DNA structure , replication and repair

A 4-year-old boy is brought to the office for evaluation of fatigue and bone pain. Physical examination shows diffuse lymphadenopathy and purpura over his arms and legs. Laboratory analysis reveals anemia and thrombocytopenia, and a peripheral blood smear shows lymphoblasts. After further work-up, acute lymphoblastic leukemia is diagnosed, and the patient begins a chemotherapy regimen that includes doxorubicin. This agent intercalates between DNA base pairs and inhibits DNA replication, a process that normally occurs at replication forks and produces 2 distinct daughter strands. Which of the following is unique to the daughter strand that is synthesized in the opposite direction of the growing replication fork?

- A. 3′→5′ exonuclease activity of DNA polymerase
- B. 3′→5′ polymerase activity of DNA polymerase
- C. 5′→3′ exonuclease activity of DNA polymerase
- D. RNA primer synthesis before DNA strand synthesis
- E. Synthesis of multiple, short DNA fragments

Proceed To Next Item

A research scientist purifies DNA polymerase III from an *Escherichia coli* extract. The isolated enzymes are then incubated in a mixture containing DNA templates, RNA primer oligonucleotides, and tagged deoxynucleotides. After analyzing the DNA molecules formed during incubation, the researcher concludes that the enzyme possesses 3′ to 5′ exonuclease activity. Which of the following enzymatic actions was most likely observed during the experiment?

- A. Cleavage of DNA strands to remove supercoils
- B. Excision of thymine dimers within DNA
- C. Removal of mismatched base pairs during DNA synthesis
- D. Removal of RNA primer nucleotides
- E. Unwinding of double-stranded DNA

Proceed To Next Item

An 18-year-old man comes to the urgent care clinic due to painful erythema affecting his extremities, trunk, and face. He is vacationing in Florida and spent 5 hours at a Gulf coast beach earlier in the day. The patient did not apply any sunscreen as it was cloudy. The physician explains that cloud cover does not afford a high degree of protection against the sun, especially with prolonged exposure in highly reflective environments like the beach. He is advised to wear protective clothing and apply sunscreen to prevent recurrence. Which of the following is most likely to happen within the patient's skin cells as a result of his exposure?

- A. Covalent bond formation between adjacent purine bases
- B. End-joining repair of double-stranded DNA breaks
- C. Endonuclease nicking of the damaged DNA strand
- D. Hypermethylation of residues in the undamaged DNA strand
- E. Removal of deaminated bases by glycosylase

Proceed To Next Item

Researchers studying molecular biology observe a eukaryotic cell via electron microscopy. During interphase of the cell cycle, they notice 10-nm thick chromatin fibers with a "beads on a string" appearance. These chromatin fibers are extracted and treated with an endonuclease, which preferentially cleaves the "string" portions of the chromatin. Further evaluation reveals that the "beads" are composed of DNA wrapped around a core of proteins. Which of the following proteins is most likely found outside this core and promotes chromatin compaction?

- A. Histone H1
- B. Histone H3
- C. Histone H4
- D. Small nuclear ribonucleoprotein
- E. Type II topoisomerase
- F. Ubiquitin

Proceed To Next Item

A 34-year-old woman with a history of recurrent urinary tract infections comes to the physician with dysuria and increased urinary frequency. Her urine culture grows colonies of Gram-negative bacteria. The bacteria are isolated and placed in a growth-enhancing nutrient solution, where they undergo rapid cellular division. As they are actively dividing, the bacterial cells are lysed and their DNA is extracted and purified. Analysis of the partially replicated DNA fragments shows the presence of uracil. This finding is most likely mediated by which of the following enzymes?

- A. DNA ligase
- B. DNA polymerase I
- C. DNA polymerase III
- D. Gyrase
- E. Helicase
- F. Primase

Proceed To Next Item

A 46-year-old woman is evaluated for a 2-month history of progressive abdominal distension, vague abdominal discomfort, and a bloating sensation. Physical examination shows moderate ascites. Laboratory evaluation reveals markedly elevated CA-125 and imaging studies show an ovarian mass. Molecular analysis of the malignant cells in ascitic fluid is performed, and these cells are found to have high telomerase activity. This enzyme promotes cell growth and malignancy by directly causing which of the following actions?

- A. Enhancing tissue invasion and metastasis
- B. Increasing transcription factor expression
- C. Preventing chromosomal shortening
- D. Promoting G1/S progression
- E. Sustaining angiogenesis

Proceed To Next Item

A 5-year-old girl is brought to the office by her mother because she is concerned that her daughter "sunburns too easily." The mother says the patient's skin becomes red and scaly with only minimal sun exposure. She first noticed the problem when her daughter was 7 months old during a trip to the beach. The mother has since avoided exposing her child to excess sunlight, but finds it difficult now that the patient has begun kindergarten. Physical examination shows thin and hyperpigmented skin. She also has a few nevi on her hands that have been enlarging rapidly. This patient's disorder is most likely due to a primary defect involving which of the following processes?

- A. DNA mismatch repair
- B. Nucleotide excision repair
- C. Ras signal transduction
- D. Regulation of apoptosis
- E. Regulation of cell cycle
- F. Repair of DNA crosslinks

Proceed To Next Item

Pharmacologic researchers develop a novel alkylating chemotherapeutic agent against glioblastoma multiforme. They find that malignant cells with methylation of the promoter region for the O^6-methylguanine-DNA methyltransferase (*MGMT*) gene are more susceptible to this drug than cells without methylation. Which of the following is the most likely function of the protein encoded by the gene?

- A. Induction of apoptosis
- B. Reducing major histocompatibility complex expression
- C. Repairing DNA damage
- D. Upregulation of telomerase

Proceed To Next Item

A 23-year-old previously healthy man comes to the office after noticing a painless, hard mass in the left testis. Scrotal ultrasound shows a solid testicular mass, and CT scan of the abdomen and pelvis shows left paraaortic lymphadenopathy. Left orchidectomy is performed and postoperative histopathology reveals seminoma of the testis. External beam radiotherapy is administered to the paraaortic metastatic area. Several weeks later, the retroperitoneal nodes are observed to have markedly decreased in size. Which of the following is the most likely effect of the therapy used on the metastatic cells in this patient?

- A. Demethylation of DNA
- B. DNA cross-linking
- C. Double-strand DNA breaks
- D. Nucleotide mismatches
- E. Pyrimidine dimers

Proceed To Next Item

A 56-year-old man comes to the office due to difficulty swallowing for the past several months. He has the most trouble with solid foods and says, "They seem to get stuck in my throat if I don't chew a lot." The patient has no chest pain or heartburn and has lost 4.5 kg (10 lb) in the last 3 months. He has been an avid hunter for many years and frequently cures the meat he eats with sodium nitrite. Physical examination is unremarkable. Endoscopy shows an ulcerated mass in the distal third of the esophagus, and biopsy samples are obtained from the mass and adjacent normal mucosa. Analysis of the samples shows accelerated cytosine deamination of chromosomal DNA in both normal and malignant epithelial cells. This damage is most likely to be repaired through which of the following enzymatic sequences?

