

X tion Id: 1434**DNA polymerase I** is unique as it is the only prokaryotic polymerase that also has **5' to 3' exonuclease**

activity. This activity functions to **remove the RNA primer** created by primase and repair damaged DNA sequences.

(Choice B) DNA polymerase III has 3' to 5' exonuclease activity; however, it does not possess 5' to 3' exonuclease activity.

(Choice C) The enzyme topoisomerase II, also known as DNA gyrase in prokaryotes, relieves tension created during DNA strand unwinding by introducing negative supercoils into the circular DNA. Fluoroquinolones (eg, ciprofloxacin) are a class of antibiotics that work by inhibiting DNA gyrase.

(Choice D) Before DNA replication begins, helicase unwinds the DNA double helix, facilitating separation of the 2 DNA strands which are then stabilized by single-stranded DNA-binding proteins.

(Choice E) Okazaki fragments of the lagging strand are bound together by the enzyme ligase.

(Choice F) DNA polymerases cannot begin synthesizing complementary DNA on a single-stranded template without an RNA primer. Primase is an RNA polymerase that synthesizes this primer, which is made up of short stretches of RNA base paired to the DNA template.

Educational objective:

In prokaryotes, only DNA polymerase I has both 5' to 3' and 3' to 5' exonuclease activities. The 3' to 5' exonuclease activity allows for a proofreading function during DNA replication, while the 5' to 3' exonuclease activity is involved in removal of RNA primers and repair of damaged DNA sequences.

References

- [DNA replication fidelity in Escherichia coli: a multi-DNA polymerase affair.](#)

Genetics

Genetics (General Principles)

Subject

System

Dna replication

Topic



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 (5%)
- B. Frameshift mutation (60%)
- C. Missense mutation (20%)
- D. Nonsense mutation (9%)
- E. Silent mutation (4%)

Omitted

Correct answer

B



60%

Answered correctly



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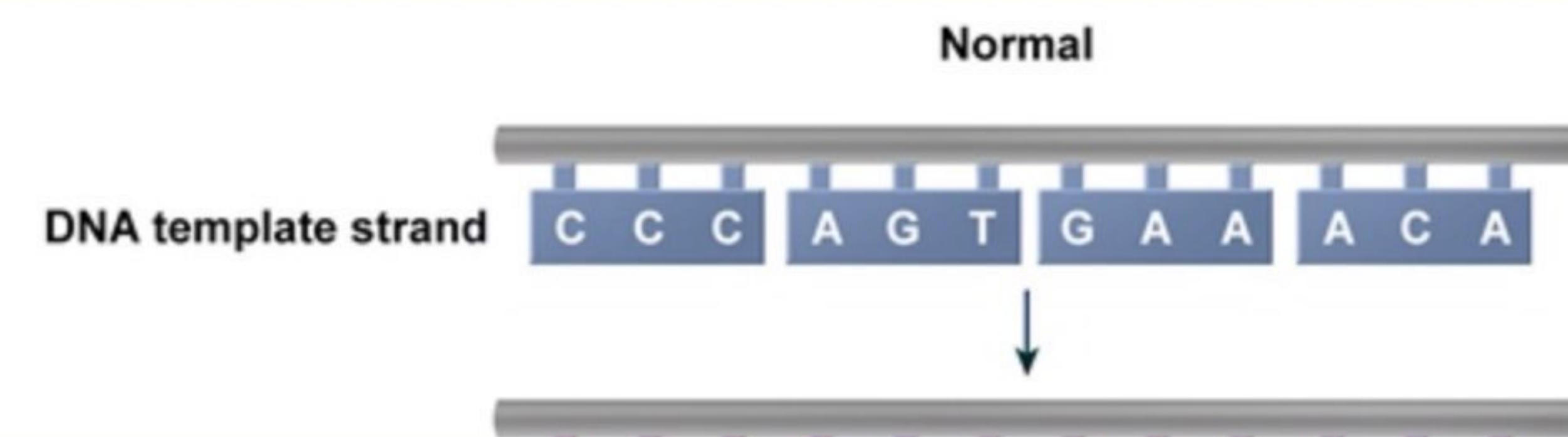
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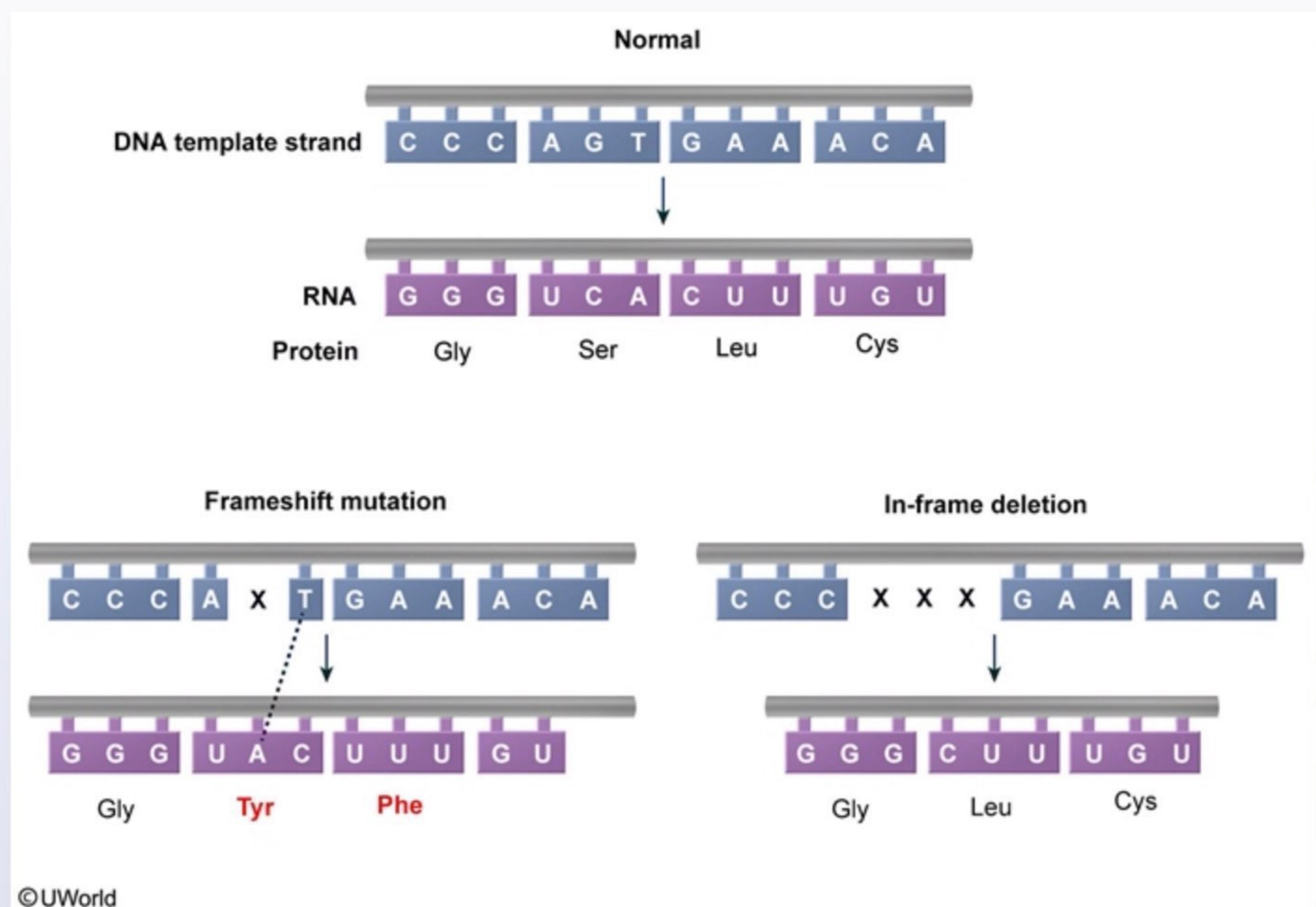
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Explanation





Explanation



Organisms that ferment lactose appear pink on MacConkey agar whereas lactose non-fermenters form white colonies. In this case, the single nucleotide deletion within the *lac* operon DNA sequence of the newer isolates impairs lactose metabolism most likely by preventing the formation of a required enzyme. Because the mutation is a **single base deletion**, it will cause a **frameshift mutation** if it occurs within the coding region (exons) of the gene.

Frameshift mutations are caused by deletion or insertion of any number of nucleotides that are not multiples





If a single base deletion, it will cause a **frameshift mutation** if it occurs within the coding region (exons) of the gene.

Frameshift mutations are caused by **deletion or insertion** of any number of nucleotides that are **not multiples of 3**. The result is a change in the reading frame during protein translation, which causes the production of an entirely different protein that is often shorter than the original due to formation of a premature stop codon.

The other mutations listed are all examples of **point mutations** (ie, single base substitutions) that can lead to a variety of changes in the coded protein.

(Choices A and C) Missense mutations are single base substitutions that result in the placement of an incorrect amino acid in a protein sequence. These mutations occur within the coding region of a gene and do not alter protein length. A conservative mutation is a type of missense mutation where an amino acid is replaced with another that has similar biochemical characteristics. Conservative mutations generally preserve protein function unless the mutation occurs in a critical region (eg, active site of enzyme).

(Choice D) Nonsense mutations introduce a premature stop codon in a coding region, resulting in the production of a truncated protein. The mutation described is not a nonsense mutation because it was caused by a single base **deletion** (not a base substitution).

(Choice E) A silent mutation is a single base substitution within a codon that does not change the amino acid (due to codon redundancy). Silent mutations have no effect on protein formation or function.

Educational objective:

A frameshift mutation occurs with the deletion/addition of a number of bases not divisible by 3 in the coding region of a gene. Frameshift mutations alter the reading frame of the genetic code, dramatically changing the protein structure and often resulting in the formation of a premature stop codon.



