6. Nucleic acids and protein synthesis

1. Explain the meaning of the term gene.
   - Sequence of nucleotides that is part of DNA
   - That codes for a polypeptide/ protein

2.

Complete Table. 5.1 by stating:

- the name of each base
- whether the base is a purine **or** pyrimidine
- whether the base is present
  - **only** in an RNA molecule (write **RNA** in the table)
  - **only** in a DNA molecule (write **DNA** in the table)
  - in RNA **and** in DNA molecules (write the word **both** in the table).

Table 5.1

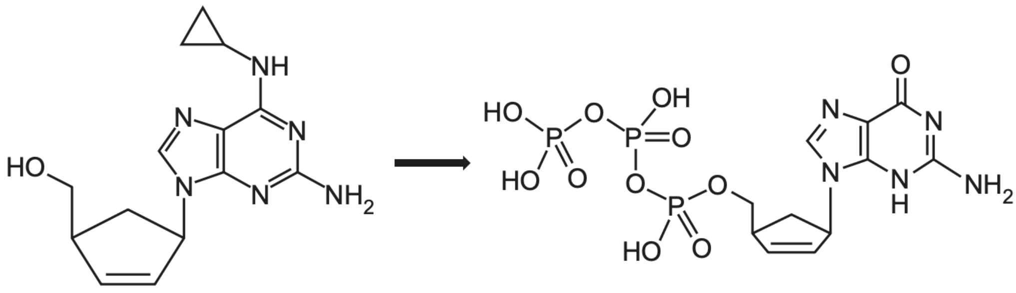
base	name of base	purine or pyrimidine	present in RNA, DNA, or both
A			
C			
G			
T			
U			

base	name of base	purine or pyrimidine	RNA or DNA or both
A	adenine	purine	both
C	cytosine	pyrimidine	both
G	guanine	purine	both
T	thymine	pyrimidine	DNA
U	uracil	pyrimidine	RNA

3.

(b) Abacavir is an analogue drug used in the treatment of some viral diseases. It enters a cell infected by a virus and is metabolised to the analogue carbovir triphosphate.

Fig. 5.1 shows the molecular structure of abacavir and carbovir triphosphate.



Carbovir triphosphate can be inserted into an elongating polynucleotide chain instead of a nucleotide. This interferes with the action of DNA polymerase during the synthesis of viral DNA.

With reference to Fig. 5.1, explain whether carbovir triphosphate will replace a purine or a pyrimidine nucleotide in the elongating polynucleotide chain.

- purine because it is a double ring structure / has two rings

With reference to Fig. 5.1 and the action of DNA polymerase, suggest why the conversion of abacavir to carbovir triphosphate increases the chance of the analogue being added to the viral polynucleotide chain.

- carbovir triphosphate is similar to / same as an activated nucleotide
- carbovir triphosphate has 3 phosphates / is activated / is phosphorylated
- DNA polymerase action: activated nucleotides are added to the growing / elongating, chain
- nucleotides form H bonds with complementary base
- nucleotides are substrates for DNA polymerase
- phosphodiester bonds form between nucleotides

Suggest and explain how carbovir triphosphate interferes with the action of DNA polymerase and how this may prevent the synthesis of viral DNA.
carbovir triphosphate can be inserted into a growing chain…

- this prevents polymerase from adding DNA nucleotide to growing chain
- similar shape to substrate / activated / phosphorylated nucleotide OR complementary shape to active site of DNA polymerase / enzyme
- acts as an inhibitor (irriversible)

- fits into / binds to active site of enzyme / DNA polymerase and competes with DNA nucleotide for active site
- fewer ES complexes form in – enzyme with DNA nucleotide
- irreversible inhibitor may cause change in shape / tertiary structure of DNA polymerase / enzyme
- DNA polymerase may not form phosphodiester bonds
- ref. to proofreading mechanism: may be too similar to be noticed as error and not repaired
- AVP: viral DNA containing analogue may not be further replicated // DNA polymerase cannot move along DNA template strand // carbovir triphosphate introduces a mutation / changes DNA formed / changes nucleotide sequence