- A. Endonuclease, polymerase, glycosylase, lyase, ligase
- B. Endonuclease, polymerase, lyase, glycosylase, ligase
- C. Glycosylase, endonuclease, lyase, polymerase, ligase
- D. Glycosylase, ligase, lyase, endonuclease, polymerase
- E. Lyase, endonuclease, glycosylase, polymerase, ligase

Proceed To Next Item

An 18-year-old woman comes to the office for evaluation of graying hair. The patient has no other concerns and has otherwise been healthy. She reports that her mother had similar features at a young age and died of progressive pulmonary fibrosis. Examination shows diffuse gray hair. There are white patches on the surface of the tongue. Cardiopulmonary examination is unremarkable, and the abdomen is soft and nondistended. Skin examination shows areas of reticular hyperpigmentation on the neck and torso. The nails of the fingers and toes appear thin. Genetic testing reveals a loss-of-function mutation affecting the telomerase reverse transcriptase gene. Which of the following cell types is most likely to be affected by this mutation?

- A. Cardiac myocytes
- B. CNS neurons
- C. Compact bone osteocytes
- D. Hematopoietic stem cells
- E. Secondary oocytes
- F. Vascular endothelial cells

Proceed To Next Item

A 65-year-old woman with chronic obstructive pulmonary disease and type II diabetes mellitus comes to the emergency department due to profound fevers and malaise. After initial evaluation, she is hospitalized for septicemia. Blood cultures plated on lactose-containing media grow rapidly dividing gram-negative bacteria. Replication of these microbial cells requires synthesis of two daughter strands of DNA using the parent strands as templates. Which of the following processes will differ the most between the 2 daughter strands formed at each replication fork?

- A. Enzymatic function of DNA helicase
- B. Interaction with single-stranded DNA-binding proteins
- C. Joining of DNA fragments by ligase
- D. Proofreading of the newly synthesized DNA
- E. Relief of supercoils by topoisomerase

Proceed To Next Item

A 24-year-old woman comes to the office for evaluation of a skin lesion. Physical examination shows a 5-mm, brown, oval macule on her anterior thigh. Biopsy of the lesion shows normal-appearing nevus cells clustered in the epidermis, consistent with a benign acquired melanocytic nevus. During histologic analysis, the patient's epithelial cells are found to each contain a condensed body composed of heavily methylated DNA at the periphery of the nucleus. This region of DNA is most likely associated with which of the following genetic findings?

- A. Extensive double-strand DNA break repair
- B. Histone acetylation
- C. Impaired mismatch repair
- D. Low transcription activity
- E. Reduced positive supercoiling

Proceed To Next Item

A 6-year-old boy is brought to the office due to a persistent facial ulcer for the past 2 months. His mother reports that the patient has extreme sensitivity to sunlight and has developed freckles on his face, neck, and limbs since infancy. On physical examination, the skin in sun-exposed areas is dry and rough with numerous freckles and erythematous macules. There is an ulcerated plaque on the left face; a biopsy reveals squamous cell carcinoma. Further testing leads to a diagnosis of xeroderma pigmentosum. A defect in which of the following enzymes is most likely causing this patient's condition?

- A. 3'→5' exonuclease
- B. DNA ligase
- C. Endonuclease
- D. Helicase
- E. Topoisomerase

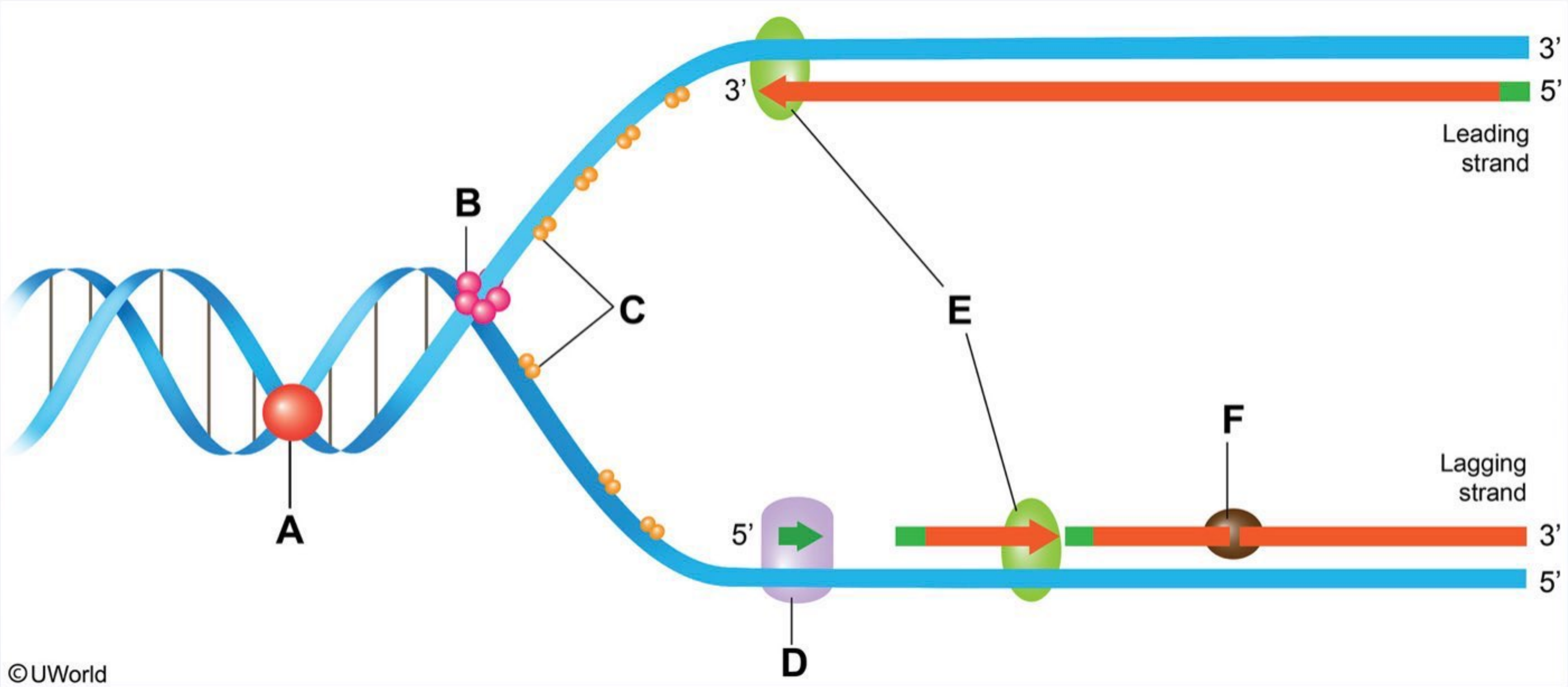
Proceed To Next Item

A genetic researcher is comparing the DNA replication process of prokaryotic and eukaryotic cells. In an experiment, *Escherichia coli* and human cells are cultured in separate media containing tagged nucleotides and their rates of DNA replication are determined. Although the eukaryotic genome is significantly larger and more complex than that of the prokaryote, eukaryotic DNA replication still occurs in a timely manner. Which of the following features of eukaryotic replication best explains this observation?