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 (75%)
- B. Erythrocytes (3%)
- C. Myocardial cells (2%)
- D. Neurons (10%)
- E. Pancreatic β cells (7%)

Omitted

Correct answer
A

75%

Answered correctly



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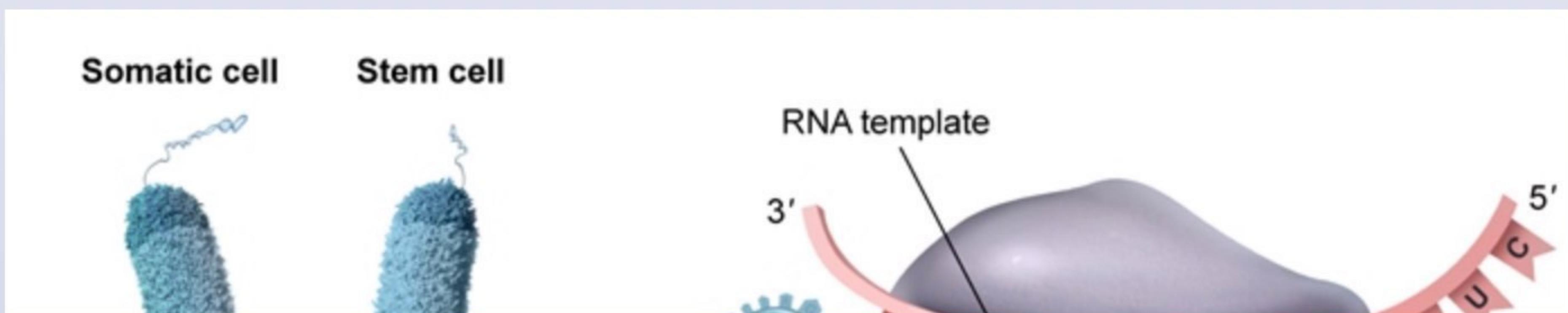
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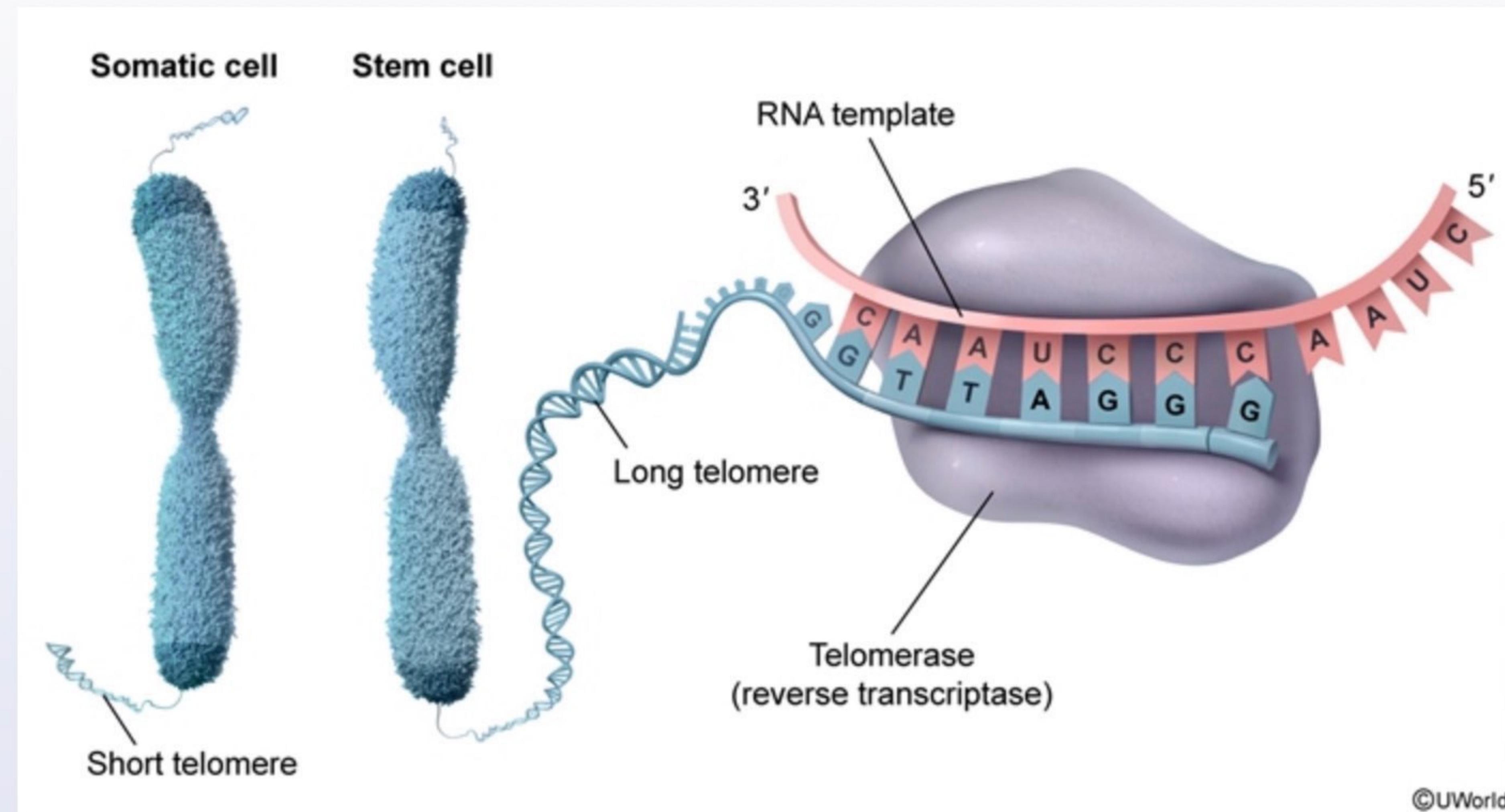
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Explanation





Explanation



Telomerase is a ribonucleoprotein that adds **TTAGGG** repeats to the **3' end of chromosomes** (telomere region). It is similar to other reverse transcriptase enzymes in that it synthesizes single-stranded DNA using single-stranded RNA as a template (**RNA-dependent DNA polymerase**). Telomerase is composed of 2 main subunits, the telomerase reverse transcriptase (TERT) subunit and the telomerase RNA component (TERC). TERC is a "built-in" RNA template that is repeatedly read by the TERT subunit to add TTAGGG DNA sequence repeats to telomeres.

Stem cells have very **long telomeres** due to their high telomerase activity, allowing them to proliferate indefinitely in a controlled manner. In contrast, most terminally differentiated adult somatic cells (eg, myocardial cells, neurons, pancreatic B cells) have short telomeres as they do not express telomerase and their telomeres

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is a built-in RNA template that is repeatedly read by the TERT subunit to add TTAGGG DNA sequence

repeats to telomeres.

Stem cells have very **long telomeres** due to their high telomerase activity, allowing them to proliferate indefinitely in a controlled manner. In contrast, most terminally differentiated adult somatic cells (eg, myocardial cells, neurons, pancreatic β cells) have short telomeres as they do not express telomerase and their telomeres shorten with every cell division (**Choices C, D, and E**). Critical shortening in telomere length is thought to be a signal for programmed cell death. In fact, syndromes of premature aging (eg, Bloom syndrome) are associated with shortened telomeres. In contrast, cancer cells upregulate their telomerase activity, preventing cell death by maintaining their telomere length.

Stem cells are undifferentiated cells with the potential to differentiate into other cell types and can be classified as either embryonic or adult stem cells. Although embryonic stem cells are present in the very early stages of embryogenesis and can give rise to every cell type in adult humans (pluripotent), adult stem cells are present in most tissues and are generally responsible for replacing dead cells. For example, the epidermis is continuously replaced by stem cells present in the basal cell layers. Bone marrow stem cells similarly replace peripheral red and white blood cells.

(Choice B) Erythrocytes have no nuclei and therefore have no potential to divide.

Educational objective:

Critical shortening in telomere length can signal for programmed cell death. Telomerase is a reverse transcriptase (RNA-dependent DNA polymerase) that lengthens telomeres by adding TTAGGG repeats to the 3' end of chromosomes. Stem cells have long telomeres due to high telomerase activity, allowing them to proliferate indefinitely in a controlled manner.

References

- Telomere structure and telomerase in health and disease (review).

RNA structure , synthesis and processing

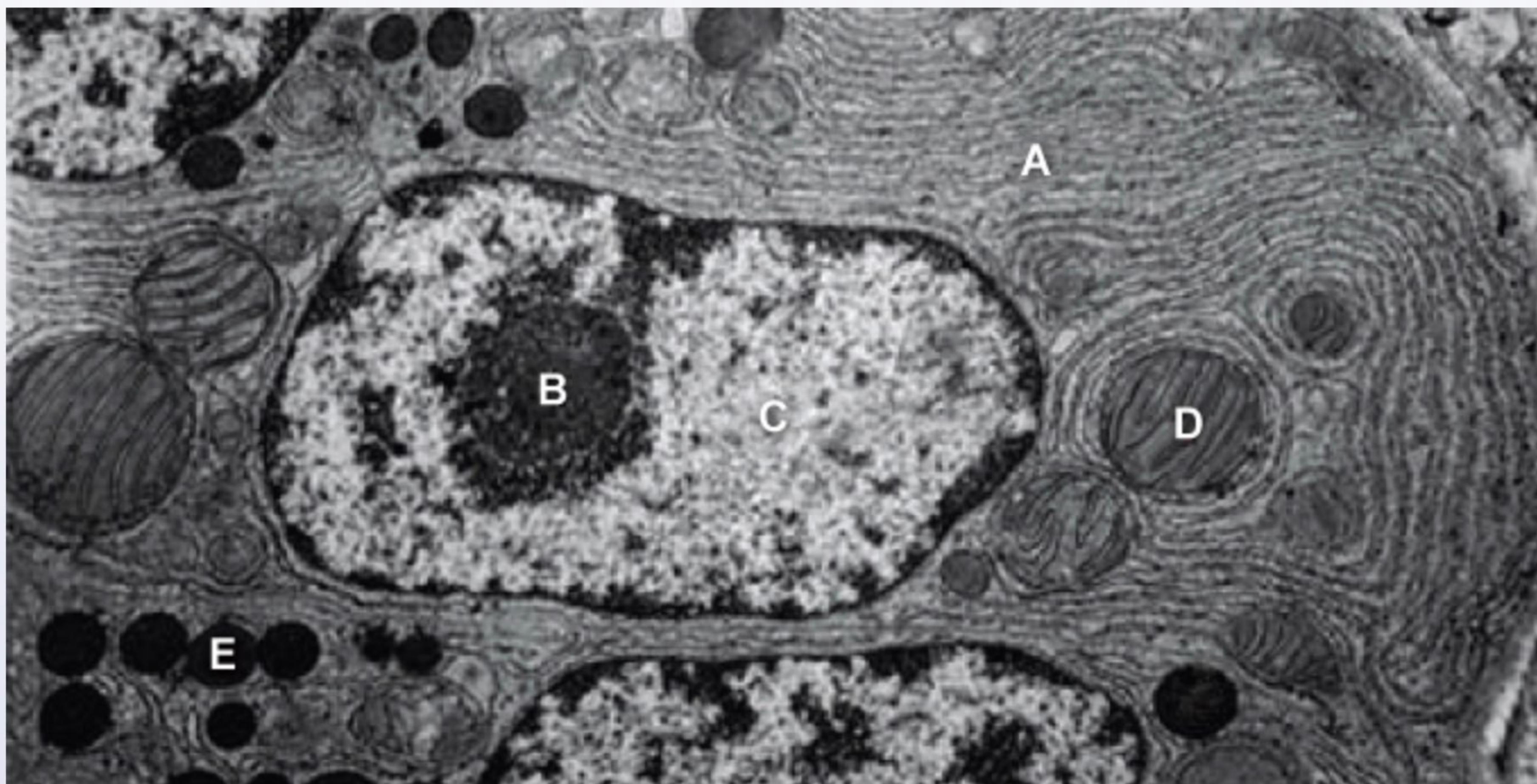
In an experiment, cultured fibroblasts are mechanically lysed, and the membrane lipids and cellular proteins are chemically removed to isolate nucleic acids. The cellular extract containing the purified nucleic acids is incubated along with short sequences of repeated deoxythymidine residues fixed to latex beads. The solution is washed several times to remove unbound molecules. Which of the following types of nucleic acid is most likely to bind the strongest to the latex beads in this experiment?

