Indian Institute of Science Education and Research, Tirupati

ABHIPRAJNA 2023 (Prelims)

BIO QUESTION PAPER

Date: September 17, 2023 Maximum points: 30

Instructions:

- *All questions are mandatory.*
- *The question paper consists of 6 questions in total, spread over 7 pages.*
- *Answers must be written in legible and readable handwriting, failing which that question shall not be considered for evaluation.*
- *Question 3 comprises of two questions, out of which you can choose one to answer.*
- ***A part of Question 2 is the Hint question, whose answer will be required to solve the puzzle question in the Theme Round.***
- *Click this link for submitting your solution PDF:* *https://forms.gle/Aq1Cc2kvXDAcb58SA*

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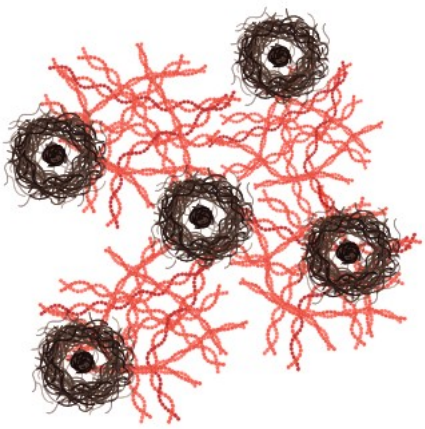
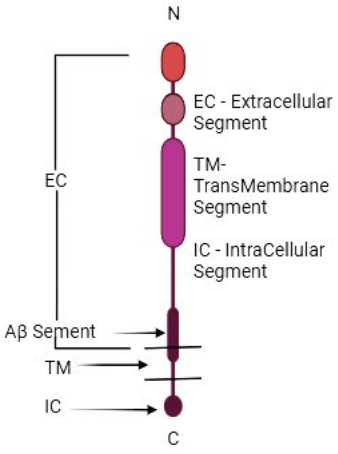
1. Alzheimer's is one of the most fatal neurodegenerative which is also progressive in nature, associated with critical clinical features like memory impairment, language deterioration, motor and sensory abnormalities, etc. Researchers have found that pathologically an increased amount of beta-amyloid peptide and plaques in mainly neocortex, allocortex, hippocampal, and amygdala regions in the patient's brain suffering from Alzheimer's.



Amyloid plaques with Tau Aggregations



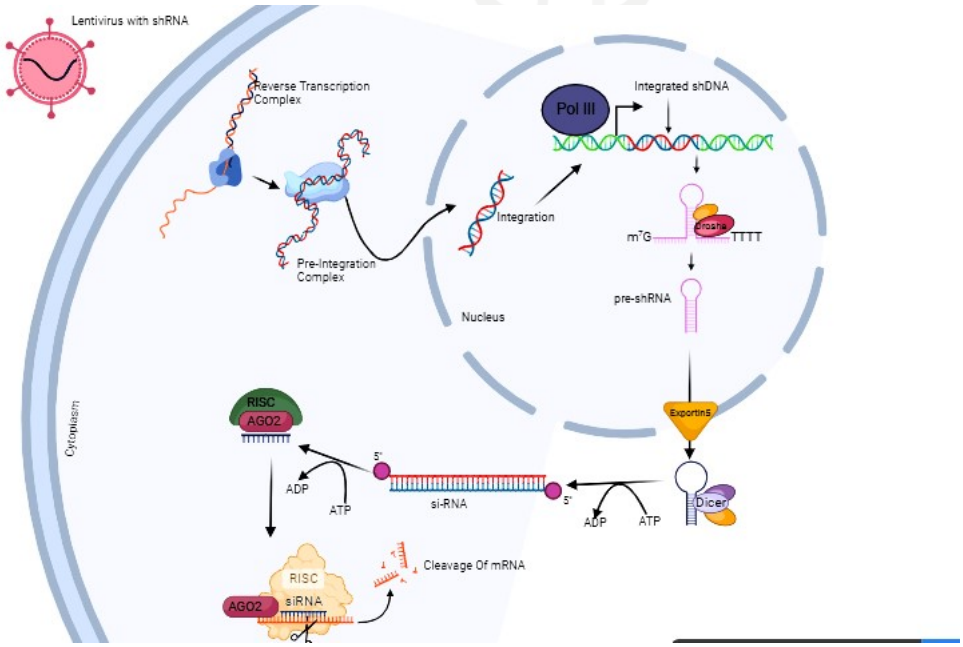
Aβ Amyloid Precursor Protein

The main component of these plaques is amyloid beta (Aβ) which is generated from APP (Amyloid Precursor Protein) [Schematic diagram is mentioned above] upon the action of two enzymes beta-secretase and followed by gamma-secretase. Earlier studies have already shown that several mutations associated with the Aβ region of APP can be a potential cause of Alzheimer's.

