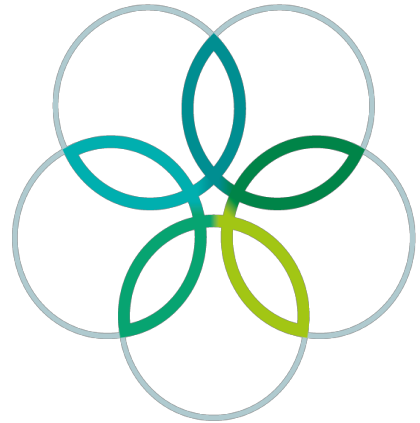
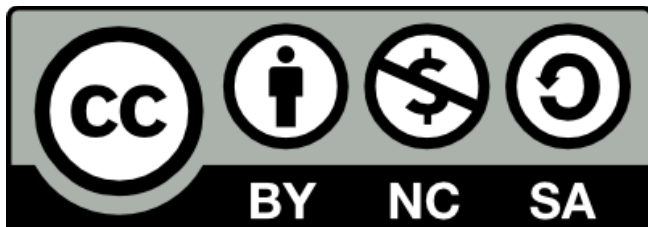


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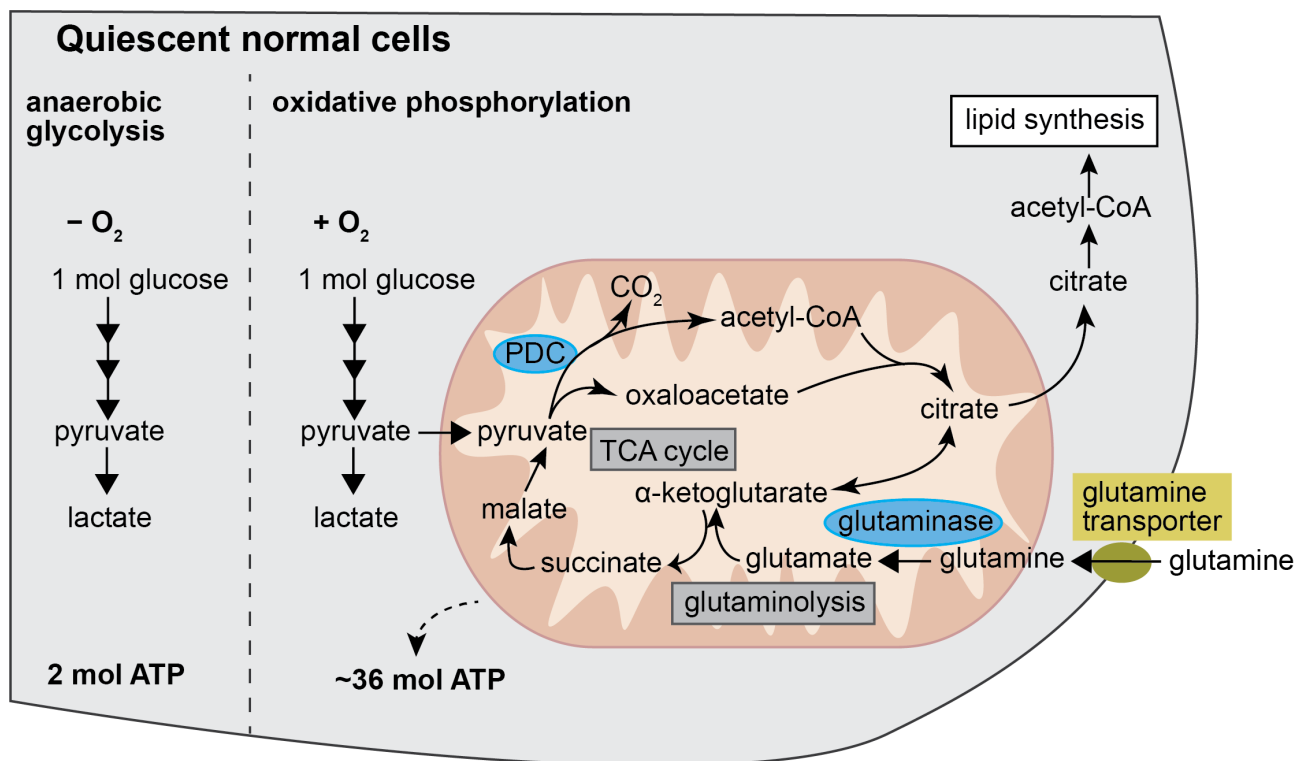
## Theoretical2



English (Official)

### Question 51

In quiescent normal cells, under normal physiological conditions, glucose is aerobically metabolized to pyruvate, most of which is transformed to acetyl-CoA by PDC (Pyruvate Dehydrogenase Complex) (Figure 1a). The resulting Acetyl-CoA enters the tricarboxylic acid cycle (TCA, also Krebs or citric acid cycle) in the mitochondria. In anaerobic microenvironment, pyruvate is almost completely converted to lactate in the cytoplasm and the production of Acetyl-CoA is inhibited. In rapidly growing cancer cells, increased expression of Pyruvate Dehydrogenase Kinases (PDKs) inactivates PDC, and inhibits the conversion of pyruvate to Acetyl-CoA (Figure 1b). Instead, the conversion of pyruvate to lactate is activated, and glycolysis takes place in the cell with high intensity.

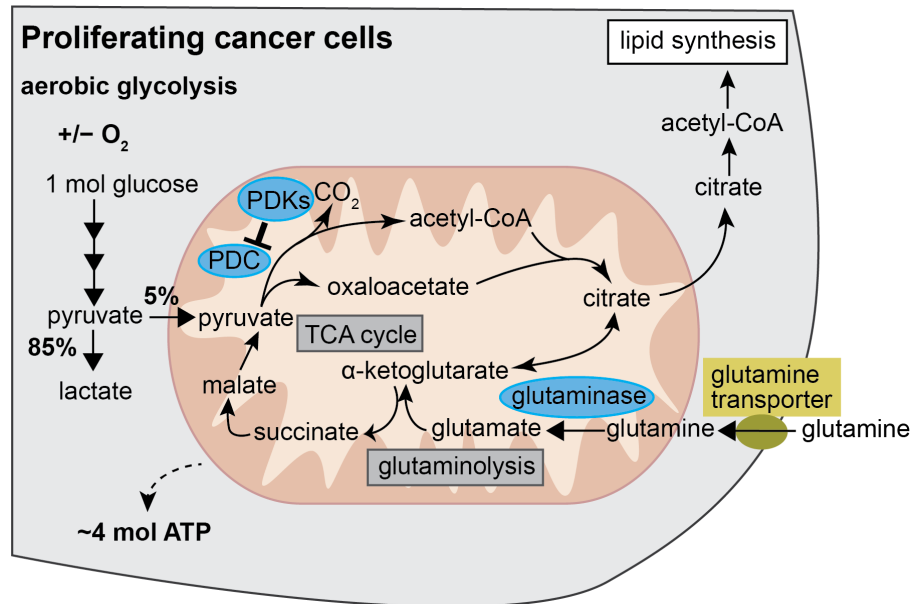


a

## Theoretical2



English (Official)



b

Figure. 1. The metabolic pathway of glucose in normal cells (a) and tumor cells (b): TCA - tricarboxylic acid, PDC – pyruvate-dehydrogenase complex; PDKs – pyruvate dehydrogenase kinases.

Use the information and figures to determine whether the following statements are true or false.

- (A) When the normal cell turns cancerous, it switches its glucose metabolism from oxidative phosphorylation to aerobic glycolysis.
- (B) Cancer cells undergo alterations in metabolic pathways that enable them to suppress glucose uptake and glycolysis. This leads to stimulation of ATP production in the TCA cycle in normal conditions.
- (C) In rapidly growing tumors where hypoxia occurs, increased glycolysis can not support sufficient ATP production and bioenergetic homeostasis of cells.
- (D) In cancer cells, beyond the increase of glycolysis, increased glutaminolysis and fatty acid biosynthesis, generate TCA cycle intermediates, which are often used for anabolic and bioenergetic purposes.

## Theoretical2



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English (Official)

### Question 52

Cryopyrin is a protein involved in the formation of enzymatically active caspase-1 from procaspase-1. p35 is a protein fragment resulting from the cleavage of procaspase-1. The conversion of pro-interleukin-1 $\beta$  to interleukin-1 $\beta$  (IL-1 $\beta$ ) is catalyzed by caspase-1. Researchers were interested in the functional properties of wild-type cryopyrin and its two mutants, R260W and D303N. They developed two cell lines: **293-ASC-caspase-1** with a stable expression of both procaspase-1 and ASC (a protein known to interact with cryopyrin) and **293-caspase-1**, with a stable expression of procaspase-1 but not ASC. They transfected cells from each cell line with one of the five vectors and then performed a Western Blot of the proteins they were interested in (Figure).

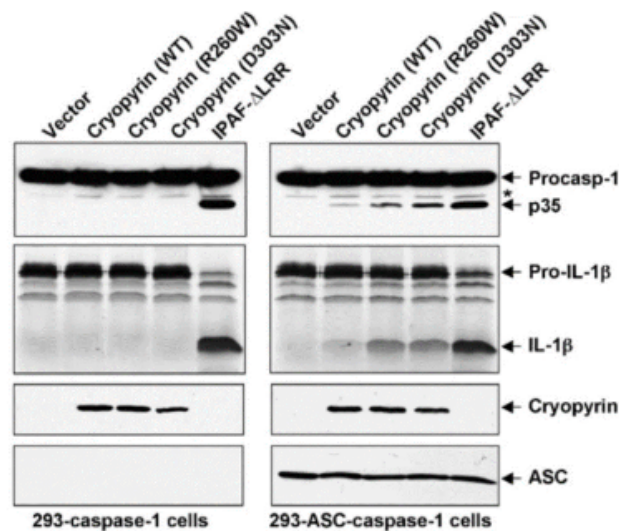


Figure. Results of Western Blot for each cell line: (1) empty vector, (2) vector with WT cryopyrin, (3) vector with the cryopyrin R260W mutant, (4) vector with the cryopyrin D303N mutant, (5) vector with IPAF- $\Delta$ LRR, which causes autocleavage of procaspase-1 independent from all other factors.

Using the information and figures, determine whether the following statements are true or false.

- A. Cryopyrin-dependent IL-1 $\beta$  production is not dependent on ASC.
- B. The R260W mutant is partially active, as compared to wild type cryopyrin.
- C. The D303N mutant does not contain a truncating mutation early in the gene sequence.
- D. IPAF- $\Delta$ LRR served as a positive control in this experiment for each cell line.



## Theoretical2



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English (Official)

### Question 53

At the ends of chromosomal DNA molecules of eukaryotes, there are special nucleotide sequences called telomeres, which shorten during each division of the somatic cell. Telomeres do not contain genes, but consist of multiple repeats of a short nucleotide sequence, such as TTAGGG. When DNA replication is completed (Fig. 1a), a single-strand protrusion (TTAGGG) occurs at the 3' end of the 5'-3' (lagging) strand of DNA. The enzyme telomerase containing the CAAUCC sequence in associated RNA allows for a complete duplicate of the DNA molecule along the entire length of the chromosome (Fig. 1b-e).

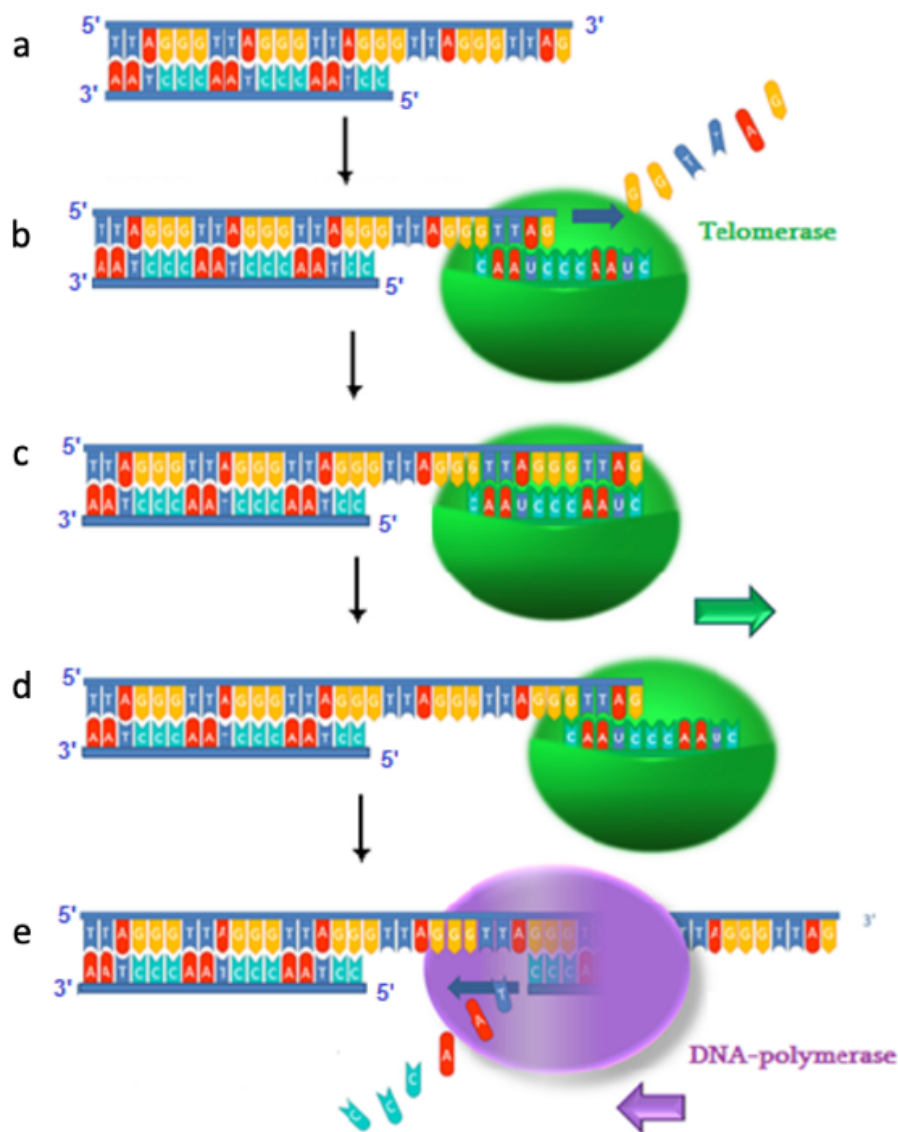


Figure 1. The mechanism of action of telomerase. 5'-3' is the "maternal" DNA strand, and 3'-5' is the "daughter" strand.

