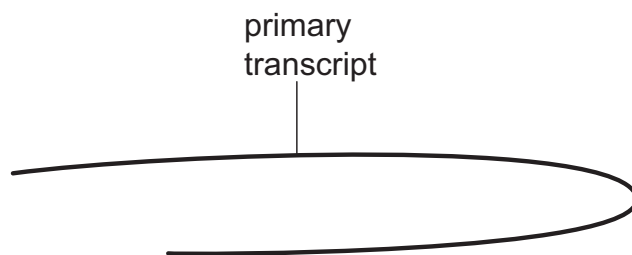


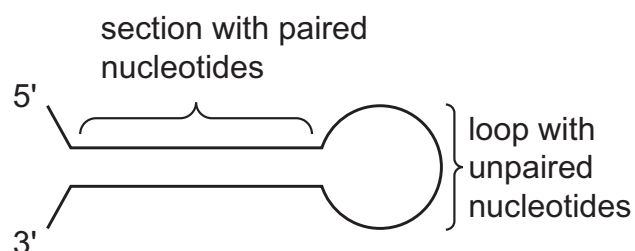
- 3** Small interfering RNA (siRNA) is a short length of double-stranded RNA (dsRNA), approximately 21 to 25 nucleotides long. siRNA helps to regulate protein synthesis in cells.

(a) Fig. 3.1 is an outline summary of one way in which a primary transcript can be processed to produce a molecule of siRNA. The transcript does **not** code for a sequence of amino acids.

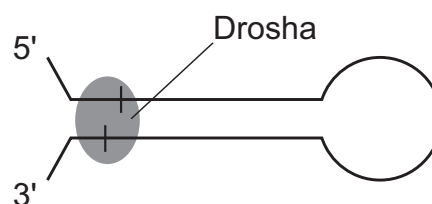
step 1: a primary transcript is synthesised from one strand of DNA



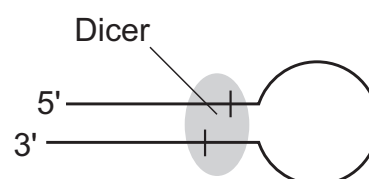
step 2: the primary transcript loops and a section of the RNA becomes double stranded



step 3: the enzyme Drosha attaches and cleaves (cuts) the RNA to produce a shorter length



step 4: in the cytoplasm, the enzyme Dicer attaches and cleaves the RNA



step 5: siRNA, which is double stranded and has 2 unpaired nucleotides at each 3' end, is produced

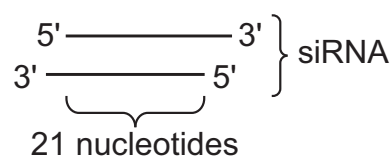


Fig. 3.1

(i) In **step 2** in Fig. 3.1, the single-stranded primary transcript loops and forms a section where dsRNA is present.

Explain how it is possible for the double-stranded section of RNA to be held together in **step 2** and maintained this way in **steps 3, 4** and **5**.

[2]

(ii) After **step 3**, the shorter dsRNA produced by the action of Drosha is transported to the cytoplasm, where it is cleaved further by Dicer to produce ds siRNA.

Suggest why two different enzymes, Drosha and Dicer, are needed to cut dsRNA into shorter lengths.

[2]

(b) From 2018, siRNA has been used as a therapeutic drug to treat a number of diseases.

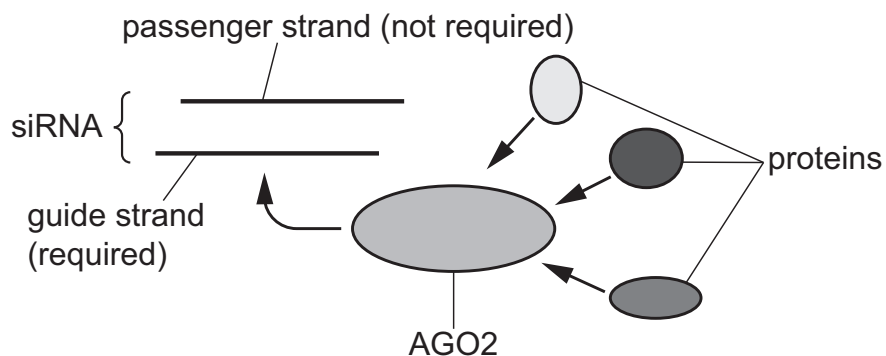
The presence of molecules of siRNA in the cytoplasm can result in the cleavage of messenger RNA (mRNA) molecules coding for a protein involved in the disease. This prevents the synthesis of the protein.