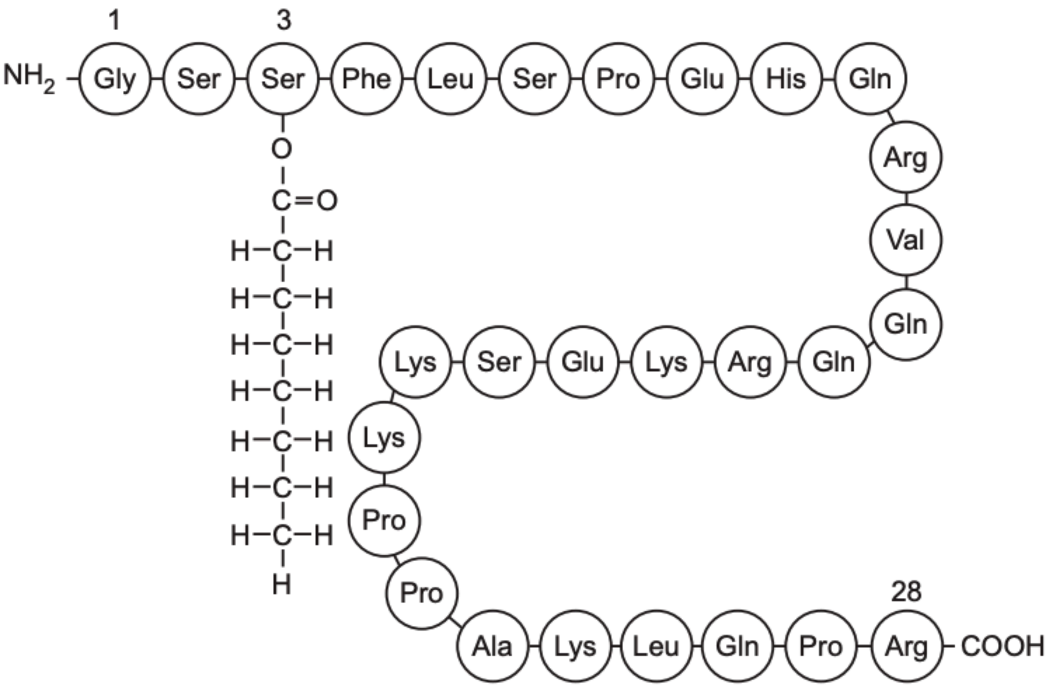
4. Many genes in eukaryotic cells contain introns. The genes that code for gliadin do not contain introns. Explain how a lack of introns in a gliadin gene affects the production of mRNA from the primary transcript.
   - RNA / gene splicing not needed / does not occur
   - no non-coding sequences so introns to not need to be removed // no nucleotides removed from the primary transcript / after transcription
   - no process of exon joining
   - all primary transcript is a coding sequence; primary transcript has the same sequence as the mRNA
   - no alternative RNA splicing / exons not joined in different combinations; only one type of mRNA formed / mRNA formed always the same

5.

The cell in Fig. 2.1 releases ghrelin, a small protein that acts as a cell signalling molecule.

Fig. 2.2 shows the sequence of amino acids in a ghrelin molecule.

The amino acid serine (Ser) in position 3 in Fig. 2.2 has been modified by the addition of a saturated fatty acid chain.



Scientists have discovered that the gene coding for ghrelin contains 5000 base pairs. This is a much larger number of base pairs than is needed to code for the ghrelin molecule shown in Fig. 2.2. Calculate the percentage of base pairs found in the gene that codes for the ghrelin molecule shown in Fig. 2.2. Show your working and give your answer to one decimal place.

