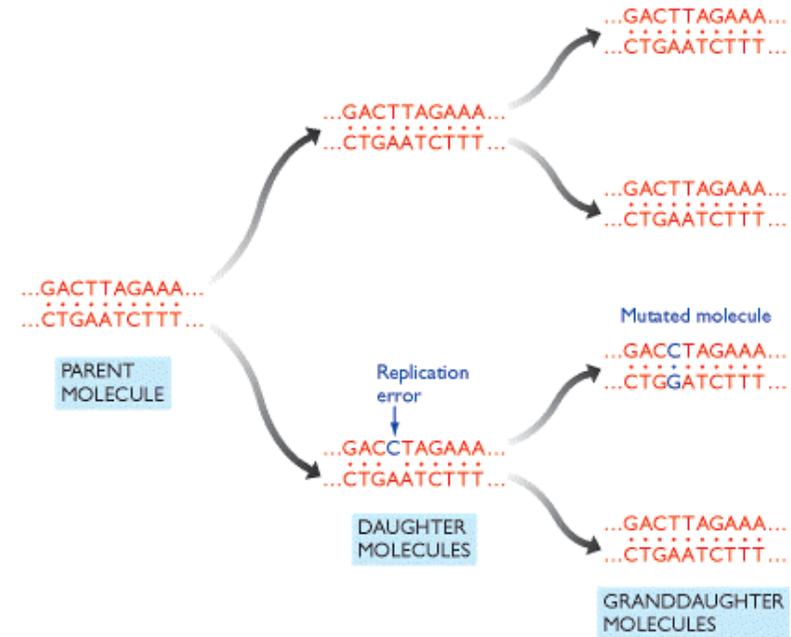


Mutazione, riparo and ricombinazione

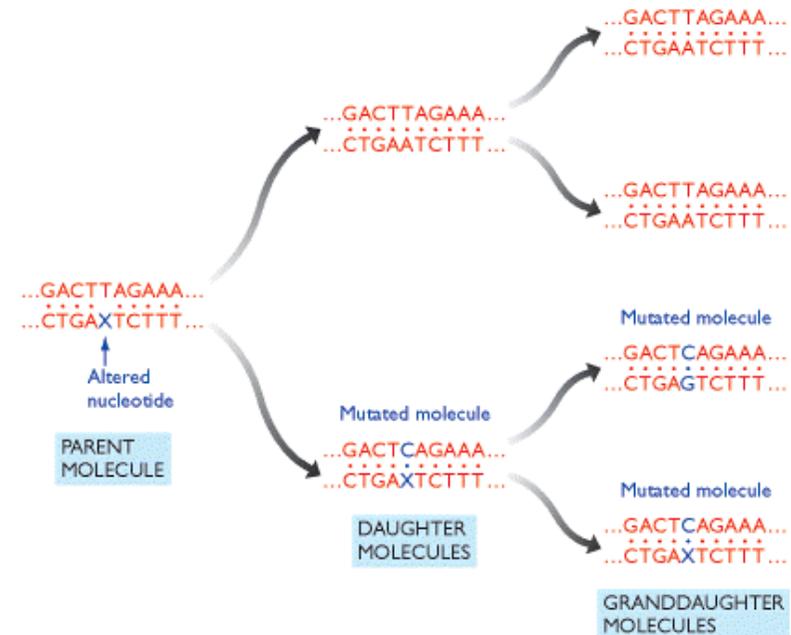
Le mutazioni si possono originare in due modi

- Alcuni sono errori spontanei nella duplicazione
- Altre insorgono perché il DNA è venuto a contatto con un mutageno

(A) An error in replication

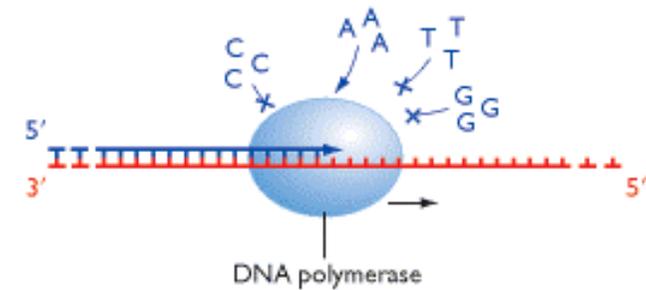


(B) One possible effect of a mutagen

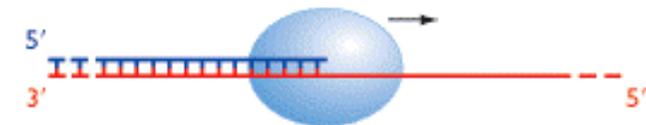


Errori nella replicazione

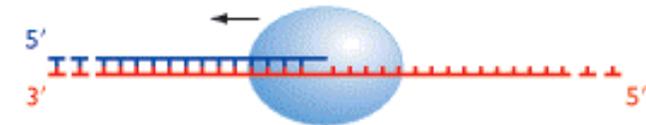
(A) Nucleotide selection



(B) 'Proofreading'



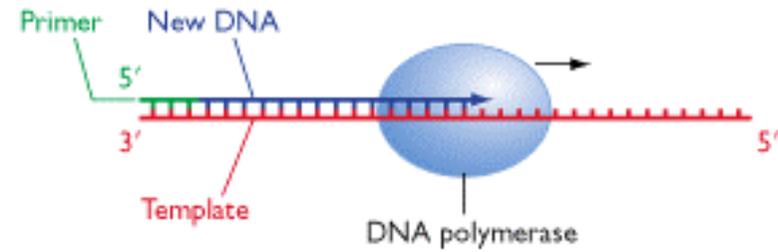
Last nucleotide is
base-paired
POLYMERASE WINS