Dr. Joseph W and his group is currently focusing on designing different shRNAs to target the Aβ region of APP mRNA and knockdown the APP gene to reduce the content of Aβ proteins in the neuronal cells.

Short hairpin RNAs are characterized by a double-stranded RNA stem, a loop structure with a 3′ overhang which is typically 70-80 nucleotide long and is greatly used for silencing a particular gene that follows mainly RNA interference (RNAi) mechanism in-vivo cellular environment. For a high level of expression generally, U6 or 7S K promoters are used and they are designed based on a target sequence that is present in the exon region of the transcript of the gene of interest. For DNA-based shRNAs mainly two methods for delivery are followed – i) Lentiviral Transduction or ii) Lipid-based transfection.

After getting integrated with the DNA or getting transcribed by the action of DNA Pol III from the plasmid delivered shRNAs are further processed by the Dicer complex and 3′ overhangs containing dsRNA are generated which will be further processed by the RNA Induced Silencing Complex and the anti-sense RNA will make a hybrid with the target mRNA and RISC will eventually cleave it.



Mechanistic Diagram of lentiviral delivery of shRNA and RNAi-mediated Gene Silencing

Dr Joseph and his team have selected one shRNA to screen it over two human microglia cell lines LHDM-5 and HUM-O which contain a pathogenic mutation in the APP gene at A region and show an increased amount of amyloid beta production and accumulation.

Interestingly they found out that though the shRNA is highly specific for its target region in the APP mRNA, it's knocking down the APP gene in the HUM-O cell line with a 97% efficacy but no knockdown is observed in the other cell line. This group of researchers has already checked for abnormalities in the molecular machinery associated with shRNA generation and processing in the LHDM-5 cells but all seems to be ok.

1. Find out the possible mechanism by which shRNA-mediated knockdown is by passed by the LHDM-5 cells (Make your own hypothesis). **[5 points]**
2. Based on your hypothesis design an experiment to check your hypothesis in in-vitro condition. **[5 points]**

2. **Bio Babble**

Please find the link for PPT here:
https://docs.google.com/presentation/d/11ypq7ltpK1YMgMP8_EeIFM9sjZ2pUw3e1oObSZ9AI4A/edit?usp=sharing

The instructions for the Bio Babble are given in the PPT. Please read them carefully before attempting to fill out the crossword. Note that you only have to do section I or the first 10 words of Bio Babble as part of this question. While submitting you don't have to make the crossword, just write the words on your answer sheet.
[5 points]

3. Aposematism is a defensive strategy in which certain species exhibit conspicuous warning colouration, patterns, or other signals to deter predators, signalling their unpalatability, toxicity, or dangerousness, thus increasing survival chances.

   Whereas mimicry is an evolutionary adaptation where one species closely resembles another, benefiting (even aposematism) by gaining protection from predators, enhanced foraging opportunities, or other advantages, further bifurcating into two categories: Batesian and Mullerian.

   Few observational scenarios are challenging the sympatric setting of mimics and models, where mimicry exists in an allopatric setting, where the environmental con-