- A. Aminoacyl-tRNA
- B. Mature mRNA
- C. Promoter regions of DNA
- D. Ribosomal RNA
- E. Splice sites of pre-mRNA
- F. Telomere regions of chromosomes

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Molecular biologists are investigating the functional significance of non-coding RNA molecules. During an experiment, they isolate large complexes containing both protein and RNA from exocrine pancreatic cells. The complexes are found both freely floating in the cytoplasm and bound to the endoplasmic reticulum. The RNA found within these complexes is primarily synthesized at which of the following intracellular sites?



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



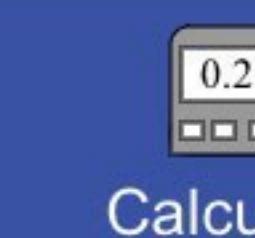
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An 8-year-old boy of Ashkenazi Jewish ancestry is brought to the office after developing reduced sensitivity to pain, impaired tear formation, and orthostatic hypotension. Familial dysautonomia is suspected due to the patient's symptoms and heritage. This disorder is caused by loss of function of the *IKAP* protein, which is essential for development and survival of sensory and autonomic neurons. *IKAP* gene sequencing reveals a single nucleotide substitution that causes a guanine residue to be replaced by adenine at the highlighted position in the normal gene sequence shown below. Exon sequences are represented by capital letters and introns by lowercase letters.

5'-GTACAAACATTGCTGGGAAAGCCGCCGCCACCATG
GGCTATGGGAGTGGTAGCACTGGAGTTAACACCGAAATTG
GCAAGATCCGGGATGAAATGGTGG AACAGAACAGGAGAGAAC
ACCCCTTCAGCAAAAAACTAGATGAATTAAAAGTCATCTCCCTTA
TTTGCATTGCAGGCTGGATCATAAAATATTGGGCACTTCAATGAC
CCGGTTGATGGAGGGTCCTGGATCAGAGGTGCTATTACTACT
TAAAAATTGCAGTGGCCCTGGCTGTAGCAGGTGATTCCATTCC
AAGgtctgcctgcagtcatcaccacacctgcctggctctggaaactcg
cagaagaaaaatgcc
cattggaaagcctcccgtctgtggaaacccttggttgtacttctgttatctgctc
cagacaagactgg
tacacttacaacaaccagatgcagtctgcag GTACAAACATTGCTGGGA
AAGCTATGGGAGTGGTAGCAAACGGAGTTAACACCGAAATT
GGCAAGATCCGGGATGAAATGGTGGCAACAGAACAGGAAGAA
CACCCCTTCAGCAAAAAACTAGATGAATTGGGGAACAGCTTTCC
AAAGTCATCTCCCTTATTGCATTGCAGTCTGGATCATAAATTG
GGACTTCAATGACCCGGTTCATGGAGGtcmgatcagaggtgctattacta
ctttaaaaattgcagtggccctggctgttagcagccattcctgaagg
tctgcagtcacac
ctgccGggctctGggaactcgcagaatggcaaagaaaaatgccatttt
tttcgaagcctcag
CTCTCTCCAAAACCGCTTCTGACTTATCTCTGACACAG

TTTGCATTGCAGGCTGGATCATAAATATTGGGCACCAATGAC
CCGGTTGATGGAGGGCCTGGATCAGAGGTGCTATTACTACT
TAAAATTGCAGTGGCCCTGGCTGTAGCAGGTGATTCCATTCC
AAGgtctgcctgcagtcatcaccacccgcctggcttggaaactcg
cagaagaaaaatgcc
cattggaagcctcccgtctgtggaaaccctgggtgtacttctgttatctgctc
cagacaagactgg
tacacttacaacaaaccagatgcagtcgcag
GTACAAACATTGCTGCTGGGA
AAGCTATGGGAGTGGTAGCAACTGGAGTTAAACCGAAATT
GGCAAGATCCGGGATGAAATGGTGGCAACAGAACAGGAAGAA
CACCCCTTCAGAAAAACTAGATGAATTGGGGAACAGCTTCC
AAAGTCATCTCCCTTATTGCATTGCAGTCTGGATCATAAATTG
GGACTTCAATGACCCGGTTCATGGAGgtcmatcagaggctattacta
ctttaaaattgcagtggccctggctgttagcagccattcctgaagg
tgcctgcagtcacac
ctgccGggctctGggaactcgcaaatggcaaagaaaaatgccatttgc
aaggcctcag
GTCTGTGGAAACCCTGGTTGACTTCTGTTATCTGCTCAGACAG
ACTGGTACACTACAACAAACCAGATGTCAGTCTGCAGGC-3'

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Which of the following is the most likely effect of this mutation?

- A. Decreased mRNA export to the cytosol
- B. Impaired ribosomal attachment to mRNA
- C. Incorrect splicing of pre-mRNA
- D. Increased degradation of mRNA by 5' exonucleases
- E. Translation of the 3'-untranslated region of mRNA

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Geneticists are studying a malfunctioning protein that causes impaired endothelial cell migration and angiogenesis. They have noticed that the amino acid sequence of the protein is truncated compared to normal controls. The mutated mRNA strand is isolated, and analysis shows a nonsense mutation located near the 3' end of the coding region. The 3' terminal coding sequence of the abnormal mRNA strand is shown below.

5'—ACG—CUA—CCA—UUG—UAA—CAA—GUU—AGC—UAG—3'

Which of the following tRNA anticodons is responsible for adding the last amino acid to the truncated polypeptide during protein translation?

- A. 5'-AAC-3'
- B. 5'-AUC-3'
- C. 5'-CAA-3'
- D. 5'-GCU-3'
- E. 5'-UCG-3'

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A researcher develops 2 functional mRNA sequences composed of CUC and CUU trinucleotide repeats, respectively. He subsequently incubates these mRNAs in a solution containing functional ribosomes and tRNAs charged with the appropriate amino acids. After several hours, it is found that both mRNA sequences produce polypeptide chains containing leucine repeats. This observed finding is due to which of the following genetic principles?

- A. Ambiguity
- B. No punctuation
- C. Transition
- D. Universality
- E. Wobble

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tion Id: 11595



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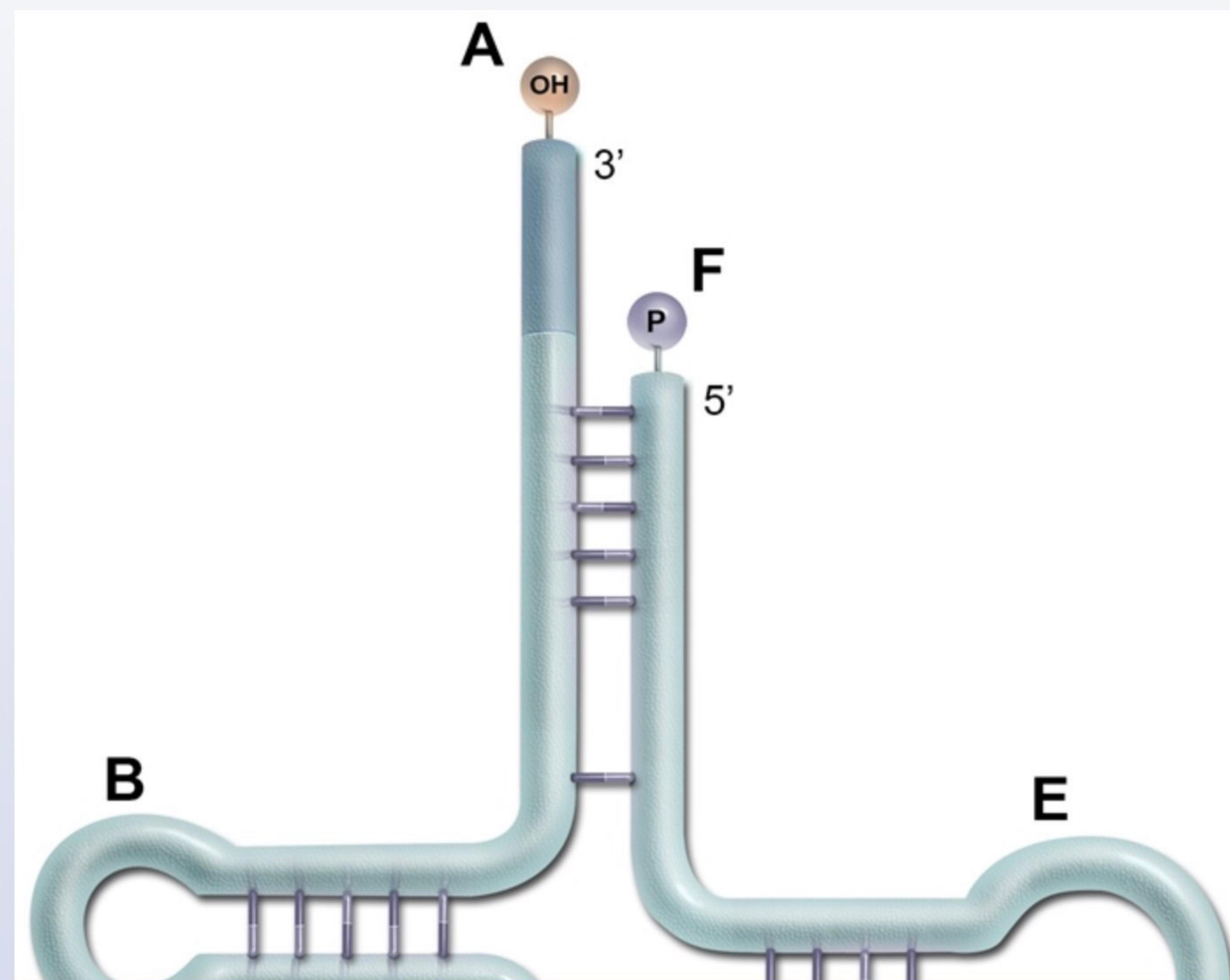
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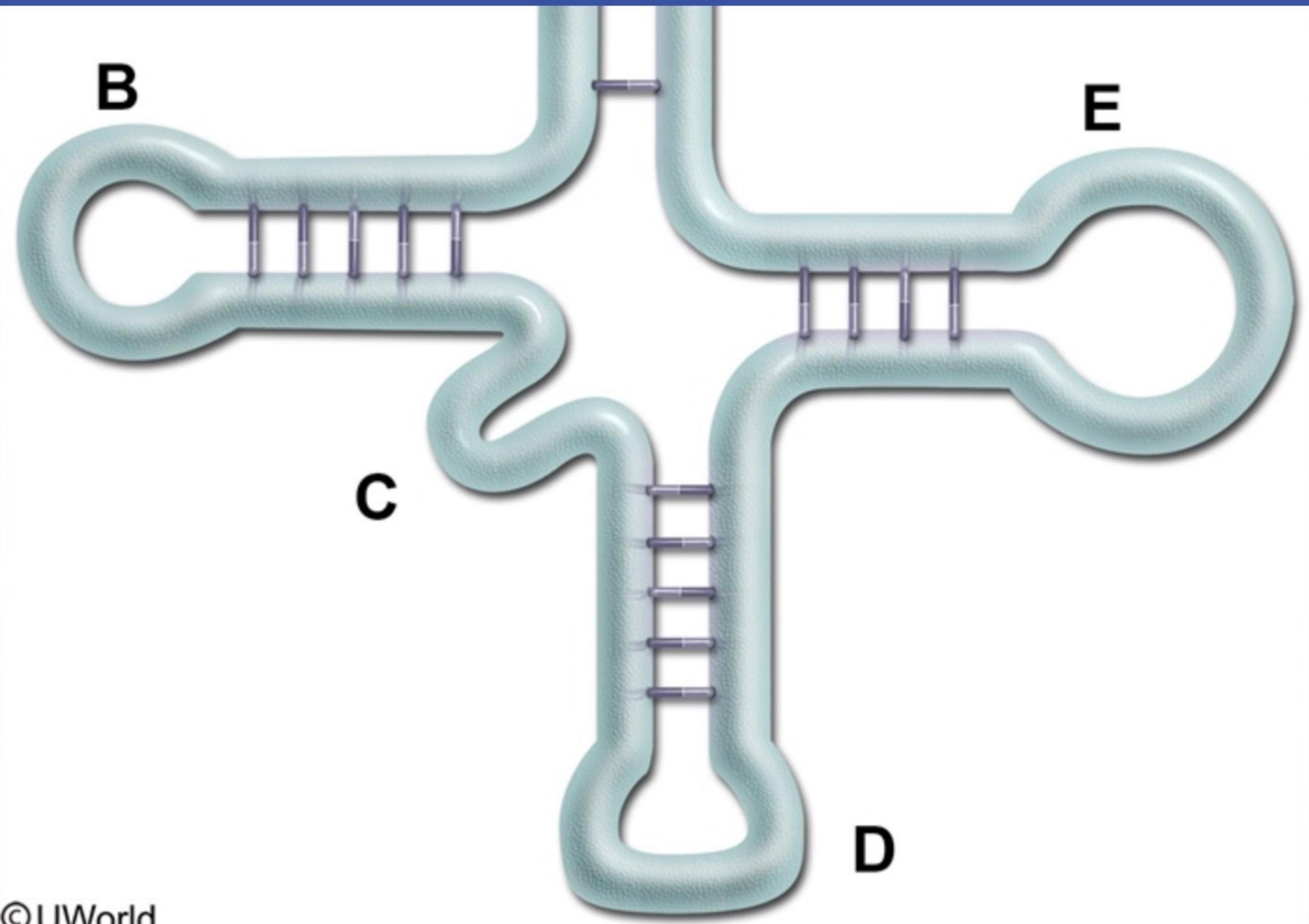
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A geneticist is performing an experiment to alter protein structures by incorporating modified amino acids into their polypeptide sequences. During the process, she incubates dermal fibroblasts in a medium containing fluorescently labeled lysine residues. After several hours, she finds that aminoacyl tRNA synthetase in the fibroblasts "loads" lysine residues onto tRNA molecules containing the anticodon UUU. This residue most likely attaches to tRNA at which of the following sites in the image shown below?