Using the information and figures, determine whether the following statements are true or false.

## Theoretical2



English (Official)

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- A. The protein component of telomerase is sufficient to elongate telomeres.
- B. The mother strand of DNA is sequentially elongated on the 3' end, using the telomerase RNA as a template.
- C. Loss-of-function mutations in the telomerase protein are likely to cause diseases such as progeria or bone-marrow failure.
- D. Telomere length has a threshold value in cells and in HeLa cells telomerase is repressed to maintain this threshold value.

## Theoretical2

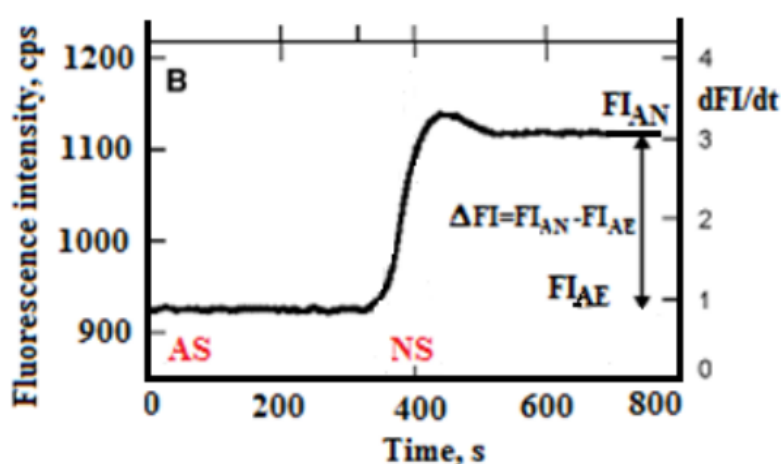


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English (Official)

### Question 54

The metabolic activity of microbial cells can be measured based on the intracellular content of different molecules, such as NAD(P)H, the reduced form of nicotinamide adenine dinucleotide (phosphate), which fluoresces at  $\lambda = 440 \text{ nm}$ . A sharp increase in fluorescence intensity of NAD(P)H is observed during a forced transition of yeast cells from aerobic to anaerobic conditions (AA transition) (Figure). The relative fluorescence increase ( $FI_{rel}$ ) during AA transition was evaluated as a measure of yeast metabolic activity.



|                             |  |
|-----------------------------|--|
| Fluorescence intensity, cps |  |
| Time, s                     |  |

Figure. NAD(P)H fluorescence intensity during the aerobic-anaerobic transition. FI – fluorescence intensity, AS - air sparging (bubbling of air), NS - nitrogen sparging,  $FI_{AN}$  – fluorescence intensity during the anaerobic phase,  $FI_{AE}$  fluorescence intensity during the aerobic phase.

Determine whether the following statements are true or false:

- The reduced phosphorylated (NADPH) and nonphosphorylated (NADH) pyridine nucleotides have essentially equivalent fluorescence properties while their oxidized forms are non-fluorescent.
- Under aerobic conditions, the oxidized nucleotides in cells are reduced, e.g., in the respiratory chain, which leads to an equilibrium between the formation and depletion of NAD(P)H.
- After the sudden alteration from aerobic to anaerobic conditions (AA transition), the microbes are not able to re-oxidize all the reduced NAD(P)H, which can be tracked as an intracellular step-like increase of NAD(P)H fluorescence intensity.
- Measurements of NAD(P)H fluorescence intensity during AA transition can indicate the increasing metabolic activity of microbes under stress conditions.

## Theoretical2

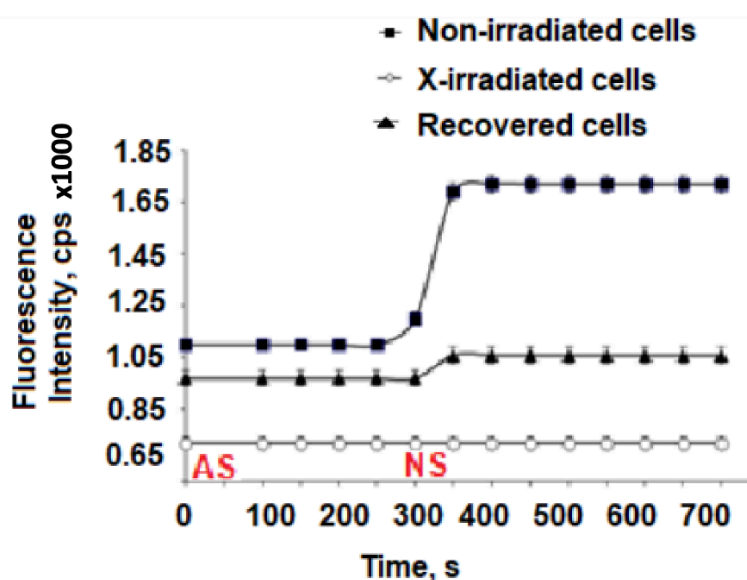


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English (Official)

### Question 55

The metabolic activity of equal-sized cultures of yeast was explored under 3 conditions: non-irradiated, X-irradiated and recovered (during 24-hour post-irradiation incubation) was determined as the relative increase in NADPH fluorescence intensity (FI) ( $FI_{rel}$ , cps) during forced aerobic - anaerobic (AA) transition, using the equation:  $FI_{rel} = (FI_{AN} - FI_{AE}) \times 100$ , where  $FI_{AN}$  and  $FI_{AE}$  represent the FI under anaerobic and aerobic conditions respectively. The following table shows the metabolic activity values of yeast under different conditions.



|                             |  |
|-----------------------------|--|
| Fluorescence Intensity, cps |  |
| Time, s                     |  |
| Non-irradiated cells        |  |
| X-irradiated cells          |  |
| Recovered cells             |  |

Figure. the fluorescence intensity curve of NADPH during the aerobic-anaerobic transition. FI - Fluorescence intensity, AS-air sparging (bubbling of air), NS-nitrogen sparging.

Using the table and data above, determine whether the following statements are true or false.

- The metabolic activity of yeast cells was disrupted under the influence of X-radiation, i.e. the metabolism of yeast cells stopped, and they all died.
- Metabolic processes in yeast changed under the influence of X-radiation, and, as a result, the fluorescent properties of intracellular NADP(H) were altered due to the structural damage of NADPH.

## Theoretical2



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English (Official)

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- C. During the post-irradiation incubation period, due to the repair processes in yeast cells, their metabolism was recovered, and they began to function like native yeasts.
- D. The weak fluorescence intensity of intracellular NADPH of X-irradiated yeasts is associated with a decrease in the amount of NADPH due to a severe decrease in metabolism.



## Question 56

Isolated cancer cells carry genetic changes and acquire an aggressive metastatic phenotype. One of these genetic changes is an activation of lysosomal exocytosis. The lysosomal system is one of the important participants of cancer transition, and thus, is a frequent target for cancer therapy. Lysosomal exocytosis is regulated by  $\text{Ca}^{2+}$  ions, which promote the fusion of lysosomes with the plasma membrane (PM) and the subsequent release of their contents into the extracellular matrix (ECM).

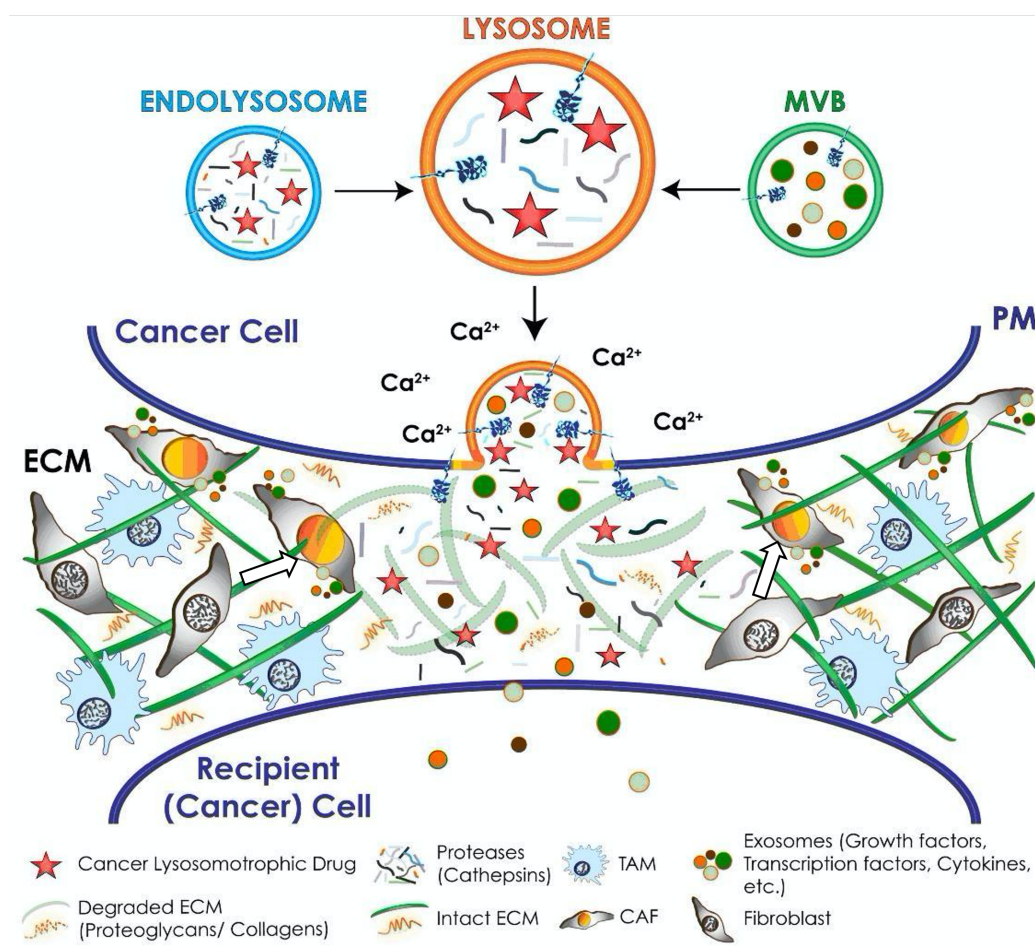


Figure. Schematic representation of downstream effects of lysosomal exocytosis in cancer cells. (TAM = tumor-associated macrophages, CAF = cancer-associated fibroblasts, MVB = multivesicular bodies)

## Theoretical2



English (Official)

|                                                                   |  |
|-------------------------------------------------------------------|--|
| Lysosome                                                          |  |
| Endolysosome                                                      |  |
| MVB                                                               |  |
| Cancer cell                                                       |  |
| ECM                                                               |  |
| PM                                                                |  |
| Recipient (cancer) cell                                           |  |
| cancer lysosomotropic drug                                        |  |
| degraded ECM<br>(proteoglycans/collagens)                         |  |
| proteases (cathepsins)                                            |  |
| intact ECM                                                        |  |
| TAM                                                               |  |
| CAF                                                               |  |
| Exosomes (growth factors, transcription factors, cytokines, etc.) |  |
| fibroblast                                                        |  |

Determine whether the following statements are true or false.

- A. Exosomes, which contain signaling molecules, leave the cell by means of lysosomal exocytosis and promote the conversion of macrophages and fibroblasts into cancer-associated fibroblasts (CAF) and tumor-associated macrophages (TAM).
- B. Weakly alkaline chemotherapeutic drugs tend to accumulate in lysosomes
- C. Lysosomal exocytosis enables the release of exosomes, which distribute signaling molecules to surround cells.
- D. One mechanism for cancer cells to become resistant against chemotherapeutics is the efflux of chemotherapeutic drugs, which could occur through lysosomal exocytosis

## Theoretical2

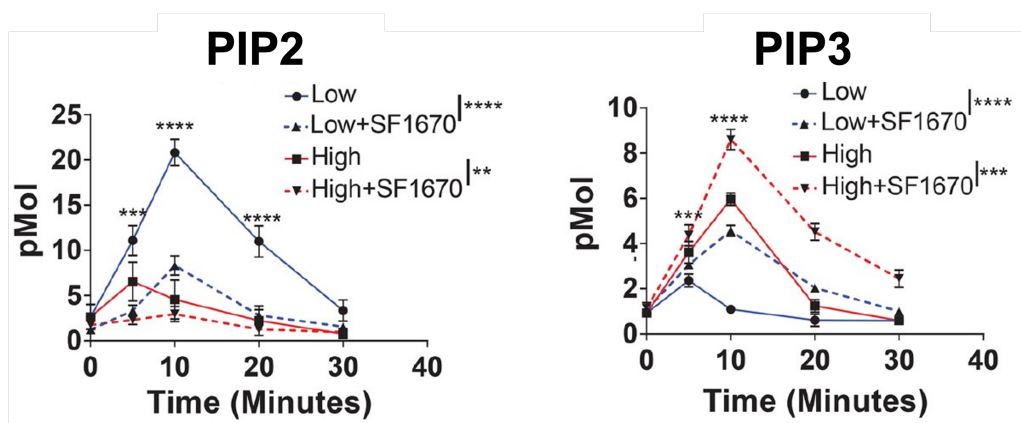


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English (Official)

### Question 57

After the antigen binds to the receptors on T cells, phosphatidylinositol-4-phosphate ( $PIP_1$ ) is phosphorylated to yield  $PIP_2$ , which is then phosphorylated again resulting in  $PIP_3$ . Both new lipid compounds are crucial messengers of the immune response. Results of a cell culture experiment to analyze this process are shown on the plots. Each trace is a time series for  $PIP_2$  or  $PIP_3$ . There are four experimental groups in total: (1) stimulated with low dosage of the antigen; (2) stimulated with low dosage of antigen, while adding SF1670 (the inhibitor of enzyme PTEN, which is a key enzyme involved in lipid signaling); (3) stimulated with high dosage of antigen; (4) stimulated with high dosage of antigen, while adding SF1670.



|                |  |
|----------------|--|
| Low            |  |
| High           |  |
| Time (Minutes) |  |

Figure. The left plot represents the experimentally measured concentration of PIP2 as a function of time, while the right plot represents the same for PIP3. On each plot, the blue color stands for low dosage stimulation, while the red one stands for high dosage. Solid lines stand for the experiments with no usage of SF1670, while dotted lines indicate that SF1670 was used in the experiment.