- A. Continuous synthesis of the lagging strand
- B. Energy-independent DNA unwinding
- C. Multiple origins of replication
- D. No proofreading of daughter strands
- E. No requirement for RNA primers

Proceed To Next Item

A 13-year-old boy is evaluated for a possible inherited genetic defect. He has growth retardation, microcephaly, sun-sensitive skin, and recurrent infections. The patient is the second-born child of 2 first cousins. His parents and siblings are healthy, but 2 of his maternal cousins have similar signs and symptoms. Genetic analysis of the patient reveals a defect in the *BLM* gene, which codes for a DNA helicase. Which of the following is the most likely site of action of this enzyme in the DNA replication fork diagram shown below?



- A. A
- B. B
- C. C
- D. D
- E. E
- F. F

A pharmaceutical researcher develops a novel antibacterial drug that works by inhibiting exonuclease activity during DNA replication. When actively dividing *Escherichia coli* is exposed to the drug, enzyme-mediated nucleotide removal in the 5' to 3' direction is impaired, leading to inhibition of bacterial growth. Which of the following enzymes is the most likely target of this drug?

A. DNA polymerase I
B. DNA polymerase III
C. Gyrase
D. Helicase
E. Ligase
F. Primase

Proceed To Next Item

A 34-year-old woman comes to the office due to dysuria. The patient has a history of recurrent urinary tract infections. A urine sample is collected and sent for culture. Gram-negative bacteria isolated from the urine are found to form pink colonies on lactose-containing MacConkey agar. Several days later, bacterial isolates from a second urine sample are found to form white colonies when plated on the same type of medium. Genetic analysis shows that the more recent isolates have a single nucleotide deletion within the *lac* operon DNA sequence. This genomic change is most consistent with which of the following?

- A. Conservative mutation
- B. Frameshift mutation
- C. Missense mutation
- D. Nonsense mutation
- E. Silent mutation

Proceed To Next Item

A cell biologist is studying the role of ribonucleoproteins in normal cellular function. He prepares a cell extract using a specific cell type obtained from a 73-year-old man. Ribonucleoproteins are separated and purified from the cell extract for structural and functional analyses. These cells are found to express higher amounts of a particular protein in comparison to other cell types. This protein has reverse transcriptase activity that functions to add TTAGGG repeats to the 3' end of chromosomes. Which of the following cell types was most likely studied in this experiment?

- A. Epidermal basal cells
- B. Erythrocytes
- C. Myocardial cells
- D. Neurons
- E. Pancreatic β cells

Proceed To Next Item

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- A. 3′→5′ exonuclease activity of DNA polymerase (10%)
- B. 3′→5′ polymerase activity of DNA polymerase (6%)
- C. 5′→3′ exonuclease activity of DNA polymerase (11%)
- D. RNA primer synthesis before DNA strand synthesis (7%)
- ✓ E. Synthesis of multiple, short DNA fragments (63%)

Omitted	63%	05 mins, 28 secs	2023
Correct answer E	Answered correctly	Time Spent	Version