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

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A genetic study performed on a 10-year-old boy reveals a single base substitution mutation involving a DNA segment that encodes a cellular protein, as shown in the image below.

Normal coding strand: 5' --- GCCCAATCT ---- TATAAA ---- CAAGCTCGTCATGCAGGAG --- 3'
Patient's coding strand: 5' --- GCCCAATCT ---- TAGAAA ---- CAAGCTCGTCATGCAGGAG --- 3'

-25 bp +1 bp

This mutation is most likely to affect which of the following processes?

- A. DNA methylation
- B. Polypeptide folding following translation
- C. Posttranscriptional RNA splicing
- D. RNA elongation
- E. Transcription initiation
- F. Translation initiation

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In an experiment, erythrocyte precursor cells are incubated in a medium containing radiolabeled cysteine. These radiolabeled cysteine residues are attached to their appropriate tRNAs by the enzyme aminoacyl-tRNA synthetase. The bound cysteine residues are then chemically modified to form alanine. The end product of this reaction is a tRNA molecule that contains the cysteine anticodon but is mischarged with alanine. Which of the following is most likely to occur to this alanine residue during polypeptide synthesis of alpha-hemoglobin?

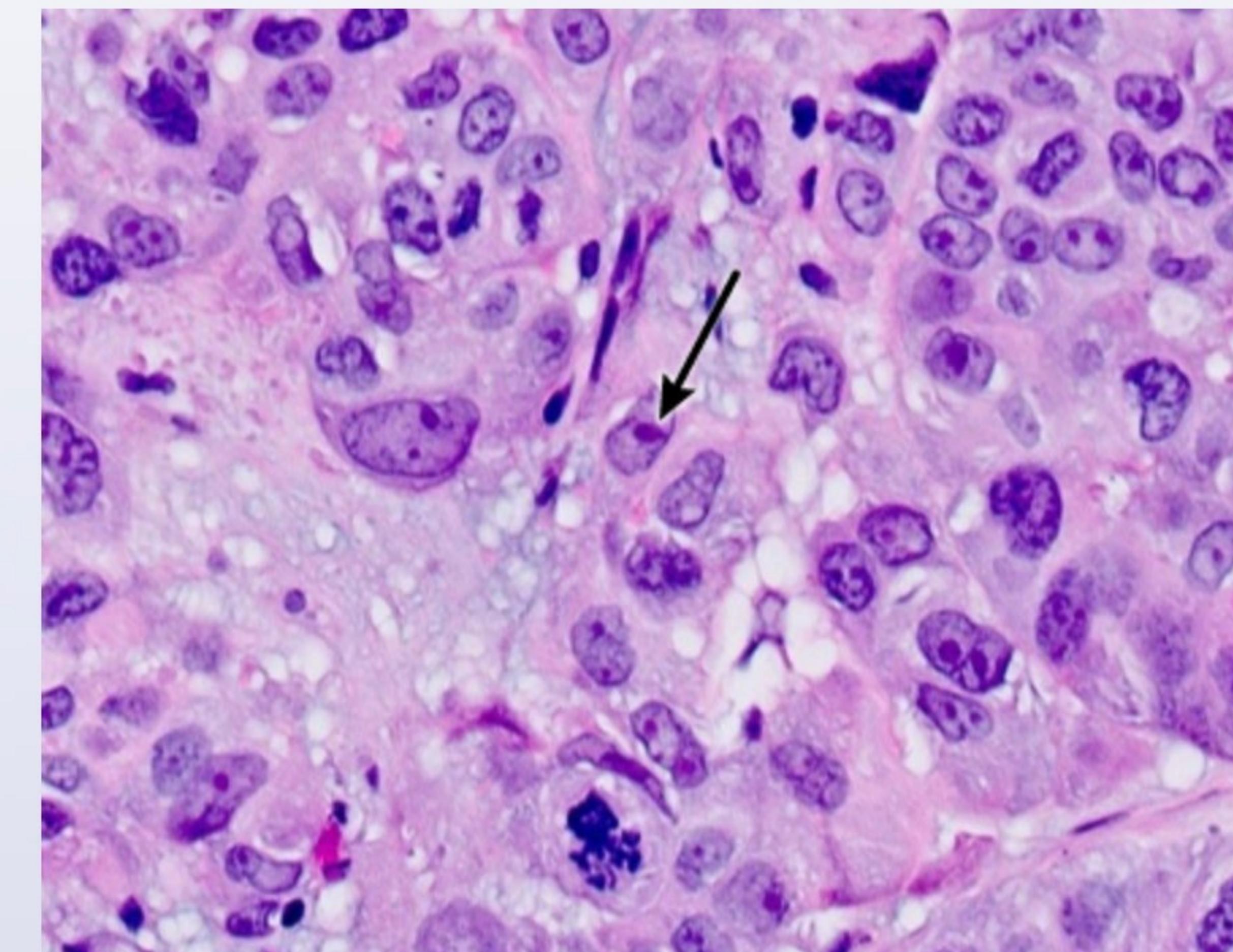
- A. It will be incorporated into the polypeptide chain at a site requiring alanine
- B. It will be incorporated into the polypeptide chain at a site requiring cysteine
- C. It will be randomly incorporated into the polypeptide chain, halting chain elongation
- D. It will be rapidly cleaved off tRNA by the enzyme glycosylase
- E. It will never be incorporated into the polypeptide chain and will remain attached to tRNA

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A 58-year-old man comes to the office with a persistent dry cough. He also has involuntarily lost 10 kg (22 lb) over the past 3 months. The patient drinks 2 or 3 beers daily and has a 40-pack-year smoking history. Physical examination shows dullness to percussion over the right lower lung base. CT scan of the chest reveals a right-sided pleural effusion and a mass in the lower lobe of the right lung. Microscopic examination of the mass demonstrates malignant cells with large nuclei that contain prominent, round, basophilic bodies, as shown in the image below:



Which of the following enzymes is most likely to function only within this basophilic region of the nucleus?

