

SBI4U Molecular Genetic Mutations

MUTATIONS

Discuss with a partner:

1. When you think about the word **mutation**, what comes to mind?

Discuss with a partner:

2. If you could invent a mutation for yourself, what would it be?

Amoeba Sister Video

MUTATION

x a permanent change in the nucleotide sequence of a cell's DNA

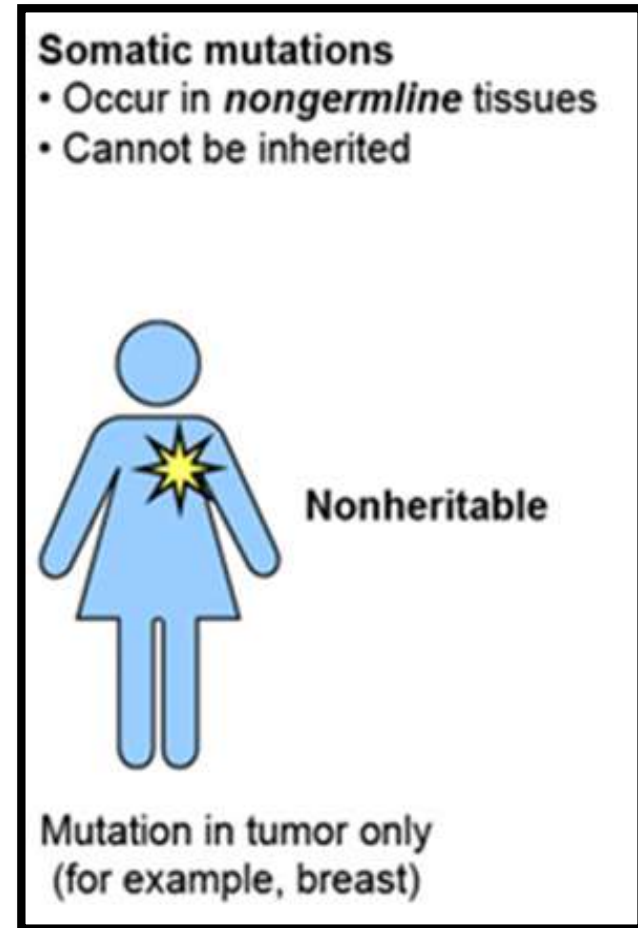
x typically neutral or harmful, *rarely beneficial*

- x allow species to change and adapt over time
- x only those adapted to their environment will survive

x can be passed onto daughter cells

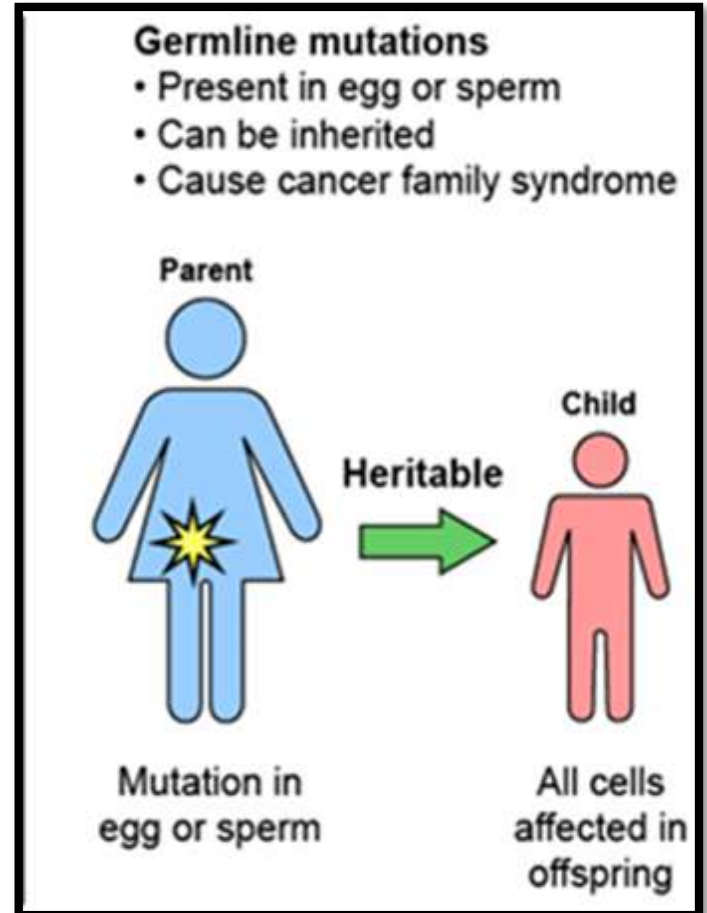
Multicellular organisms have two types of mutations:

1. Somatic mutations:
passed on during mitosis,
but not to subsequent
generations



Multicellular organisms have two types of mutations:

2. Germ-line mutations:
occur in cells that give rise to gametes, passed to subsequent generations



Mutations Can Be:

- Spontaneous or Induced
- Caused by Physical or Chemical
- Chromosomal (large-scale) or Single-gene (small-scale)

Mutations Can Be:

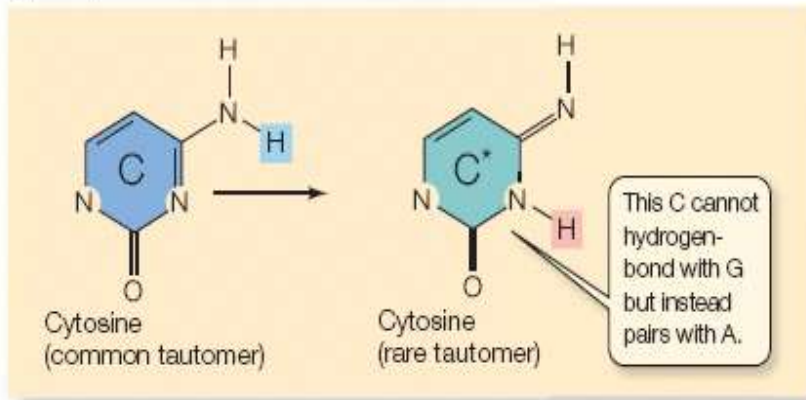
Spontaneous

- X take place naturally as a result of normal molecular interactions (ex. DNA pol made a mistake)
- X ex. DNA replication, transposons (jumping genes)