- Number of base pairs needed = (28 + 2) x 3 = 90
  REMEMBER to account for the start and end codon
- Percentage = (90/5000) x 100 = 1.8%

6. The primary transcript produced from the ghrelin gene is a longer molecule than the mRNA found in the cytoplasm. Explain how the primary transcript is modified before translation.
   - Introns / non-coding regions removed
   - exons / coding regions are joined together
   - gene splicing / RNA splicing
   - AVP: e.g. guanine (cap) added (to 5' end); poly A tail / many As added (to 3' end)

7. A triplet of bases codes for one amino acid. This fact only partly explains how the activity of gene ABCA3, which is 80kb (80000 base pairs) long, can result in the protein ABCA3, which is only 1704 amino acids long. Suggest other reasons to explain the difference in the number of base pairs in gene ABCA3 compared with the number of amino acids in protein ABCA3.
   - introns are non-coding / do not code for amino acids / are not involved in polypeptide synthesis
   - introns are removed after transcription / from primary transcript / before mRNA is formed
   - only exons join to form mRNA: gene splicing / RNA splicing
   - some DNA triplets / mRNA codons are STOP codons: eg. UAA / UAG / UGA STOP codons do not code for an amino acid / terminate translation
   - met / first amino acid / amino acid coded for by START codon, and may be removed after translation

8.

(a) Table 4.1 shows a sequence of 12 nucleotides in the template strand of a short length of a DNA molecule, the corresponding primary transcript and the four amino acids coded for by the sequence. The table is incomplete.

(i) Complete Table 4.1 to show the sequence of nucleotides in the primary transcript that would result from transcription of this short length of DNA.

Table 4.1

position of nucleotide	1	2	3	4	5	6	7	8	9	10	11	12
DNA template strand	C	A	C	T	A	C	T	C	C	A	A	C
primary transcript												
amino acid	aa1			aa2			aa3			aa4		

[1]

(ii) Table 4.2 shows all the possible template strand DNA triplets that code for the amino acids labelled aa1, aa2, aa3 and aa4 in Table 4.1.

Table 4.2

amino acid	DNA triplets
val	CAA, CAG, CAT, CAC
arg	GCA, GCG, GCT, GCC, TCT, TCC
met	TAC
leu	AAT, AAC, GAA, GAG, GAT, GAC

A second type of gene mutation is caused by the deletion of a DNA nucleotide. Using the information in Table 4.2, state and explain the effect on the final protein structure of a deletion of the nucleotide at position 3 in Table 4.1.

- first amino acid unchanged / still val
- changes the reading frame / described OR all codons from mutation on will change / frameshift mutation
- deletion alters all amino acids after the mutation / amino acid sequence / primary structure
- stop codon causing premature chain termination / leading to shorter polypeptide
- leading to changes in the tertiary structure / active site

9.

Fig. 4.1 shows the structure of an ATP molecule.

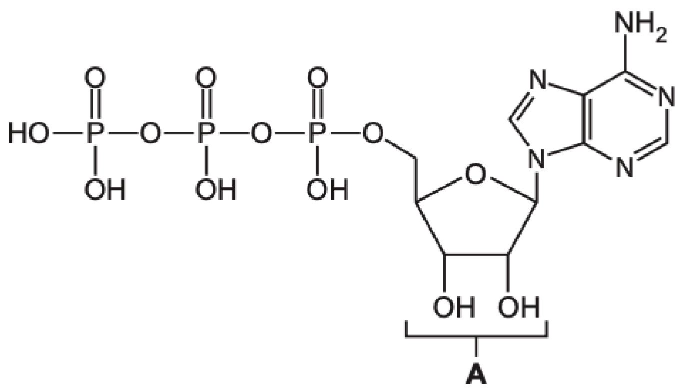


Fig. 4.1

State the name of the part of the ATP molecule labelled **A** in Fig. 4.1.

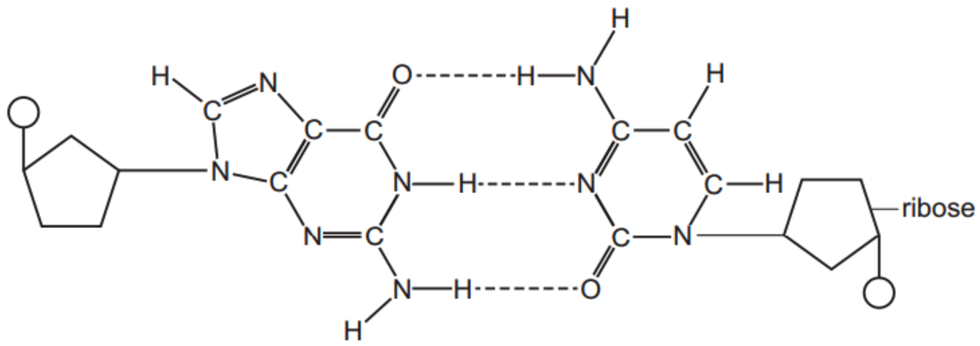
- Ribose

10.