- A. Peptidyltransferase
- B. RNA polymerase I

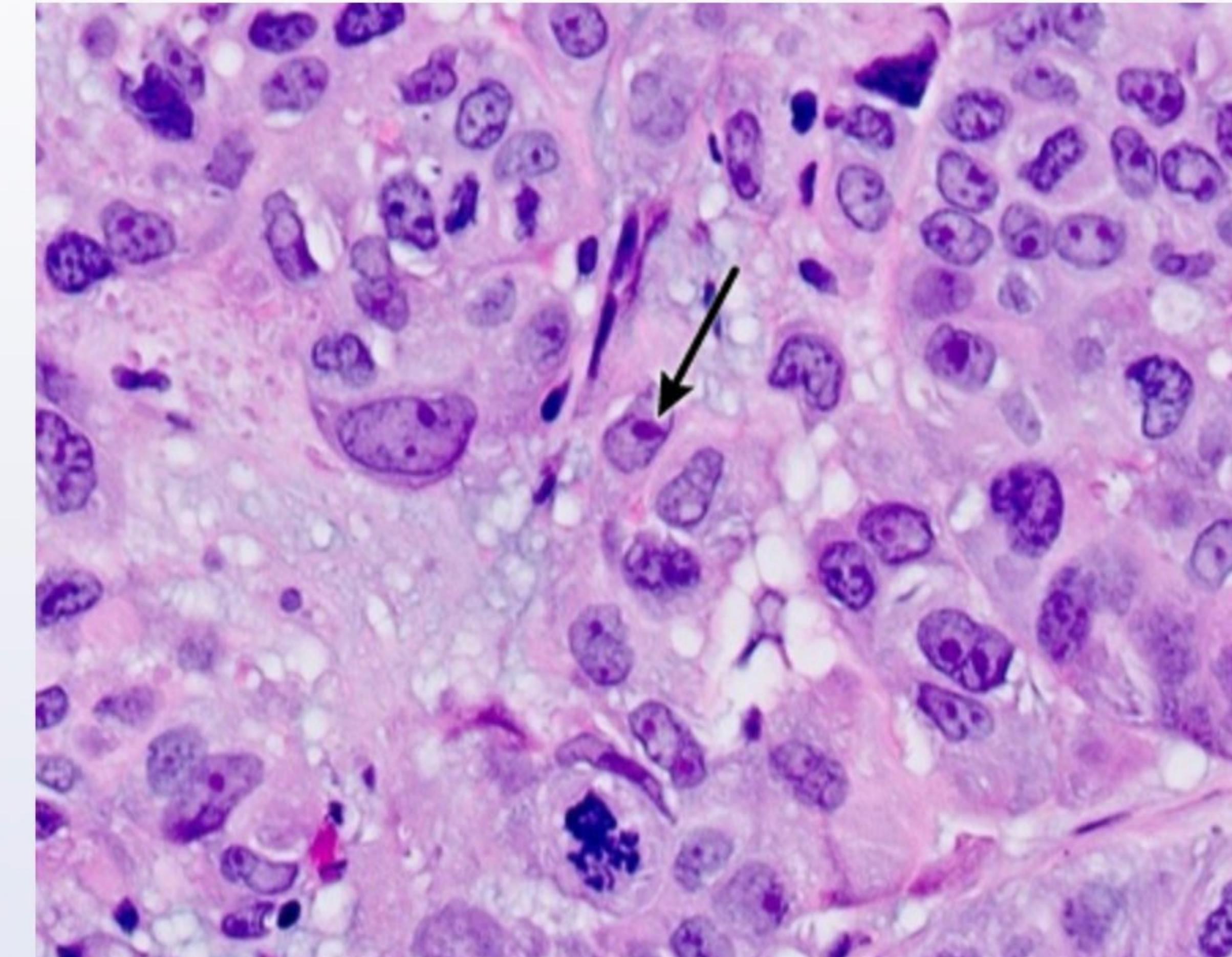
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demonstrates malignant cells with large nuclei that contain prominent, round, basophilic bodies, as shown in the image below:



Which of the following enzymes is most likely to function only within this basophilic region of the nucleus?

- A. Peptidyltransferase
- B. RNA polymerase I
- C. RNA polymerase II
- D. Ubiquitin ligase

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A pharmaceutical researcher develops a new drug that affects bacterial protein synthesis. In an experiment, *Escherichia coli* is exposed to the drug and serially cultured in media containing tagged nucleotides and amino acids. It is found that the drug inhibits molecules that recognize the highlighted codon in the bacterial mRNA fragment shown in the image below.

5' --- ACG CUA CCA UUG CAA GUU AGC **UAA** AUA GCG UUC --- 3'

Which of the following molecules is the most likely target of this drug?

- A. Charged tRNA
- B. Elongation factor 2
- C. Releasing factor 1
- D. snRNP
- E. Transcription factor II D
- F. Uncharged tRNA

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A 32-year-old man is recovering from extensive burns. Fibroblasts near the site of injury actively synthesize precursor mRNA to be used as templates for protein synthesis. After transcription, extensive processing of the precursor RNA occurs to form the finalized mRNA sequence. The finalized mRNA then exits the nucleus and undergoes translation by ribosome complexes before being degraded. Which of the following steps involving the processing and handling of mRNA occurs only within the cytoplasm of cells?

- A. 5'-terminal guanosine triphosphate addition
- B. Methylation of the 5'-terminal guanine
- C. Multiple adenine nucleotide attachment to the 3'-end
- D. Interaction with snRNP
- E. Removal of intervening sequences
- F. Interaction with P bodies

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A series of experiments is being conducted to determine the structure and function of different types of bacterial RNA. Cultures of *Staphylococcus aureus* are exposed to chemicals that lyse the bacterial cells, and the RNA molecules are then extracted. A specific RNA consisting of 90 nucleotides is purified for further analysis. It is found to contain high amounts of chemically modified bases such as dihydrouridine, pseudouridine, and ribothymidine, and its secondary structure arises from base pairing within the chain. Which of the following is the most likely composition of the 3'-end of this molecule?

- A. AUG
- B. CCA
- C. Methylguanosine triphosphate
- D. Poly-A
- E. TATA
- F. UAG

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Incubated along with short sequences of repeated deoxythymidine residues fixed to latex beads. The solution is washed several times to remove unbound molecules. Which of the following types of nucleic acid is most likely to bind the strongest to the latex beads in this experiment?

- A. Aminoacyl-tRNA (13%)
- B. Mature mRNA (28%)
- C. Promoter regions of DNA (28%)
- D. Ribosomal RNA (7%)
- E. Splice sites of pre-mRNA (5%)
- F. Telomere regions of chromosomes (15%)

Omitted

Correct answer

B



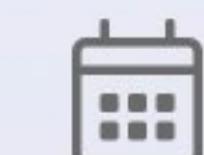
28%

Answered correctly



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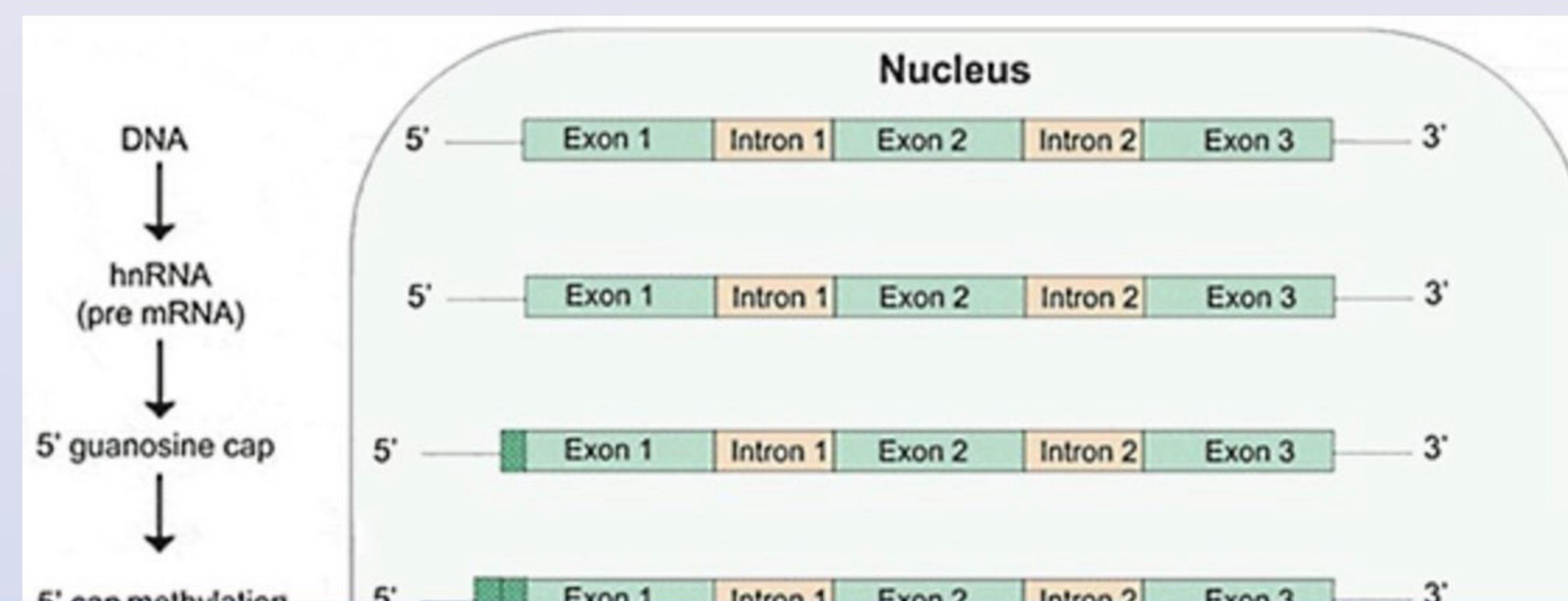
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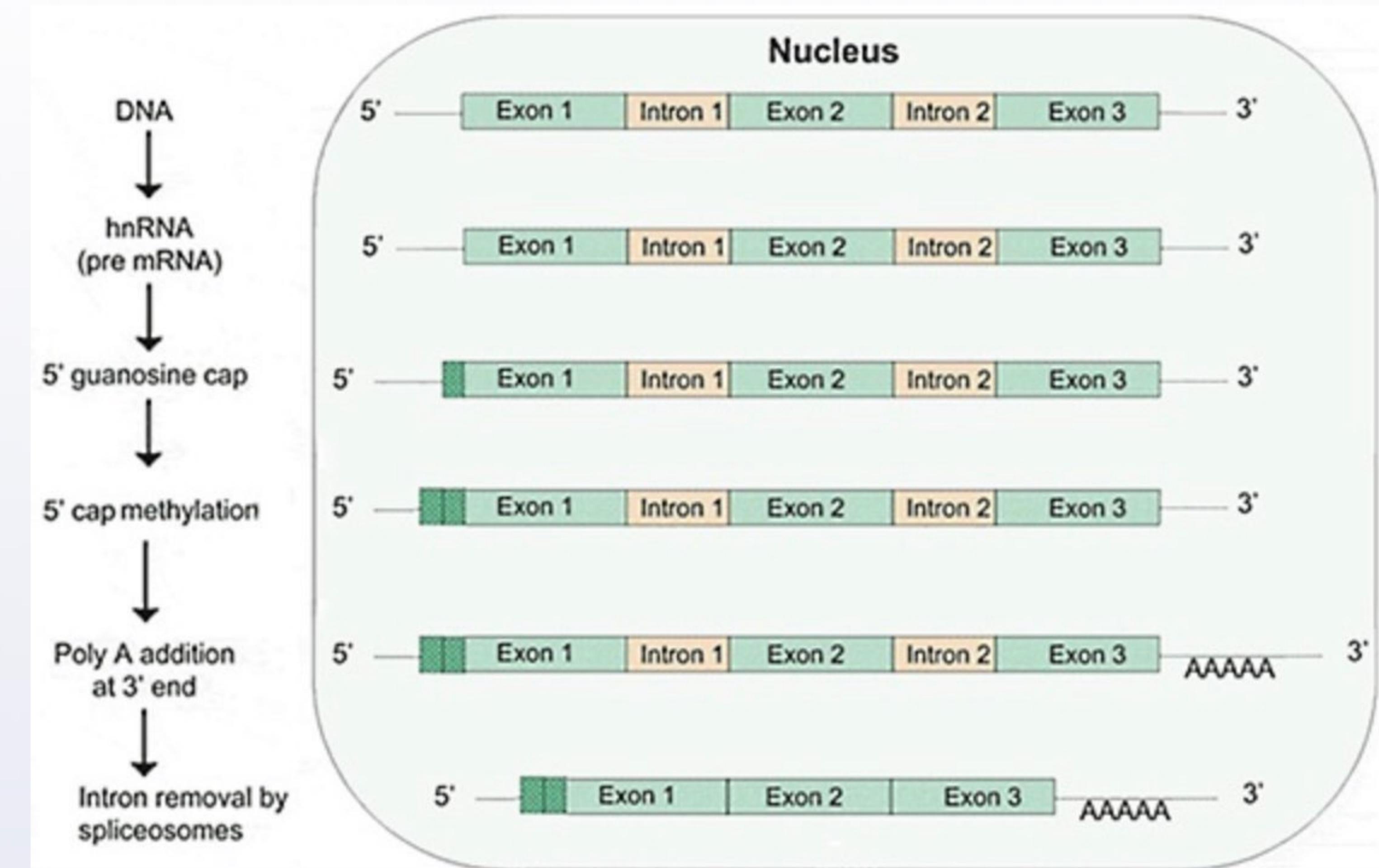


