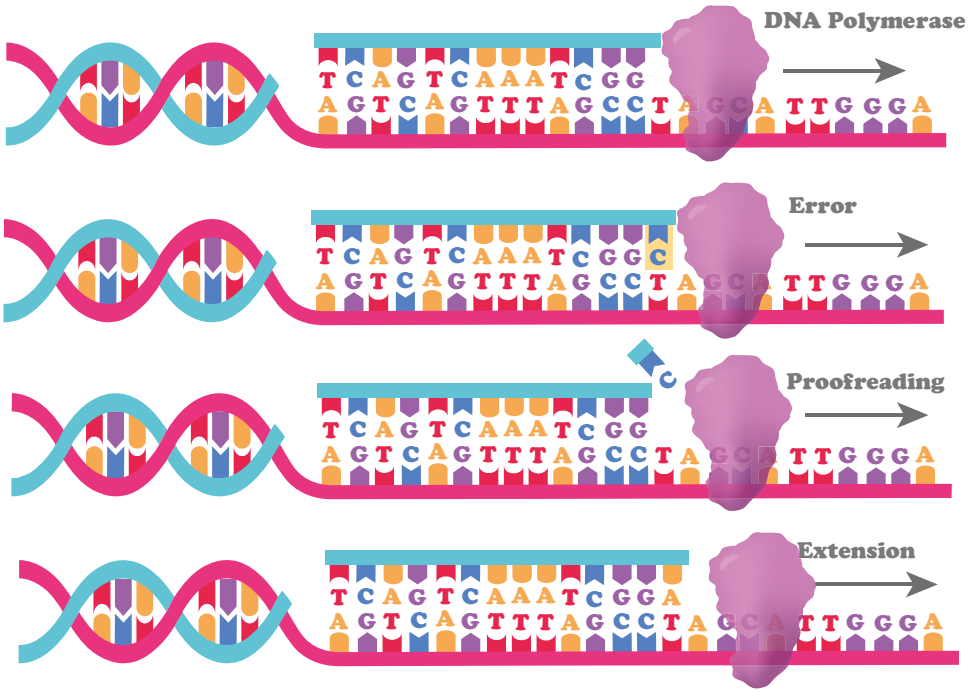
CONCEPT: DNA REPAIR

- DNA damage is repaired in a lot of different _____-
  - □ DNA polymerase proofreading quickly fixes a mispaired base
  - □ Enzymes can reverse damaged DNA
    - Many different enzymes exist to counteract damaged DNA
      - Ex: CPD photolyase is an enzyme that repairs dimers caused from UV light

EXAMPLE:



Repair Pathways

□ **Base-excision repair (BER)** removes and replace damaged nucleotides

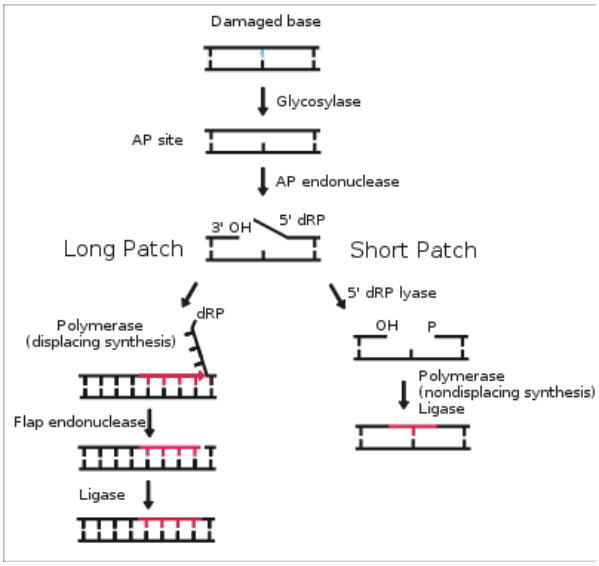
- DNA glycoslyases are enzyme that remove the damaged base from the sugar

- A deoxyribophosphodiesterase enzyme removes a stretch of neighboring DNA

- DNA polymerase fills the gap with complementary nucleotides

- DNA ligase seals the new nucleotides into the backbone

EXAMPLE:



□ **Nucleotide-excision repair (NER)** repairs damage that _____ the DNA helix

1. **Global genomic NER** repairs damage anywhere in the genome

2. **Transcription-coupled NER** repairs only transcribed regions of DNA

- Damaged base is recognized by proteins, which recruit more proteins

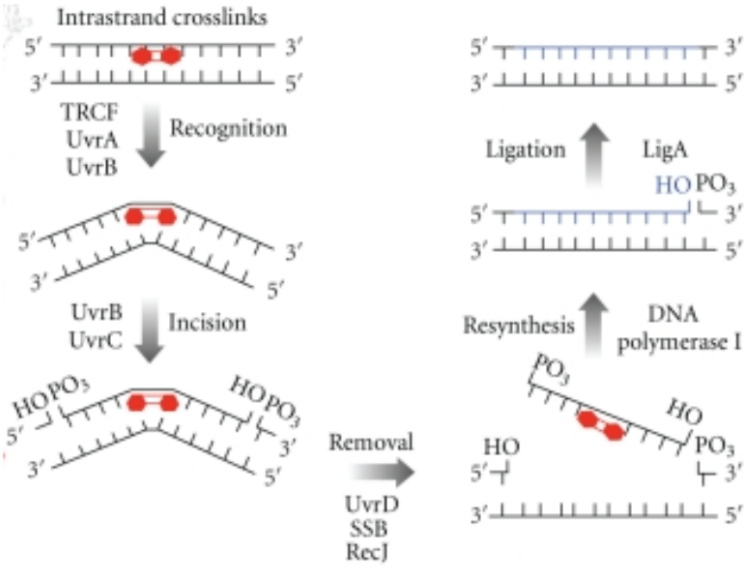
- A 30 nucleotide segment of DNA is removed from the damaged area

- DNA polymerase fills the gap, and DNA ligase seals the new nucleotides to the backbone

- Distortions in NER cause diseases like Xoderma pigmentosum and cockayne syndrome

    - Causes light sensitivities

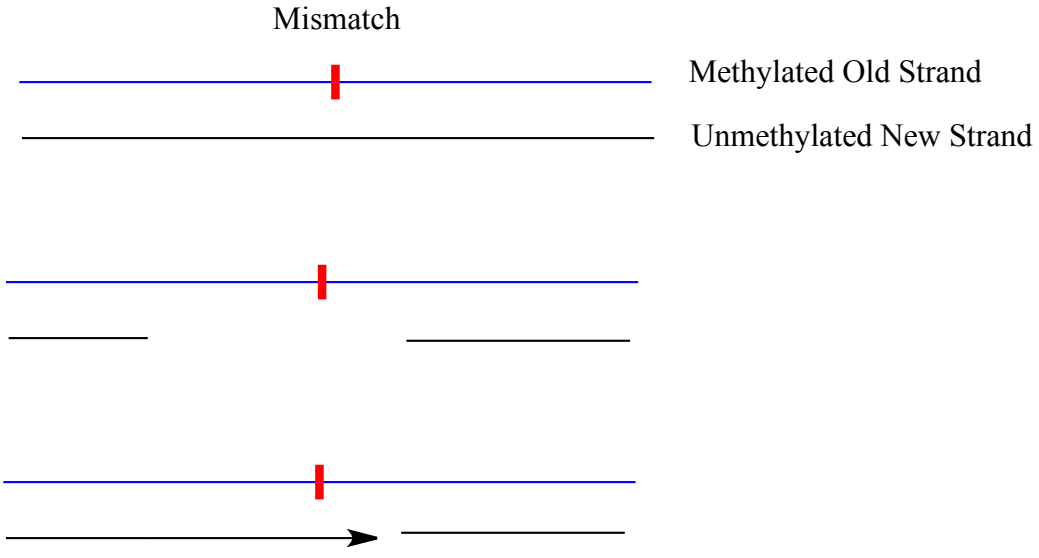
EXAMPLE:



□ **Mismatch repair** repairs damaged from insertions or deletions that occur immediately following replication

- First, the mismatched base is recognized, and proteins are recruited to the area
- The methylation status of the DNA strands is used to determine which is the mismatched base
    - Methylated strand = old strand, unmethylated strand = new strand
- DNA polymerase fills the gap, and DNA ligase seals the new nucleotides to the backbone

EXAMPLE:



Translesion Synthesis

□ **Translesoin DNA synthesis** is a last resort mechanism the cell uses to prevent mutations from causing death