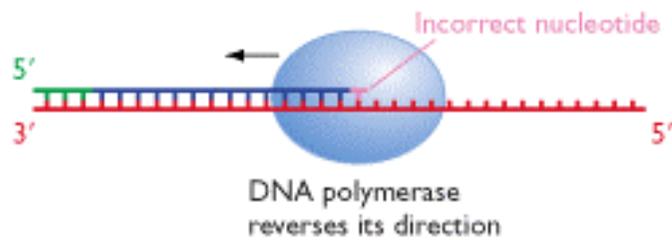
Last nucleotide is not
base-paired
EXONUCLEASE WINS

Esistono meccanismi che assicurano la corretta replicazione del DNA

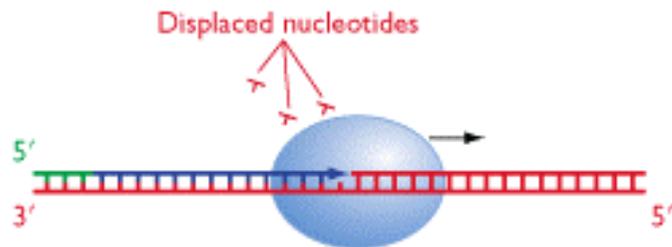
(A) 5'→3' DNA synthesis



(B) 3'→5' exonuclease activity



(C) 5'→3' exonuclease activity



Sintesi del DNA e attività esonucleasica della DNA polimerasi

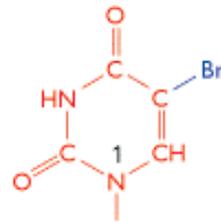
Mutageni causano mutazioni in tre modi diversi:

- Alcuni si comportano come analoghi delle basi e sono erroneamente utilizzati come substrati quando nuovo DNA si duplica.
- Alcuni reagiscono direttamente con il DNA, causando delle modificazioni strutturali che portano a degli errori nella duplicazione
- Alcuni reagiscono indirettamente con il DNA. Essi non influenzano direttamente la struttura, ma fanno sì che la cellula produca essa stessa dei mutageni come il perossido.

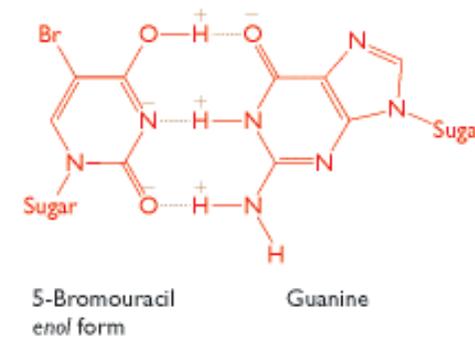
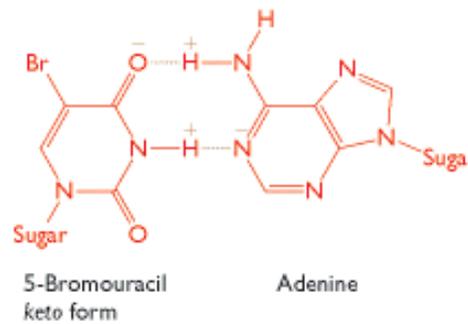
Analogo delle basi