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Explanation





In the experiment described above, the poly-A tail on mature mRNA is most likely to bind the latex beads because the adenine residues in this tail would form complementary base pairs with the repeated deoxythymine residues fixed to the beads.

Mature mRNA refers to mRNA that has been processed and is ready for nuclear export and translation into protein. mRNA processing (**post-transcriptional modification**) involves the following steps:

1. **5' capping:** A 7-methyl-guanosine cap is added to the 5' end of the mRNA.
2. **Polyadenylation:** A **poly-A tail** (chain of adenine residues) is added to most eukaryotic mRNA molecules by poly-A polymerase. Poly-A tails are not transcribed from the DNA template. Instead, a **consensus sequence (AAUAAA)** located near the **3'** end of the RNA molecule directs the addition of the poly-A tail. This tail protects the mRNA from degradation within the cytoplasm after it exits the nucleus.
3. **Splicing:** The initial mRNA transcript (pre-mRNA) contains sequences from coding and noncoding regions of

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sequence (AAUAAA) located near the 3' end of the RNA molecule directs the addition of the poly-A tail.

This tail protects the mRNA from degradation within the cytoplasm after it exits the nucleus.

3. Splicing: The initial mRNA transcript (pre-mRNA) contains sequences from coding and noncoding regions of DNA, known as exons and introns, respectively. Spliceosomes (complexes of small nuclear ribonucleoproteins [snRNPs] and other proteins) remove introns containing GU at the 5' splice site and AG at the 3' splice site (**Choice E**).

(Choice A) Aminoacyl-tRNA is tRNA charged with its amino acid. The cloverleaf structure of tRNA consists of a 3' CCA tail (amino acid binding site); a T loop abundant in ribothymidine, pseudouridine, and cytidine residues; a D loop rich in dihydrouridine residues; and an anticodon loop.

(Choice C) DNA promoter regions help initiate transcription by binding transcription factors and RNA polymerase II. Promoter regions contain consensus sequences that are typically AT-rich (eg, TATA and CAAT boxes) or GC-rich (eg, GC box).

(Choice D) Ribosomal RNA (rRNA) is a component of the ribosome that catalyzes peptide bond formation during translation.

(Choice F) Telomeres are located at the ends of chromosomes and contain TTAGGG repeats, which are added by the enzyme telomerase (RNA-dependent DNA polymerase). Critical shortening in telomere length is thought to signal programmed cell death.

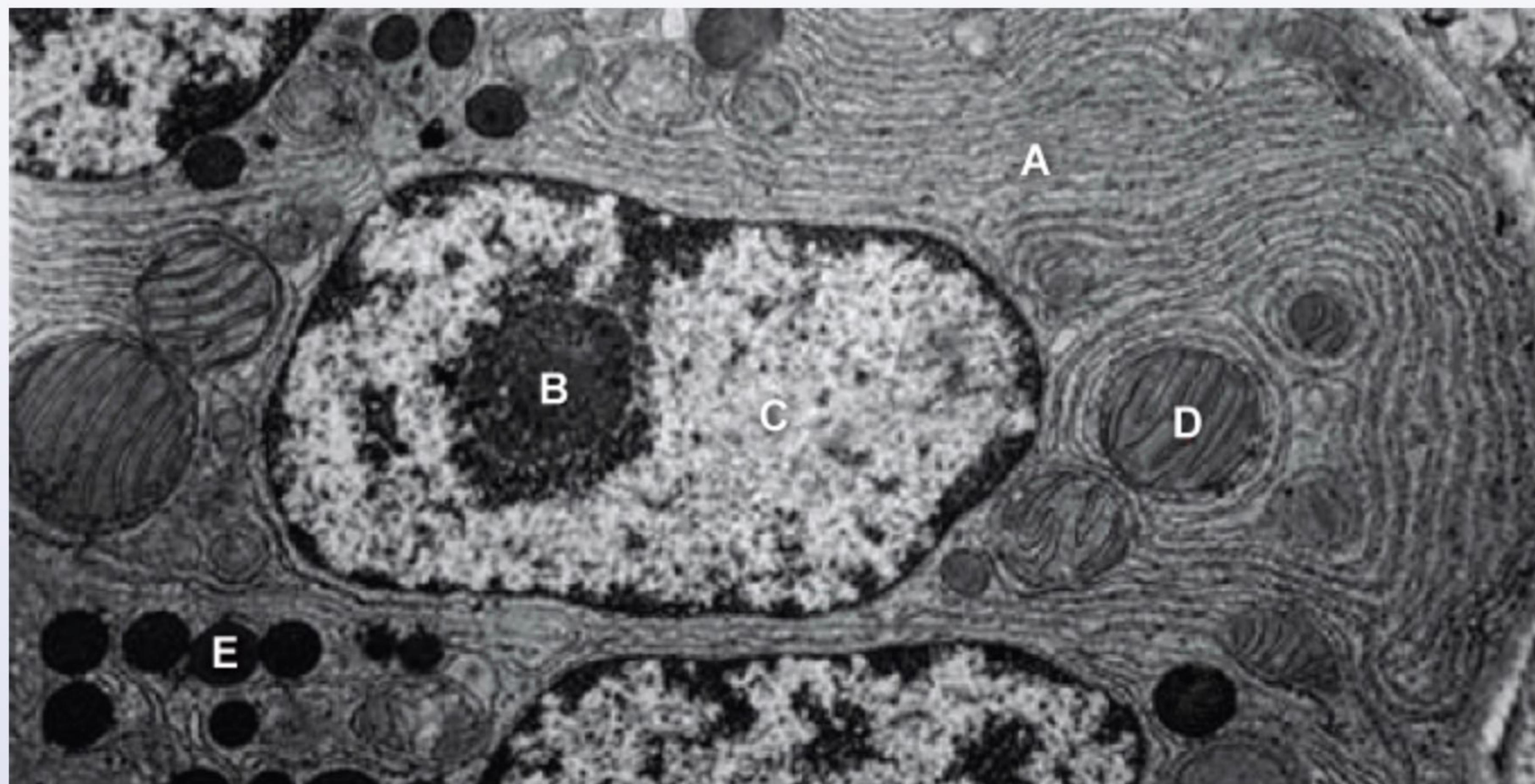
Educational objective:

The poly-A tail is not transcribed from DNA; instead, it is added as a post-transcriptional modification downstream of the consensus sequence (AAUAAA) located near the 3' end of the mRNA molecule. This tail protects mRNA from degradation within the cytoplasm after it exits the nucleus.

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Molecular biologists are investigating the functional significance of non-coding RNA molecules. During an experiment, they isolate large complexes containing both protein and RNA from exocrine pancreatic cells. The complexes are found both freely floating in the cytoplasm and bound to the endoplasmic reticulum. The RNA found within these complexes is primarily synthesized at which of the following intracellular sites?



- A. A (10%)
- B. B (54%)
- C. C (23%)
- D. D (8%)
- E. E (3%)

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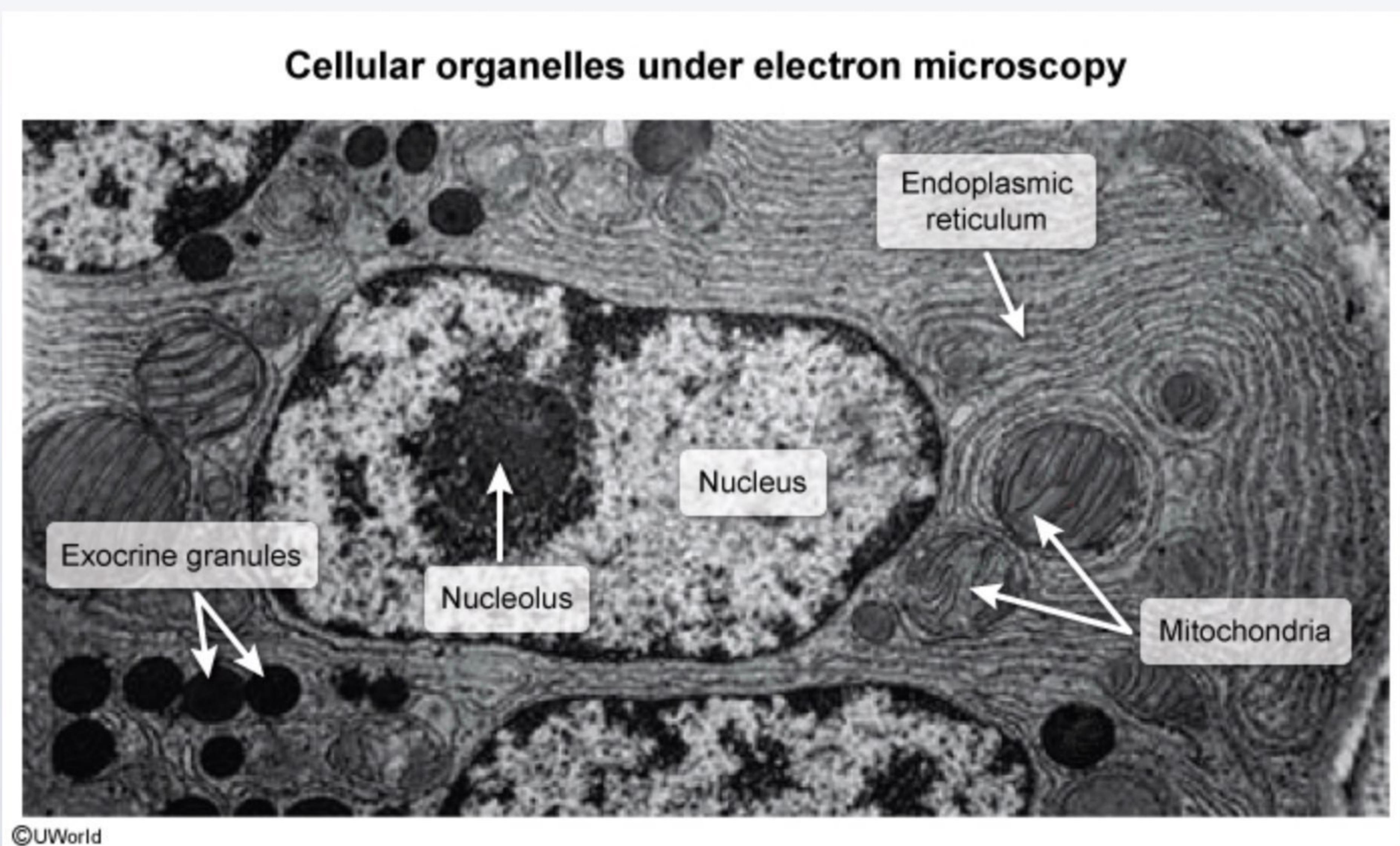
Omitted
Correct answer
B