- DNA damage causes DNA polymerase to _____- while replicating

- **Translesion (bypass) polymerases** are recruited to the area

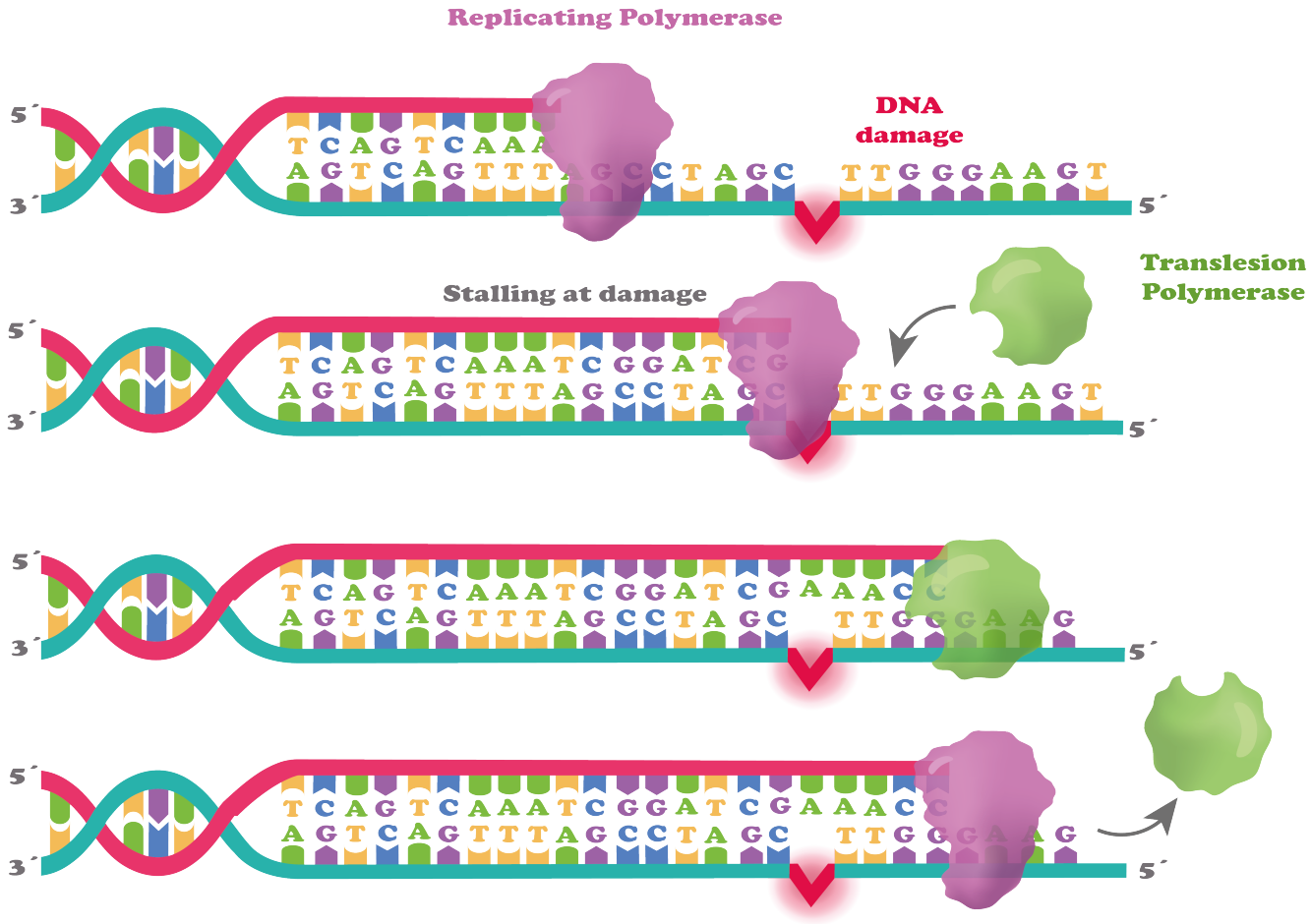
  - These polymerases can overcome helical distortions and continue replicating

  - But they have problems including: high error rate, no proofreading, and only add few nt at a time

- So translesion polymerases unblock stalled replication forks to allow for replication to continue

- They don't fix the damage that caused the stall and they can miss mutations without proofreading

EXAMPLE:

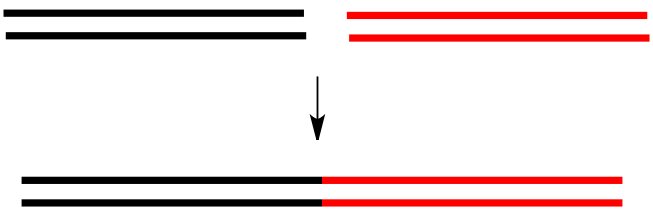


Double Strand Breaks

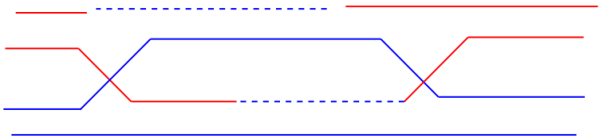
- Double strand breaks can be repaired in _____ ways
  - □ **Nonhomologous end joining** connects two broken ends together
    - Proteins recognize DNA damage
    - Other proteins are recruited which trim nucleotides off the damaged ends
    - DNA ligase connects the two broken ends
    - This type of repair occurs outside of S phase
  - □ **Homologous recombination** repairs double strand breaks directly after replication
    - *Synthesis-dependent strand annealing* uses sister chromatids as a template to repair the broken strands
    - Process is similar to crossing over, but uses sister chromatids instead of nonsister chromatids

EXAMPLE:

Nonhomologous end joining



Homologous Recombination



PRACTICE:

1. Which of the following repair pathways repairs damage that causes distortions in the double helix?
    a. Base Excision Repair
    b. Nucleotide Excision Repair
    c. Mismatch Repair
    d. Homologous Recombination

2. Which of the following repair pathways uses a methylated strand of DNA to correct DNA damage?
    a. Base Excision Repair
    b. Nucleotide Excision Repair
    c. Mismatch Repair
    d. Homologous Recombination

3. True or False: Translesion DNA synthesis is the first mechanism the cell uses to repair DNA damage?
    a. True
    b. False

4. Which of the following pathways is an error-free way to repair double-stranded breaks?
    a. Homologous recombination
    b. Non-homologous end joining
    c. Translesion synthesis
    d. Mismatch repair