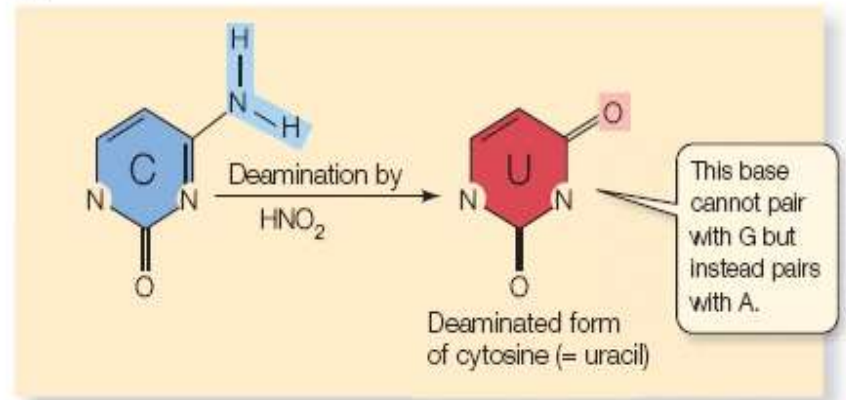
Induced

- X caused by agents outside the cell
- X mutagen: a substance that increases the rate of mutation

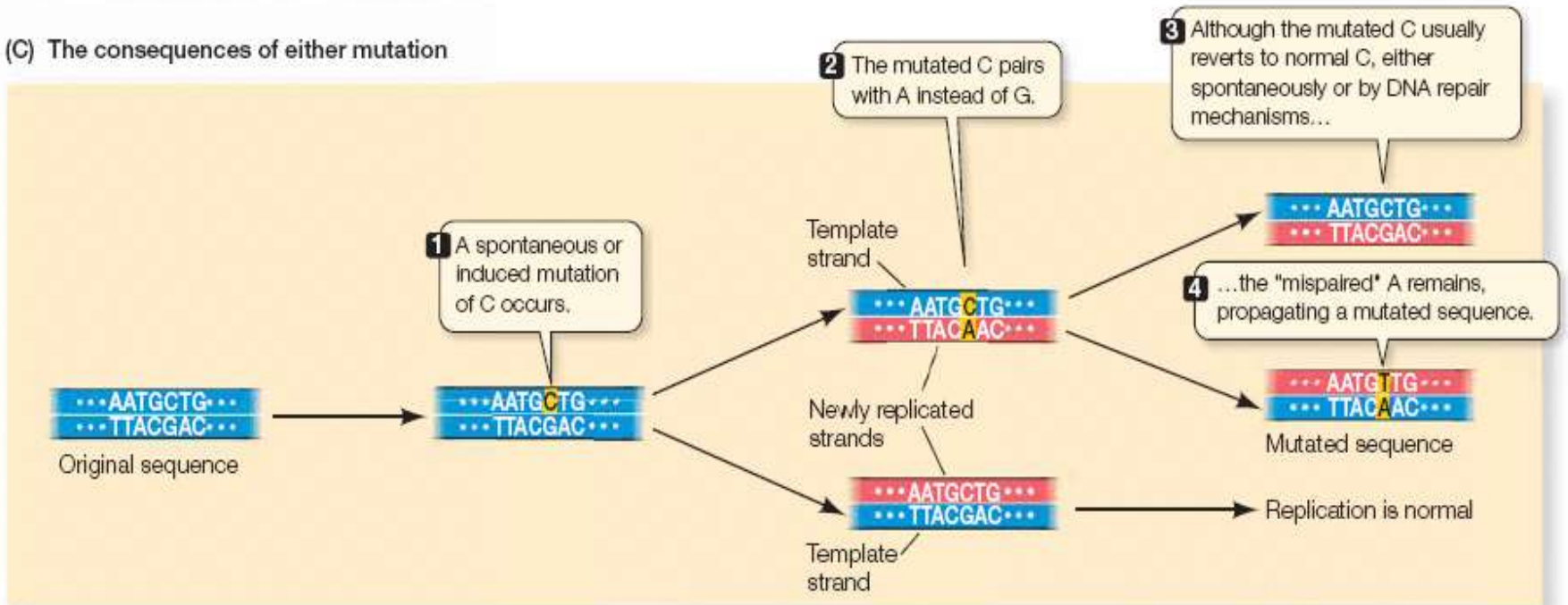
(A) A spontaneous mutation



(B) An induced mutation



(C) The consequences of either mutation



With your partner, discuss which type of mutation is this considered?

1. Nitrous acid (HNO_2) and can turn C in DNA into U
2. Benzpyrene, a component of cigarette smoke, adds a large chemical group to G, making it unavailable for base pairing

With your partner, discuss which type of mutation is this considered?

1. Nitrous acid (HNO_2) and can turn C in DNA into U
 - a) Induced!
2. Benzpyrene, a component of cigarette smoke, adds a large chemical group to G, making it unavailable for base pairing
 - a) Induced!

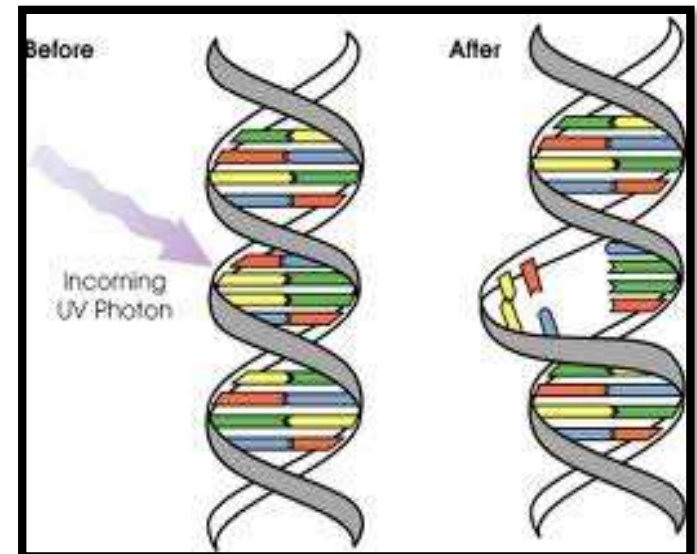
With your partner, discuss which type of mutation is this considered?

3. Ionizing radiation (X-rays)

With your partner, discuss which type of mutation is this considered?