Determine whether the following statement are true or false:

- PIP2 concentration quickly returns to initial levels even when the antigen is still present; thus, it cannot mediate long-term changes in cell fate
- Presence of PTEN activity reliably increases the concentration ratio of PIP2 to PIP3
- Concentration ratio of PIP2 to PIP3 contains information on the strength of the antigen.
- Since antigen binding mediates production of PIP2, more antigen binding will result in more PIP2 under intact PTEN



## Theoretical2

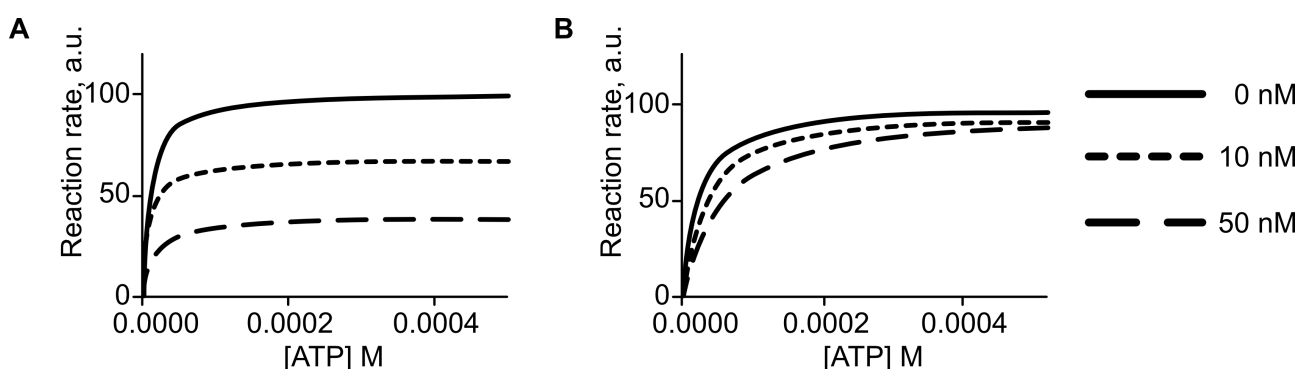


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English (Official)

### Question 58

TAK1 is a protein kinase which transfers a phosphate group from ATP to a substrate. In order to elucidate the action mechanism of Takinib, a novel inhibitor of TAK1, two experiments were carried out. In experiment A, TAK1 was added to the solution of ATP, Takinib and TAK1 substrate, and the initial reaction rate was measured for different ATP concentrations and different amounts of Takinib. In experiment B, TAK1 was pre-incubated with 5  $\mu$ M ATP for 3 hours and then the same steps as in experiment A were carried out with the pre-incubated TAK1. The results of experiments A and B are summarized below, with the amount of inhibitor used indicated to the right.



|                     |  |
|---------------------|--|
| Reaction Rate, a.u. |  |
| Time (Minutes)      |  |

Figure. The dependence of initial reaction rate (in arbitrary units) on the starting concentration of ATP (in M). Different colors indicate the concentration of Takinib used. The legend on the right side applies to both plots.

Determine whether the following statements are true or false:

- A. If TAK1 is pre-incubated with 5  $\mu$ M ATP for 3 hours, then Takinib, added later, acts as a competitive inhibitor.
- B. In both experiments, Takinib significantly affects TAK1's Michaelis constant with respect to ATP.
- C. Experiments A and B indicate that TAK1 has another interaction site, in addition to the enzymatic active center.
- D. If TAK1 was not pre-incubated, then the presence of Takinib could be compensated by an excess of ATP.

## Theoretical2



English (Official)

### Question 59

Mitochondria are a convergence point of cellular signals and are closely related to signalling pathways of innate immunity. The immune response enhances antiviral immunity and protects nuclear DNA from damage.

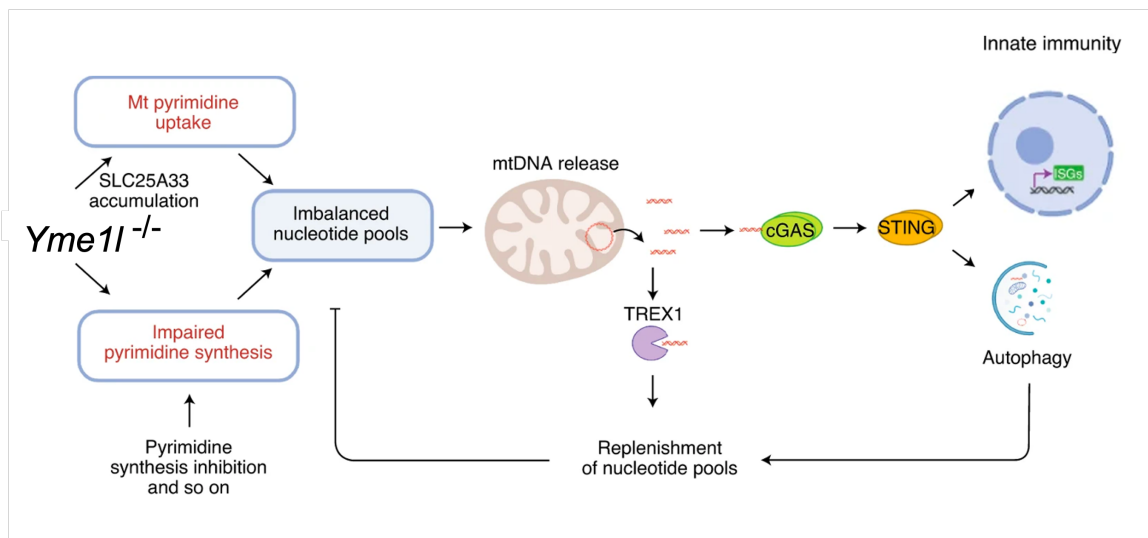


Figure. mtDNA-dependent innate immunity is coupled to cellular nucleotide metabolism

*Yme1L* = an ATP-dependent proteolytic complex of the internal mitochondrial membrane responsible for maintaining mitochondrial morphology; STING = an adaptive protein responsible for stimulating interferons; SLC25A33 = pyrimidine transporter; TREX1 = exonuclease; cGAS = cGMP-AMP-synthase. This immune response boosts antiviral immunity and protects cell nucleus DNA from damage.

|                                           |  |
|-------------------------------------------|--|
| Mt pyrimidine uptake                      |  |
| SLC25A33 accumulation                     |  |
| impaired pyrimidine synthesis             |  |
| pyrimidine synthesis inhibition and so on |  |
| imbalanced nucleotide pools               |  |
| mtDNA release                             |  |
| replenishment of nucleotide pools         |  |
| innate immunity                           |  |
| autophagy                                 |  |

Determine whether the following statements are true or false:

- The knockout of *Yme1L* in cells supports pyrimidine metabolism by maintaining de novo synthesis of nucleotides and proteolysis of SLC25A33.
- The information presented in this figure indicates that the accumulation of SLC25A33 can cause an

## Theoretical2



English (Official)

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immune response.

C. TREX1-mediated lysis of DNA can restore the imbalance of nucleotides in the cell.

D. The inhibition of the mitochondrial protease *Yme1L* downregulates the expression of genes needed for interferon production.

## Theoretical2

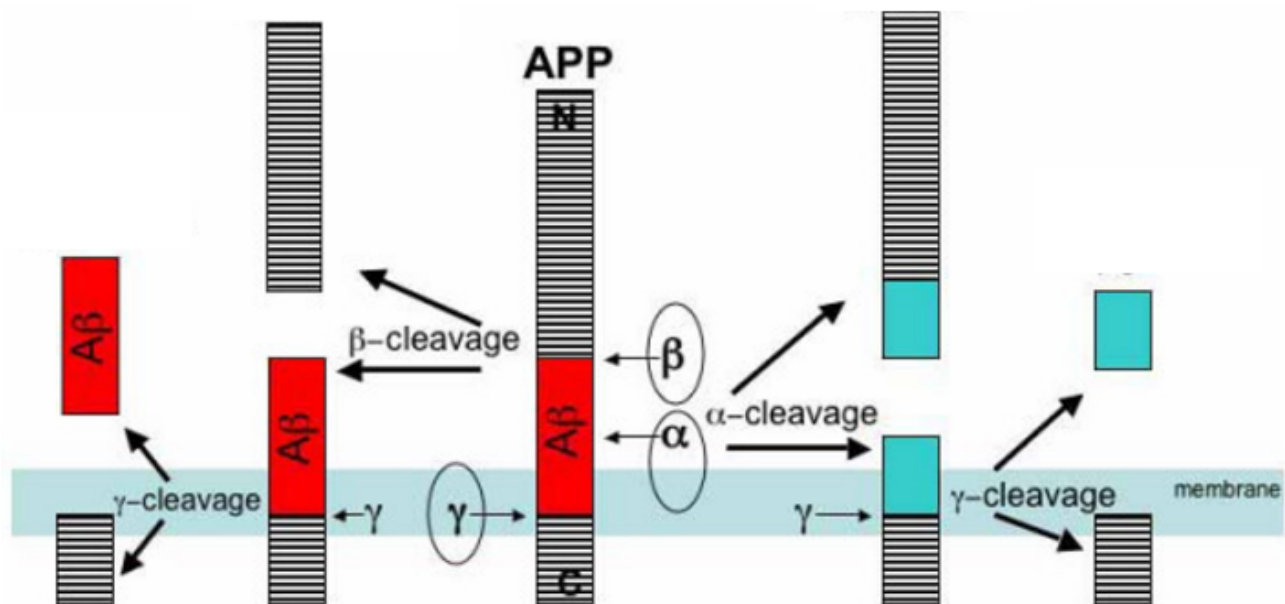


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English (Official)

### Question 60

Alzheimer's disease is related to the aggregation of amyloid peptides, followed by the degeneration of neurons and disruption of cholinergic transmission. Among patients suffering from Alzheimer's disease, the  $\beta$ -amyloid peptides ( $A\beta$ ) are formed from the cleavage of the protein APP. The normal protein (APP) is composed of many  $\alpha$ -helices, making it highly soluble. The  $\beta$ -amyloid, in contrast, has a secondary structure rich in  $\beta$ -sheets, which aggregate easily and create insoluble fibers. APP is a multi-domain transmembrane protein. There are three proteases, which take part in the proteolytic processing of APP:  $\alpha$ -,  $\beta$ -, and  $\gamma$ -secretases.



|          |  |
|----------|--|
| cleavage |  |
|----------|--|

Figure 1 APP multi-domain protein modification

Determine whether the following statements are true or false:

- A.  $\alpha$ -secretase cleaves the mature APP in a certain location and, thus, prevents the formation of  $\beta$ -amyloid.
- B.  $\beta$ - and  $\gamma$ -secretases take part in the formation of the  $\beta$ -amyloid peptide.
- C. Two transmembrane protein fragments are formed due to  $\beta$ -secretase activity: the N-terminal fragment and the C-terminal fragment.
- D. In the C-terminal transmembrane fragment, formed due to  $\beta$ -secretase activity, the  $\alpha$ -helical structure dominates.

## Theoretical2



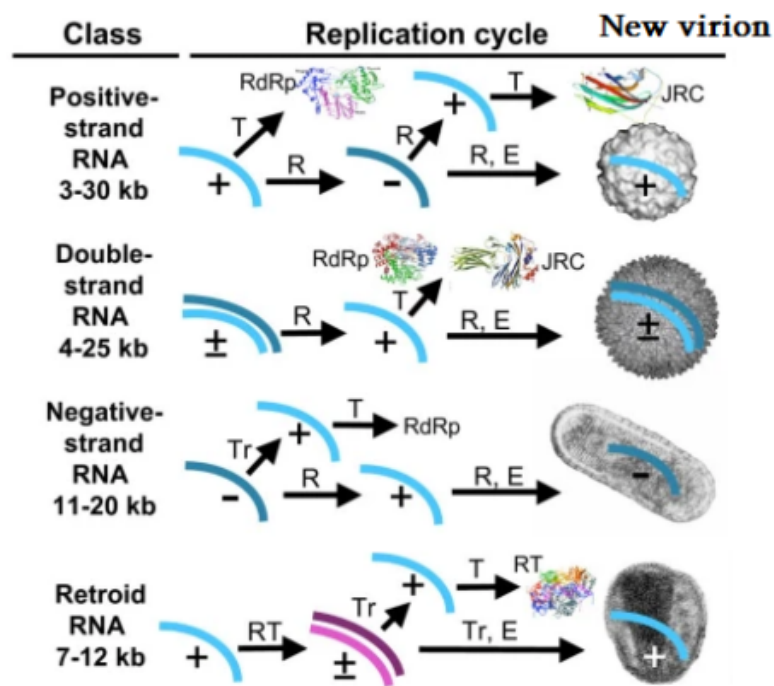
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English (Official)

### Question 61

Based on the structure of their genome and specific features of the replication process, RNA viruses are divided into the following groups:

- Single-strand (+) RNA viruses
- Single-strand (-) RNA viruses
- Double-strand (+-) RNA viruses
- Retroid viruses (including retroviruses)



|                     |  |
|---------------------|--|
| Class               |  |
| Double-strand RNA   |  |
| Negative-strand RNA |  |
| New virion          |  |
| Positive-strand RNA |  |
| Replication cycle   |  |

Figure. Replication cycles of different RNA viruses. '+' denotes a positive strand of RNA; '-' denotes a negative strand of RNA. Tr - transcription; T - translation; R - replication; E - encapsidation; RdRp - RNA-dependent RNA polymerase; JRC - capsid protein; RT - reverse transcriptase.