Describe the differences between a molecule of mRNA and a molecule of siRNA, such as the siRNA shown in **step 5** in Fig. 3.1.

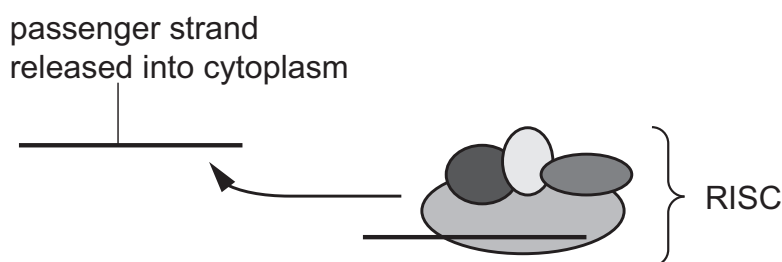
[2]

(c) Fig. 3.2 summarises how mRNA coding for a protein involved in disease can be targeted and cleaved by siRNA.

presence of siRNA activates a protein, AGO2, which binds siRNA and other proteins to form a complex known as RISC



passenger strand is separated from RISC



RISC uses guide strand to target and bind mRNA for cleavage

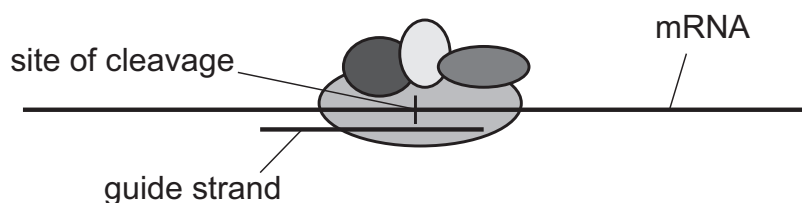


Fig. 3.2

(i) With reference to Fig. 3.2, state why the passenger strand needs to be separated and released from the RISC.

[1]

(ii) The aim of siRNA therapy is to prevent or decrease the synthesis of a protein involved in the disease being treated.

A target mRNA molecule can be cleaved in a different location by a RISC with a different siRNA.

Suggest how cleaving mRNA in different locations will have different effects on protein synthesis **and** explain how these different effects can result in a lack of functioning protein.

[3]

[Total: 10]

- 1 Guinea pigs, *Cavia porcellus*, vary in the length and colour of their fur.

Fig. 1.1 shows a guinea pig with short black fur.



Fig. 1.1

Two genes that determine the length and colour of the fur occur at the **A/a** locus and the **B/b** locus. These two gene loci are on separate autosomal chromosomes.

- The allele **A** results in short fur.
- The allele **a** results in long fur.
- **A** is dominant to **a**.
- The allele **B** results in black fur.
- The allele **b** results in chocolate fur.
- **B** is dominant to **b**.

- (a) (i) List **all** the possible genotypes of a guinea pig with short black fur.

.....
.....
..... [2]

- (ii) A test cross could be used to determine the genotype of a female guinea pig with short black fur.

Describe the **phenotype** of the male guinea pig that could be used to carry out this test cross.

..... [1]

(b) A black guinea pig with long fur that was homozygous at both loci was crossed with a chocolate guinea pig with short fur that was homozygous at both loci. The F1 offspring of this cross had short black fur. F1 offspring were mated together to produce the F2 offspring.

- Complete the Punnett square to:
- show the cross between the F1 offspring
 - predict the F2 offspring genotypes.
- You should include the gametes in your answer.

State the ratio of F2 offspring phenotypes. You should include a key to link phenotypes to genotypes.

ratio of F2 offspring phenotypes:

[4]

(c) Some genes in guinea pigs are structural genes and some are regulatory genes.

Describe the difference between a structural gene and a regulatory gene.

[2]