3. Ionizing radiation (X-rays): Induced!

- Produces highly reactive chemical species called free radicals. Free radicals can change the bases in DNA to unrecognizable forms by the DNA polymerase.
- It can break the sugar–phosphate backbone of DNA, causing chromosomal abnormalities
- UV radiation is absorbed by thymine in DNA, causing it to form inter-base covalent bonds with adjacent nucleotides, called dimers. This can cause chaos in DNA replication.



Mutagens

- Physical: X-rays, UV
- Chemical: Nitrites, Gasoline Fumes, Cigarette Smoke

Mutations can be:

- At the level of the chromosome, considered large-scale
- At the level of the base, considered small-scale.

Exploration Genetic Mutation Scratch Program

With your partner, complete the program
with the handout

Types of Mutations: Single-Gene Mutations

Changes in nucleotide sequence of one gene

Mutations Sentence Exploration

1. The cat had the hat
2. The bat had the hat

Analyze sentence 1 and sentence 2, then discuss the changes required to change sentence 1 into sentence 2 with a partner.

Mutations Sentence Exploration

1. The cat had the hat
3. The cat had the mat

Analyze sentence 1 and sentence 3, then discuss the changes required to change sentence 1 into sentence 3 with a partner.

Mutations Sentence Exploration

1. The cat had the hat
4. The ath adt heh at

Analyze sentence 1 and sentence 4, then discuss the changes required to change sentence 1 into sentence 4 with a partner.

Mutations Sentence Exploration

1. The cat had the hat

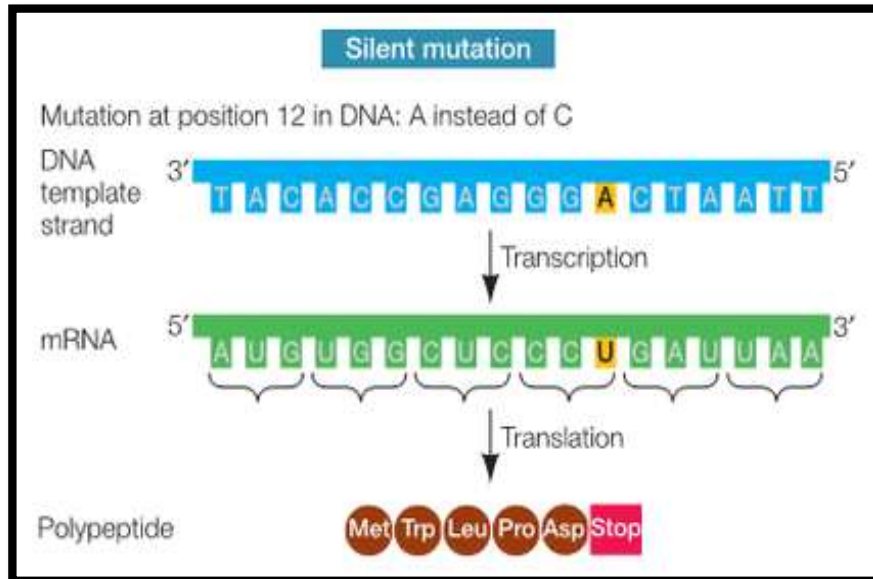
5. The cda tha dth eha

Analyze sentence 1 and sentence 5, then discuss the changes required to change sentence 1 into sentence 5 with a partner.

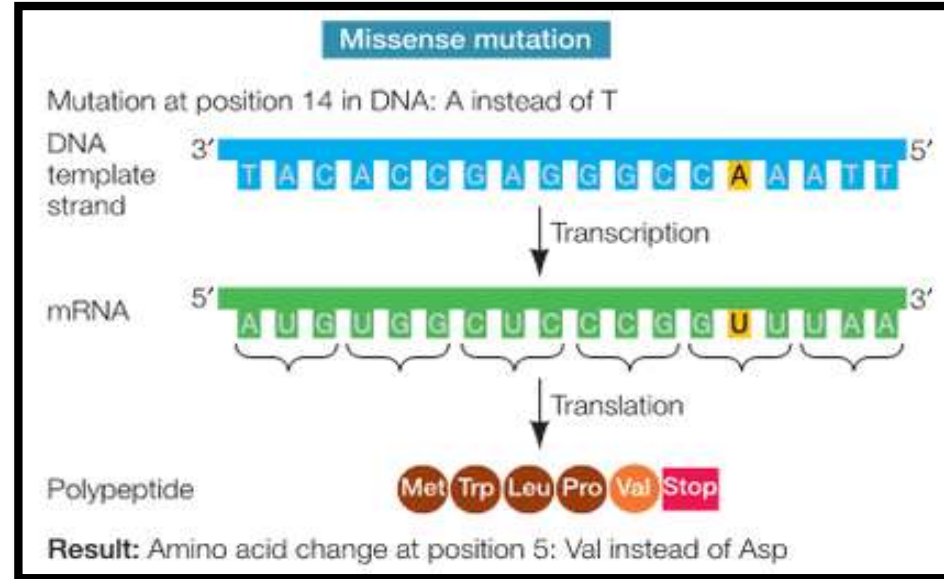
Single-Gene Mutations

Point mutation (mispairing): most frequent type and a single base pair is substituted/inserted/deleted. The effect could be minor, or not, depending on final codon sequence!

Silent Mutation: Sequence stays the same



Missense Mutation: Alters sequence of a protein



Single-Gene Mutations

Nonsense Mutation: inserts a “stop” earlier than it was supposed to

Frameshift Mutation: Changes reading frame and all subsequent amino acids are affected

Nonsense mutation

Mutation at position 5 in DNA: T instead of C

DNA template strand 3' T A C A T C G A G G G C C T A A T T 5'

Transcription

mRNA 5' A U G U A G C U C C C G G A U U A A 3'

Translation

Polypeptide Met Stop

Result: Only one amino acid translated; no protein made

Frame-shift mutation

Mutation by insertion of T between bases 6 and 7 in DNA

DNA template strand 3' T A C A C C G A G G G C C T A A T T 5'

DNA template strand 3' T A C A C C T G A G G G C C T A A T T 5'

Transcription

mRNA 5' A U G U G G A C U C C C G G A U U A A 3'

Translation

Polypeptide Met Trp Thr Pro Gly Leu

Result: All amino acids changed beyond the insertion

Reading the Codon!