## Theoretical2



English (Official)

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Determine whether the following statements are true or false:

- A. The genome of (+)RNA viruses encodes many proteins, including the RNA-dependent RNA-polymerase
- B. In all RNA-containing viruses, the RNA-dependent RNA-polymerase enters the target cell with RNA.
- C. During the replication process of double-strand (+-) RNA viruses, the single-stranded (+) RNA molecules synthesized in the target cells ensure viral protein synthesis by the host cell's ribosomes and serve as a template for the synthesis of (-) RNA chains with the participation of viral RNA polymerase.
- D. The genome of retroviruses encodes the reverse transcriptase enzyme, which is included in the viral particle and ensures the synthesis of DNA from viral RNA upon infection.

## Theoretical2

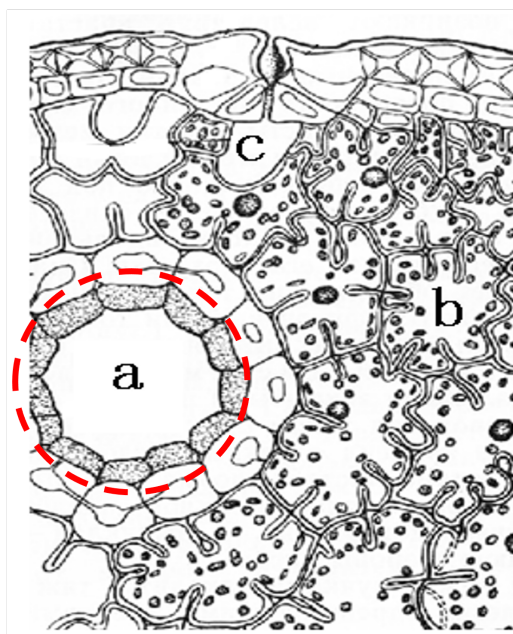


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English (Official)

### Question 62

The figure depicts a cross-section of a plant organ. Observe the figure and choose whether the following statements are true or false.



- A. The cells labeled with b capture and assimilate CO<sub>2</sub> into sugars.
- B. The space labeled with c regulates water loss.
- C. The structure labeled with a carries water and nutrition to different parts of the plants.
- D. The structure labeled with a produces and stores resin.

## Theoretical2

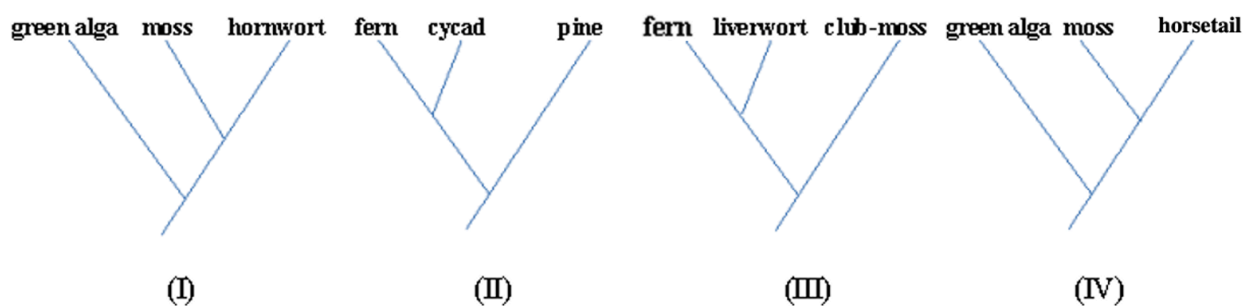


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English (Official)

### Question 63

The following cladograms show the course of the evolution of green algae and land plants.



|            |  |
|------------|--|
| club-moss  |  |
| cycad      |  |
| fern       |  |
| green alga |  |
| hornwort   |  |
| liverwort  |  |
| moss       |  |
| pine       |  |
| horsetail  |  |

Observe them and determine if they describe the evolution correctly (true) or incorrectly (false). A. Cladogram I.

B. Cladogram II.

C. Cladogram III.

D. Cladogram IV.



## Theoretical2



English (Official)

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### Question 64

The C4 Rice Project aims to introduce C4 photosynthetic traits into rice, *Oryza sativa*, a C3 species.

Choose whether the following statements are true or false:

- A. The modified C4 rice plants will have both altered biochemical and developmental pathways.
- B. The enzyme Rubisco will be non-functional in modified C4 rice plants.
- C. C4 rice plants must have smaller stomatal pore size to decrease rates of transpiration and increase photosynthetic water use efficiency.
- D. Genes for decarboxylase enzymes will need to be introduced into the C4 rice plants.



## Question 65

The following images are cross-sections of two different leaves of the same individual of *Arabidopsis thaliana*.

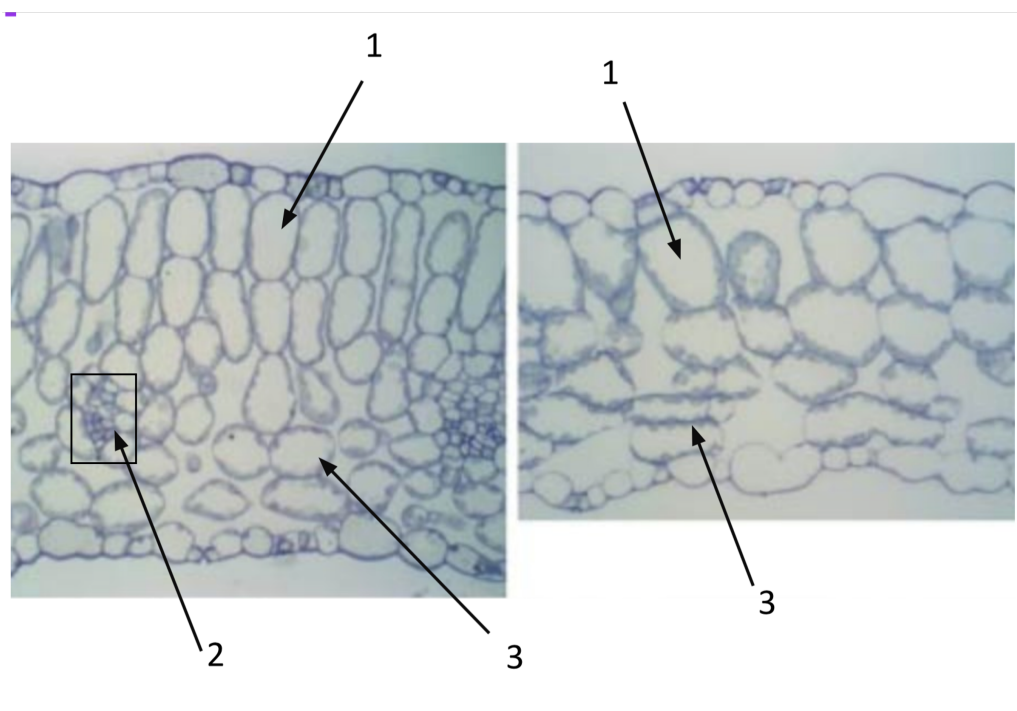


Figure 1. Cross-sections of two leaves of *A. thaliana*

Use the information and figures to determine whether the following statements are true or false.

- A. The cells labeled with 1 capture and assimilate CO<sub>2</sub> into sugars.
- B. The cells labeled with 2 demonstrate Kranz anatomy.
- C. The leaf on the left was grown under direct sunlight, while the leaf on the right was in the shade.
- D. The cells labeled with 3 have a lower Rubisco/chlorophyll ratio than cells labeled with 1.

## Theoretical2

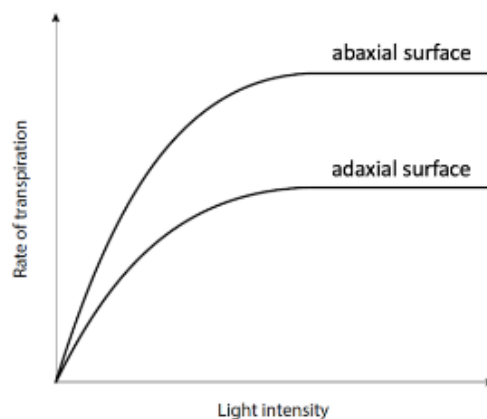


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### Question 66

The following diagram demonstrates the impact of light intensity on transpiration rate from the adaxial (upper) and abaxial (lower) surfaces of a eudicot leaf. All other abiotic factors are the same for both conditions. How can we explain the discrepancy in transpiration rates?



|                       |  |
|-----------------------|--|
| abaxial surface       |  |
| adaxial surface       |  |
| Light intensity       |  |
| Rate of transpiration |  |

Use the information and figure to determine whether the following statements are true or false.

- A. Spongy mesophyll causes faster transpiration because it has more air cavities.
- B. Transpiration decreases the water potential in the leaves
- C. Transpiration from the upper surface is slower because it has fewer stomata.
- D. Air movement would increase transpiration rates from both surfaces.

## Theoretical2

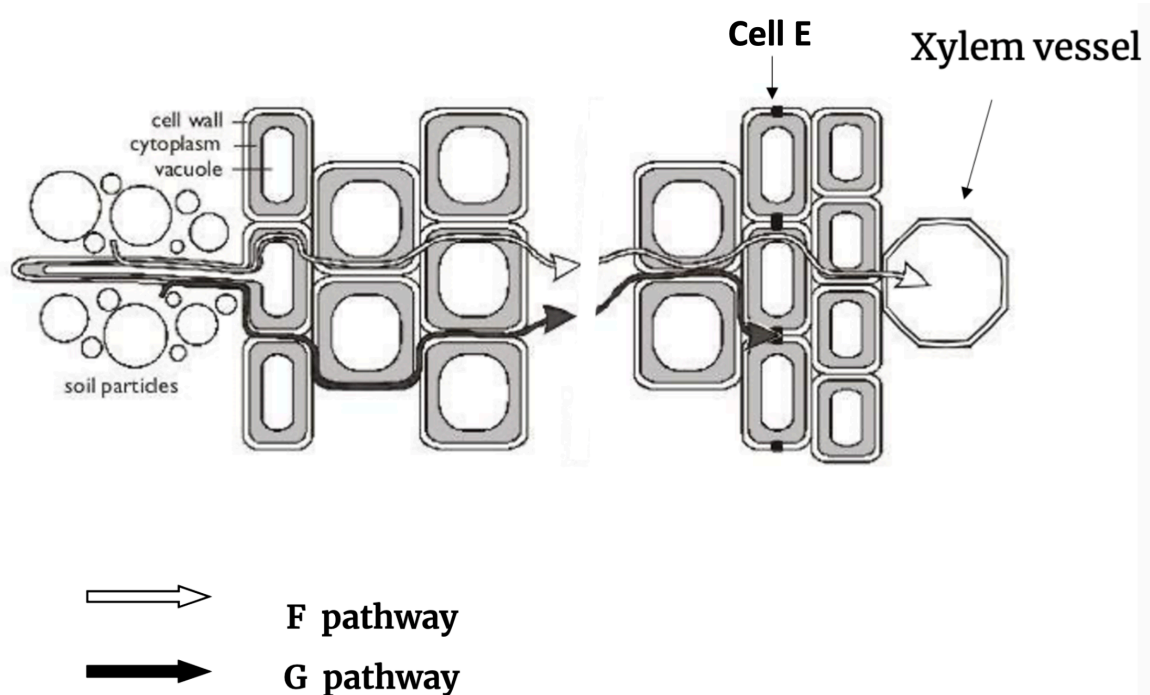


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English (Official)

### Question 67

Water that is absorbed by the roots of a plant, moves from the roots to the xylem. The figure shows these pathways in the root of *Ranunculus acris*.



|                |  |
|----------------|--|
| cell wall      |  |
| cytoplasm      |  |
| cell E         |  |
| F pathway      |  |
| G pathway      |  |
| soil particles |  |
| vacuole        |  |
| Xylem vessel   |  |

Use the information and figure to determine whether the following statements are true or false.

- A. Cell E regulates the entry of ions into the xylem vessels.
- B. G pathway is the symplastic pathway
- C. The movement of water along pathway F is slower than along pathway G.
- D. Water can move from cell to cell only with the help of plasmodesmata.

## Theoretical2

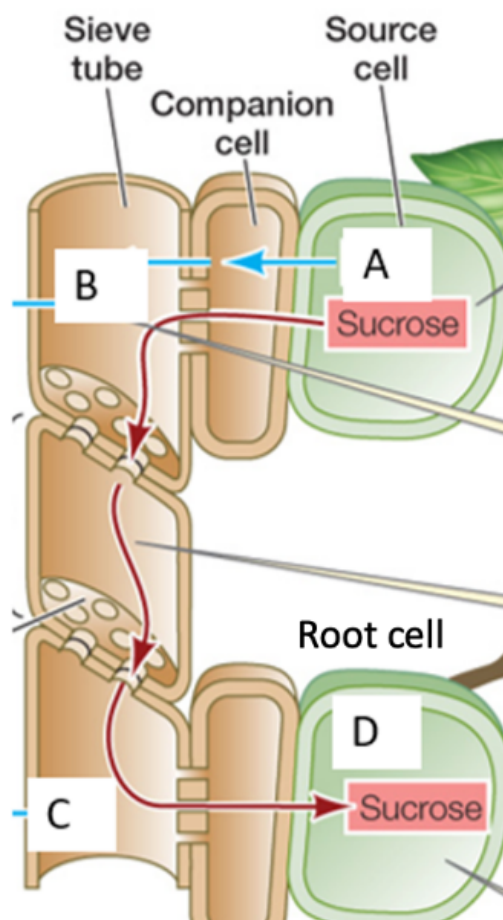


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English (Official)

### Question 68

The picture shows the tissues involved in the transport of sucrose in plants: the sieve tube cells and the companion cells.



|                |  |
|----------------|--|
| Companion cell |  |
| Root cell      |  |
| Sieve tube     |  |
| Source cell    |  |
| Sucrose        |  |

Use the information and figures to determine whether the following statements are true or false.

- A. The water potential in cell B is the highest
- B. The concentration of sucrose in cell A is the highest
- C. The difference in pressure potential is the driving force of the transport of sucrose along sieve cells.

