Proofreading

DNA polymerases are the enzymes that build DNA in cells. During DNA replication (copying), most DNA polymerases can “check their work” with each base that they add. This process is called proofreading. If the polymerase detects that a wrong (incorrectly paired) nucleotide has been added, it will remove and replace the nucleotide right away, before continuing with DNA synthes

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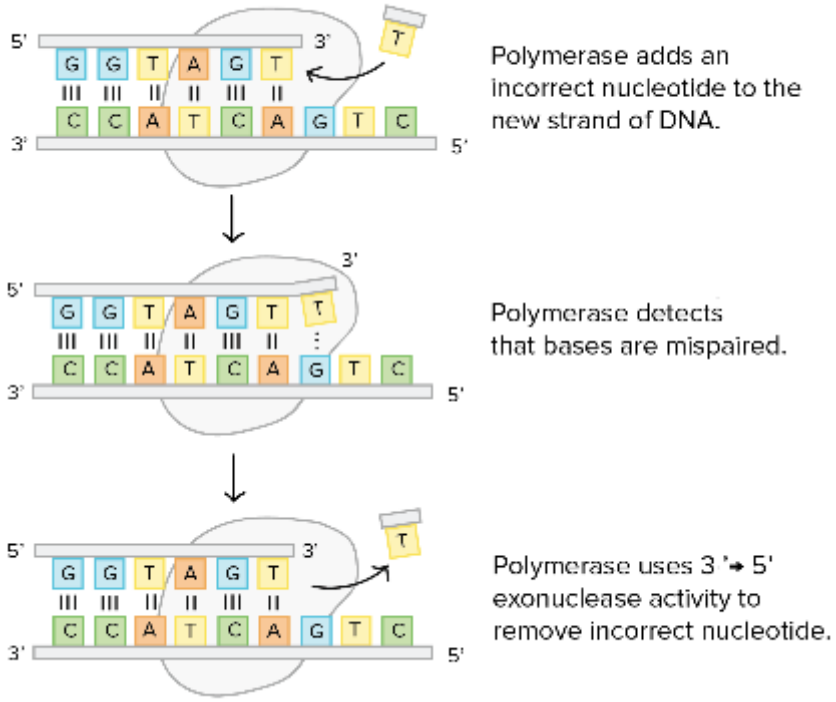
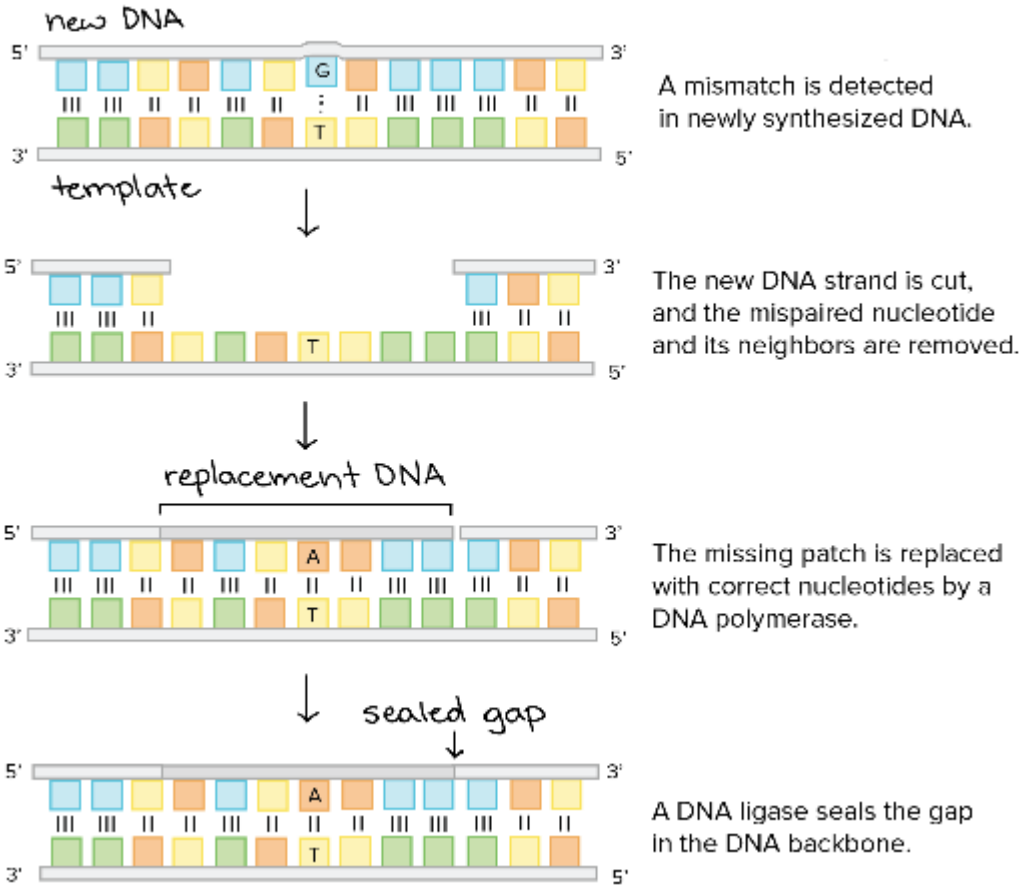


Mismatch repair

Many errors are corrected by proofreading, but a few slip through. Mismatch repair happens right after new DNA has been made, and its job is to remove and replace mis-paired bases (ones that were not fixed during proofreading). Mismatch repair can also detect and correct small insertions and deletions that happen when the polymerases "slips," losing its footing on the template.