First Base	Second Base				Third Base
	U	C	A	G	
U	UUU phenylalanine	UCU serine	UAU tyrosine	UGU cysteine	U
	UUC phenylalanine	UCC serine	UAC tyrosine	UGC cysteine	C
	UUA leucine	UCA serine	UAA stop**	UGA stop**	A
	UUG leucine	UCG serine	UAG stop**	UGG tryptophan	G
C	CUU leucine	CCU proline	CAU histidine	CGU arginine	U
	CUC leucine	CCC proline	CAC histidine	CGC arginine	C
	CUA leucine	CCA proline	CAA glutamine	CGA arginine	A
	CUG leucine	CCG proline	CAG glutamine	CGG arginine	G
A	AUU isoleucine	ACU threonine	AAU asparagine	AGU serine	U
	AUC isoleucine	ACC threonine	AAC asparagine	AGC serine	C
	AUA isoleucine	ACA threonine	AAA lysine	AGA arginine	A
	AUG methionine*	ACG threonine	AAG lysine	AGG arginine	G
G	GUU valine	GCU alanine	GAU aspartate	GGU glycine	U
	GUC valine	GCC alanine	GAC aspartate	GGC glycine	C
	GUA valine	GCA alanine	GAA glutamate	GGA glycine	A
	GUG valine	GCG alanine	GAG glutamate	GGG glycine	G

* AUG is an initiator codon. It also codes for the amino acid methionine.

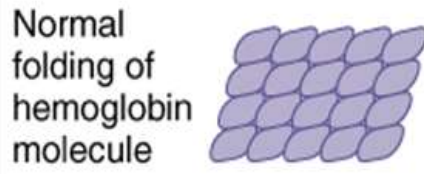
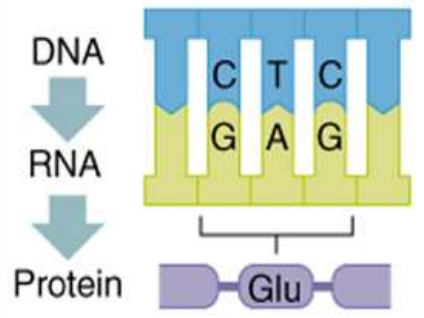
** UAA, UAG, and UGA are terminator codons.