## Theoretical2



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D. Sucrose is transported from the mesophyll cell to B cell without energy expenditure

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English (Official)

### Question 69

Mechanically activated channels (MA) transfer physical force into electrical current. Piezo1 is a well-characterized subtype of the MA channel. OSCA proteins have been described as sensing receptors that exist not only in mammals but various other eukaryotes like plants and flies. In order to understand the role of OSCA proteins to different stimuli, cells were treated with hyperosmolarity and cell stretching, and the electrical response was recorded. Cells expressing different OSCA variants, OSCA1.1 and OSCA1.2, were compared with Piezo1, in their electrical response, in the figure below.

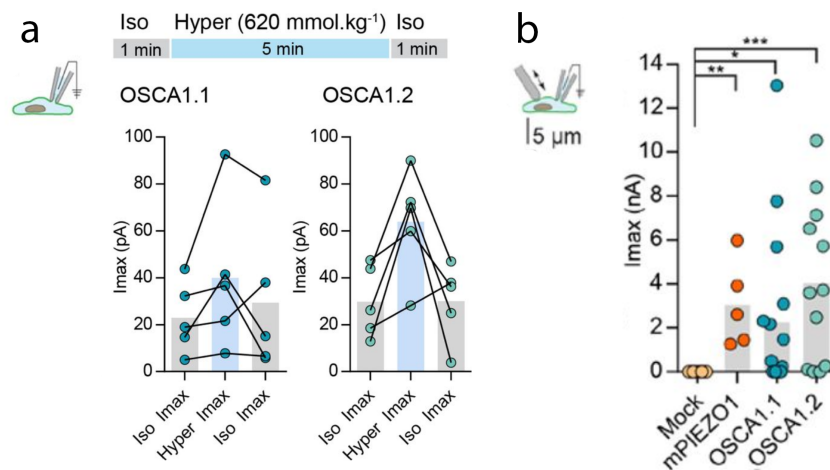


Figure 1. Left half: response to hyperosmolarity, right half: response to mechanical stimuli, recorded by glass electrodes inserted into single cells (patch-clamp recording). Imax is the current peak. Mock cells do not express any of those proteins and PIEZO1, OSCA1.1 and OSCA1.2 are the mock cells that were transfected to express the corresponding protein. Line connects biological replicates.

Use the information and figures to determine whether the statements are true or false.

- A. In plants, the MA channels can play a role in adaptation of the roots to the soil environment and gravity.
- B. OSCA-expressing cells respond to hyperosmolarity less intensely, as compared to mechanical stimuli.
- C. OSCA-expressing cells have a similar response to mechanical stimuli as Piezo1 expressing cells.
- D. From the graphs, we can conclude that OSCA 1.2 protein has no role in sensing mechanical stimuli.

## Theoretical2



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English (Official)

### Question 70

Over the last 470Ma, plant evolution has seen major evolutionary transitions, such as the move from water to land. The following figure shows the phylogenetic tree of the major plant groups.

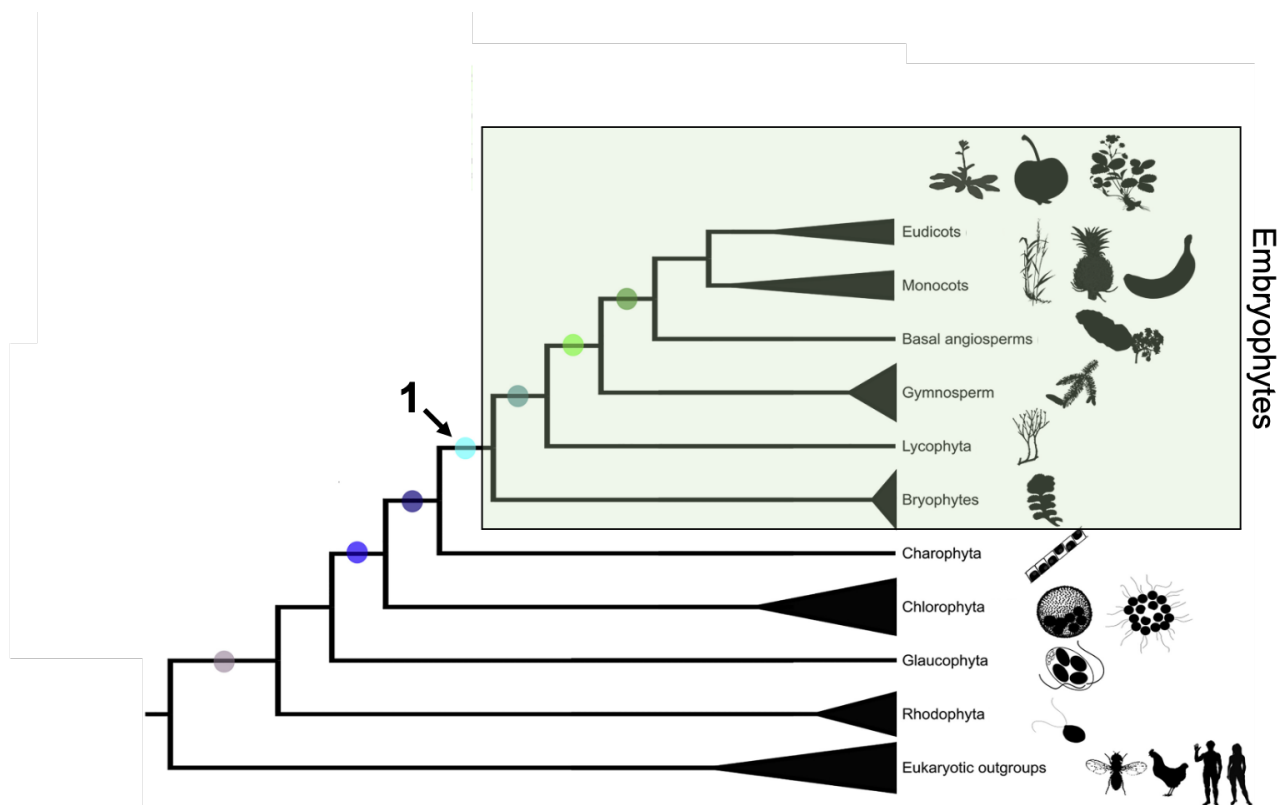


Figure 1: The phylogenetic tree of plants and algae. Each colored circle indicates an unspecified shared derived characteristic of a taxon. Other eukaryotic outgroups included as a cluster for reference.

Use the information and figure to determine whether the following statements are true or false.

- A. The shared derived characters of land plants (cyan colored circle labeled 1 on the figure) include multicellular embryos as adaptations for terrestrial life.
- B. The cladogram suggests that Charophyta is the direct common ancestor of all terrestrial plants.
- C. Multicellularity was lost in some embryophyte taxa.
- D. Rhodophyta are most closely related to Glaucophyta, based on their proximity in the phylogenetic tree.



## Question 71

One week after fertilization, human embryos implant into the uterus. In order to implant, the embryo needs to develop into a blastocyst (blastoid), a spherical structure covered with cells. Researchers simulated a blastocyst model, using pluripotent stem cells. They also modeled the endometrial layer of the uterus in the dish and blastocyst implantation in the endometrium (Figure 1). They hormonally stimulated endometrial cells, and tested blastocyst attachment (Figure 2). In order to check the effect of the Hippo pathway on blastoid development, researchers tested them under exposure to different concentrations of lysophosphatidic acid (LPA) (a Hippo-pathway inhibitor) (Figure 3). YAP1 is the downstream effector that activates cavitation, after Hippo inhibition, by binding to the TEAD transcription factor. The researchers tested different settings on the appearance of cavitation, an important event in blastocyst formation. They used two different YAP1-overexpressing (OE) blastocysts, overexpressing two different YAP1-mutants: one has a mutation in the TEAD binding site (S94A), while the other is constitutively active (5SA) (Figure 3).

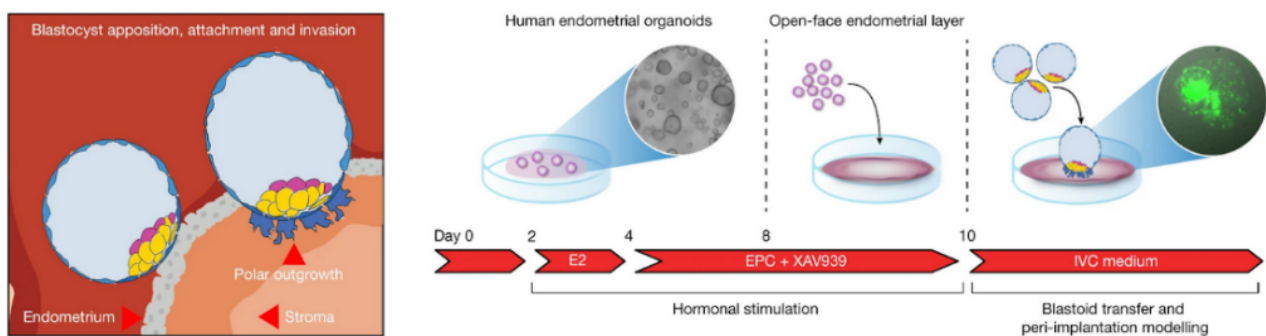


Figure 1. Diagram of attachments of the blastoid to endometrial cells (a). Method for production of the endometrial organoids for in vitro implantation modelling (b)

|                                                  |  |
|--------------------------------------------------|--|
| Blastocyst apposition, attachment and invasion   |  |
| Endometrium                                      |  |
| Polar outgrowth                                  |  |
| Stroma                                           |  |
| Human endometrial organoids                      |  |
| Hormonal stimulation                             |  |
| Open-face endometrial layer                      |  |
| Blastoid transfer and peri-implantation modeling |  |

## Theoretical2



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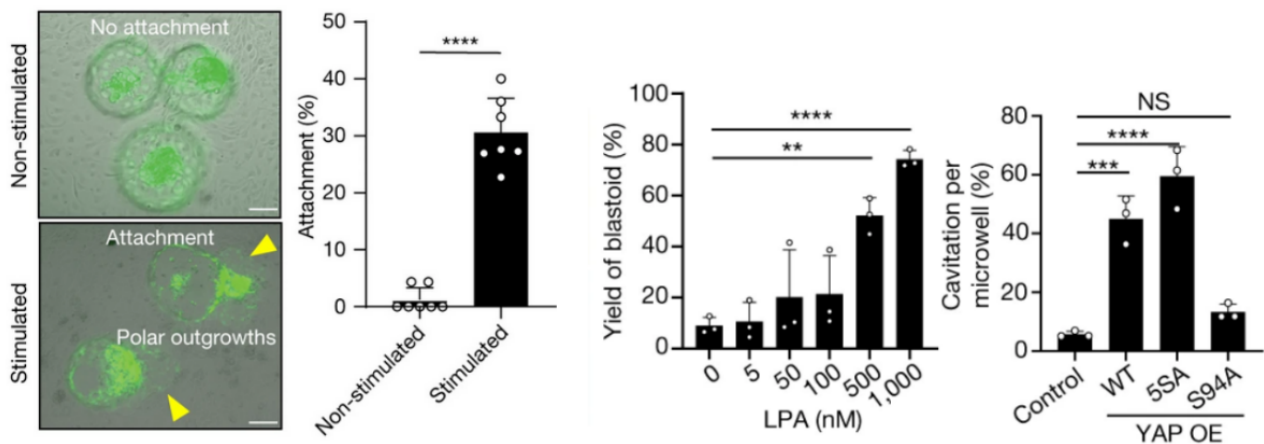


Figure 2 (left), Figure 3 (right)

|                          |  |
|--------------------------|--|
| Non-stimulated           |  |
| No attachment            |  |
| Stimulated               |  |
| Attachment               |  |
| Polar outgrowths         |  |
| Yield of blastoid        |  |
| Cavitation per microwell |  |
| Control                  |  |

Use the information and figures 1-3 to determine whether the following statements are true or false.

- Blastocysts attach to the hormonally stimulated endometrial cells but not to unstimulated ones. Absence of hormonal stimulation will result in almost inevitable failure of implantation of the blastocyst.
- Blastocysts develop polar outgrowths when attaching to the endometrium that contribute to the attachment.
- Hippo pathway activation is crucial for blastoid development.
- The interaction with TEAD is important for the function of YAP1 in cavitation.

## Theoretical2



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### Question 72

Neurons interact with each other to form the complex circuits that underlie brain function. This process is conventionally divided into three steps:

1. axons find their way to appropriate target areas (axon guidance),
2. they choose appropriate synaptic partners within those areas (synaptic specificity),
3. functional synapses are formed (synaptogenesis).