Explanation

DNA replication fork

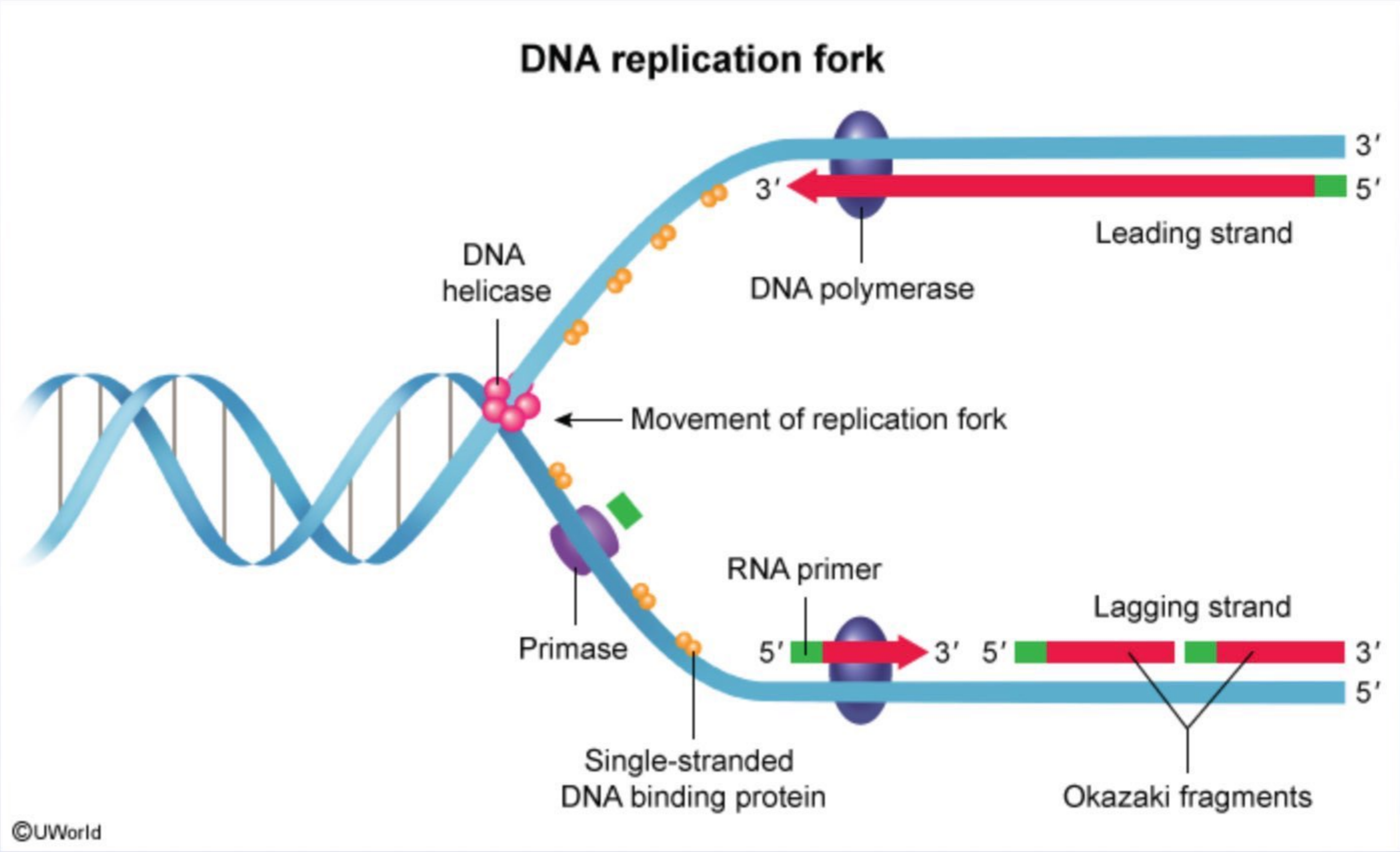
Omitted
Correct answer
E

63%
Answered correctly

05 mins, 28 secs
Time Spent

2023
Version

Explanation



DNA replication begins at **multiple sites**—origins of replication—within eukaryotic chromosomes. At these sites, the parent DNA double helix is separated and unwound in a process facilitated by the helicase enzyme and single-stranded DNA binding proteins. The locations at which unwound DNA meets the double helix are known

DNA replication begins at **multiple sites**—origins of replication—within eukaryotic chromosomes. At these sites, the parent DNA double helix is separated and unwound in a process facilitated by the helicase enzyme and single-stranded DNA binding proteins. The locations at which unwound DNA meets the double helix are known as replication forks. Replication forks travel bidirectionally away from the origin of replication as DNA polymerase synthesizes complementary daughter DNA strands.

Synthesis of the daughter strands occurs simultaneously from both parent strands. However, because **DNA synthesis can occur in only the 5′→3′ direction**, only 1 daughter strand is synthesized continuously toward the replication fork; this is the leading strand. The other strand, called the **lagging strand**, must be synthesized **discontinuously** in a direction away from the replication fork; more segments are added as the replication fork moves across the DNA double helix. This results in the formation of **Okazaki fragments**, short stretches of newly synthesized DNA that are separated by RNA primers. These primers are then removed and replaced with DNA, and the Okazaki fragments are subsequently joined together by DNA ligase.

(Choice A) DNA polymerases have 3′→5′ exonuclease activity (proofreading function) that allows them to reverse direction and remove incorrectly placed bases. This process occurs on both newly formed daughter strands (not just the lagging strand) to help reduce replication errors.

(Choice B) DNA polymerases do not have 3′→5′ polymerase activity; all polymerases synthesize in the 5′→3′ direction.

(Choice C) During the synthesis of the lagging strand, 5′→3′ exonuclease activity is needed to remove RNA primers. However, it is also used to remove primers when joining leading strands from separate origins of replication and is therefore not a unique mechanism in the creation of the lagging strand.

(Choice D) Before DNA polymerase can initiate DNA synthesis, RNA primers must first be synthesized by the enzyme primase (DNA-dependent RNA polymerase). This process is necessary for synthesis of both daughter

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(Choice D) Before DNA polymerase can initiate DNA synthesis, RNA primers must first be synthesized by the enzyme primase (DNA-dependent RNA polymerase). This process is necessary for synthesis of both daughter strands and is therefore not unique to the lagging strand.

Educational objective:

DNA synthesis occurs in the 5′→3′ direction only. During DNA replication, one daughter strand is synthesized continuously toward the replication fork (leading strand), whereas the other daughter strand is synthesized discontinuously away from the replication fork (lagging strand). The lagging strand is formed from short stretches of newly synthesized DNA separated by RNA primers (Okazaki fragments).

References

- Eukaryotic DNA replication fork.

Genetics	Genetics (General Principles)	Dna replication
Subject	System	Topic

A research scientist purifies DNA polymerase III from an *Escherichia coli* extract. The isolated enzymes are then incubated in a mixture containing DNA templates, RNA primer oligonucleotides, and tagged deoxynucleotides. After analyzing the DNA molecules formed during incubation, the researcher concludes that the enzyme possesses 3′ to 5′ exonuclease activity. Which of the following enzymatic actions was most likely observed during the experiment?

- A. Cleavage of DNA strands to remove supercoils
- B. Excision of thymine dimers within DNA
- ✓ C. Removal of mismatched base pairs during DNA synthesis
- D. Removal of RNA primer nucleotides
- E. Unwinding of double-stranded DNA

Omitted
Correct answer
C

Collecting Statistics

05 secs
Time Spent

2023
Version

Explanation

Proteins & their functions in prokaryotic DNA replication	
Helicase	• Unwinding of double helix
DNA gyrase (type II topoisomerase)	• Removal of supercoils

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Helicase	• Unwinding of double helix
DNA gyrase (type II topoisomerase)	• Removal of supercoils
Single-stranded DNA binding protein	• Stabilization of unwound template strands
Primase (RNA polymerase)	• Synthesis of RNA primer
DNA polymerase III	• DNA synthesis (5′ → 3′ polymerase activity) • Proofreading (3′ → 5′ exonuclease activity)
DNA polymerase I	• Same as DNA polymerase III • Removal of RNA primer (5′ → 3′ exonuclease activity) & replacement with DNA
DNA ligase	• Joining of Okazaki fragments (lagging strand)

DNA replication is coordinated by the actions of multiple enzymes and proteins. It requires a high degree of fidelity to ensure preservation of the genetic code in daughter cells and to prevent accumulation of mutations.

Prokaryotes have 3 types of **DNA polymerase** (I, II, III), all of which perform the following functions:

- **DNA synthesis** (**5′ → 3′ polymerase** activity): DNA chain synthesis and elongation first require the presence of an RNA primer (created by an RNA polymerase, or primase). DNA polymerases then add individual nucleotides to the 3′ end of the growing daughter strand.
- **Proofreading** (**3′ → 5′ exonuclease** activity): As the DNA daughter strand is synthesized, DNA

individual nucleotides to the 3′ end of the growing daughter strand.

- **Proofreading** (**3′ → 5′ exonuclease** activity): As the DNA daughter strand is synthesized, DNA polymerases check that each added nucleotide is appropriately matched to its complementary base. Incorrect base pairs are removed (via hydrolysis of their phosphodiester bonds), and the correct complementary bases are added.

In this experiment, the researcher most likely observed **removal of mismatched base pairs** during DNA replication to conclude that DNA polymerase III has 3′ to 5′ exonuclease activity.

(Choice A) During DNA replication in prokaryotes, the circular DNA strands are unwound, creating tension. DNA gyrase (type II topoisomerase) temporarily cleaves both strands of the DNA double helix and introduces negative supercoils to relieve this tension.

(Choice B) Ultraviolet (UV) light can damage DNA by covalently bonding adjacent pyrimidine (typically thymine) bases to form dimers. These thymine dimers are usually removed via nucleotide excision repair by the enzyme UV-specific endonuclease.