Bromouracile ed il suo effetto mutageno

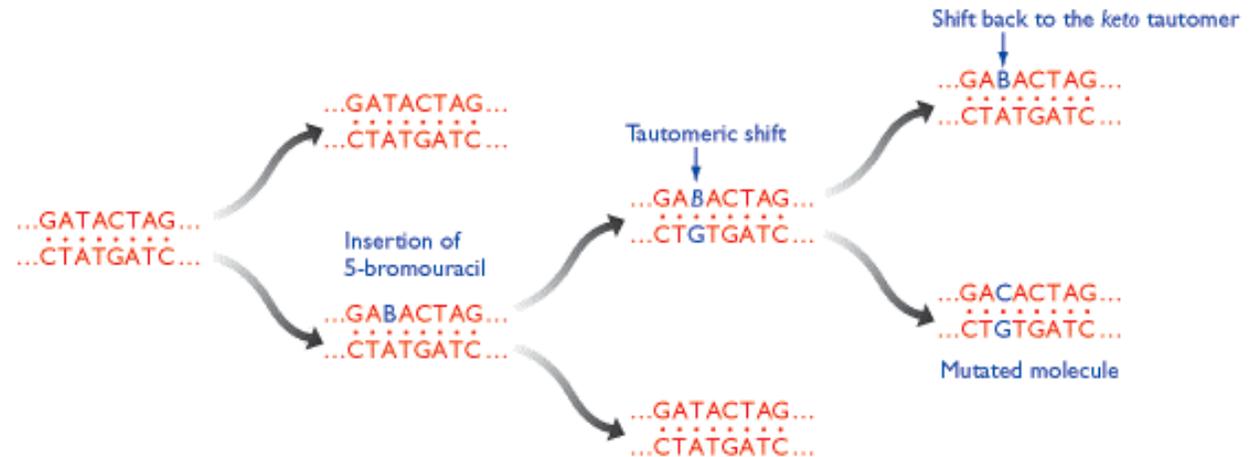
(A) 5-Bromouracil



(B) Base-pairing with 5-bromouracil



(C) The mutagenic effect of 5-bromouracil

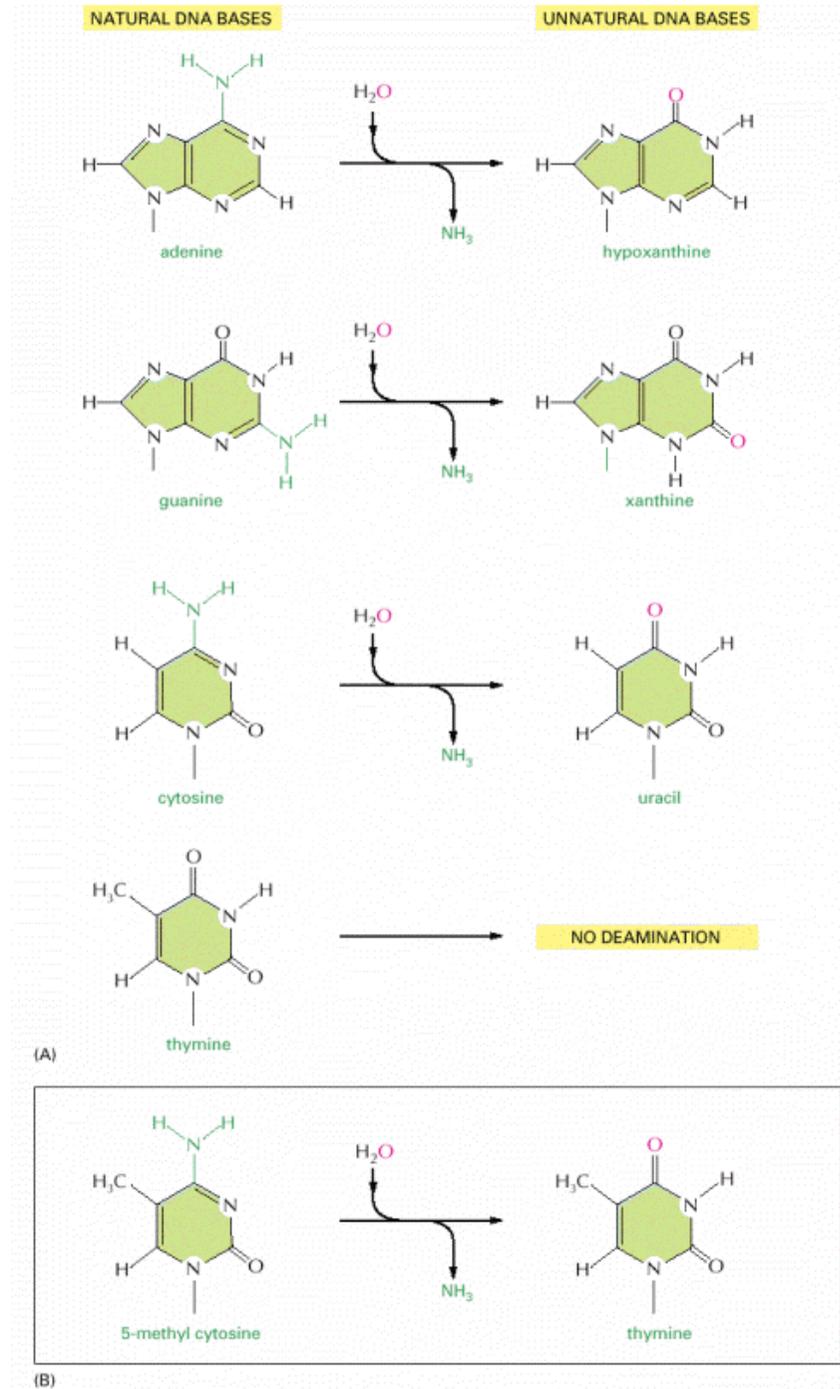