54% Answered correctly

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Explanation



The large complexes containing both protein and RNA that are found freely floating and bound to the endoplasmic reticulum are most likely **ribosomes**. Ribosome biogenesis occurs primarily within the **nucleolus**, a dense **round structure** inside the nucleus that is in direct contact with the rest of the nucleoplasm. The nucleolus contains ribosomal DNA coding for the 28S, 5.8S, and 18S ribosomal RNA (rRNA) components, and it

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The large complexes containing both protein and RNA that are found freely floating and bound to the endoplasmic reticulum are most likely **ribosomes**. Ribosome biogenesis occurs primarily within the **nucleolus**, a dense **round structure** inside the nucleus that is in direct contact with the rest of the nucleoplasm. The nucleolus contains ribosomal DNA coding for the 28S, 5.8S, and 18S ribosomal RNA (rRNA) components, and it is here where most of the **rRNA is transcribed**. After synthesis, rRNA is combined with ribosomal protein components that are translated in the cytoplasm and then imported into the nucleus. The immature 60S and 40S ribosomal subunits are then exported from the nucleus to fully mature in the cytoplasm.

(Choice A) The rough endoplasmic reticulum is identifiable due to its characteristic long, folded membranes that are coated with ribosomes, giving it a speckled or rough appearance.

(Choice C) The nucleus is identifiable as a membrane-bound structure that contains the nucleolus, electron-lucent euchromatin, and electron-dense heterochromatin (condensed DNA typically found around the periphery). However, most of the ribosomal DNA is found in the form of tandem repeats within the nucleolus; only the 5S rRNA is transcribed outside of the nucleolus.

(Choice D) Mitochondria are organelles with dual phospholipid bilayer membranes that can be recognized by the presence of foldings (ie, cristae) in their inner membranes. Mitochondria have their own ribosomes, but they are typically found within the mitochondrial matrix or bound to the inner mitochondrial membrane.

(Choice E) Pancreatic zymogen granules are electron-dense structures containing digestive proenzymes that are released from the cell via exocytosis.

Educational objective:

The nucleolus is a dense intranuclear body visible by light and electron microscopy that functions as the primary

The large complexes containing both protein and RNA that are found freely floating and bound to the endoplasmic reticulum are most likely **ribosomes**. Ribosome biogenesis occurs primarily within the **nucleolus**, a dense **round structure** inside the nucleus that is in direct contact with the rest of the nucleoplasm. The nucleolus contains ribosomal DNA coding for the 28S, 5.8S, and 18S ribosomal RNA (rRNA) components, and it is here where most of the **rRNA is transcribed**. After synthesis, rRNA is combined with ribosomal protein components that are translated in the cytoplasm and then imported into the nucleus. The immature 60S and 40S ribosomal subunits are then exported from the nucleus to fully mature in the cytoplasm.

(Choice A) The rough endoplasmic reticulum is identifiable due to its characteristic long, folded membranes that are coated with ribosomes, giving it a speckled or rough appearance.

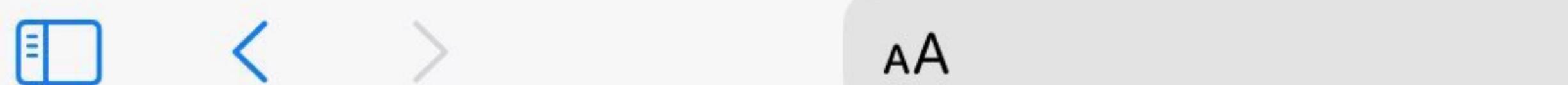
(Choice C) The nucleus is identifiable as a membrane-bound structure that contains the nucleolus, electron-lucent euchromatin, and electron-dense heterochromatin (condensed DNA typically found around the periphery). However, most of the ribosomal DNA is found in the form of tandem repeats within the nucleolus; only the 5S rRNA is transcribed outside of the nucleolus.

(Choice D) Mitochondria are organelles with dual phospholipid bilayer membranes that can be recognized by the presence of foldings (ie, cristae) in their inner membranes. Mitochondria have their own ribosomes, but they are typically found within the mitochondrial matrix or bound to the inner mitochondrial membrane.

(Choice E) Pancreatic zymogen granules are electron-dense structures containing digestive proenzymes that are released from the cell via exocytosis.

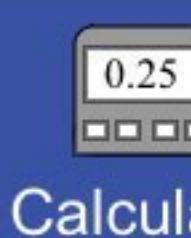
Educational objective

The nucleolus is a dense intranuclear body visible by light and electron microscopy that functions as the primary site of ribosome synthesis and assembly. All ribosomal RNA except 5S rRNA is transcribed in the nucleolus.



Item 3 of 13

Question Id: 2038



An 8-year-old boy of Ashkenazi Jewish ancestry is brought to the office after developing reduced sensitivity to pain, impaired tear formation, and orthostatic hypotension. Familial dysautonomia is suspected due to the patient's symptoms and heritage. This disorder is caused by loss of function of the *IKAP* protein, which is essential for development and survival of sensory and autonomic neurons. *IKAP* gene sequencing reveals a single nucleotide substitution that causes a guanine residue to be replaced by adenine at the highlighted position in the normal gene sequence shown below. Exon sequences are represented by capital letters and introns by lowercase letters.

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AAGCTATGGGAGTGGTAGCAACTGGAGTTAAACCGAAATT
GGCAAGATCCGGGATGAAATGGTGGCACAGAACAGGAAGAA
CACCCCTTCAGCAAAAAACTAGATGAATTGGGGAACAGCTTCC
AAAGTCATCTCCCTTATTGCATTGCAGTCTGGATCATAAATTG
GGACTTCAATGACCCGGTTCATGGAGgtcmgatcagaggctattacta
ctttaaaattgcagtggccctggctgttagcagccattcctgaaggctgcctgcagtcatcacac
ctgccGggctctGgaaactcgcagaatggcaaagaaaaatgccattttcgaagcctcag
GTCTGTGGAAACCCTGGTTGACTTCTGTTATCTGCTCAGACAG
ACTGGTACACTTACAACAAACCAAGATGTCAGTCTGCAGGC-3'

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Which of the following is the most likely effect of this mutation?

- A. Decreased mRNA export to the cytosol (2%)
- B. Impaired ribosomal attachment to mRNA (4%)
- C. Incorrect splicing of pre-mRNA (86%)
- D. Increased degradation of mRNA by 5' exonucleases (3%)
- E. Translation of the 3'-untranslated region of mRNA (3%)