(Choice D) A unique function of DNA polymerase I is its 5′ to 3′ exonuclease activity, which is used to remove the RNA primer synthesized by RNA primase. DNA polymerase III does not have 5′ to 3′ exonuclease activity.

(Choice E) Helicase promotes unwinding and dissociation of parent DNA strands at the replication fork.

Educational objective:
All prokaryotic DNA polymerases (I, II, and III) remove mismatched nucleotides via their 3′ to 5′ exonuclease (proofreading) activity. Only DNA polymerase I has 5′ to 3′ exonuclease activity, which is used to remove the RNA primer synthesized by RNA primase.

References

An 18-year-old man comes to the urgent care clinic due to painful erythema affecting his extremities, trunk, and face. He is vacationing in Florida and spent 5 hours at a Gulf coast beach earlier in the day. The patient did not apply any sunscreen as it was cloudy. The physician explains that cloud cover does not afford a high degree of protection against the sun, especially with prolonged exposure in highly reflective environments like the beach. He is advised to wear protective clothing and apply sunscreen to prevent recurrence. Which of the following is most likely to happen within the patient's skin cells as a result of his exposure?

- A. Covalent bond formation between adjacent purine bases (20%)
- B. End-joining repair of double-stranded DNA breaks (13%)
- ✓ C. Endonuclease nicking of the damaged DNA strand (57%)
- D. Hypermethylation of residues in the undamaged DNA strand (3%)
- E. Removal of deaminated bases by glycosylase (5%)

Omitted
Correct answer
C

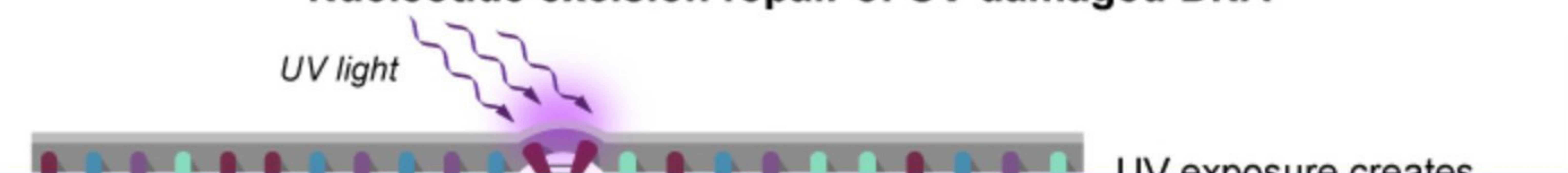
57%
Answered correctly

01 sec
Time Spent

2023
Version

Explanation

Nucleotide excision repair of UV damaged DNA



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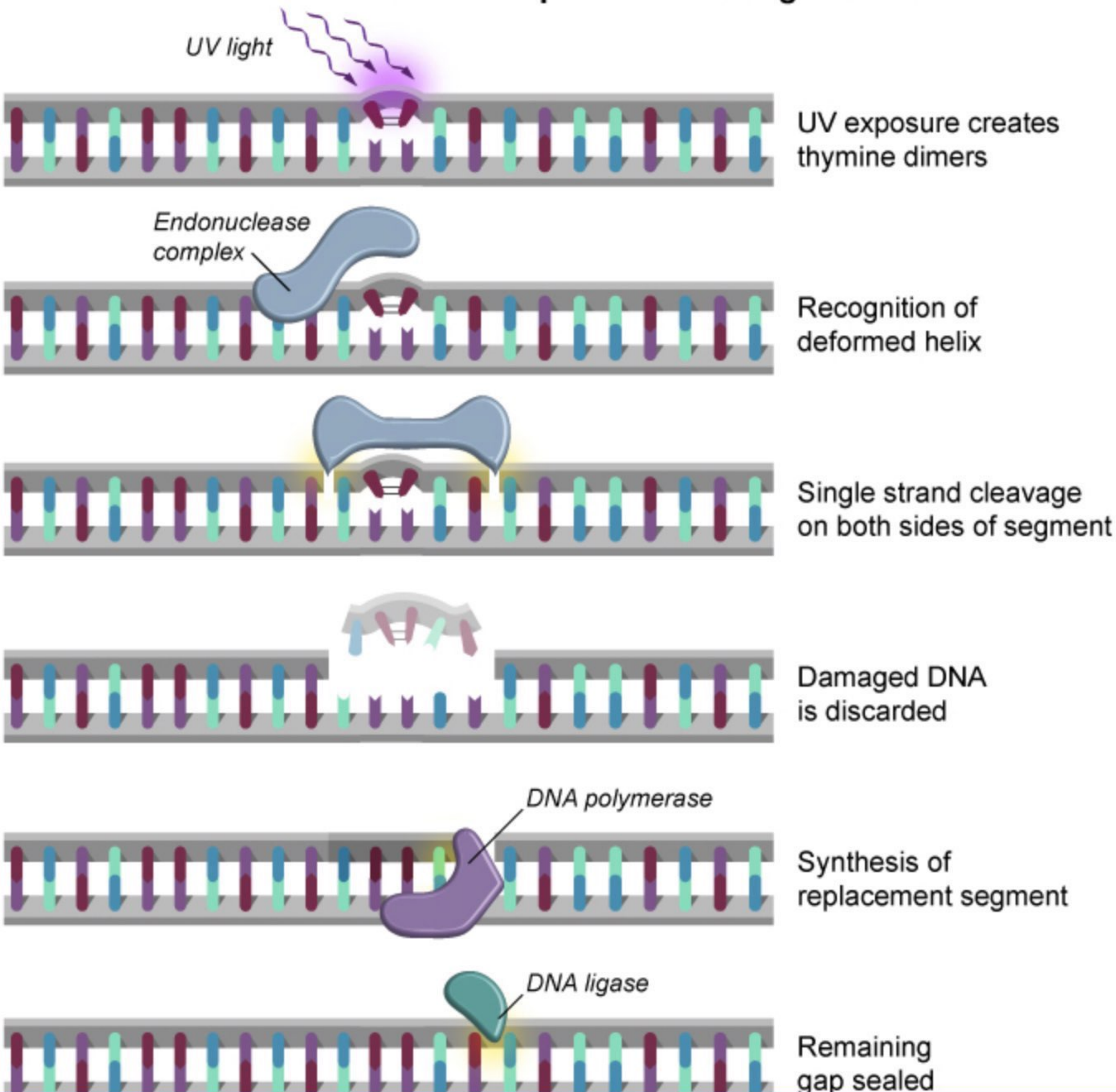