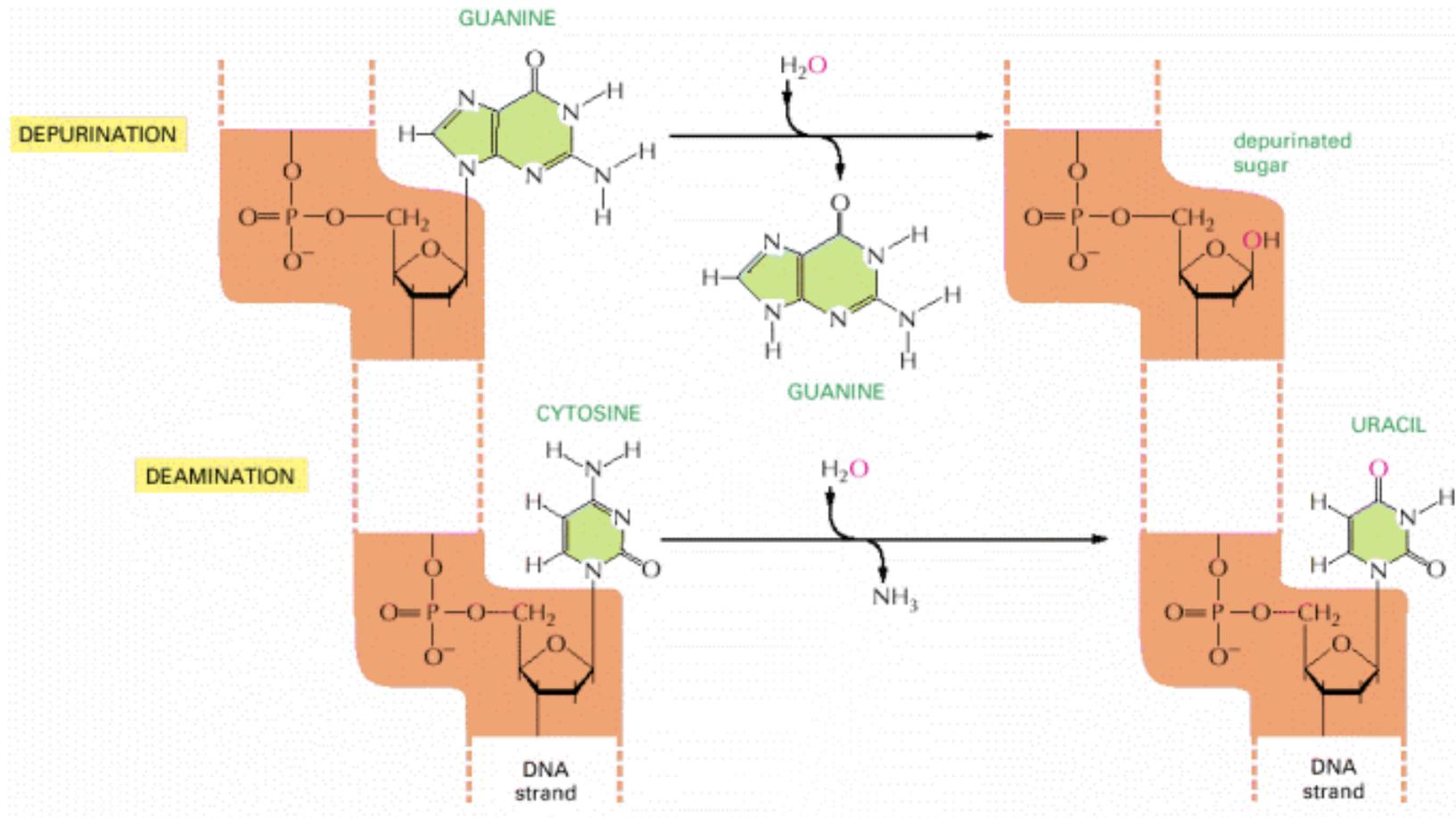
Agenti deaminanti



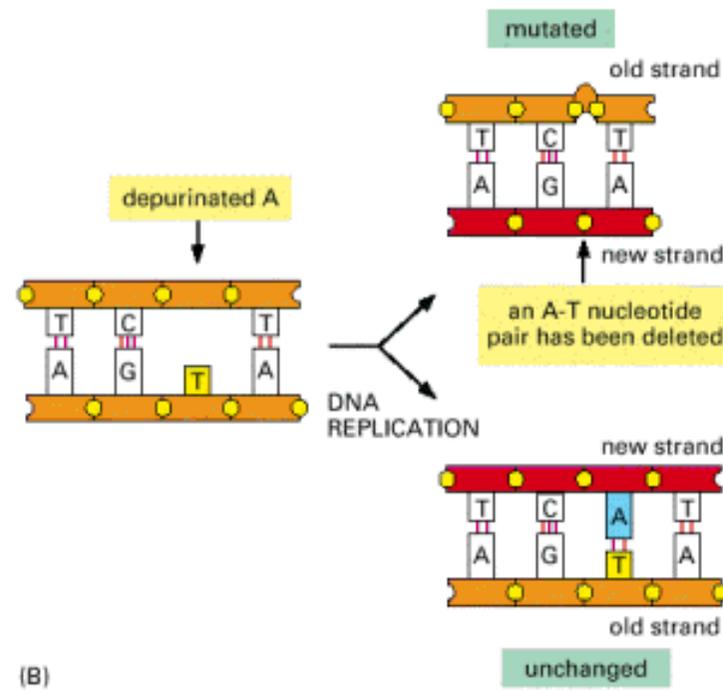
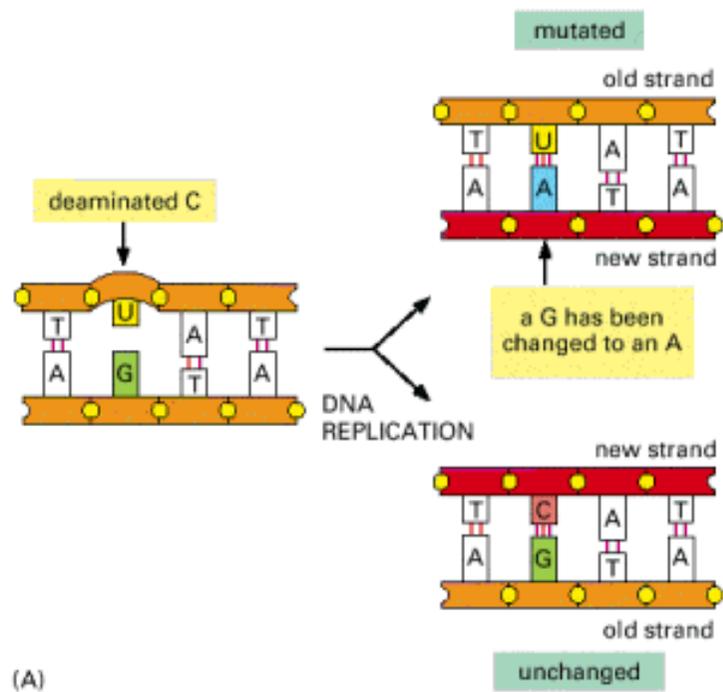
A-T → **Ipoxantina-C**

Deaminazione dei nucleotidi del DNA





Depurinazione e deaminazione. La depurinazione ha come risultato la perdita di G e A dal DNA. La più comune reazione di deaminazione converte la citosina in una base alterata per il DNA, l'uracile, ma la deaminazione avviene anche su altre basi..

