Questions and Answers for Genetics and Genomics in Medicine Chapter 2

Question 1

The sequence at the beginning of a human protein-coding gene is shown below. The sequence shown in capital letters is exon 1, and the ATG triplet shown in bold is translated to give the initiation codon of an mRNA.

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1      gtcagggcag agccatctat tgcctACATT TGCTTCTGAC ACAACTGTGT TCACTAGCAA
61     CCTCAAACAG ACACCATGGT GCACCTGACT CCTGAGGAGA AGTCTGCCGT TACTGCCCTG
121    TGGGGCAAGG TGAACGTGGA TGAAGTTGGT GGTGAGGCCC TGGGCAGgtt ggt
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What is the number of the nucleotide that is the first to be transcribed into the mRNA sequence?

Answer

The first nucleotide to be transcribed into mRNA is the adenine at position number 26.

Question 2

The sequence below is from a central exon within a gene, with the exon nucleotides shown in bold capital letters flanked by conserved dinucleotides (underlined) from the flanking intron sequences.

ag**AACCAGAGCCACTAGGCAGTCTTCGGACTACCGAGAGAGCCCCGTTTAAGTGCTGGATCGA**gt

Translate the exon sequence in all three forward-reading frames.
Is the exon likely to be coding DNA?

Answer

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AAC CAG AGC CAC TAG GCAGTCTTCGGACTACCGAGAGAGCCCCGTTTAAGTGCTGGATC
Asn Gln Ser His STOP

A ACC AGA GCC ACT AGG CAG TCT TCG GAC TAC CGA GAG AGC CCC GTT TAA GTGCTGGATC
  Thr Arg Ala Thr Arg Gln Ser Ser Asp Tyr Arg Glu Ser Pro Val STOP

AA CCA GAG CCA CTA GGC AGT CTT CGG ACT ACC GAG AGA GCC CCG TTT AAG TGC TGG ATC GA
   Pro Glu Pro Leu Gly Ser Leu Arg Thr Thr Glu Arg Ala Pro Phe Lys Cys Trp Ile
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Translation in the third reading frame is compatible with the exon containing coding DNA, but this is merely 19 codons long. Greater confidence that this gene has a coding DNA sequence would be justified if the same reading frame were maintained in adjacent exons to give a large open reading frame.

Question 3

Polypeptides are composed of amino acids that become covalently joined by peptide bonds. Illustrate how a peptide bond is formed by a condensation reaction between two amino acids—NH_2-CH(R^1)-COOH and NH_2-CH(R^2)-COOH—by giving the chemical reaction (continue to use different colors for the chemical groups that originate from the original two amino acids).

Answer

NH_2-CH(R^1)-COOH + NH_2-CH(R^2)-COOH $\longrightarrow$ NH_2-CH(R^1)-CO-NH-CH(R^2)-COOH + H-OH (= H_2O).

Question 4

Describe the two different phosphodiester bonds in an mRNA and their functions.

Answer

The general 3'⟶5' phosphodiester bond joins neighboring nucleotides that were transcribed from the genomic DNA sequence (the phosphate group is linked to the carbon 5' atom of the ribose of one nucleotide and the carbon 3'atom of ribose on the neighboring nucleotide). This type of bond gives an unambiguous orientation to the mRNA (and to any nucleic acid).

In addition, the cap at the 5' end is formed when a 7-methylguanosine that is not transcribed from the genomic DNA is covalently attached to the nucleotide at the 5' end by a 5'⟶5' phosphodiester bond. This distinctive type of phosphodiester bond effectively blocks any cellular exonuclease from nibbling away at the 5' end of the mRNA.

Question 5

A natural form of chemical crosslinking is often important in protein structure. Describe the mechanism and explain why it is important.

Answer

Many proteins have covalent bonding that joins *certain* cysteines at different locations within a single polypeptide or on different polypeptides. The chemical reaction is a reducing one in which the sulfhydryl groups on the two participating cysteine residues form a disulphide bond as follows:

Cysteine 1 –SH + Cysteine 2 –SH ⟶Cysteine 1 –S–S– Cysteine 2.

Disulfide bonding is important in protein structure because it helps to constrain protein structure more effectively than through hydrogen bonding and so it is valuable in proteins that need to have globular shapes for their function, and in making globular domains.

Question 6

The nuclear and mitochondrial DNAs of human cells differ widely in many properties. Give four examples.

Answer

- Length: nuclear DNA molecules are much bigger than mtDNA.
- Presence of ends: nuclear DNA molecules are linear; mtDNA molecules are circular.
- Nucleoprotein structure: nuclear DNA is heavily complexed with proteins to form chromatin; mtDNA has few attached proteins.
- Gene density: low in nuclear DNA; high in mtDNA.
- Transcription: multigenic transcription in mtDNA; but usually individual gene transcription in nuclear DNA.
- Mutation rate: generally much higher in mtDNA than in nuclear DNA.
- Copy number: often two copies of a nuclear DNA molecule per cell, but hundreds or thousands of mtDNA molecules per cell.

Question 7

Gene families have arisen in evolution by mechanisms that copy DNA sequences. Give three examples of these mechanisms

Answer

- Whole-genome duplication.
- Subchromosomal duplication at the level of genomic DNA by unequal crossover.
- Retrotransposition (a gene makes an RNA transcript that is copied into a cDNA by a reverse transcriptase within the cell and the cDNA then integrates into some other location in the genome; see Figure 2.15).

Question 8

What are pseudogenes? Explain how they originate and explain how some pseudogenes are functionally important.

Answer

Pseudogenes are non-allelic copies of a functional gene that have arisen in evolution by some gene copying mechanism. Subchromosomal gene duplication at the level of genomic DNA gives rise to *nonprocessed pseudogenes* that may initially have copies of all exons and introns of the parent gene plus upstream regulatory sequences such as the promoter. They pick up inactivating mutations and become liable to loss of DNA sequences. Retrotransposition gives rise to *processed pseudogenes* that have copies of the exons of the parental gene but lack copies of introns or upstream regulatory sequences.

Most pseudogenes are thought to be functionally inactive, but some pseudogene copies of a protein-coding gene are transcribed and are functionally important, even though they are not capable of making

a protein. This happens when RNA transcripts of the pseudogene compete with the mRNA from the parent gene for binding to regulators, giving the pseudogene a role in regulating the expression of the parent gene.