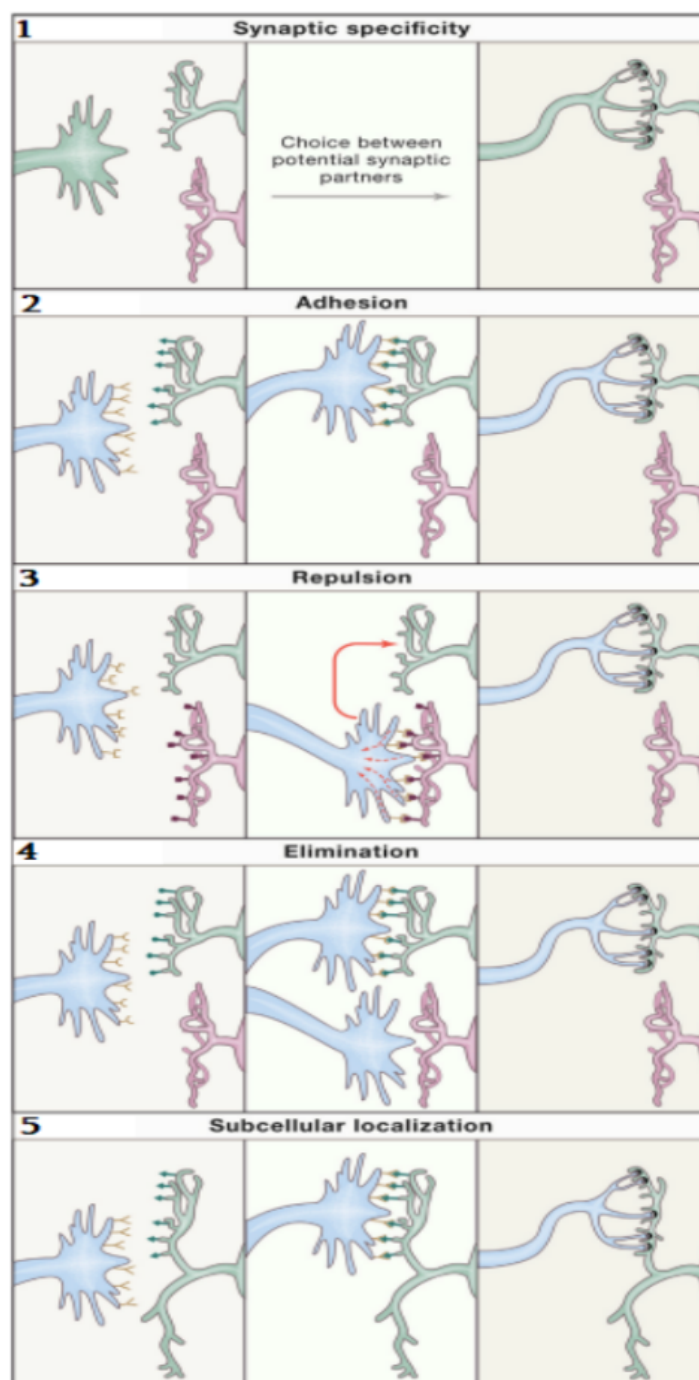


Figure. Mechanisms of synaptic specificity

## Theoretical2



English (Official)

|                                            |  |
|--------------------------------------------|--|
| Synaptic specificity                       |  |
| Choice between potential synaptic partners |  |
| Adhesion                                   |  |
| Repulsion                                  |  |
| Elimination                                |  |
| Subcellular localization                   |  |

Use the information and the figure to determine whether the following statements are true or false.

- A.** One neuron type has cell recognition proteins, which bind selectively to receptors on the surface of postsynaptic cells; recognition leads to an adhesive interaction which facilitates or blocks synapse formation between appropriate partners.
- B.** In traumatic brain injuries, cell adhesion molecules direct cellular processes that inhibit post-traumatic neuronal plasticity during recovery.
- C.** Synaptic connections could rewire as a result of suboptimal functionality of the original connection.
- D.** In many regions of the nervous system, axons or dendrites branch in just one or a few of several narrow, parallel strata within a target area.

## Theoretical2



English (Official)

### Question 73

Immune checkpoint molecules regulate the immune system and prevent excessive immune response. The programmed death molecule 1 or PD-1 is expressed on the T cells and is involved in a co-inhibitory pathway that suppresses T cell function. PD-1 has an important role in the immune system development, and allows tolerance to its own proteins. There are two known ligands for PD-1, the PD-L1 and PD-L2, and they are both known to induce the co-inhibitory signaling. Cancer cells take advantage of this signaling pathway to avoid being killed by immune cells. Researchers have found a way to target those molecules and this resulted in reduction of tumor volume, mediated through the immune system.

Determine whether the following statements are true or false.

- A.** PD-1 dysfunction can lead to development of autoimmune diseases.
- B.** PD-1, when binding to its ligand-PD-L1, activates antitumor immune response.
- C.** The inhibition of the PD-1/PD-L1-axis prevents T cells from recognizing tumor cells as "self" and enables their destruction
- D.** The inhibition of the PD1-PD-L2 axis will lead to recovery from an autoimmune disorder.

## Question 74

The biochemical and physiological processes, accompanying cerebral injuries, frequently turn into sources of secondary tissue damage themselves. These processes can be caused by many factors, e.g., dysfunction of mitochondria, anaerobic stress, peroxide-mediated oxidation of lipids, axon degeneration and cell death. Due to demyelination and disruption of the axonal cytoskeleton, the accumulation of transport proteins at the axon terminus takes place, which leads to accumulation of neurotransmitters in the synaptic cleft. Then, NMDA and AMPA receptors in postsynaptic membranes are activated, thus enhancing  $Ca^{2+}$  influx from intracellular stores.

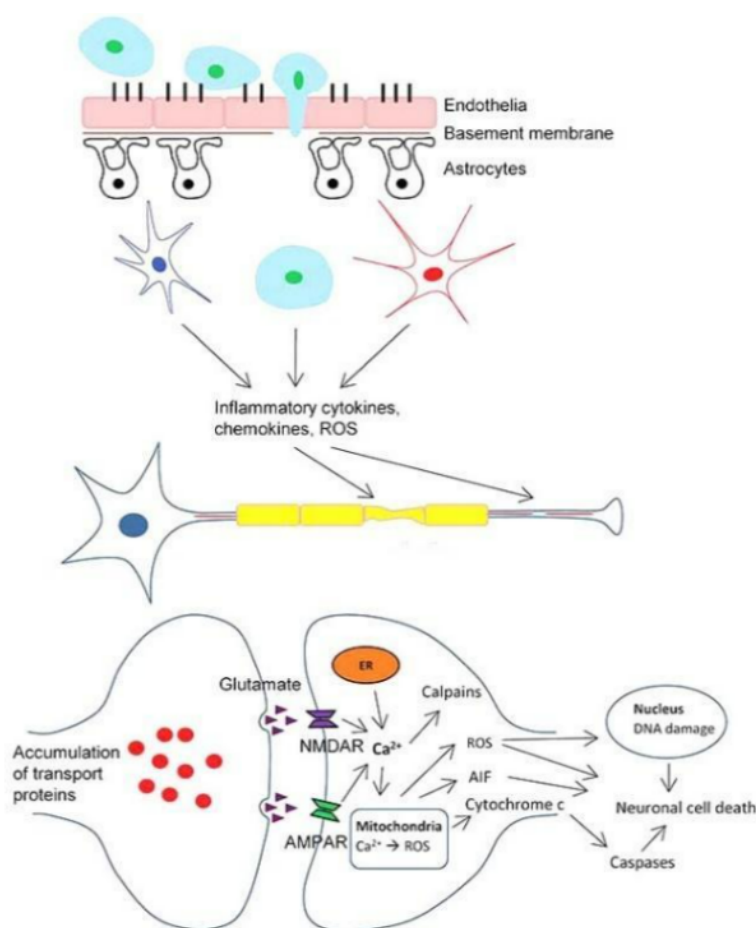


Figure. Schematic representation of pathophysiology of traumatic brain injury (TBI)

## Theoretical2



English (Official)

|                                         |  |
|-----------------------------------------|--|
| Endothelia                              |  |
| Basement membrane                       |  |
| Astrocytes                              |  |
| Inflammatory cytokines, chemokines, ROS |  |
| Accumulation of transport proteins      |  |
| Glutamate                               |  |
| Calpains                                |  |
| Mitochondria                            |  |
| Cytochrome                              |  |
| Nucleus DNA damage                      |  |
| Caspases                                |  |

ROS - reactive oxygen species

AMPA -  $\alpha$ -amino-3-hydroxy-5-methyl-4-isoxazole propionic acid receptor

NMDAR - N-methyl-D-aspartate receptor

ER - endoplasmic reticulum

AIF - apoptosis-inducing factor protein

Using this information, determine whether the following statements are true or false.

- A.** Demyelination of the axons causes disruption of the axonal cytoskeleton leading to accumulation of transport proteins at the axon terminus, and thus, making it hyperactive.
- B.**  $Ca^{2+}$  channel blockers have potential therapeutic value in spinal cord injuries.
- C.** Accumulation of free radicals results in intensive peroxidation of membraneous lipids, which leads to mitochondrial dysfunction
- D.** Excess glutamate is released following head injury which activates AMPA and NMDA receptors.



## Theoretical2



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English (Official)

### Question 75

Measurement of blood plasma enzymes allows precise diagnosis of some diseases. Creatine kinase (CK), lactate dehydrogenase (LDH) and  $\beta$ -hydroxybutyrate dehydrogenase ( $\beta$ -HBDH) were measured in the blood of a patient with acute chest pain. Additionally, electrophoretic separation of creatine kinase isoforms was performed. Creatine kinase is an enzyme composed of two subunits, the brain-typical subunit B and the muscle-typical subunit M, encoded by different genes. Different tissues have different isoforms of the enzymes: BB occurs in the brain, MB in the heart muscle and MM in skeletal muscles.

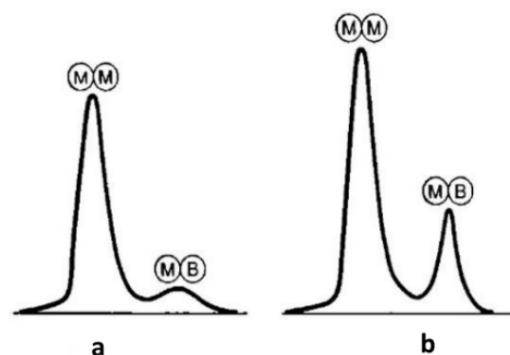
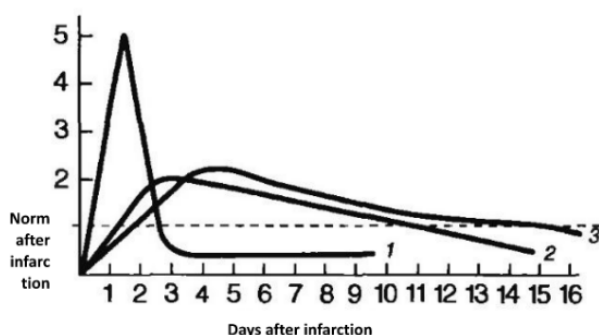


Image 1: Change in the activity of enzymes after myocardial infarction; 1-CK, 2-LDH, 3- $\beta$ -HBDH

Image 2: Isoforms of CK in blood plasma; a - healthy individual, b - patient following myocardial infarction

|                       |  |
|-----------------------|--|
| Norm after infarction |  |
| Days after infarction |  |

Based on this biochemical analysis, determine whether the following statements are true or false.

- A.** Elevated levels of CK, LDH and  $\beta$ -HBDH in the plasma can be caused by tissue and cell damage due to pathological conditions.
- B.** The rapid rise in CK activity, 24-48 hours after the emergence of pain, points to the developing dystrophy in the skeletal muscles of the chest.
- C.** The three- to four-fold increase in the activity of the MB isoenzyme is caused by the developing damage to the heart muscle.
- D.** All enzymes discussed, i.e. CK, LDH and  $\beta$ -HBDH, participate in the energy supply in muscles.

## Theoretical2

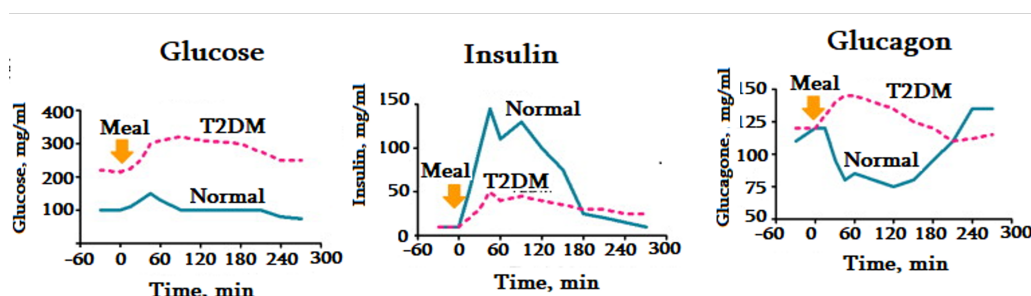


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English (Official)

### Question 76

Insulin and glucagon hormones are synthesized in the islets of the pancreas. The balance of their production ensures a stable level of glucose in the blood. Increased glucose levels stimulate the production of insulin by  $\beta$ -cells, while in hypoglycemia, glucagon is released by  $\alpha$  cells.



|           |  |
|-----------|--|
| Glucose   |  |
| Insulin   |  |
| Glucagon  |  |
| Meal      |  |
| T2DM      |  |
| Normal    |  |
| mg/ml     |  |
| Time, min |  |

The figure shows changes in glucose, insulin and glucagon levels in healthy individuals and individuals with type 2 diabetes (T2DM).

Based on this biochemical analysis, determine whether the following statements are true or false.

- The increase in glucose levels in the plasma of healthy people after a meal is due to heightened glucagon levels.
- The increase in glucose levels in the plasma leads to a more pronounced increase in insulin levels in type 2 diabetes (T2DM) patients than in healthy individuals.
- Glucagon production in healthy people is suppressed by an increase in glucose levels in plasma and by subsequent stimulation of insulin production.
- In T2DM patients, the suppressive effect of glucose on glucagon disappears, and may even be replaced by the stimulation of glucagon production.

English (Official)

Synaptic plasticity in the adult brain underlies the cellular mechanisms of learning and memory. Mitochondria contribute to the process of synaptic plasticity. The figure shows the regulatory role of mitochondria in the functions and plasticity of synapses, as well as the effect of mitochondrial dysfunction on synaptic transmission (solid lines show excitatory processes, dotted lines show inhibitory processes).