During transcription, base pairing occurs between nucleotides.

Fig. 3.1 is a diagram to show complementary base pairing between a DNA nucleotide and an RNA nucleotide.

Only the base pair is shown in molecular detail.

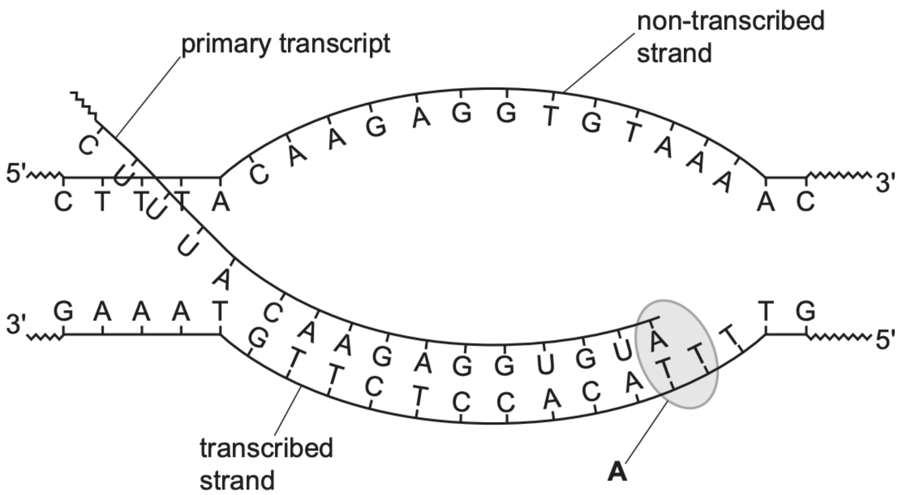


Identify and describe the DNA-RNA nucleotide pair shown in Fig. 3.1.

- base / nucleotide on left identified as guanine and base / nucleotide on right identified as cytosine
- dotted line as hydrogen bond / there are three hydrogen bonds between the bases
- circle is phosphate
- pentagon / pentose on left is deoxyribose
- double ring / base on left identified as purine
- single ring / base on right identified as pyrimidine
- AVP: label to any solid line bond as covalent bond
- ref. to antiparallel nature of base-pair

11.

Fig. 4.1 is a diagram showing the transcription of part of the *COL1A2* gene that codes for a collagen polypeptide. The part of the *COL1A2* gene shown is a section of exon. Structure **A** represents an enzyme involved in transcription.



12. State the number of amino acids that are coded for by the sequence of nucleotides on the primary transcript shown in Fig. 4.1.
    - 5

13. Use the information in Fig. 4.1 to explain why one of the strands of DNA is not transcribed.
    - other strand is not the template strand / only the template strand is transcribed
    - mRNA is single stranded
    - if transcribed, sequence of nucleotides / bases in mRNA codes for a different sequence of amino acids
    - if transcribed, results in a non-functional polypeptide / codes for a polypeptide with different function
    - translation would be a waste of energy / translation will not occur
    - AVP: RNA polymerase synthesises RNA in the 5' to 3' direction

14. Choleragen is composed of two subunits:
    - subunit A consists of one polypeptide
    - subunit B consists of five identical polypeptides

    The polypeptide in subunit A is different from the polypeptides in subunit B. Two genes, ctxA and ctxB, are needed to produce choleragen. Only one strand of the DNA forming gene ctxA is involved in the production of subunit A. Only one strand of the DNA forming gene ctxB is involved in the production of subunit B. Explain why only one strand of the DNA of each gene is involved in the production of the subunits.
    - one strand only needed to form mRNA / mRNA is single-stranded

- mRNA is used / needed to produce subunits / polypeptides
- only one strand of DNA is the template / transcribed strand
- copying / transcribing other DNA strand would not result in desired mRNA / polypeptide

15.