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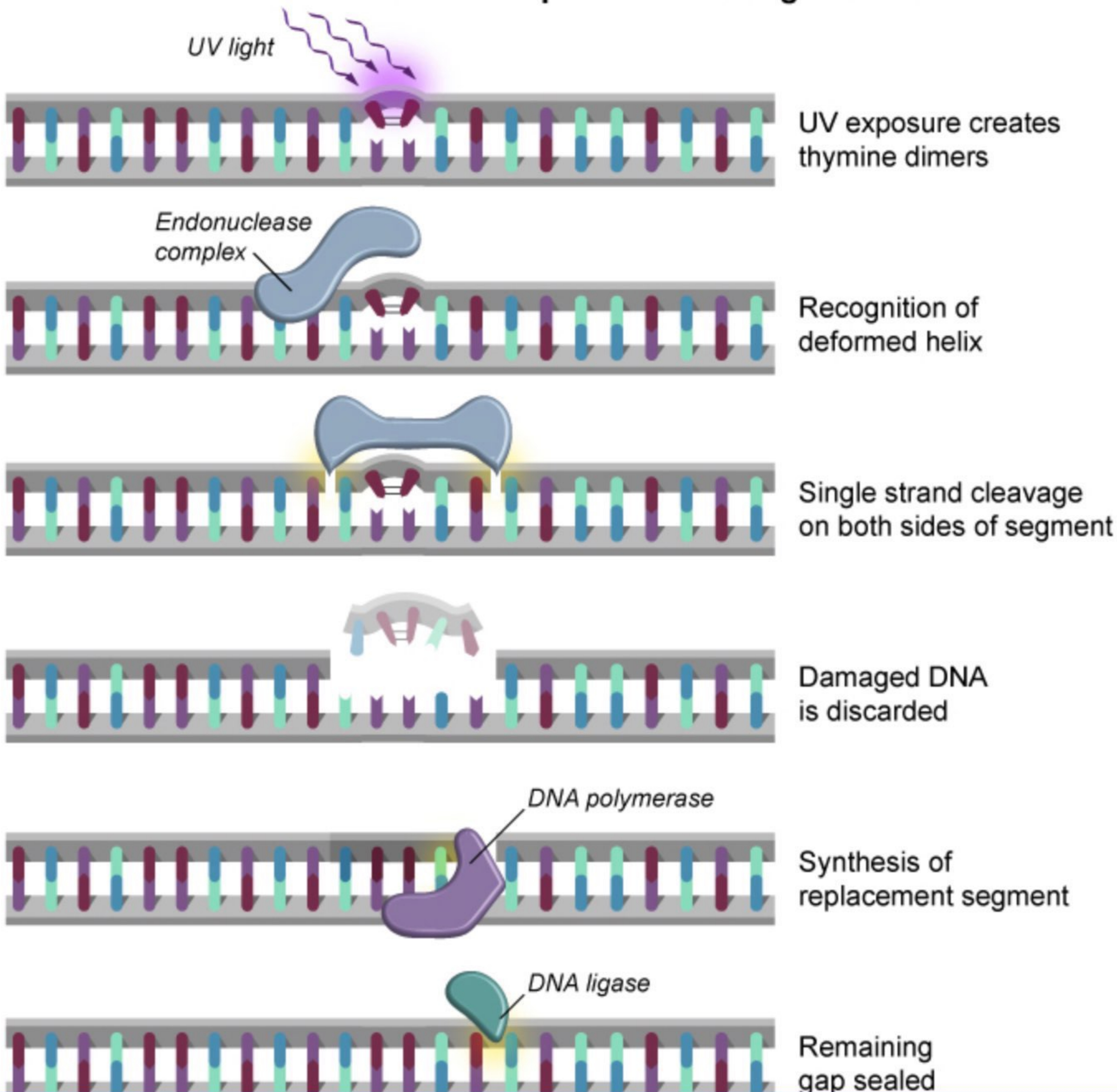

DNA can be damaged by a number of agents, including chemicals, ultraviolet radiation, and ionizing radiation. **Ultraviolet rays** damage DNA primarily through formation of abnormal covalent bonds between adjacent thymine or cytosine residues (**pyrimidine dimers**). The presence of pyrimidine dimers interferes with base recognition during transcription and replication, and **DNA mutations** can result if the damage is not repaired.

Pyrimidine dimers are removed by **nucleotide excision repair**. In this process, a specific endonuclease complex detects abnormalities in the DNA structure caused by the formation of DNA photoproducts. The endonuclease complex then **nicks** the damaged strand on both sides of the pyrimidine dimer, and the defective region is excised. DNA polymerase synthesizes new DNA in the place of the damaged DNA, and DNA ligase seals the final remaining nick.

Mutations that impair the components involved in nucleotide excision repair cause **xeroderma pigmentosum**, a condition characterized by severe photosensitivity and the development of skin cancers at a young age.

(Choice A) Ultraviolet radiation causes the formation of pyrimidine-pyrimidine dimers, not purine-purine dimers.

(Choice B) Exposure to ionizing radiation (x-rays and gamma rays) causes double-strand DNA breaks. The fractured ends can be joined by nonhomologous end joining.

(Choice D) Incorrect base substitution occurs during normal DNA replication and can result in mutations if they are not corrected. DNA mismatch repair in certain prokaryotes is guided by hypermethylation of the parent strand, which helps to identify the non-mutated strand for use as a template.

(Choice E) Deamination of DNA bases (eg, cytosine conversion to uracil, adenine to hypoxanthine) can occur spontaneously or secondary to chemical exposure. These errors are corrected by **base excision repair**. In this process, abnormal bases are recognized and removed by specific glycosylases without disruption of the phosphodiester backbone. The apurinic and apyrimidinic residues are then removed by specific endonucleases region is excised. DNA polymerase synthesizes new DNA in the place of the damaged DNA, and DNA ligase seals the final remaining nick.

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Educational objective:
Pyrimidine dimers are formed in DNA as a result of ultraviolet light exposure. They are recognized by a specific endonuclease complex that initiates the process of repair by nicking the damaged strand on both sides of the pyrimidine dimer. The damaged segment is then excised, and replacement DNA is synthesized by DNA polymerase.

Genetics | Genetics (General Principles) | Sunburn

Researchers studying molecular biology observe a eukaryotic cell via electron microscopy. During interphase of the cell cycle, they notice 10-nm thick chromatin fibers with a "beads on a string" appearance. These chromatin fibers are extracted and treated with an endonuclease, which preferentially cleaves the "string" portions of the chromatin. Further evaluation reveals that the "beads" are composed of DNA wrapped around a core of proteins. Which of the following proteins is most likely found outside this core and promotes chromatin compaction?