With your partner, discuss

- 1. Which single-gene mutation would have the largest effect?**

2. With your partner, discuss which single-gene mutation is sickle red blood cells are an example of.

wildtype allele

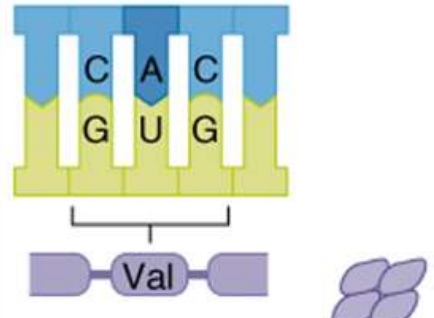


Normal red blood cells



wildtype phenotype

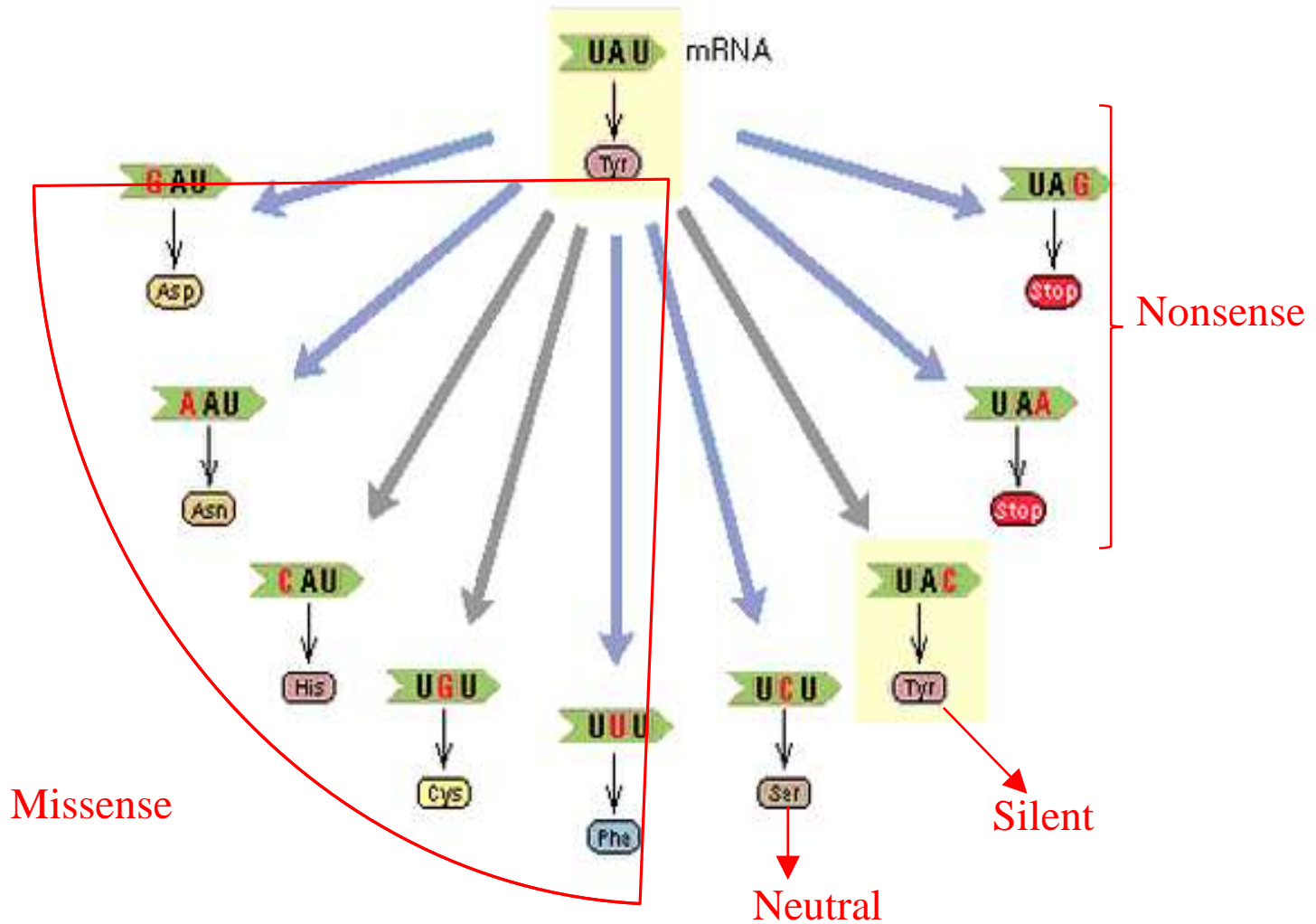
mutant allele



Sickled red blood cells

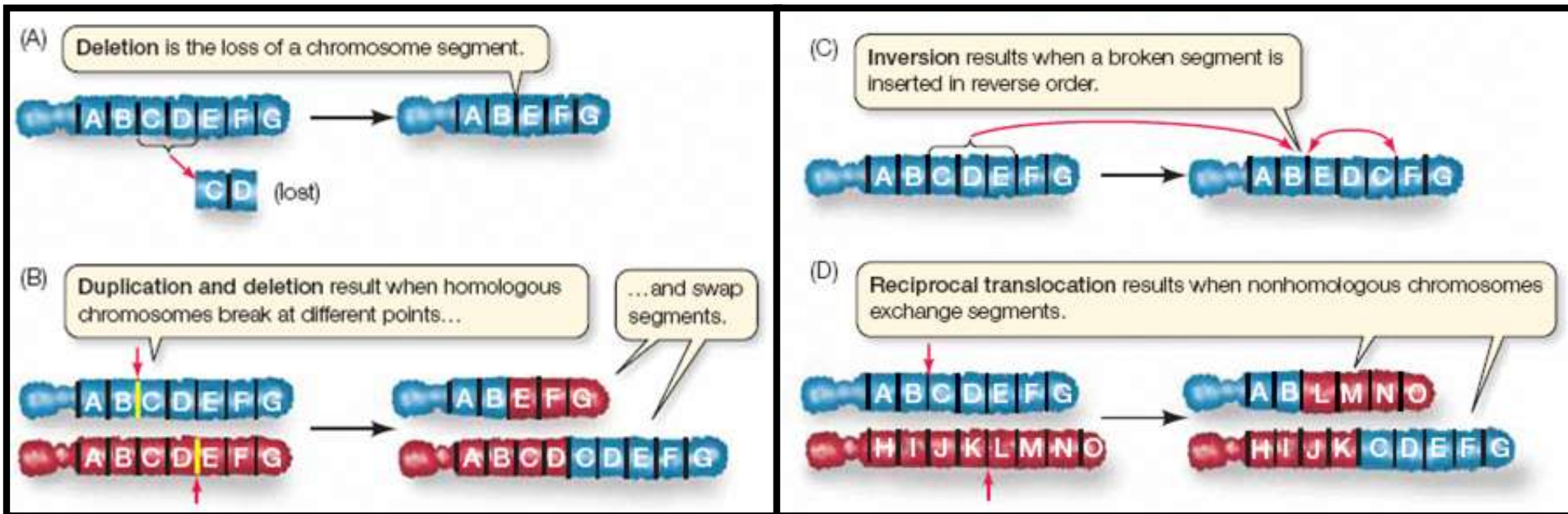


mutant phenotype



Types of Mutations: Chromosome Mutations

Changes in chromosomes can involve many genes, and are usually a consequence of crossing-over gone wrong during meiosis

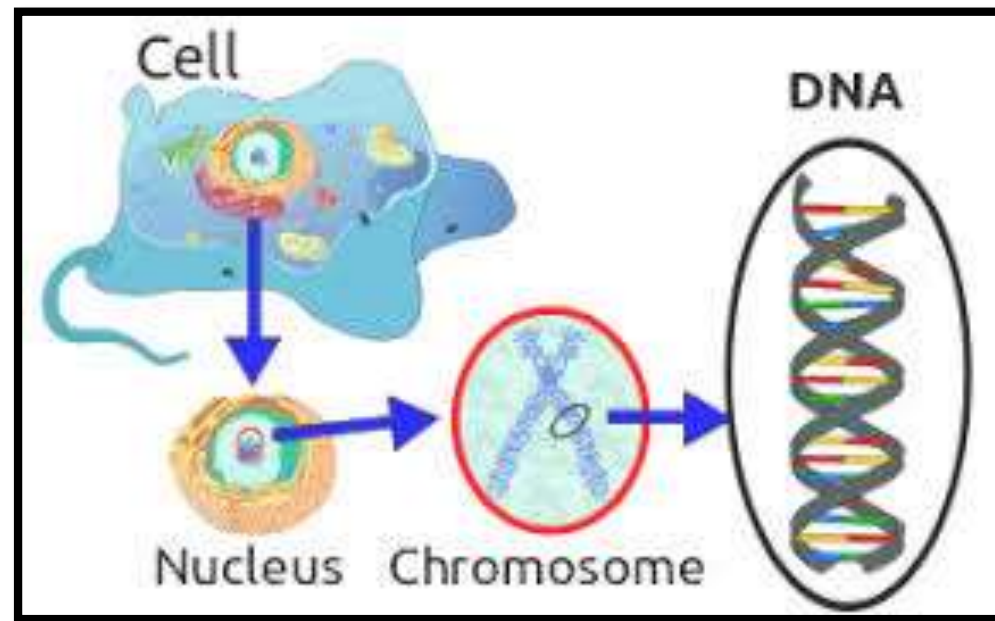


Can these mutations
be fixed?

ERROR CORRECTION

A human cell can go through mitosis and make a copy its DNA in a few hours!