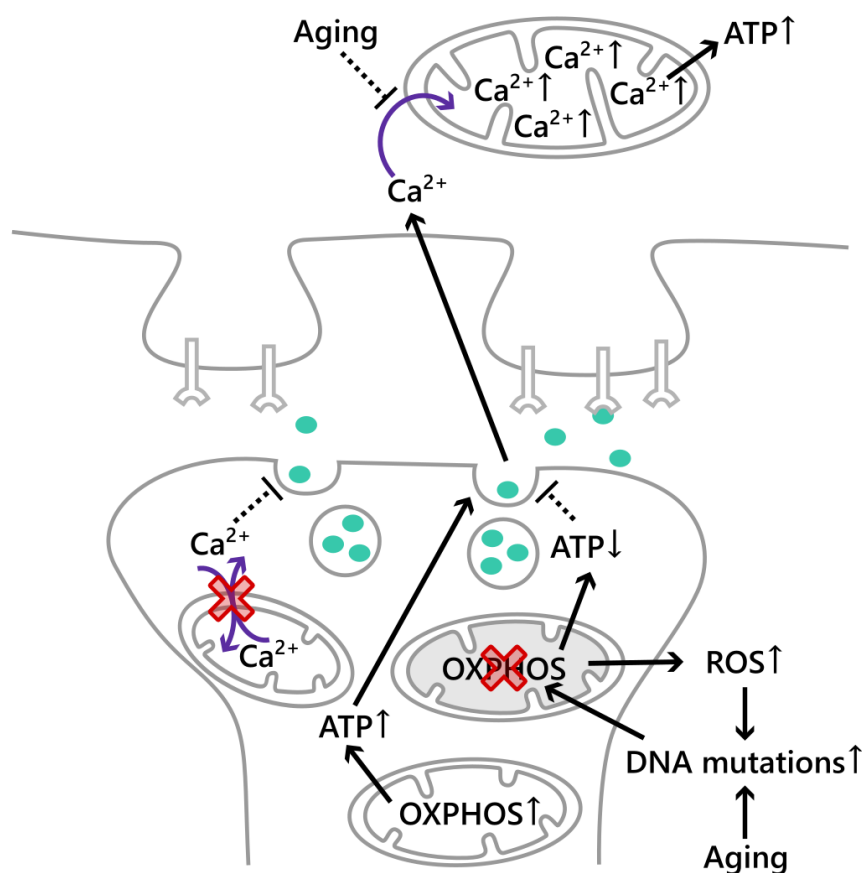


Figure. Role of mitochondria in synaptic plasticity.

|               |  |
|---------------|--|
| Aging         |  |
| DNA mutations |  |

Based on this diagram, determine whether the following statements are true or false.

- A.** The disruption of mitochondrial calcium exchange can block neurotransmitter release from vesicles.
- B.** The process of aging leads to blocking the entry of calcium into postsynaptic mitochondria, which, in turn, activates oxidative phosphorylation.

## Theoretical2



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English (Official)

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**C.** The process of aging suppress mitochondrial respiration, leading to increased release of neurotransmitters into the synaptic cleft.

**D.** Deficiency of components of the electron transport chain (ETC) may result in the accumulation of reactive oxygen species (ROS). Subsequently, high levels of ROS may cause DNA mutations, resulting in mitochondrial damage and further ETC deficiency.

## Theoretical2

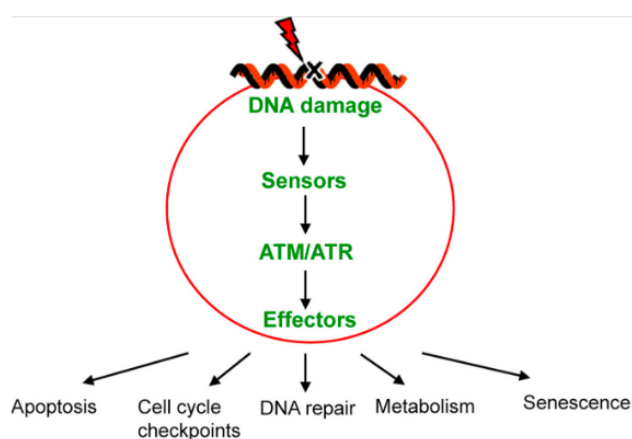


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English (Official)

### Question 78

Cell response to DNA damage is intricately regulated and can lead to different pathways. On one hand, cells try to repair the breaks in the DNA helix, on the other hand, they proceed to the apoptosis and mitotic arrest, if it fails. Cancer cells are typically treated with DNA-damaging agents like irradiation and many chemotherapeutics lead to proliferation inhibition and ultimately cell death. To escape this fate, some cancer cells develop various resistance mechanisms that allow them to survive and proliferate further.



|                        |  |
|------------------------|--|
| DNA damage             |  |
| Sensors                |  |
| ATM/ATR                |  |
| Effectors              |  |
| Apoptosis              |  |
| Cell cycle checkpoints |  |
| DNA repair             |  |
| Metabolism             |  |
| Senescence             |  |

Using this information, determine whether the following statements are true or false.

- A.** Genetic diseases that lead to genomic instability often contain defects in DNA repair mechanisms and may lead to cancer.
- B.** If the DNA damage is not repaired, normal cells will be arrested in the cell cycle but cancer cells will not.
- C.** Cancer cells carrying mutations in the DNA-damage sensing proteins may escape apoptosis.
- D.** DNA damage is more dangerous for the cells in G0 phase when compared to S or M phase.

## Theoretical2

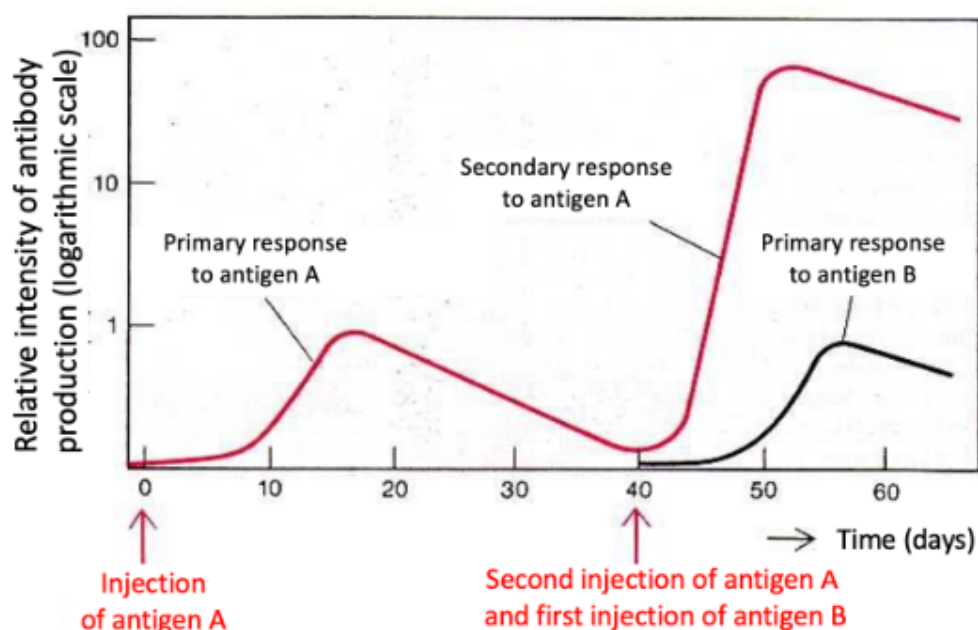


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English (Official)

### Question 79

It is known that the humoral immune system responds to the antigens entering an organism by producing antibodies. The diagram shows the immune response (production of antibodies) during the initial (first) and repeated (secondary) introduction of the antigen. Note that the time from infection to the presence of significant amount of antibody in the bloodstream is called a latent period.



|                                                                |  |
|----------------------------------------------------------------|--|
| Relative intensity of antibody production (logarithmic scale)  |  |
| Primary response to antigen A                                  |  |
| Secondary response to antigen A                                |  |
| Primary response to antigen B                                  |  |
| Injection of antigen A                                         |  |
| Second injection of antigen A and first injection of antigen B |  |

Using this information, determine whether the following statements are true or false.

- A.** After a second injection of antigen A not only quantity, but also quality (eg. affinity) of the antibodies are substantially enhanced.
- B.** Any antigenic stimulation nonspecifically activates the immune system leading to generally stronger and quicker humoral response to all antigens.
- C.** Secondary response against antigen A benefits from already differentiated antigen-specific B cells and helper T cells from the primary response.

## Theoretical2



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**D.** Primary response to antigen A is due to rapid innate immune mechanisms like phagocytosis of the antigen, localized in immunized tissue.

## Theoretical2



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English (Official)

### Question 80

One of the main symptoms of depression, which often develops after stress, is anhedonia, the loss of the ability to feel pleasure. Dopamine (DA) signals, which are sent to certain parts of the brain, play a key role in the pursuit of rewards, motivation for behavior and learning from positive experiences.

One assumption is that stress leads to anhedonia through dopamine neurons although little evidence is available to support this claim. Experiments were performed on mice to study the neurological mechanisms of anhedonia using the method of "intracranial electroencephalography" (iEEG), assessing the activity of dopaminergic (DA), (Figure 1a) and Gamma-Aminobutyric Acid (GABA) (Figure 1b) neurons. Mice in the experimental group (+stress) were rewarded with water after being exposed to stress. Mice in the control group were not exposed to stress. A sound stimulus (as a CS) alerted mice to the reward of water.

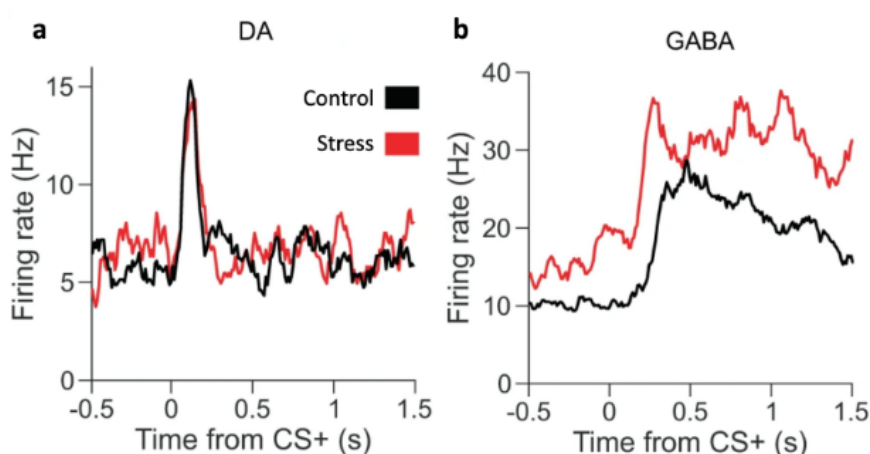


Figure 1. The activity of (a) DA neurons and (b) GABA neurons in the midbrain (firing rate, fluctuations in neuronal activity in hertz) in response to a sound signal. On the horizontal axis - time in seconds (s), the moment of sound signal (CS +) onset is assumed as 0. Black curve, neuronal activity of control mice; Red curve - the neuronal activity of experimental (stress) mice.

|                  |  |
|------------------|--|
| Firing rate (Hz) |  |
| Time from CS+    |  |

Using the information and the figures above, determine whether the following statements are true or false.

- A. The response of DA to the expected reward does not change after stress.
- B. DA responds to expected reward with a short-term increase in activity, while GABA-neurons respond long-term.
- C. Both DA and GABA neurons participate in the development of post-stress anhedonia.
- D. GABA-neuronal activity does not decrease back to baseline even after the stress is over, potentially leading to alterations in further downstream processes.



## Theoretical2

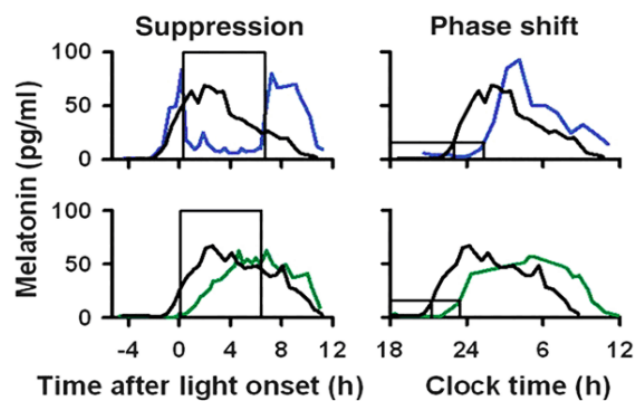


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English (Official)

### Question 81

The human biological "internal clock" located in the suprachiasmatic nucleus (SCN) of the hypothalamus ensures the shift from sleep to waking state. To synchronize activity with the solar cycle, the SCN receives information from the light-sensing cells of the retina (rods, cones, ganglion cells), and reduces the synthesis of melatonin, which affects the activity of various processes. To assess the role of the retinal cells in regulating the sleep/wake cycle, a group of volunteers were kept in conditions of constant blue light ( $\lambda_{\max} = 460 \text{ nm}$ ) for 6.5h at night. Another group was kept in similar conditions but with green light ( $\lambda_{\max} = 555 \text{ nm}$ ). Cones have been shown to absorb green light, and retinal ganglion cells are capable of absorbing only blue light ( $\lambda_{\max} = 480 \text{ nm}$ ) with the help of melanopsin pigment. Melatonin levels of the subjects and the change in circadian rhythms - "phase shift" were measured. The results are shown below.



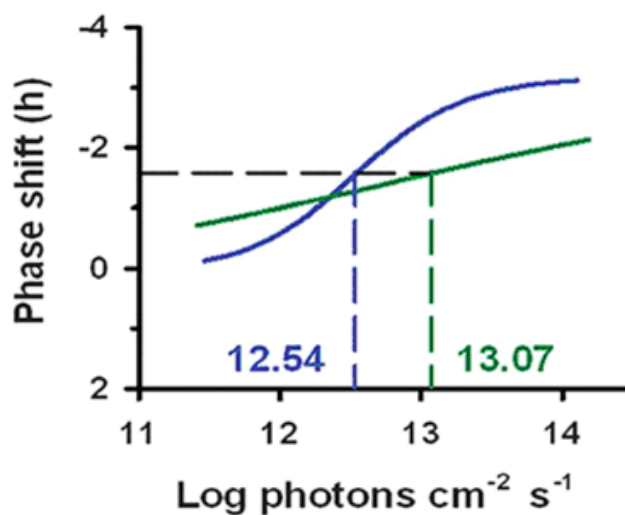
|                            |  |
|----------------------------|--|
| Suppression                |  |
| Phase shift                |  |
| Melatonin ( <i>pg/ml</i> ) |  |
| Time after light onset (h) |  |
| Clock time (h)             |  |

Figure 1. Melatonin levels, during the experiment (left panels, exposure to light indicated by the black box) and the day after the experiment (right panels). Black curves are fluctuations in melatonin levels the day before the experiment. Blue curves (top panels) = blue light treatment (460nm), green curves (bottom panels) = green light treatment (555nm).

## Theoretical2



English (Official)



|                                            |  |
|--------------------------------------------|--|
| Phase Shift (h)                            |  |
| Log photons $\text{cm}^{-2} \text{s}^{-1}$ |  |

Figure 2. Dependence of the phase shift / change in circadian rhythm on the amount of light received. The dashed horizontal line shows half of the maximum daily rhythm shift, the dashed vertical lines show the proportions of light corresponding to those changes.