HIV has a nucleic acid core of RNA. The virus also contains the enzyme reverse transcriptase.

After HIV enters T-lymphocytes, reverse transcriptase catalyses the formation of DNA using activated DNA nucleotides with the viral RNA as a template.

Some drugs, such as tenofovir, have been developed to inhibit the action of reverse transcriptase.

The structure of tenofovir is similar to the structure of deoxyribose adenosine monophosphate, as shown in Fig. 3.2.

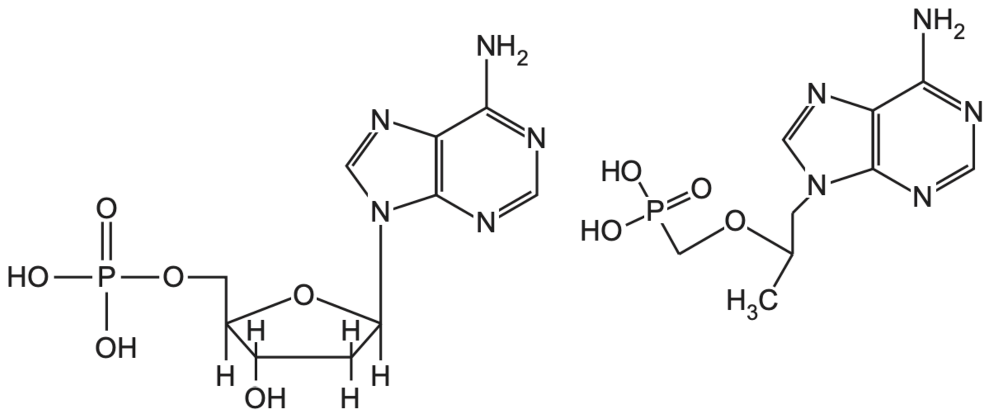


Fig. 3.2

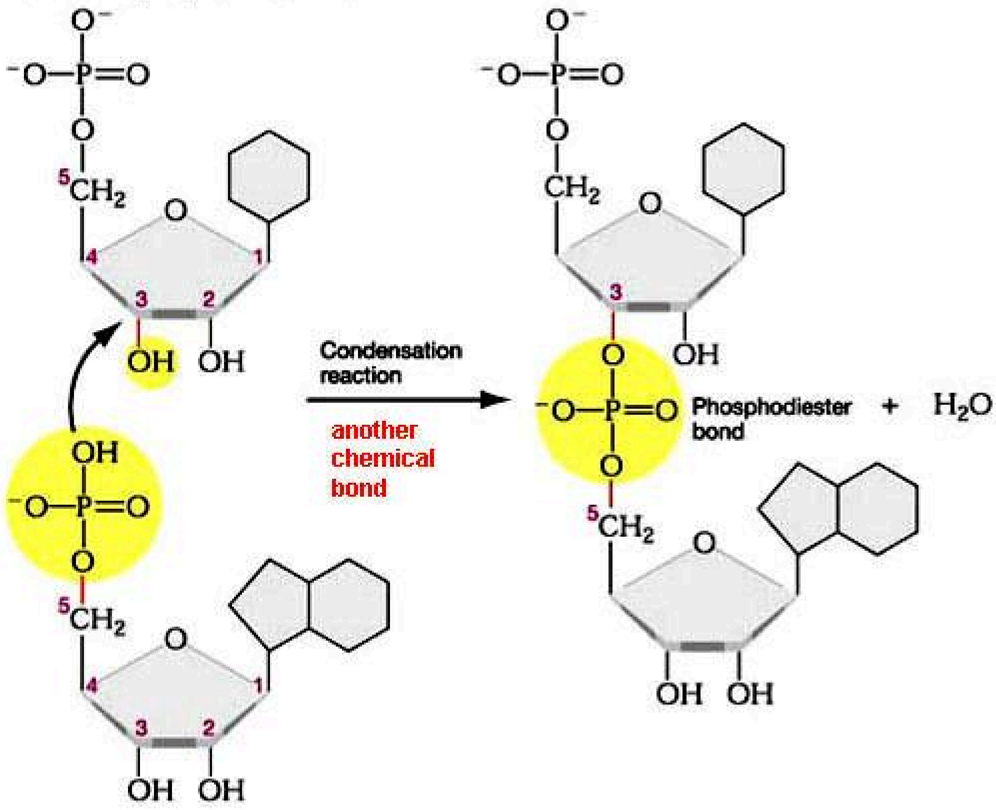
After tenofovir is absorbed into cells it is phosphorylated twice and can be used by reverse transcriptase in the synthesis of DNA.