Omitted
Correct answer
C

86%
Answered correctly

13 secs
Time Spent

2023
Version

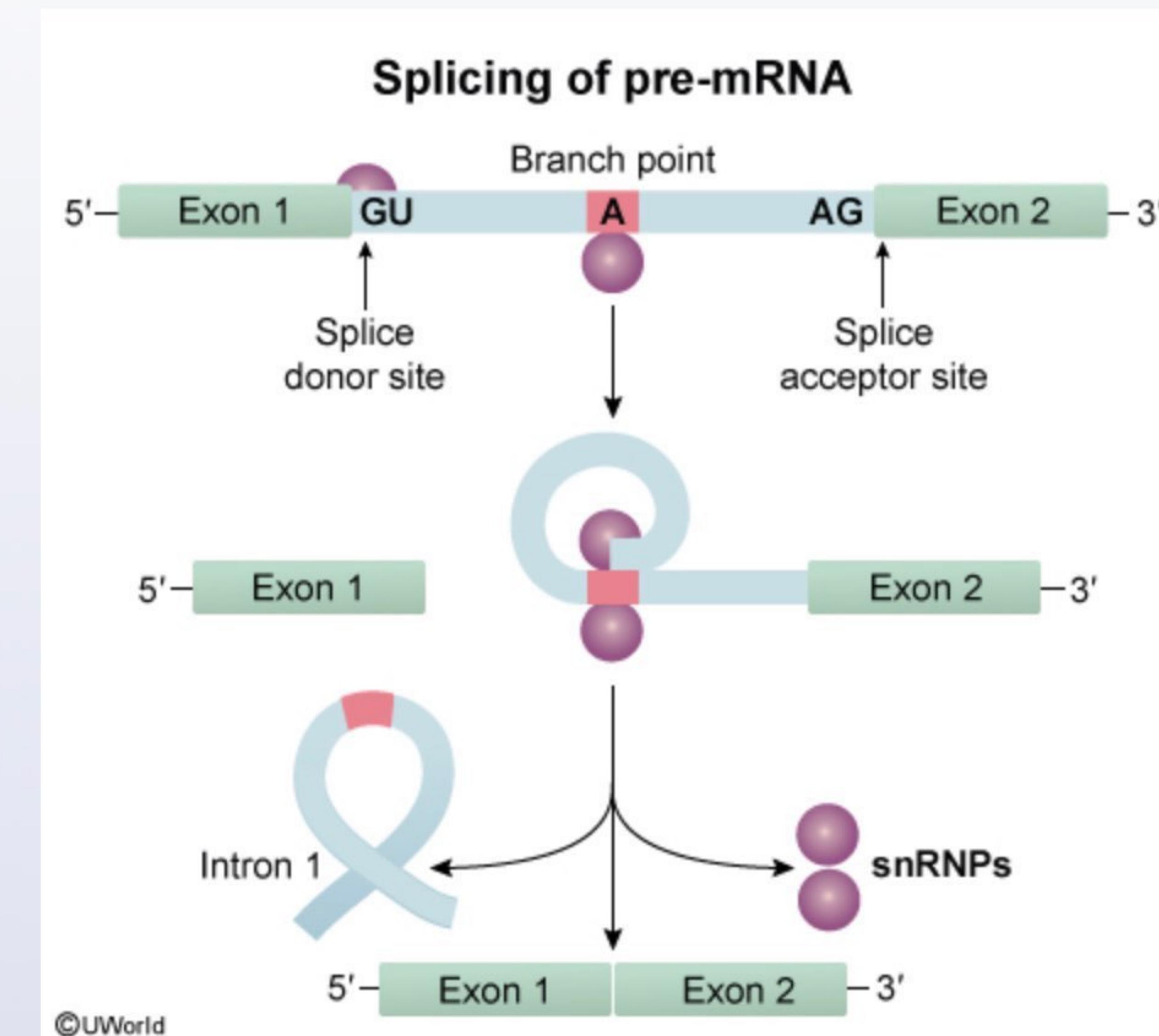
Explanation

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Mark

Explanation



Following transcription, pre-mRNA is the initial transcript that contains both intron and exon sequences. Before leaving the nucleus, pre-mRNA must be processed to mature mRNA by 3 post-transcriptional modifications: 5' methylguanosine capping, addition of a 3' polyadenine (Poly A) tail, and splicing.

Splicing is performed by **spliceosomes**, which are complexes of small nuclear ribonucleoproteins (snRNPs) and other proteins that assemble on pre-mRNA. Spliceosomes remove introns containing GU at the 5' splice site.

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methylguanosine capping, addition of a 3' polyadenine (Poly A) tail, and splicing.

Splicing is performed by **spliceosomes**, which are complexes of small nuclear ribonucleoproteins (snRNPs) and other proteins that assemble on pre-mRNA. Spliceosomes **remove introns** containing **GU** at the **5' splice site** and **AG** at the **3' splice site**. Initially, the 5' end of intron 1 (splice donor site) is cleaved and joined to the branch point. The freed 3'-OH of exon 1 then forms a phosphodiester bond with the 5'-phosphate at the splice acceptor site, joining exons 1 and 2. Mutations at splice sites may result in inappropriate removal of exons and retention of introns. This often leads to the formation of proteins with impaired structure and function as described in the case above.

(Choice A) Polyadenylation of the 3' end of mRNA is performed by the enzyme polyadenylate polymerase. This process stabilizes mRNA and helps it exit the nucleus.

(Choices B and D) In eukaryotes, translation is initiated when the small ribosomal subunit attaches to the 5' cap of mRNA and then scans for the AUG start codon within the Kozak consensus sequence. The 5' cap also protects against exonucleases and helps stabilize mRNA in the cytosol.

(Choice E) Termination of polypeptide synthesis occurs at the 3 stop codons (UAA, UAG, UGA) in mRNA. Mutations in stop codons (nonstop mutations) can result in continued and inappropriate translation of mRNA into the 3'-untranslated region, producing an extremely long, nonfunctional polypeptide.

Educational objective:

Splicing is performed by spliceosomes, which remove introns containing GU at the 5' splice site and AG at the 3' splice site. Splice site mutations may result in inappropriate removal of exons and retention of introns, leading to the formation of dysfunctional proteins.

References

- [Familial dysautonomia is caused by mutations of the IKAP gene](#)

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Item 4 of 13 Question Id: 1420

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Geneticists are studying a malfunctioning protein that causes impaired endothelial cell migration and angiogenesis. They have noticed that the amino acid sequence of the protein is truncated compared to normal controls. The mutated mRNA strand is isolated, and analysis shows a nonsense mutation located near the 3' end of the coding region. The 3' terminal coding sequence of the abnormal mRNA strand is shown below.

5'—ACG—CUA—CCA—UUG—UAA—CAA—GUU—AGC—UAG—3'

Which of the following tRNA anticodons is responsible for adding the last amino acid to the truncated polypeptide during protein translation?

- A. 5'-AAC-3' (6%)
- B. 5'-AUC-3' (38%)
- C. 5'-CAA-3' (32%)
- D. 5'-GCU-3' (15%)
- E. 5'-UCG-3' (8%)

Omitted
Correct answer
C

32%
Answered correctly

03 secs
Time Spent

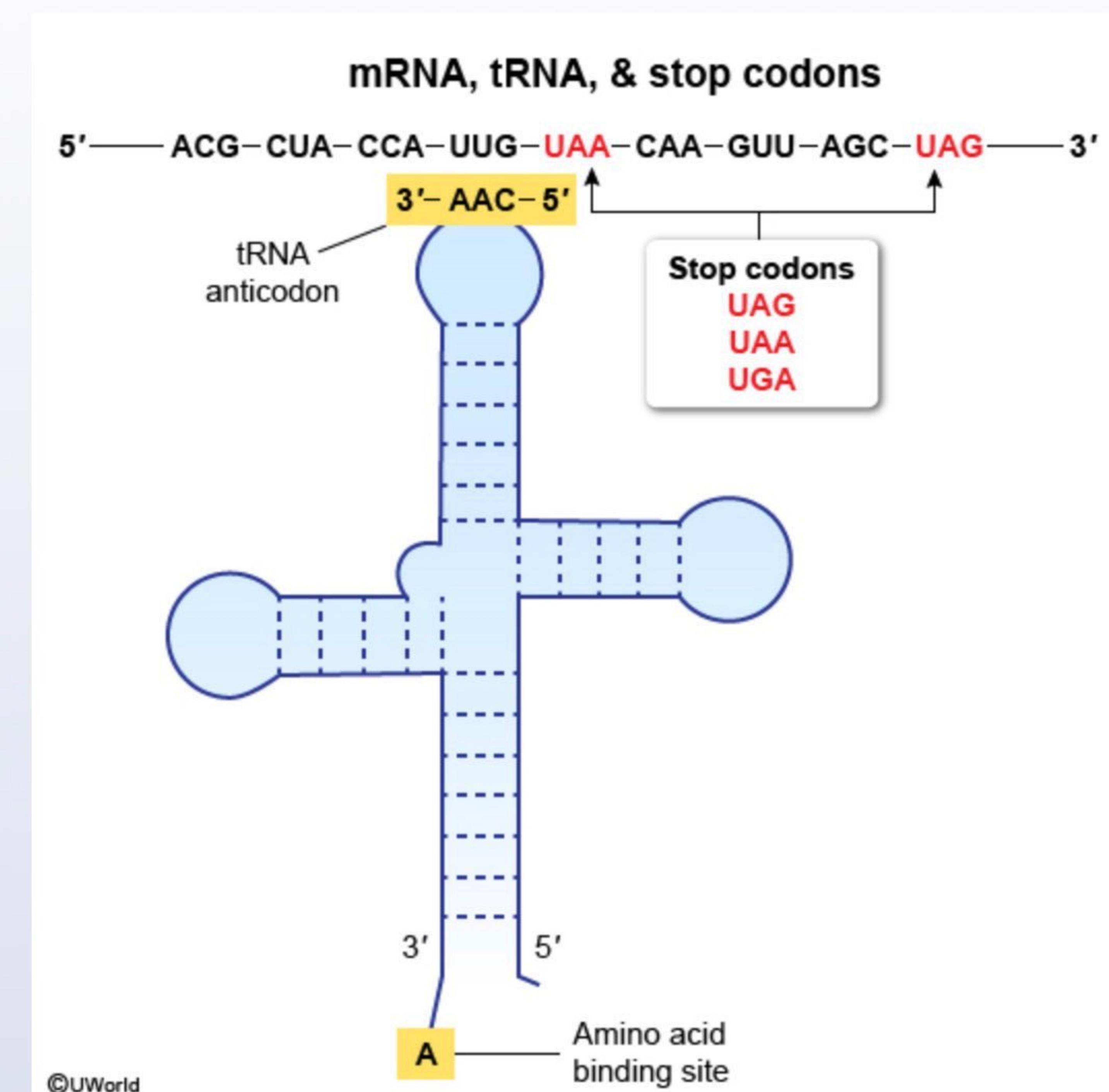
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Explanation

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Item 4 of 13 Question Id: 1420 Explanations

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One codon (AUG) signals initiation of protein synthesis and 3 codons (**UAA**, **UAG**, and **UGA**) stop protein synthesis. **Stop codons** function only to terminate translation; they do not add amino acids to the polypeptide chain.

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Transfer RNA molecules (**tRNA**) transport amino acids to the ribosome and ensure placement of the proper amino acid. One end of the molecule serves as the amino acid binding site; the opposite end contains a specific nucleic acid sequence known as the **anticodon** that is **complementary** to one or more **mRNA codons** (due to base wobbling). The type of amino acid that is bound to each tRNA molecule is determined by its anticodon sequence; this ensures that the proper amino acid is added at each mRNA codon during protein synthesis.

Translation of the mRNA template proceeds in the 5' to 3' direction. The mRNA of the dysfunctional protein in the question stem contains an extra stop codon (UAA) before the normal stop codon (UAG) at the end of the template. During protein translation, the **first stop codon** encountered will **bind a release factor**, halting protein synthesis. Therefore, the codon just prior to the first stop codon will be the last codon to add an amino acid. In this case, (**5'-UUG-3'**) is the last codon to add an amino acid to the truncated protein, and this amino acid will be carried by the **5'-CAA-3'** anticodon (codon-anticodon binding occurs in opposite directions [ie, **5' to 3' binds 3' to 5'**]).

(Choice A) Because complementary sequences align in antiparallel fashion, during translation the tRNA anticodons will bind the 5' to 3' mRNA in the (opposite) 3' to 5' direction. Therefore, the **5'-UUG-3'** mRNA codon will bind the **5'-CAA-3'** tRNA anticodon, not the **5'-AAC-3'** anticodon.

(Choices B and E) The **5'-AUC-3'** and **5'-UCG-3'** anticodons will bind to the **5'-GAU-3'** and **5'-CGA-3'** codons, respectively (**5' to 3' binds 3' to 5'**). These are not present in the above mRNA sequence.

(Choice D) The last codon shown in the above mRNA sequence is **5'-UAG-3'** (a stop codon), with the second-to-last codon being **5'-AGC-3'**. Therefore, **5'-GCU-3'** would be the tRNA anticodon responsible for adding the last amino acid to the normal (non-truncated) protein.

Educational objective:

Translation of the mRNA template proceeds in the 5' to 3' direction. Because complementary sequences align in