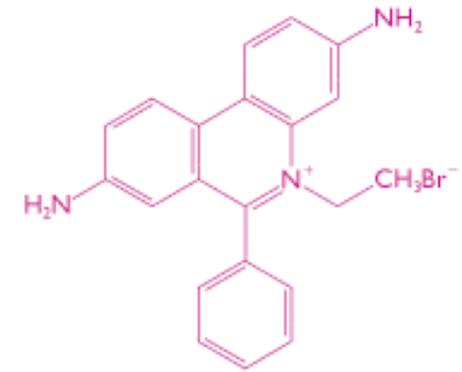


Come sostanze chimiche possono produrre della mutazioni

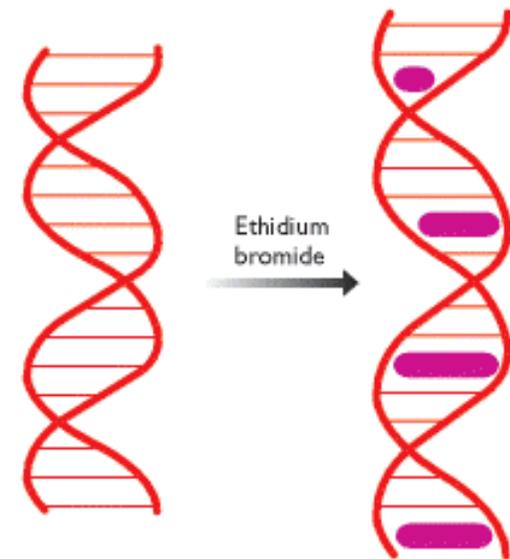
agenti intercalanti

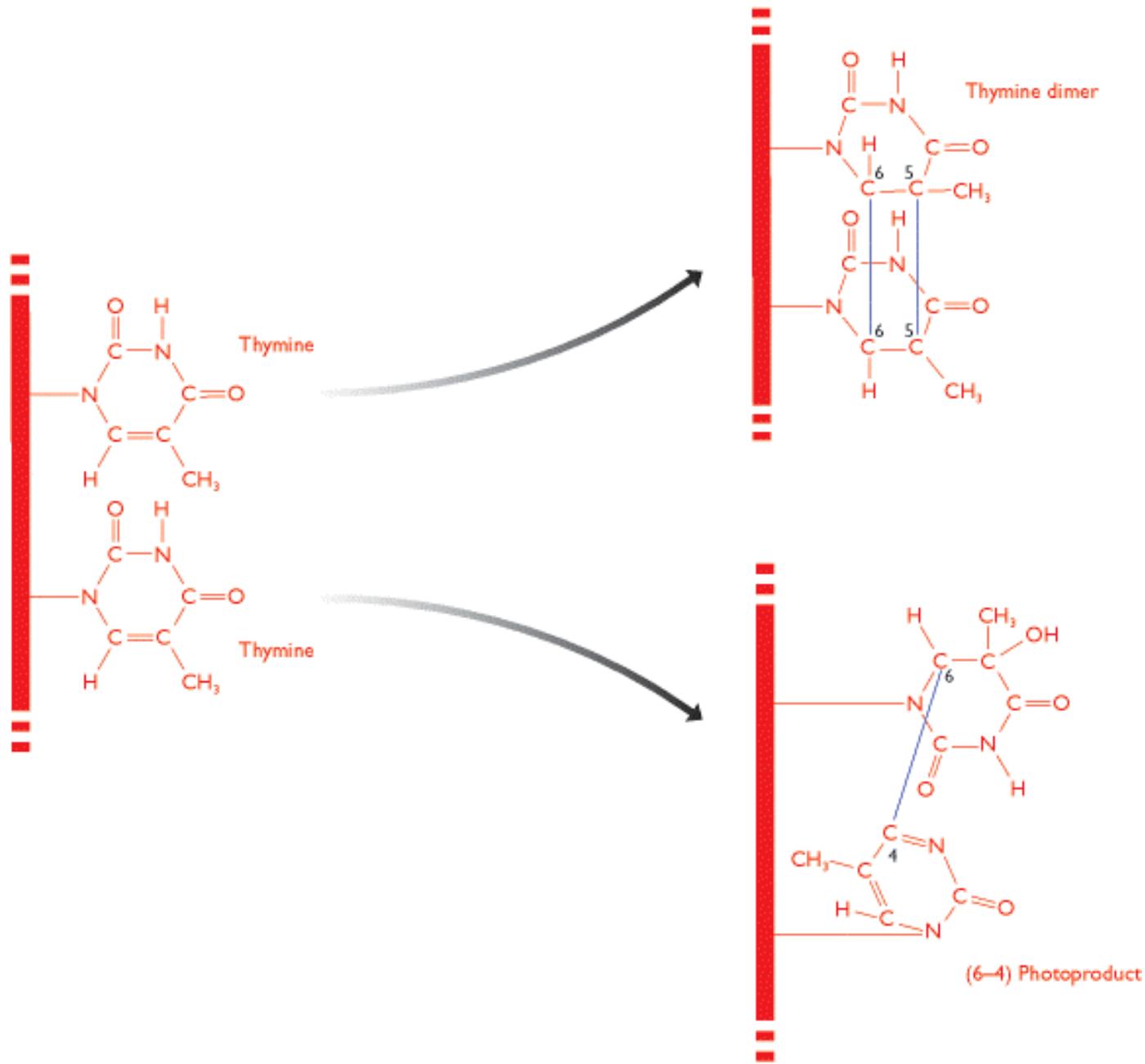
Effetto mutageno dell'etidio bromuro

(A) Ethidium bromide



(B) The mutagenic effect

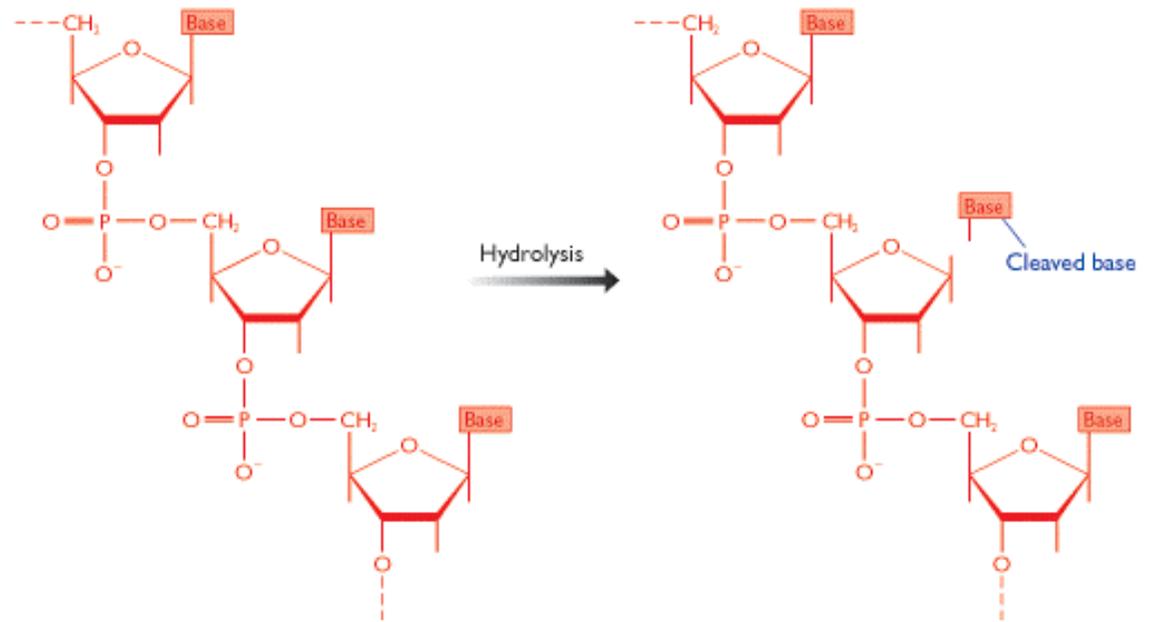




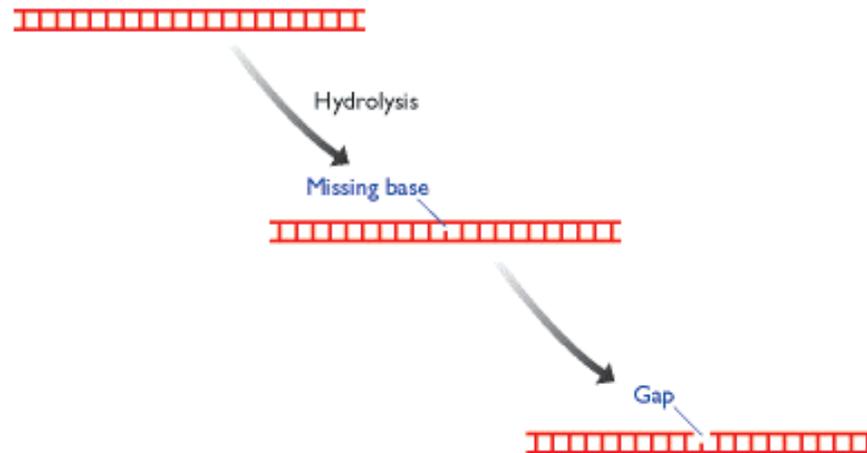
Radiazioni ultraviolette

L'effetto mutageno del calore

(A) Heat-induced hydrolysis of a β -N-glycosidic bond



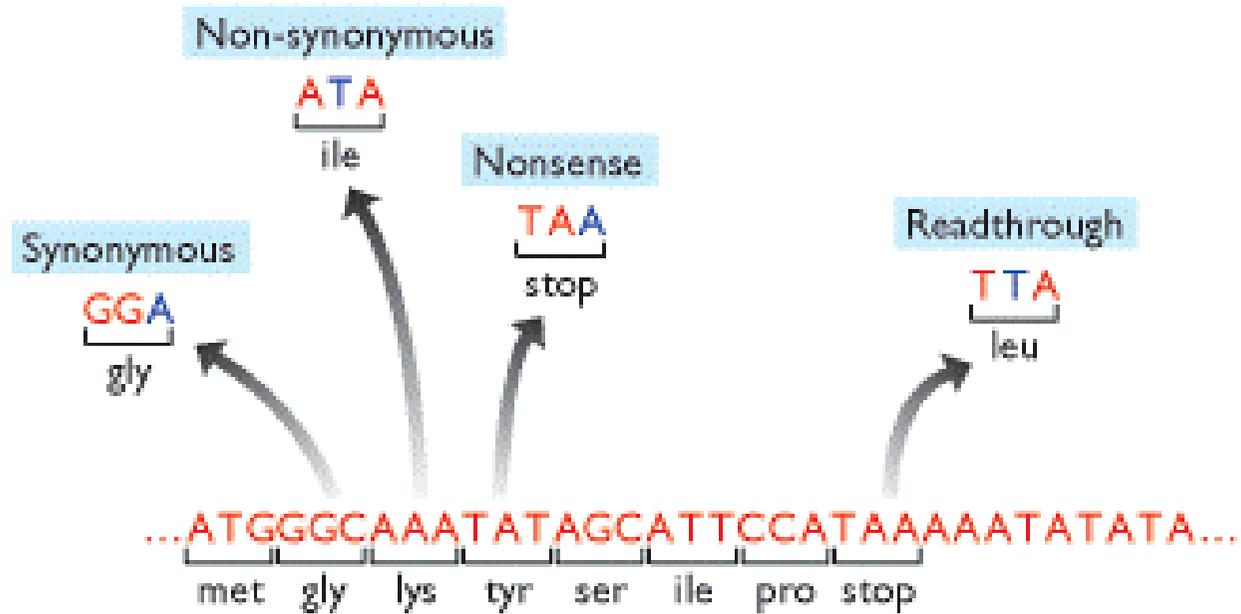
(B) The effect of hydrolysis on double-stranded DNA



Effetti delle mutazioni

Mutazione silente

Un cambiamento del DNA che non produce nessun effetto nella espressione o nel funzionamento di un gene o di un prodotto di un gene



Effetto di una mutazione puntiforme sulla regione codificante

(a) Point mutations and small deletions

Wild-type sequences

Amino acid	N-Phe	Arg	Trp	Ile	Ala	Asn-C
mRNA	5'-UUU	CGA	UGG	AUA	GCC	AAU-3'
DNA	3'-AAA	GCT	ACC	TAT	CGG	TTA 5'
	5'-TTT	CGA	TGG	ATA	GCC	AAT 3'

Missense

3'-AAT	GCT	ACC	TAT	CGG	TTA-5'
5'-TTA	CGA	TGG	ATA	GCC	AAT-3'
N-Leu	Arg	Trp	Ile	Ala	Asn-C

