REG.NO.:

VIT
Vellore Institute of Technology
(Deemed to be University under section 3 of UGC Act, 1956)

SCHOOL OF BIO SCIENCES AND TECHNOLOGY
CONTINUOUS ASSESSMENT TEST - II
WINTER SEMESTER 2025-2026

Programme Name & Branch	**: Integrated M.Sc. Biotechnology**
Course Code	**: TBIT408L**
Course Name	**: Gene Therapy**
Slot	**: D2+TD2**
Faculty Name	**: Prof. Everette Jacob Remington N**
Class Number	**: VL2025260503479**
Date of Examination	**: 18th Mar 2026**
Exam Duration	**: 90 minutes** **Maximum Marks: 50**

General instructions:

- Answer All Questions
- M – Maximum Mark; CO – Course Outcome; BL – Bloom's Taxonomy Level (1 – Remember, 2 – Understand, 3 – Apply, 4 – Analyse, 5 – Evaluate, 6 – Create)
- Course Outcomes:
  3. Identify suitable viral vectors based on their simplicity, genotoxicity, and immunotoxicity.
  4. Examine various factors that could influence the progress of a gene therapy clinical trial.
  5. Appraise gene therapy for a disease based on the need, safety, and success of previous trials.

Q. No.	Question	M	CO	BL
1.	ADA-SCID was the first human monogenic disorder to be treated by gene therapy. Since the prevalent disease manifestations of ADA-SCID are in the T lymphocytes, several of which are long-living cells, the first gene therapy clinical trial was performed by gene transfer into the peripheral blood T lymphocytes. The cells were recovered by apheresis and cultured *ex vivo* in the presence of a mitogen and IL-2, following which they were transduced with a gammaretroviral vector expressing the ADA cDNA and then reinfused. The first trials performed by gene transfer into T lymphocytes showed that gene therapy was safe and devoid of any adverse effects. In some patients, a relatively high number of transduced lymphocytes, up to 20% could be detected even more than 10 years after the transplant with a significant immune function recovery. a. Assume the choice of T lymphocytes for gene transfer. b. Infer the need for administering PEG-ADA to the patients. c. Examine some of the drawbacks of this clinical protocol.	 3 3 4	5	4
2.	The first clinical trial for hemophilia B was conducted in 1999 based on the intramuscular injection of an AAV2 vector. Patient follow-up effectively confirmed the safety of AAV vectors and revealed factor expression for at least a few years after injection. However, the levels of circulating FIX were too low (<1–2% of normal) to allow therapeutic benefit to these patients. The results of subsequent studies entailing AAV vector transduction of the liver by direct injection or portal vein inoculation generated much more encouraging results. After these treatments, therapeutic or even higher than normal levels of FIX were detected in the circulation in mice, hemophilic dogs, and non-human primates, which prompted the organization of clinical trials entailing portal vein inoculation of AAV2 vectors. a. Analyze the reason for very low levels of circulating FIX. b. Contrast the benefits of portal vein inoculation in this protocol. c. Inspect some of the drawbacks of AAV2 used in this clinical trial.	 3 3 4	5	4

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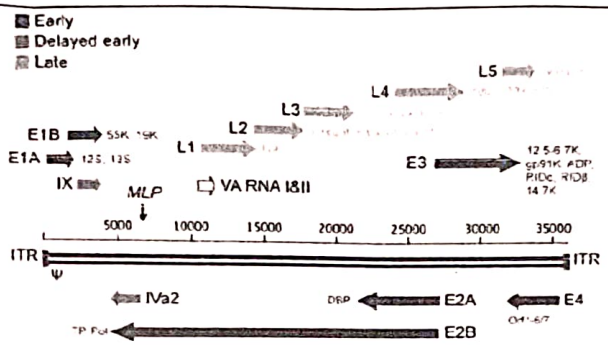
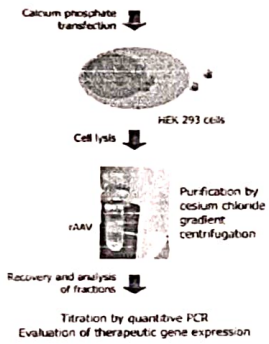
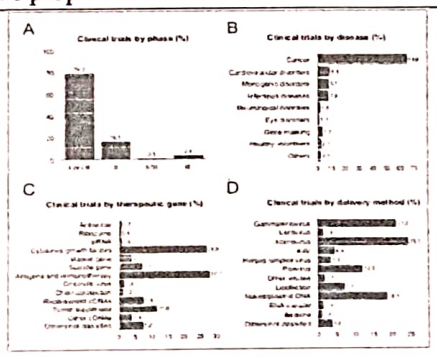
3.			3	2
	a. Relate some of the specific functions of the E1 gene products.	3		
	b. Summarize the major effects of the E3 gene products.	3		
	c. Compare the 1st, 2nd, and 3rd generation adenoviral vectors.	4		
4.			3	2
	a. Interpret that the packaging cells do not stably express the *rep* gene.	3		
	b. Adeno-associated viruses are incapable of autonomous infection. Explain.	3		
	c. Outline some of the properties of adeno-associated virus vectors.	4		
5.			4	4
	a. Classify the different types of viral vectors used in gene therapy.	3		
	b. Distinguish the two broad approaches employed in cancer treatment.	3		
	c. Simplify the important aspects of a Phase III gene therapy clinical trial.	4		