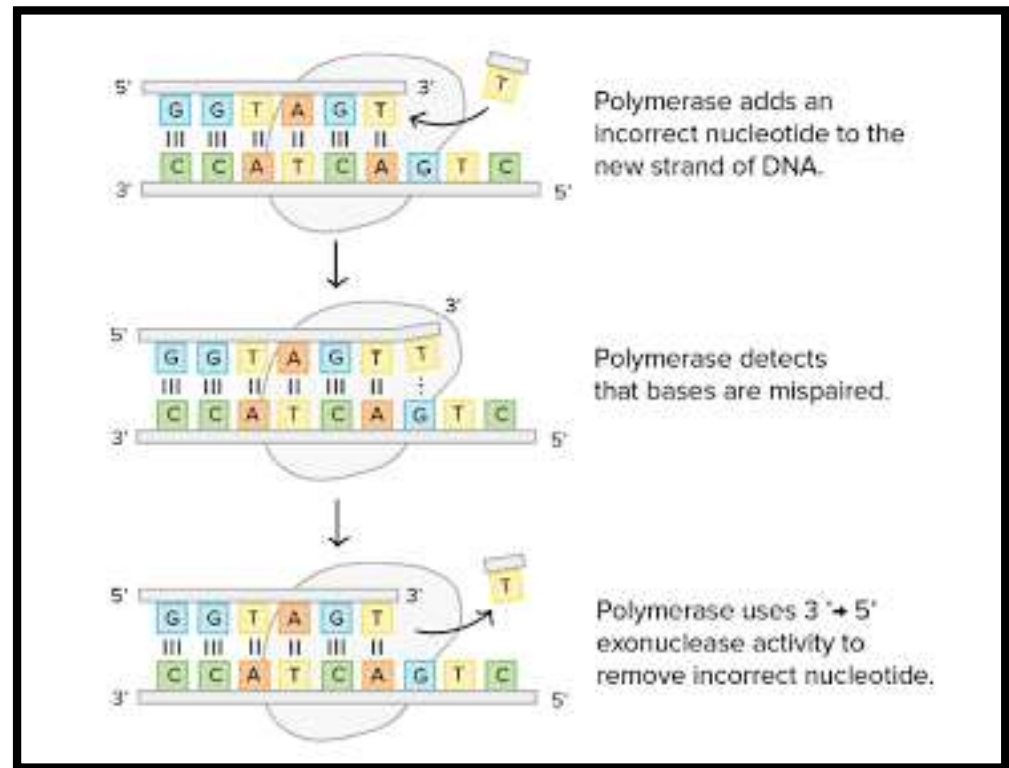
If you stretched the DNA in one cell all the way out, it would be about 2m long and all the DNA in all your cells put together would be about twice the diameter of the Solar System.



Mechanisms of Repair

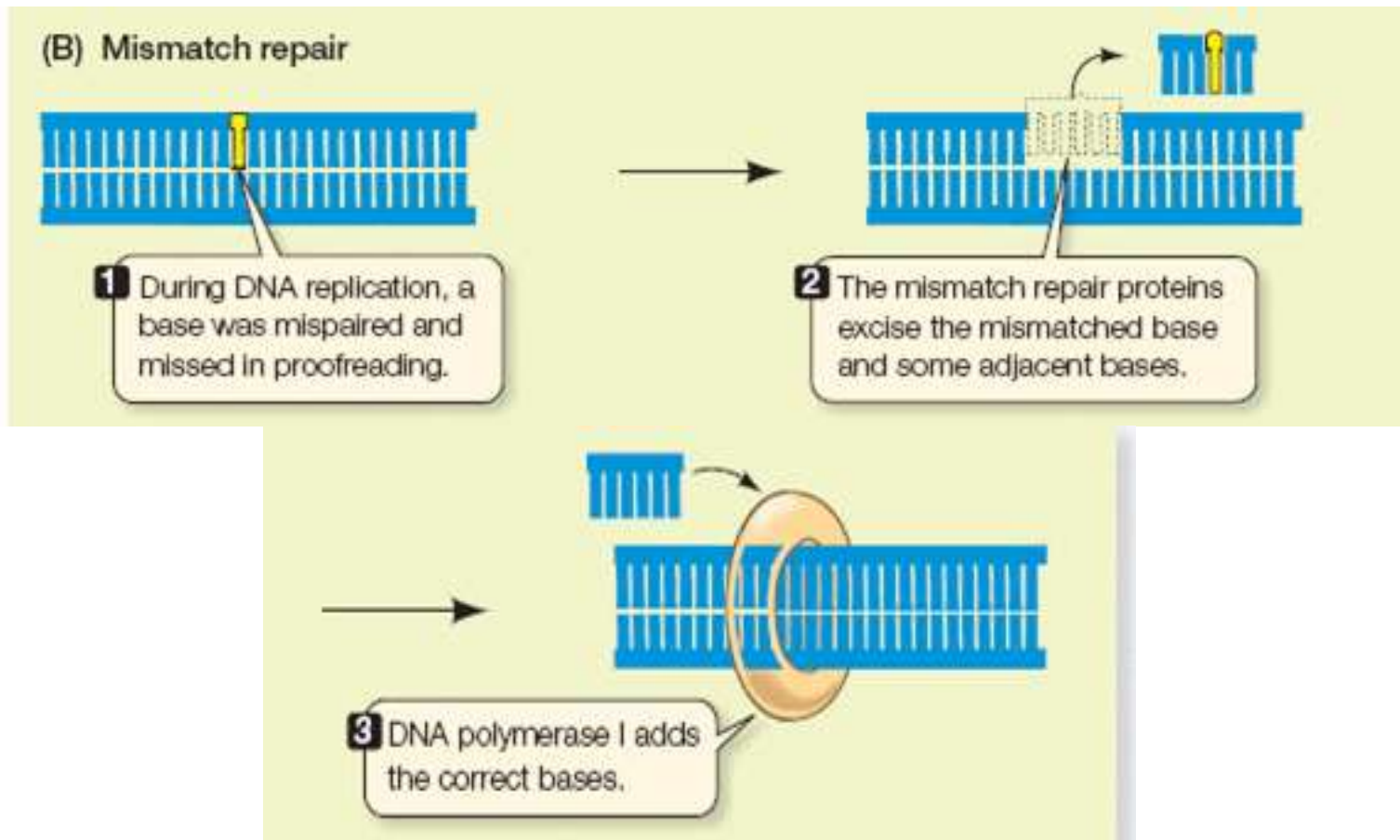
Proofreading – DNA Polymerase I and DNA Polymerase II

- x Both proof-read and “fix” mistakes as new DNA is being made.
- x 99% of mistakes are caught this way
- x The incorrect base is taken out, and the based correct added