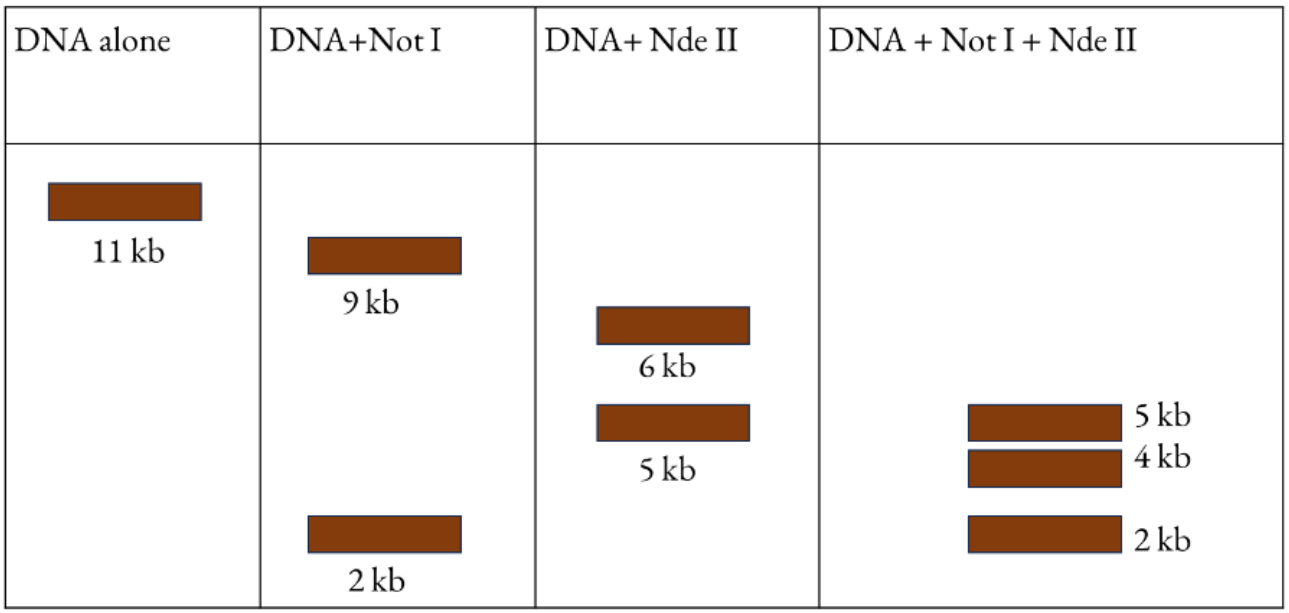
ditions are similar. What are the factors that allow mimicry to be sustained in such an environment?

Two species of ants co-exist; species 2 mimics the pheromones of species 1. Suppose we isolate species 2 geographically for a few generations. Later, reintroduce them into the previous environment, where species 1 exists. What would be the impact on mimicry? [**5 points**]

OR

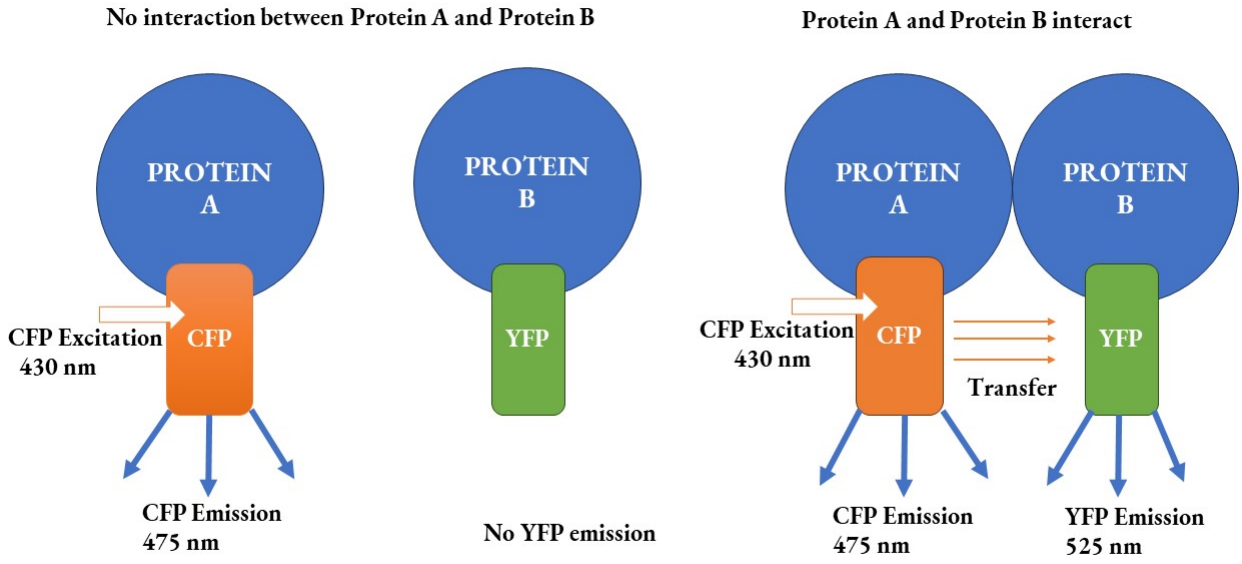
Biobabble Section II: [**5 points**]
https://docs.google.com/presentation/d/11ypq7ltpK1YMgMP8_EeIFM9sjZ2pUw3e1oObSZ9AI4A/edit?usp=sharing

4. One fine day, Professor Phunsukh Wangdu entered the lab brimming with excitement. He shared an idea with his intern Raju: a mysterious DNA fragment from an Adenovirus might hide a unique NSP gene, which could be useful for the further characterization of that viral species. As an initial step, he told Raju to digest the fragment with restriction enzymes and identify where the restriction enzymes were cutting the DNA fragment. To start, Raju used precision enzymes (Not I and Nde II) to cut the DNA, revealing distinct patterns on gel images. When both enzymes teamed up, the gel showed even more complexity.