- A. Histone H1 (66%)
- B. Histone H3 (10%)
- C. Histone H4 (9%)
- D. Small nuclear ribonucleoprotein (3%)
- E. Type II topoisomerase (4%)
- F. Ubiquitin (3%)

Omitted
Correct answer
A

66%
Answered correctly

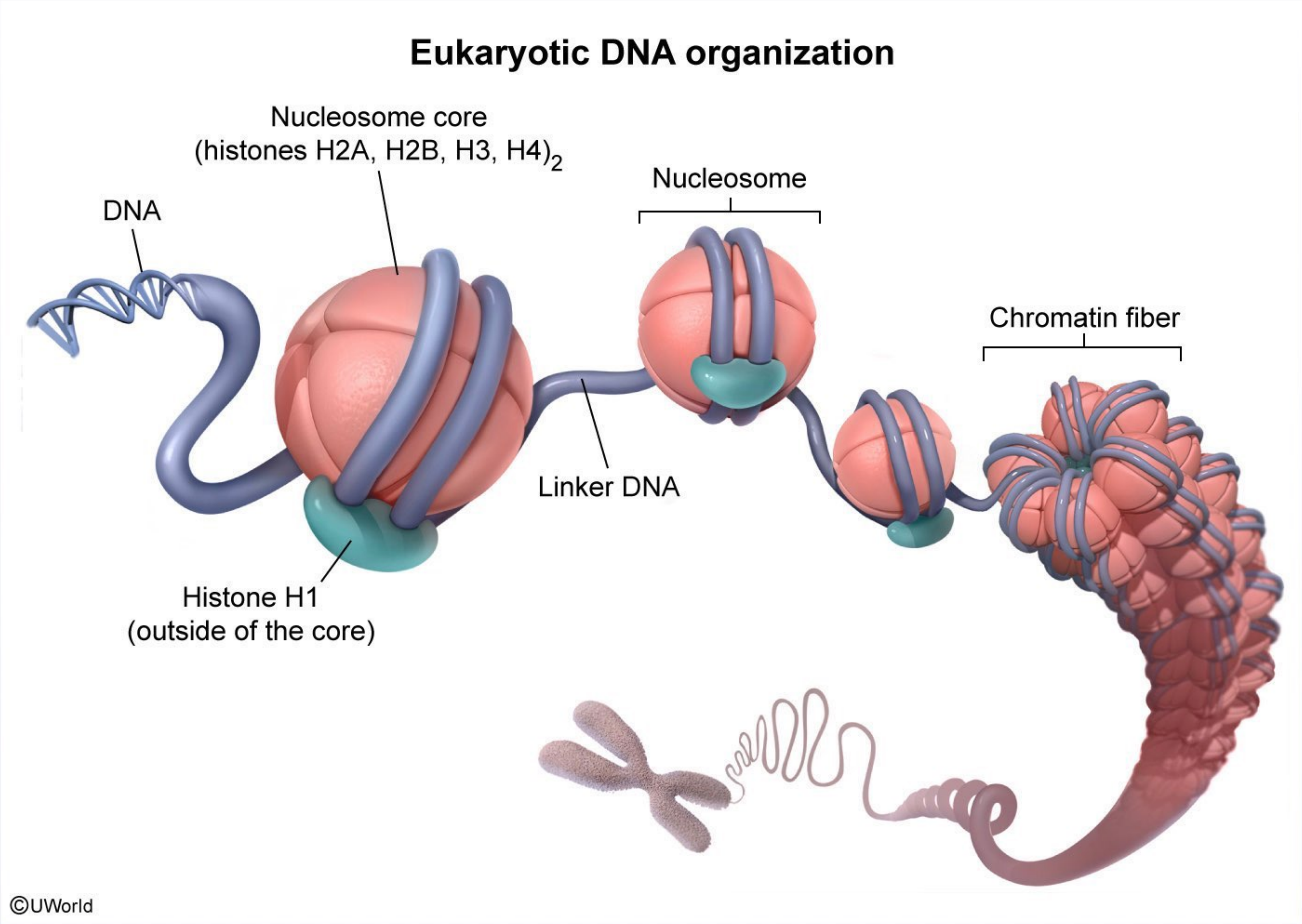
02 secs
Time Spent

2023
Version

Explanation

Eukaryotic DNA organization

Explanation



Chromatin is made up of DNA (negatively charged) wrapped twice around an octamer of histone proteins (positively charged). This core of histones is composed of 2 molecules each of histones H2A, H2B, H3, and H4. Together, these histone proteins and wrapped DNA are known as a **nucleosome**. Nucleosomes are separated

Chromatin is made up of DNA (negatively charged) wrapped twice around an octamer of histone proteins (positively charged). This core of histones is composed of 2 molecules each of histones H2A, H2B, H3, and H4. Together, these histone proteins and wrapped DNA are known as a **nucleosome**. Nucleosomes are separated by a stretch of DNA, or **linker DNA**, giving them the appearance of **beads on a string**. This loose structure of DNA organization is about 10 nm in diameter and provides a high degree of transcriptional access (euchromatin).

The degree to which nucleosomes can be compacted is dynamic and changes based on epigenetic modification (eg, histone acetylation) and binding of additional DNA structural proteins. One such protein is **histone H1**, which, in contrast to the other histone proteins, is located **outside the nucleosome core**. Histone H1 binds to both the nucleosome and adjacent linker DNA, which facilitates packaging of chromatin into a thicker (30-nm), **more compact** structure (heterochromatin) that limits transcriptional access to the DNA.

During cell division, chromatin interacts with additional proteins (eg, nuclear scaffold protein) and undergoes further rounds of coiling, ultimately forming condensed chromosomes.

(Choices B and C) Histones H3 and H4 are components of the nucleosome core.

(Choice D) Small nuclear ribonucleoproteins help splice out introns from pre-mRNA, forming mature mRNA.

(Choice E) During DNA replication, topoisomerase relieves the tension created during DNA strand unwinding by introducing negative supercoils into the DNA. It does not promote chromatin compaction.

(Choice F) Ubiquitin is a small protein present in the cytoplasm and nucleus of all eukaryotes. It is typically covalently attached to various intracellular proteins to signal for their degradation by the proteasome (ubiquitin-proteasome pathway).

Educational objective:

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(Choice F) Ubiquitin is a small protein present in the cytoplasm and nucleus of all eukaryotes. It is typically covalently attached to various intracellular proteins to signal for their degradation by the proteasome (ubiquitin-proteasome pathway).

Educational objective:

Nucleosomes are composed of DNA wrapped around a core of histone proteins. Histone H1 is unique in that it is located outside this histone core and helps package nucleosomes into more compact structures, limiting transcriptional access to DNA.

References

- H1 histones: current perspectives and challenges.

Genetics	Genetics (General Principles)	Dna structure & function
Subject	System	Topic

A 34-year-old woman with a history of recurrent urinary tract infections comes to the physician with dysuria and increased urinary frequency. Her urine culture grows colonies of Gram-negative bacteria. The bacteria are isolated and placed in a growth-enhancing nutrient solution, where they undergo rapid cellular division. As they are actively dividing, the bacterial cells are lysed and their DNA is extracted and purified. Analysis of the partially replicated DNA fragments shows the presence of uracil. This finding is most likely mediated by which of the following enzymes?

