SISSA PhD Course in Functional and Structural Genomics
Academic year 2019-20, admission exam - spring session, written test
SISSA Main building, room 005
11 April 2019

Please choose 1 question from Set 1 and 1 question from Set 2 and elaborate on them.

Set 1

1. Methods to downregulate/ablate expression of a gene of interest: provide a synthetic and comprehensive description.

2. Conditional gain-of-function gene manipulations: provide a synthetic and comprehensive description.

3. How does excitotoxicity play a role in neurodegeneration?

4. Prion and prion-like mechanisms

5. Do prions form in the aggregation process of Abeta and alpha synuclein?

6. Detection systems of aggregated forms of proteins involved in neurodegeneration.

7. Methods to downregulate/ablate expression of a gene of interest: provide a synthetic and comprehensive description.

8. Conditional gain-of-function gene manipulations: provide a synthetic and comprehensive description.

9. Split reads and discordant reads. Explain what they are, why they are useful and which kind of variations they can identify.

Set 2

1. A primary neural culture gain of function for X-gene displays an increased ratio of Y-protein to Y-mRNA. Are we allowed to conclude that X stimulates translation of Y-mRNA? Are there any alternative explanations? If so, which ones? Which experimental strategy would you employ to distinguish among them?

2. The mRNA-encoding X gene and its diverging-antisense lncRNA-encoding Y companion are co-expressed by a first set of cell lines and are both not expressed by a second set of cell lines. We suspect that expression of Y promotes expression of X. How can we prove that? How can we demonstrate that *Y transcription per se* rather than *Y-lncRNA* promotes X transcription?

3. Both overexpression and downregulation of X-gene result into a comparable reduction of the neuronal output originating from a culture of neuronogenic committed progenitors. Provide explanatory hypotheses accounting for this phenomenon and propose a simple experimental strategy to distinguish among them.

4. Our preferred X gene, encoding for a canonical mRNA, has an Y pseudogene companion, lying on a different chromosome and subject of distinct transcriptional regulation. We found that if we artificially upregulate or downregulate Y, then the translation of X is promoted or depressed, respectively. Propose explanatory hypotheses and suggest a simple experimental strategy to validate/confute them.

5. Color blindness is a vision disorder caused by a recessive mutation of the gene D which is found on the X chromosome. A healthy man and woman had 4 sons of which 2 affected by color blindness and 3 healthy daughters. Explain what the genotype of the parents is and calculate the probability that the first daughter is a healthy carrier of the mutation. Motivate your responses.

6. Analyzing sequencing data mapped on the genome from DNA of a single human you find that, in a unique specific genomic location, the mapped reads display the presence of 3 different nucleotides: G, C and A. The G results to be present in about 48% of the reads, the C is present in 47% of reads while the A is present only in 5% of reads mapping on that position. The coverage of the region is very high and there are no errors; therefore these nucleotides are real and their frequencies are not an error or an artifact. How can you explain this result? What G, C and A represent?

7. Along the sequence of a gene a spontaneous mutation occurs that causes the substitution of a thymine with a cytosine. The resulting protein is identical to the original protein, its amino acid sequence has not been altered. Describe and motivate what has happened.

8. A species of squirrel has evolved a particular behavior. If an individual sees a predator, it makes strong calls for warn the other members of the colony and encourage them to seek shelter. Such behavior manifests itself in adult individuals who are no longer fertile, and puts the life of the individual making the call at serious risk, because the call might draw the attention of the predator on it. How do you explain this behavior in relation to natural selection?

9. The same transcript transcribed in the genome of the *Octopus vulgaris* displays, in two different populations, a different nucleotide in a specific position. However, when researchers sequenced the genome for this locus, both the *Octopus* populations presented the same nucleotide in that position. How can you explain the existence of the different nucleotide at the RNA level and not in the DNA?