How does mismatch repair work? First, a protein complex (group of proteins) recognizes and binds to the mispaired base. A second complex cuts the DNA near the mismatch, and more enzymes chop out the incorrect nucleotide and a surrounding patch of DNA. A DNA polymerase then replaces the missing section with correct nucleotides, and an enzyme called a DNA ligase seals the gap



Mismatch repair:

1- A mismatch is detected in newly synthesized DNA , there is a G in the new stand paired with a T in the template (old) strand
2- The new DNA strand is cut, and a patch of DNA containing the mispaired nucleotide and its neighbors is removed
3- The missing patch is replaced with correct nucleotides by a DNA polymerase
4- A DNA ligase seals the remaining gap in the DNA backbone

DNA damage repair mechanisms

Bad things can happen to DNA at almost any point in a cell's lifetime, not just during replication. In fact, your DNA is getting damaged all the time by outside factors like UV light, chemicals, and X-rays—not to mention spontaneous chemical reactions that happen even without environmental insults.

Fortunately, your cells have repair mechanisms to detect and correct many types of DNA damage. Repair processes that help fix damaged DNA include:

Direct reversal: Some DNA-damaging chemical reactions can be directly "undone" by enzymes in the cell.

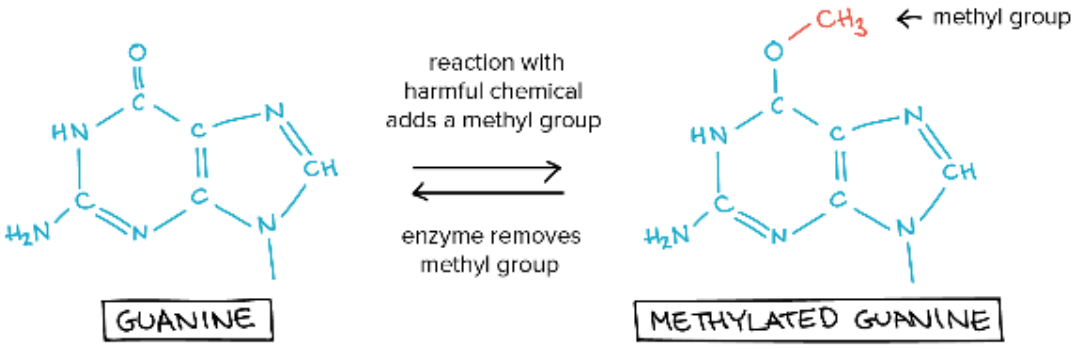
Excision repair: Damage to one or a few bases of DNA is often fixed by removal (excision) and replacement of the damaged region. In base excision repair, just the damaged base is removed. In nucleotide excision repair, as in the mismatch repair we saw above, a patch of nucleotides is removed.

Double-stranded break repair: Two major pathways, non-homologous end joining and homologous recombination, are used to repair double-stranded breaks in DNA (that is, when an entire chromosome splits into two pieces).

Reversal of damage

In some cases, a cell can fix DNA damage simply by reversing the chemical reaction that caused it. To understand this, we need to realize

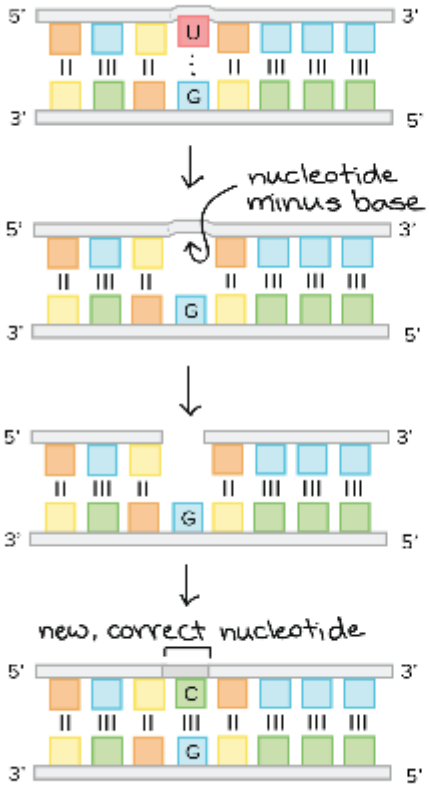
that "DNA damage" often just involves an extra group of atoms getting attached to DNA through a chemical reaction.
For example, guanine (G) can undergo a reaction that attaches a methyl (
−CH3 group to an oxygen atom in the base. The methyl-bearing guanine, if not fixed, will pair with thymine (T) rather than cytosine (C) during DNA replication. Luckily, humans and many other organisms have an enzyme that can remove the methyl group, reversing the reaction and returning the base to normal



Base excision repair
Base excision repair is a mechanism used to detect and remove certain types of damaged bases. A group of enzymes called glycosylases play a key role in base excision repair. Each glycosylase detects and removes a specific kind of damaged base.
For example, a chemical reaction called deamination can convert a cytosine base into uracil, a base typically found only in RNA. During DNA replication, uracil will pair with adenine rather than guanine (as it would if the base was still cytosine), so an uncorrected cytosine-to-uracil change can lead to a mutation

To prevent such mutations, a glycosylase from the base excision repair pathway detects and removes deaminated cytosines. Once the base has

been removed, the "empty" piece of DNA backbone is also removed, and the gap is filled and sealed by other enzymes



Deamination converts a cytosine base into a uracil.

The uracil is detected and removed, leaving a base-less nucleotide.

The base-less nucleotide is removed, leaving a small hole in the DNA backbone.

The hole is filled with the right base by a DNA polymerase, and the gap is sealed by a ligase.