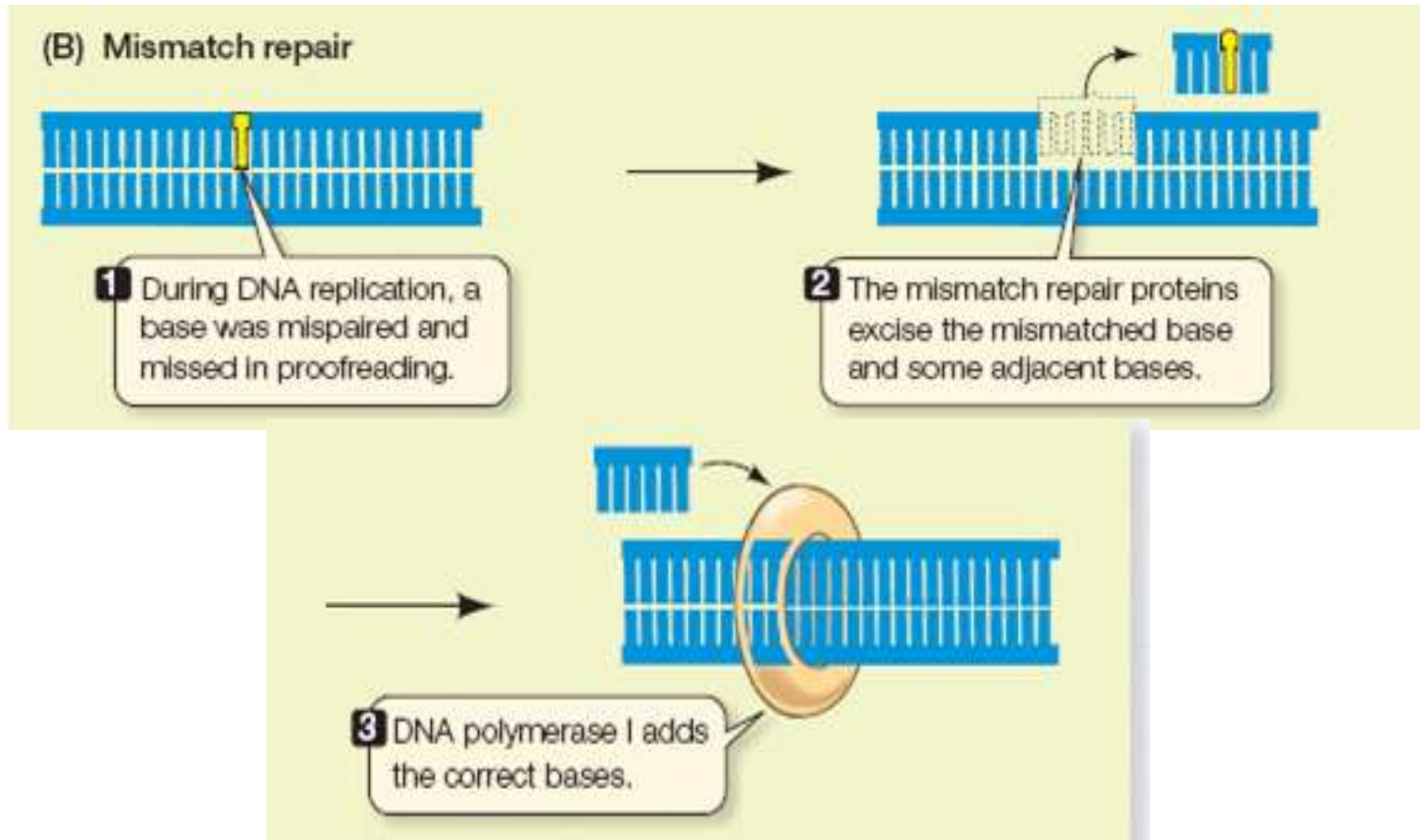
Mismatch Repair

Similarly in prokaryotes and eukaryotes, a protein group replaces mismatched nucleotides with the correct ones.



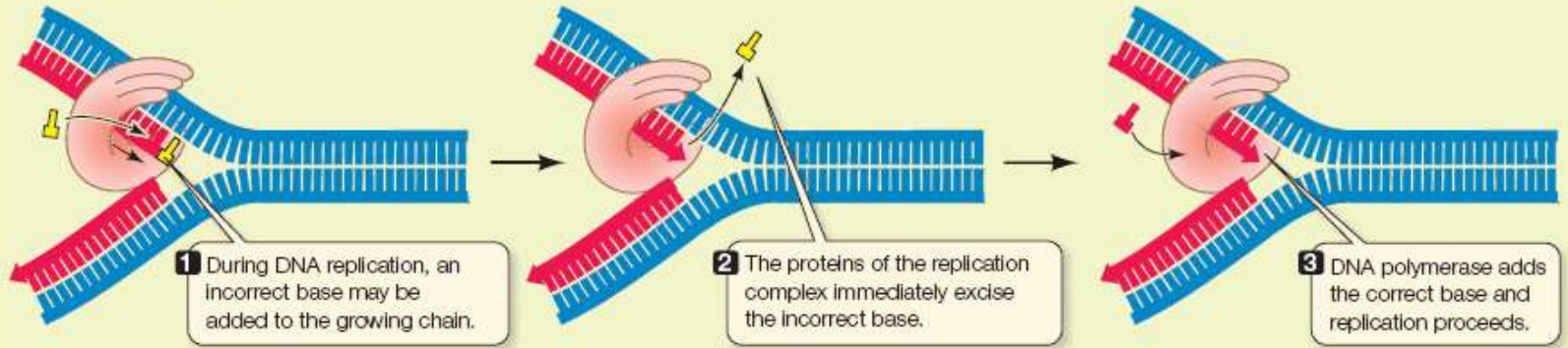
Excision Repair

Damage to one or a few bases of DNA is often fixed by removal and replacement of the damaged region. In base excision repair, just the damaged base is removed.