Nonsense

3'-AAA	GCT	ATC	TAT	CGG	TTA-5'
5'-TTT	CGA	TAG	ATA	GCC	AAT-3'
N-Phe	Arg	Stop			

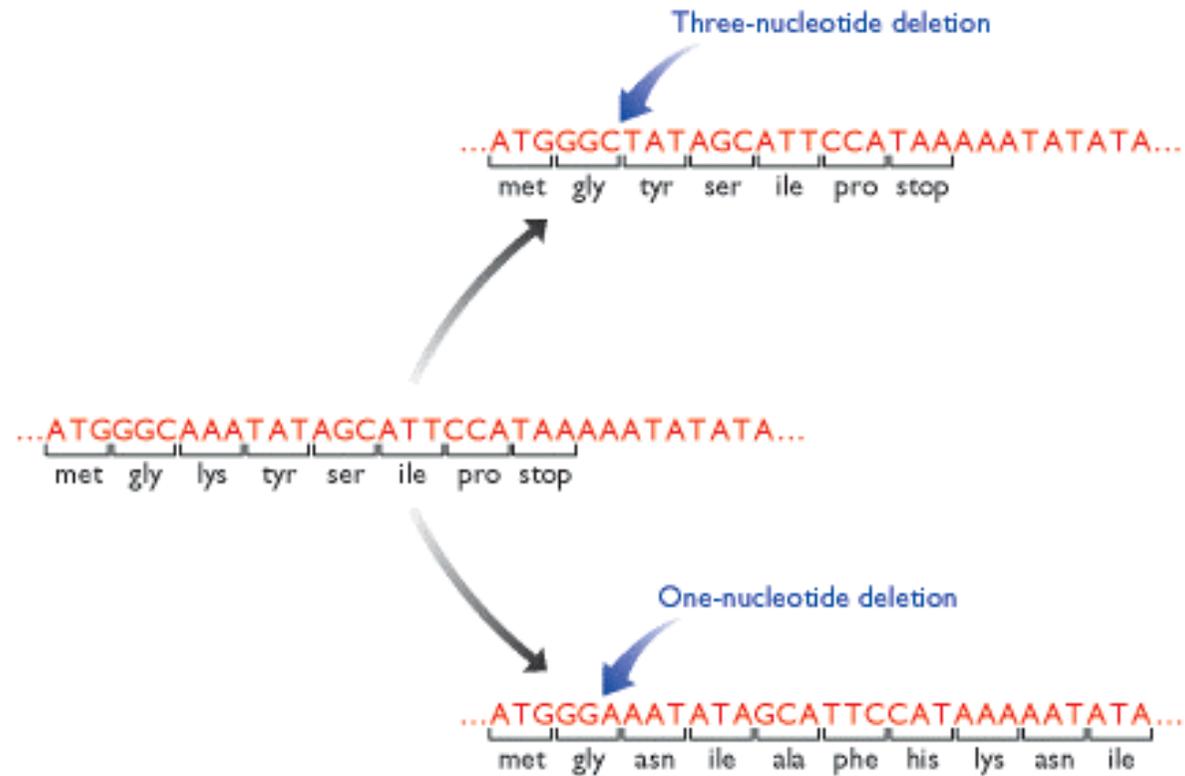
Frameshift by addition

3'-AAA	GCT	ACC	ATA	TCG	GTT A-5'
5'-TTT	CGA	TGG	TAT	AGC	CAA T-3'
N-Phe	Arg	Trp	Tyr	Ser	Gln

Frameshift by deletion

	GCTA				
	CGAT				
3'-AAA	↓ CCT	ATC	GGT	TA-5'	
5'-TTT	GGA	TAG	CCA	AT-3'	
N-Phe	Gly	Stop			

Differenti tipi di mutazione



mutazioni per delezione per
inserzione

—————> **Frameshift**

(A) Direct repair



(B) Excision repair



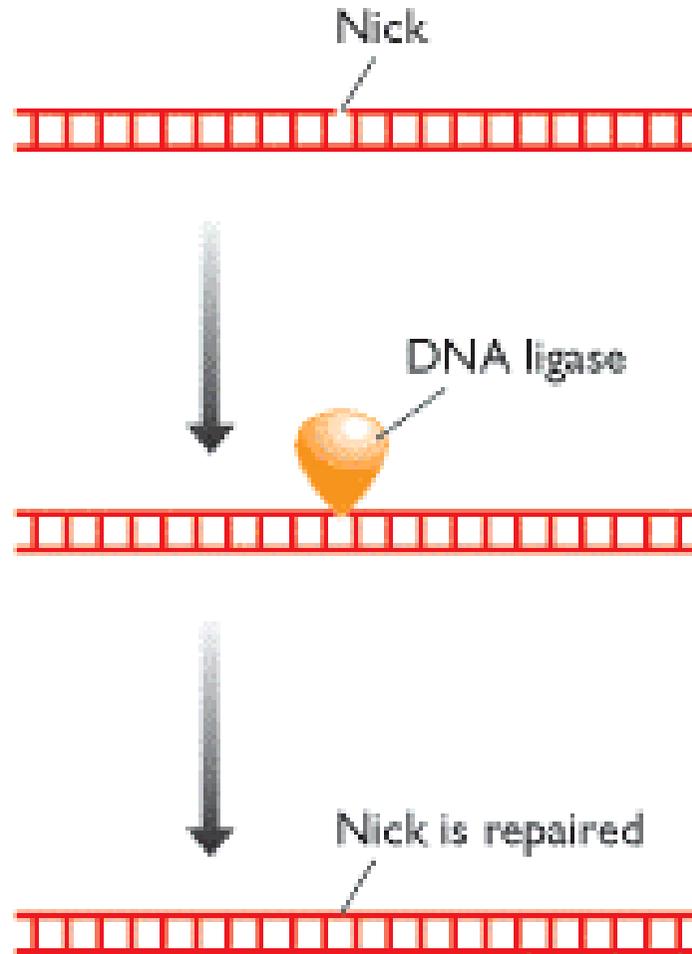
(C) Mismatch repair



(D) Recombination repair



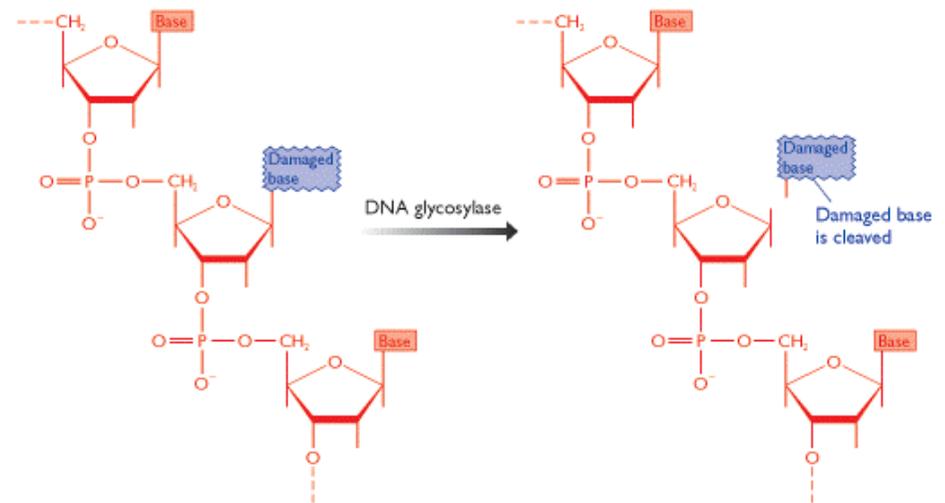
Quattro tipi di sistemi di riparo del DNA



**Riparo di una interruzione tramite la
DNA ligasi**

Riparo per escissione di basi (A) la DNA glicosilasi rimuove la base danneggiata. (B) rappresentazione schematica della riparazione

(A) Removal of a damaged base by DNA glycosylase



(B) Outline of the pathway

