Genetic technology – 2018 Biology A2 9700

1. Nov/2018/Paper_41/No.5

(a) Leber's congenital amaurosis (LCA) is an autosomal recessive eye disease. LCA results in eye disorders, including severe loss of vision, at birth. LCA has been successfully treated by gene therapy, using a virus instead of a plasmid as the vector.

Adeno-associated virus (AAV) vectors containing the therapeutic allele were injected directly into the retina, the layer at the back of the eye containing the photoreceptor cells. People who had been blind from a young age were able to see again.

There is a risk associated with the injection method used to deliver the vectors, as it might cause the retina to detach, damaging vision. This method of delivery was first used for LCA before being trialled on other retinal diseases that gradually reduce the vision of people as they get older.

(i) Suggest the main steps involved in creating recombinant DNA for this example of gene therapy.

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(ii) Explain why the fact that LCA is an autosomal recessive genetic disease makes it suitable for treatment with gene therapy.

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(iii) Suggest why the retinal injection method of gene therapy was used for LCA before it was trialled on other retinal diseases that gradually reduce the vision of people as they get older.

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(b) Scientists tried to create an improved virus vector for gene therapy.

step 1 – The scientists used a special form of the polymerase chain reaction (PCR). This form of PCR causes mutations in the DNA sequence of AAV by base substitution.

step 2 – The viruses containing different base substitutions were tested. This was done by using the different viruses to deliver a new gene, the gene for green fluorescent protein (GFP), into the photoreceptor cells of mice, using the retinal injection method.

step 3 – The best virus, known as 7m8, caused the photoreceptor cells in the retina of the mouse to fluoresce brightly, even when the recombinant virus was injected into the fluid inside the eye instead of into the retina itself.

step 4 – The 7m8 virus was used to cure a mouse with LCA by injecting this virus containing the therapeutic allele into the fluid inside the eye of the mouse.

(i) Suggest how errors occurring during PCR can cause base substitution mutations in the DNA sequence of AAV.

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(ii) Explain why the photoreceptor cells of the mouse fluoresced in step 3.

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(iii) Predict the impact of the 7m8 AAV on treatment for age-related retinal diseases.

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[Total: 14]