When a tenofovir molecule is added to the DNA strand being synthesised, the process stops.

Suggest the mechanism of action of tenofovir to prevent the synthesis of DNA by reverse transcriptase. Use the information in Fig. 3.2 in your answer.

- tenofovir competes with activated / phosphorylated adenine nucleotide / deoxyribose adenosine triphosphate / active site / to prevent nucleotides being added to elongating chain OR tenofovir acts as a competitive inhibitor of reverse transcriptase
- tenofovir forms a phosphodiester bond to elongating DNA strand but stops further reactions
- tenofovir has no 3´ -OH so next nucleotide cannot form a phosphodiester bond / no deoxyribose so cannot form phosphodiester bond

Phosphodiester bond:



16. Suggest how this modification of the primary transcripts occurs in plasma cells.
    - removal of introns from primary transcript
    - after removal of introns) exons, are joined together, in different, sequences / combination(s) ; A alternative splicing
    - 3 not all the exons are used (in making the polypeptides) ; I capping and polyA tail

17. Suggest how different forms of a proteins can be formed from the same primary transcript.
    - differences owing to RNA / gene splicing
    - removal of introns / non-coding sequences
    - exons / coding sequences joined differently / in a different combination
    - so messenger RNA / mRNA formed is different

18. Suggest how the two different forms of a protein can still have similar functions, even though they have a different primary structure.
    - similar tertiary structure / binding site shape / 3D shape
    - removed amino acids are not structural amino acids
    - removed amino acids are not part of binding site
    - R-group interactions (still) the same / similar

19. Some people become ill when they have sucrose in their diet. These people have a gene mutation in the gene coding for sucrase and cannot hydrolyse sucrose in the digestive system. Scientists studying the DNA of people with this condition identified a deletion mutation in the gene coding for sucrase. Suggest and explain why a person with this deletion mutation cannot digest sucrose.

- deletion mutation is loss of one or more nucleotides in the gene coding for sucrase
- causes a change in the sequence of nucleotides / base pairs in the DNA molecule
- causes a change in the sequence of nucleotides / bases in mRNA
- consequence to codons: all the codons after the deletion mutation are altered – causes a frameshift
- mutation may form a premature stop codon / introduce a stop codon
- structural change to sucrase: change in the primary structure / different amino acid OR polypeptide does not fold into correct tertiary structure
- why sucrase is non-functional: active site not complementary

1.

(d) Row 1 and row 2 of Table 2.1 show the DNA base sequences of part of the normal *CFTR* allele and the same part of a mutated *CFTR* allele. The base sequences shown are for the DNA strands used in the synthesis of RNA. When Table 2.1 is completed, row 3 will show the base sequence of the RNA synthesised from the same part of the mutated *CFTR* allele.

Table 2.1

1	DNA base sequence of part of the normal *CFTR* allele	T	A	G	T	A	G	A	A	A	C	C	A
2	DNA base sequence of part of the mutated *CFTR* allele	T	A	G	T	A	A	C	C	A	C	A	A
3	RNA base sequence synthesised from the mutated *CFTR* allele												

a. The difference between the DNA base sequence in row 1 and the DNA base sequence in row 2 is caused by a single gene mutation. State the name of this type of gene mutation.
Deletion mutation

b. Complete Table 2.1 to show the missing bases in row 3.

AUC AUU GGU GUU

REMEMBER to replace T with U!!