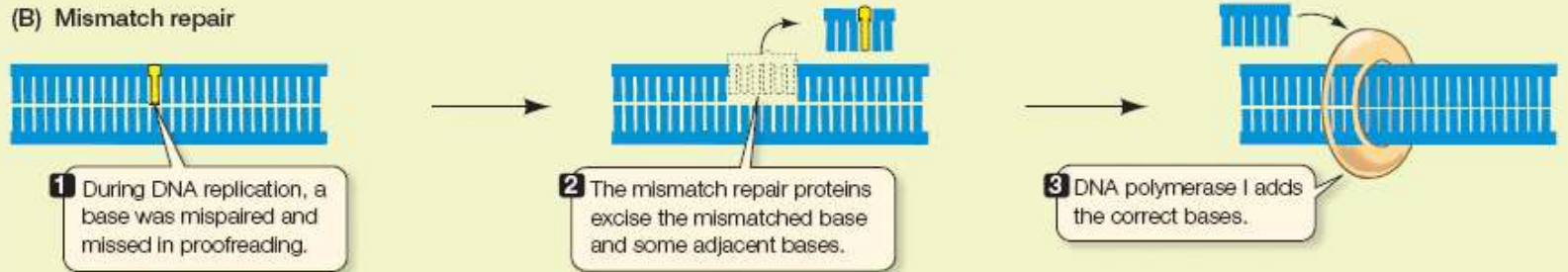


Error Correction Recap

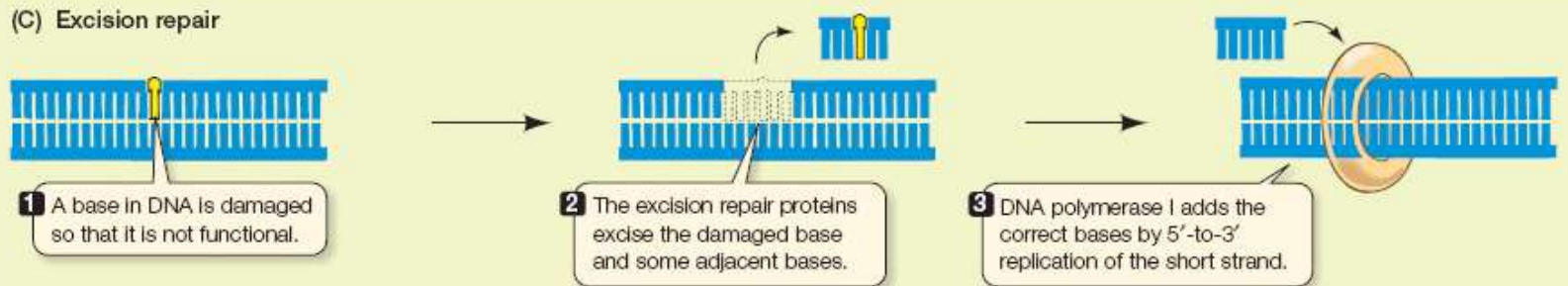
(A) DNA proofreading



(B) Mismatch repair

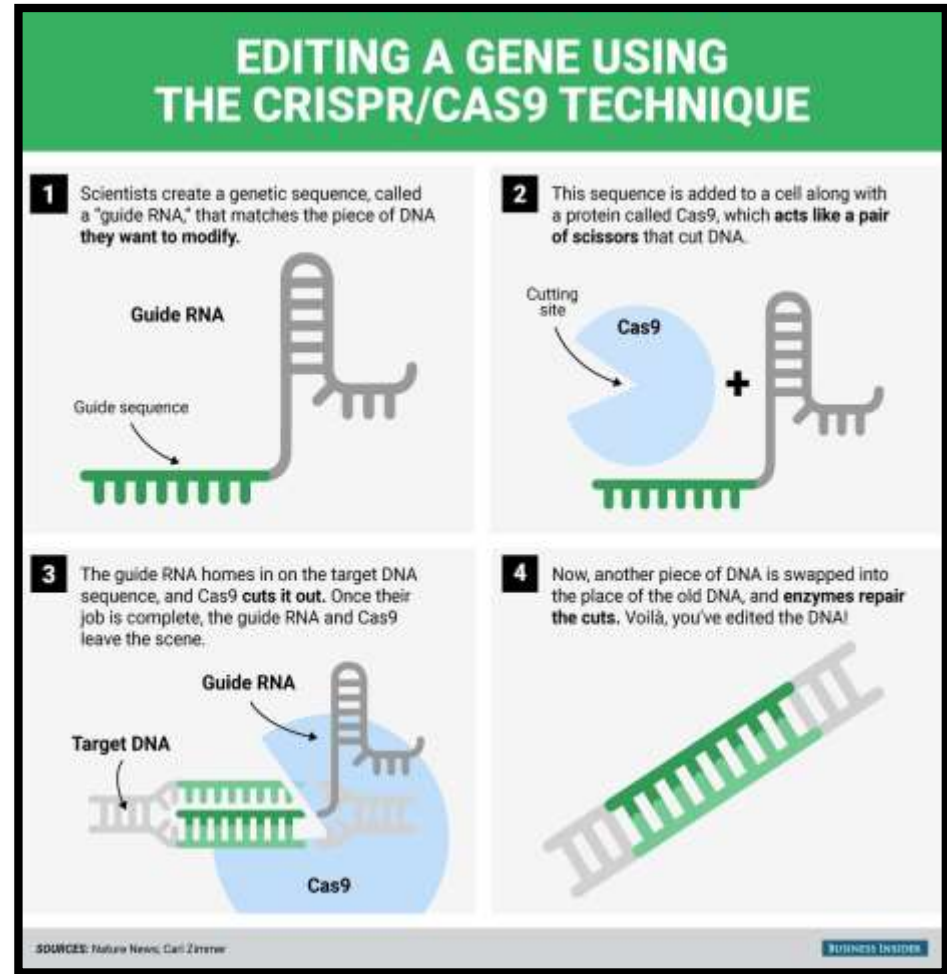


(C) Excision repair



Targeted Mutagenesis

x Researchers have developed many ways of targeting specific locations for mutation, so that they may better study the effects of certain genes and changes to them. One method that is gaining a lot of attention now is called [CRISPR](#).



Example Nucleotide Matching Scratch Game

This game asks players to match nucleotides!

The checkmark will light up, stating the answer is correct, or the X mark to light up, asking the player to try again!



CRISPR Resources

CRISPR Explained Youtube Video

<https://www.youtube.com/watch?v=UKbrwPL3wXE>

How CRISPR lets you edit DNA – Andrea M. Henle

<https://www.youtube.com/watch?v=UKbrwPL3wXE>

Genetic Engineering Will Change Everything Forever –CRISPR

<https://www.youtube.com/watch?v=jAhjPd4uNFY>

With CRISPR Prime, gene therapies are one step closer to curing millions

<https://synbiobeta.com/with-crispr-prime-gene-therapies-are-one-step-closer-to-curing-millions/>

New Details About The Infamous 'CRISPR Babies' Experiment Have Just Been Revealed

<https://www.sciencealert.com/china-s-failed-experiment-proves-we-re-not-ready-for-human-gene-editing>

Chinese scientist's claims he created HIV-resistant 'CRISPR babies' a 'deliberate falsehood', researchers say

<https://nationalpost.com/news/world/chinese-scientists-claims-he-created-hiv-resistant-crispr-babies-a-deliberate-falsehood-researchers-say>