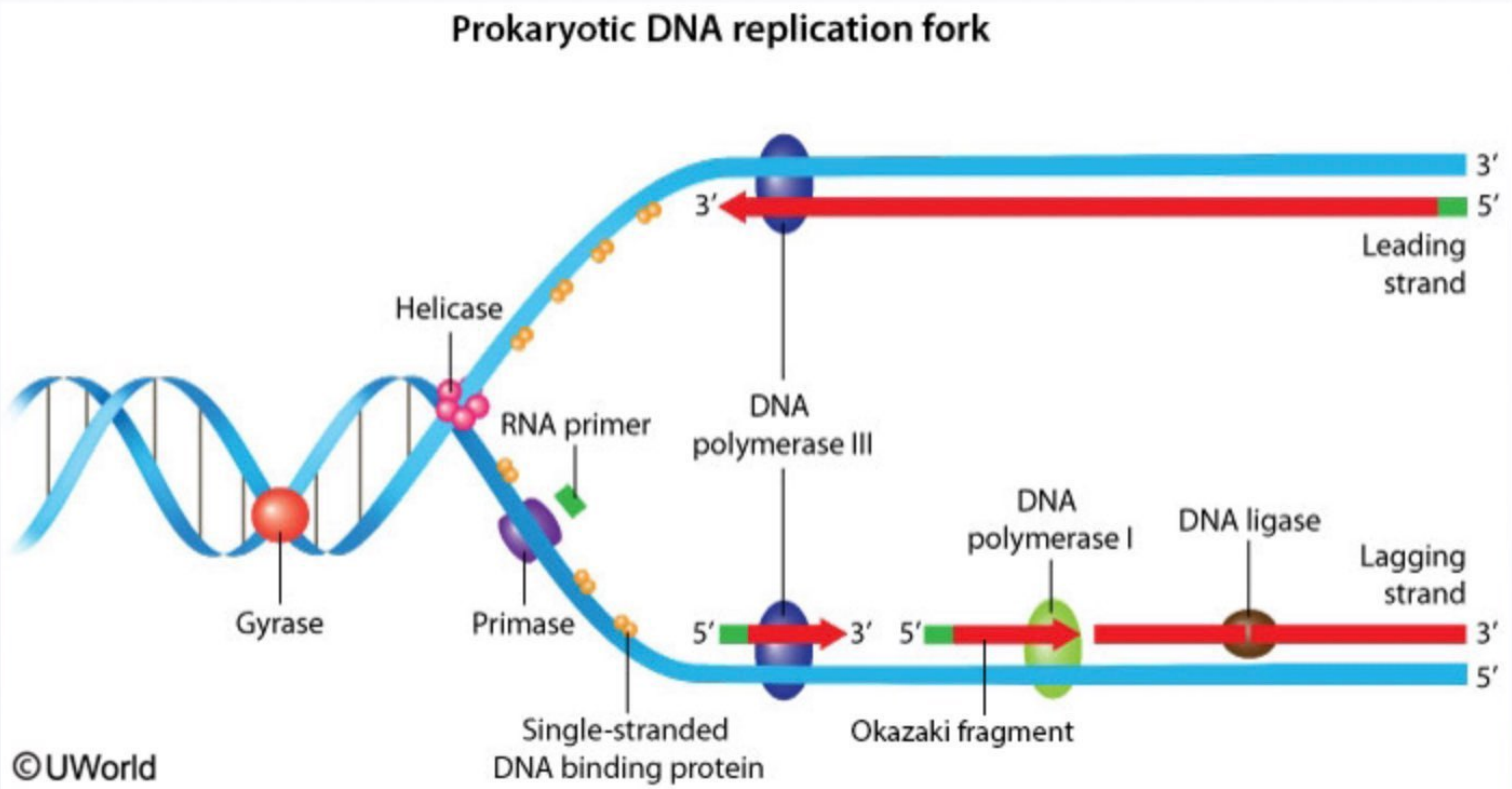
- A. DNA ligase (2%)
- B. DNA polymerase I (15%)
- C. DNA polymerase III (18%)
- D. Gyrase (2%)
- E. Helicase (1%)
- ✓ F. Primase (59%)

Omitted	59%	01 sec	2023
Correct answer F	Answered correctly	Time Spent	Version

Explanation

Prokaryotic DNA replication fork

Explanation



This question describes a scenario in which uracil is found in association with bacterial DNA during prokaryotic DNA replication. In general, uracil is found only in RNA, so the question essentially asks which enzyme involved in DNA synthesis catalyzes the formation of RNA strands. In prokaryotic DNA replication, primase (an RNA polymerase) is responsible for synthesizing a short RNA primer using the separated strands of DNA at the replication fork as templates. DNA replication then proceeds, with DNA polymerase using the 3' hydroxyl group of the RNA primer as a starting point for synthesis. Primase is a crucial enzyme for bacterial replication as DNA polymerase cannot initiate DNA synthesis without this short nucleic acid sequence primer.

(Choice A) DNA ligase is the enzyme that repairs single-strand breaks in duplex DNA during DNA replication and repair.

This question describes a scenario in which uracil is found in association with bacterial DNA during prokaryotic DNA replication. In general, uracil is found only in RNA, so the question essentially asks which enzyme involved in DNA synthesis catalyzes the formation of RNA strands. In prokaryotic DNA replication, primase (an RNA polymerase) is responsible for synthesizing a short RNA primer using the separated strands of DNA at the replication fork as templates. DNA replication then proceeds, with DNA polymerase using the 3' hydroxyl group of the RNA primer as a starting point for synthesis. Primase is a crucial enzyme for bacterial replication as DNA polymerase cannot initiate DNA synthesis without this short nucleic acid sequence primer.

(Choice A) DNA ligase is the enzyme that repairs single-strand breaks in duplex DNA during DNA replication and repair.

(Choices B and C) During replication, DNA polymerase III is the primary enzyme responsible for synthesis of daughter DNA strands; DNA polymerase I functions chiefly to replace the RNA primers with DNA segments. Unlike DNA polymerase III, DNA polymerase I has 5'→ 3' exonuclease activity that can remove RNA primers and damaged DNA segments. The 3'→ 5' exonuclease activity of DNA polymerase I and III provides a proofreading function that fixes mismatched nucleotides in the newly formed daughter strands.

(Choices D and E) Helicase unwinds DNA at the replication fork. However, this process results in supercoiling of the DNA. DNA gyrase is a type II topoisomerase that helps to relieve the resultant strain.

Educational objective:
Primase is a DNA-dependent RNA polymerase that incorporates short RNA primers into replicating DNA.

Biochemistry	Genetics (General Principles)	Transcription
Subject	System	Topic