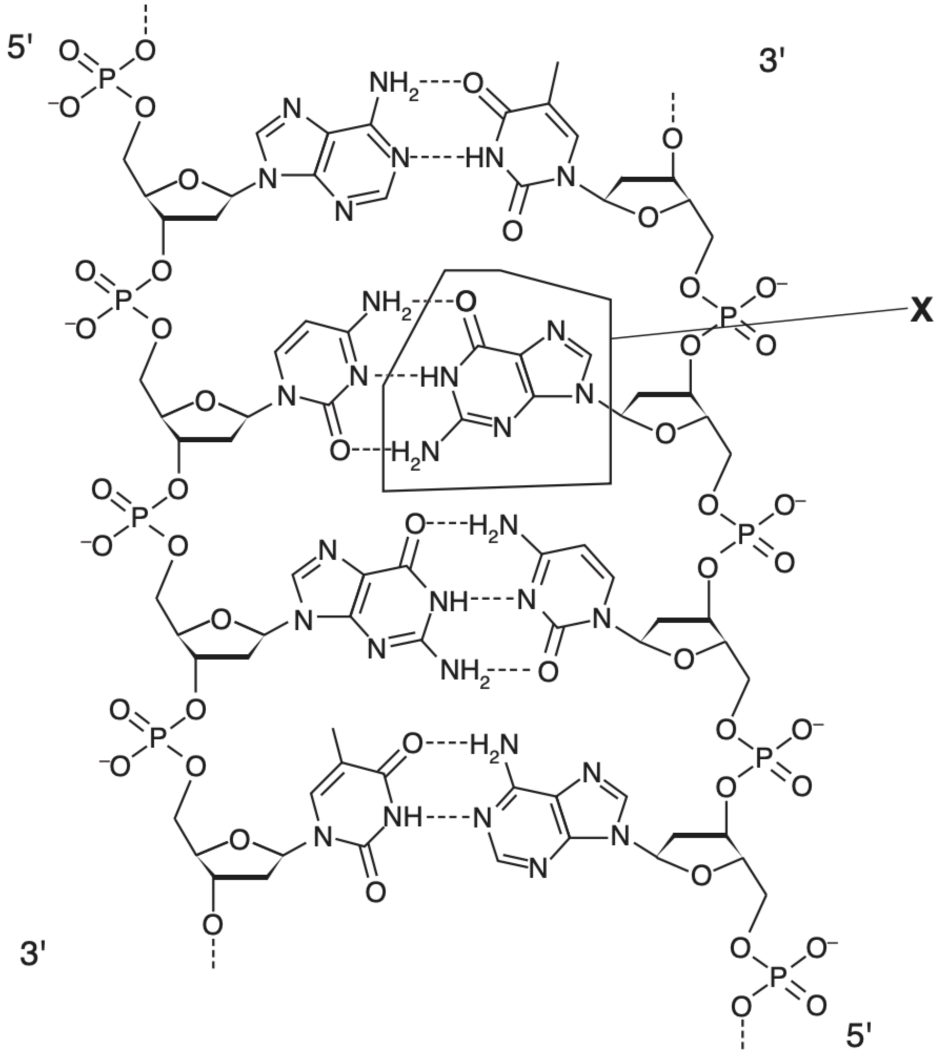
2. State the term used to describe the DNA strand that is used in the synthesis of RNA.
   Template strand / transcribed strand

3. The normal CFTR allele is approximately 189000 base pairs in length. The CFTR polypeptide consists of only 1480 amino acids. Explain the reasons for this difference between the number of base pairs and the number of amino acids.
   - 3 bases code for 1 amino acid.
   - During gene splicing/ RNA splicing, introns that do not code for amino acids are are removed from the primary transcript RNA.
   - Only the exons that code for amino acids are joined together to form mRNA.
   - DNA triplet / mRNA codon for STOP does not code for an amino acid.
   - methionine at start / first amino acid / amino acid coded for by START codon is removed.
   - AVP: ref. to (upstream) enhancer sequences // ref. to (downstream) terminator sequences // ref. to (non-coding) regulatory sequences / promoter