Based on the above gel images, Raju predicted where the enzymes should cut the DNA and drew the map on a sheet. Draw the map that Raju predicted. Explain the logic behind his prediction. **[3 points(1+2)]**

5.



Förster Resonance Energy Transfer (FRET) is a process by which energy is transferred between two fluorophores (molecules that can emit light) without the emission of a photon. In FRET, there is a donor fluorophore and an acceptor fluorophore. The donor fluorophore is initially in an excited state and transfers its energy to the acceptor fluorophore through non-radiative mechanisms. As a result, the donor fluorophore's excited state is quenched (reduced), and the acceptor fluorophore becomes excited and emits light of a relatively higher frequency.

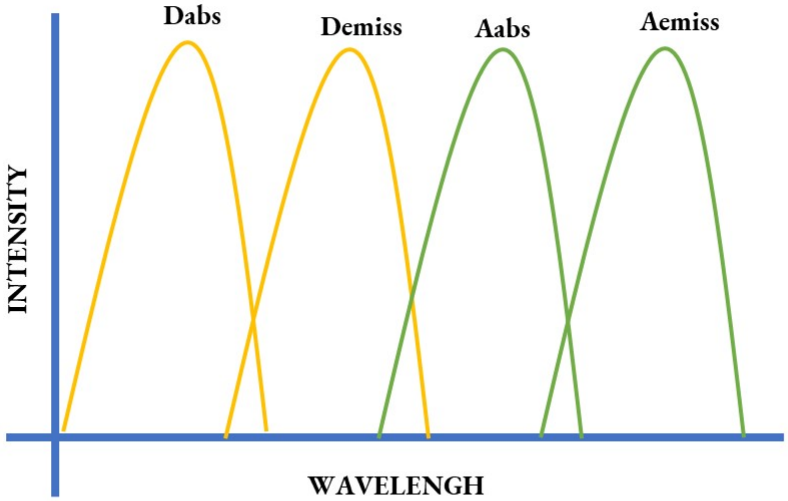
One example of FRET in biology is the study of protein-protein interactions within living cells. Researchers can attach a donor fluorophore to one protein of interest and an acceptor fluorophore to another protein of interest. If these two proteins come close enough due to a molecular interaction, FRET can occur, indicating their proximity and interaction.

Spectral overlap between fluorophores could indicate whether FRET is happening and quantify its efficiency. FRET efficiency (E) is a measure of how effectively energy is transferred between the fluorophore molecules.

Based on the above information, tell if FRET is happening in the below profile at

all. Show the overlap region that indicates FRET and explain your thought process. Comment on the relationship between FRET efficiency and the area of the overlap region. **[4 points(1+2+1)]**

[Dabs: Donar absorption, Demiss: Donar emission, Aabs: Acceptor absorption, Aemiss: Acceptor emission]



6. Aposematism is a defensive strategy in which certain species exhibit conspicuous warning colouration, patterns, or other signals to deter predators, signalling their unpalatability, toxicity, or dangerousness, thus increasing survival chances.

   In turn, mimicry is an evolutionary adaptation where one species closely resembles another, benefiting from the resemblance by gaining protection from predators, enhanced foraging opportunities, or other advantages, further bifurcating into two categories: Batesian and Mullerian. Batesian mimicry is when a harmless species imitates the warning signals of a dangerous species to deter predators, while Müllerian mimicry is when two or more harmful species share similar warning signals, reinforcing their mutual protection.

   Species A uses echolocation to detect species B around and catch them. However, B has evolved a signal (auditory) that helps it escape. by either jamming the signal or transmitting the message of unpalatability. How will you experimentally determine if it is jamming or emitting a message?

Species C mimics the B signal to avoid species A, which is a common predator for both. How do you determine if it is Mullerian or Batesian? Design an experimental study. [**3 points**]

Click this link for submitting your solution PDF:
https://forms.gle/Aq1Cc2kvXDAcb58SA

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