4. HIV protease is an enzyme composed of two identical polypeptide chains. Each polypeptide chain is 99 amino acids long. During translation, the amino acids are joined by peptide bonds to form the polypeptide chain. Describe how a polypeptide of HIV protease is produced by the process of translation.
   - mRNA attaches to / associates with ribosome.
   - 2 two codons, exposed: A and P sites / first and second binding sites on the ribosome.
   - tRNA carries an amino acid to ribosome / each type carries a specific amino acid / first amino acid is met / tRNA with met / tRNAmet.
   - anticodon (on tRNA) binds to codon (on mRNA): complementary base pairing between codon and anticodon; H-bonds form between bases on codon and anticodon.
   - START (mRNA) codon / (mRNA) AUG first codon.
   - second tRNA with its amino acid binds next to first tRNA / (two) amino acids are held in place close to each other by tRNA binding.
   - (after peptide bond formation) first tRNA detaches / ribosome moves along one codon.
   - tRNA molecules reused / leave ribosome to attach to another amino acid.
   - process repeats / elongation occurs until STOP codon / polypeptide chain synthesis (and released from ribosome).

5.

Fig. 3.1 is a diagram of a small section of a DNA molecule.



Identify the base X and state the evidence in Fig. 3.1 that supports this identification.

- Base X = guanine
- Evidence
    - double ring base / purine base ;
    - forms three hydrogen bonds with complementary base ;

NOTE:

- Adenine & guanine = purines = double-ring structure
- Thymine, uracil, cytosine = pyrimidines = single-ring structure
- Adenine-thymine = 2 hydrogen bonds
- Guanine-cytosine = 3 hydrogen bonds

6. The section of the DNA molecule in previous figure is part of a gene coding for a polypeptide. Base X is located in an exon on the strand of DNA that is transcribed during protein synthesis. A mutation that results in the deletion of base X will affect the polypeptide produced. Explain how this deletion may affect the polypeptide produced during protein synthesis.
   - three bases / triplet of bases / codon code(s) for one amino acid ;
   - change in triplet of bases / codon ;
   - frameshift mutation occurs;
   - every, triplet / codon, after deletion will be different ;
   - primary structure / sequence of amino acids / AW, will be altered ;
   - may introduce a stop codon ;
   - (stop codon results in) formation of, shortened / truncated, polypeptide ;
   - AVP ;
     - e.g. ref. to errors in RNA splicing
     - ref. to affects post-translational modification
     - bonds that form between R groups, will / may, be altered
     - tertiary structure of protein will be altered
     - non-functional protein formed
     - altered function of the protein

7. Gene mutations can occur in either introns or exons. Suggest the effect of a gene mutation in an intron.
   - no effect on protein structure (because introns are non-coding) ;
   - non-functional / reduced function of, protein (as intron not spliced after transcription) ;
   - may affect regulation of gene expression ;
     - e.g. reduction in the rate of transcription
     - RNA polymerase does not bind
   - ref. to errors in RNA splicing ;
   - ref. to formation of an oncogene ;

8.

PfK13 is a protein that has an important role in the development of the trophozoite stage of *P. falciparum*. The gene *kelch13* codes for PfK13.

Two different mutations of *kelch13*, known as F446I and C580Y, were investigated to see if they were associated with partial artemisinin resistance. Details of these mutations are summarised in Table 3.1.

Table 3.1

name of mutation	**change in DNA**		**change in protein PfK13**	
	nucleotide present in *kelch13*	**nucleotide present after mutation**	**amino acid before mutation**	**amino acid after mutation**
F446I	thymine (T)	adenine (A)	phenylalanine (phe)	isoleucine (ile)
C580Y	guanine (G)	adenine (A)	cysteine (cys)	tyrosine (tyr)

Using gene kelch13 and mutation F446I as examples, explain the difference between a gene and a gene mutation.

- Correct use of example:
    - gene = kelch13
    - gene mutation = kelch13 mutation or F446I
    - protein/polypeptide = PfK13
- (mutation has), changed / altered / AW, sequence / arrangement / order, of nucleotides / bases, (in DNA)
- (gene) codes for the production of a, polypeptide / protein AW