Using the information and data, determine which of the statements are true or which are false.

- A. Both melanopsin-containing cells and cones are involved in the generation of circadian rhythms.
- B. In both groups of subjects, the brighter the light the smaller the phase shift/change of rhythms.
- C. At low light intensities, blue light is much more efficient for phase shift than green light, and at high intensities, the opposite is true.
- D. Ganglion cells act as the main modulators of circadian rhythms of the organism, and the cones play a supplementary role.

## Theoretical2

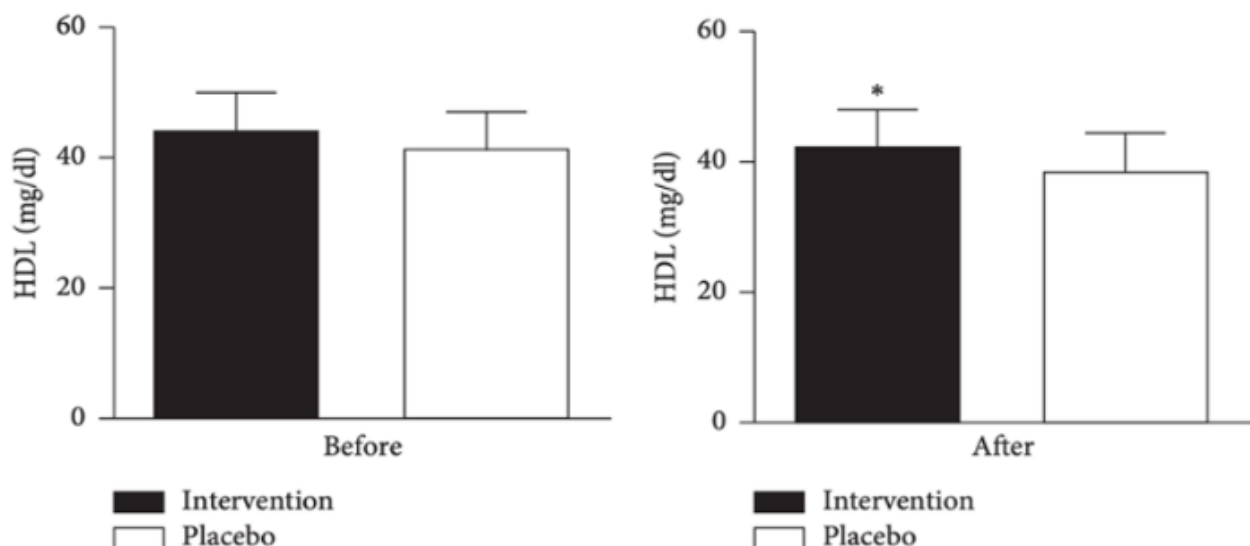
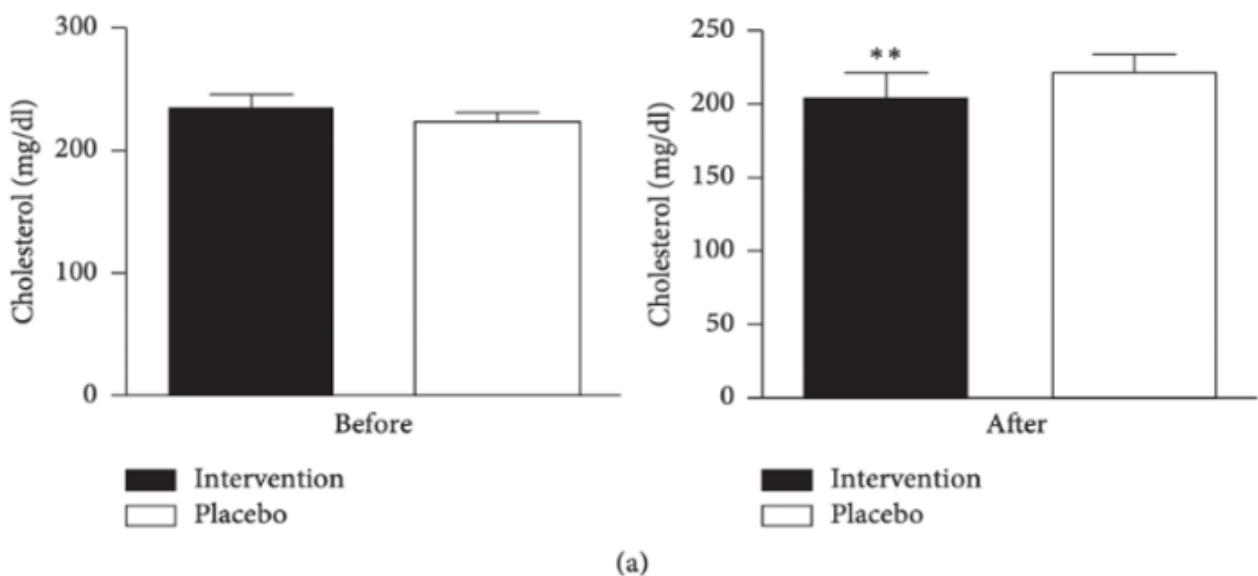


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English (Official)

### Question 82

A herbal treatment was tested on patients with lipid imbalance in their blood. Patients with lipid imbalance in the blood were divided into two groups – the control group received a placebo, while the intervention group received a herbal preparation. During the experiment, which lasted 6 weeks, both patient groups received statin therapy, which inhibits cholesterol production in the liver. At the end of 6 weeks, both groups were measured for average cholesterol, high-density lipoprotein (HDL) and low-density lipoprotein (LDL) levels in the blood, and the results were plotted in a bar chart to compare against pre-treatment levels.



## Theoretical2



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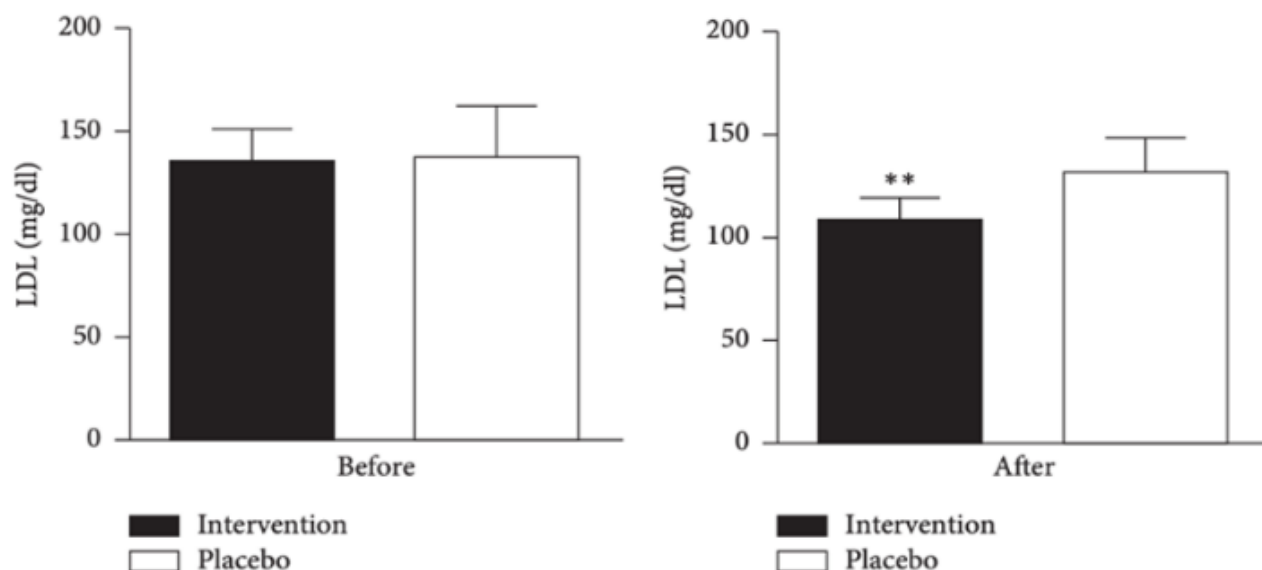


Figure. 1. Summary of the results of a controlled experimental trial of the herbal preparation intervention. \* and \*\* indicate statistically significant differences. compared to placebo.

|                     |  |
|---------------------|--|
| Cholesterol (mg/dl) |  |
| HDL (mg/dl)         |  |
| LDL (mg/dl)         |  |
| Intervention        |  |
| Placebo             |  |
| Before              |  |
| After               |  |

Using the information and the data in the graphs, determine which of the statements are true or which are false.

- A. The results in this figure alone are sufficient to assert that statin therapy decreases cholesterol levels in the blood.
- B. The information presented here is not sufficient to claim that herbal preparation would reduce LDL levels in the absence of a statin therapy.
- C. The reduced LDL concentration in the intervention group relative to the control group could imply an improved cardiovascular prognosis for patients in the intervention group.
- D. The LDL-reducing effect of the herbal preparation after 6 weeks cannot be established since the case group had a lower LDL concentration to start with.

## Theoretical2

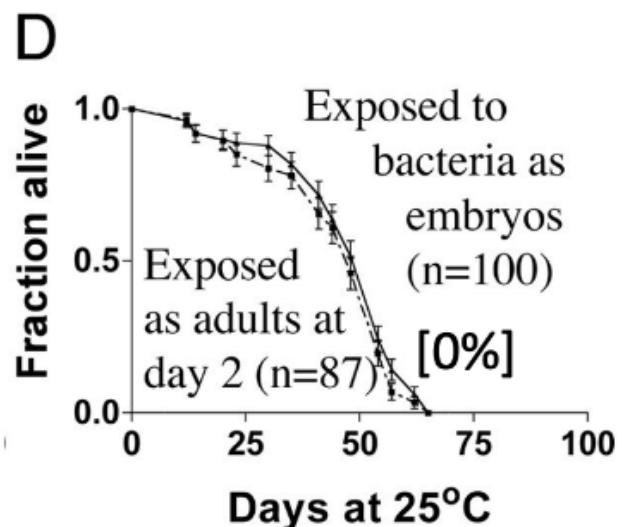
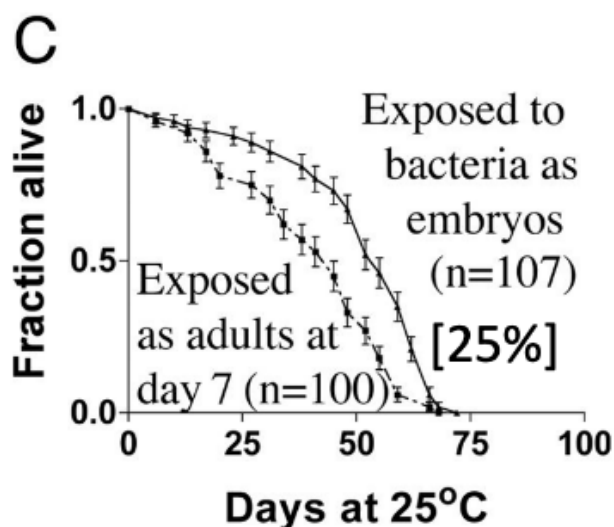
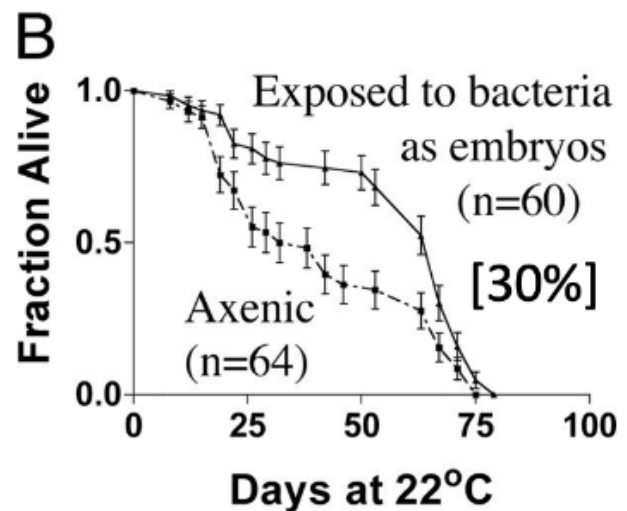
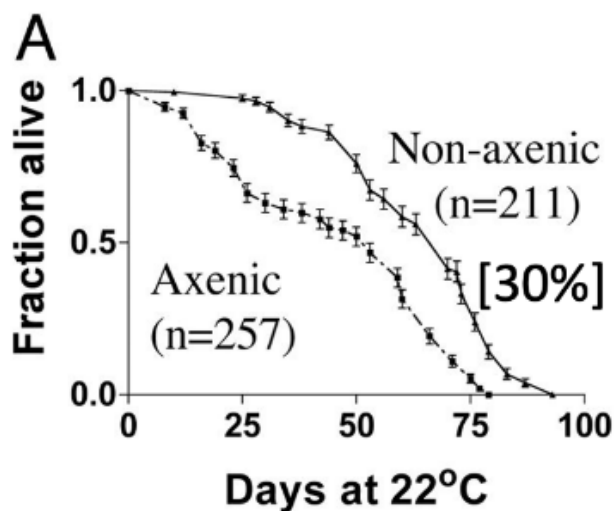


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### Question 83

Researchers investigated the effect of the microbiome on the lifespan of the fruit fly (*D. melanogaster*). To this end, they disinfected fly eggs and transferred them to a sterile food substrate. The non-disinfected eggs served as a control group ("non-axenic", figure A). Another cohort of the flies (originating from disinfected eggs) was kept on a sterile substrate for the entire lifespan ("axenic", figures A and B). The rest of the eggs were separated into three groups. They were treated with bacterial cultures either as embryos right after disinfection (figures B, C, D), at day 2 of adulthood (figure D) or at day 7 of adulthood (figure C). The researchers evaluated the fraction of individuals still alive in each population for 100 days, summarizing their results in the graphs below. The percentage in square brackets shows the difference in average lifespan between two populations.



## Theoretical2



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|                                |  |
|--------------------------------|--|
| Fraction alive                 |  |
| Days at                        |  |
| Axenic                         |  |
| Non-axenic                     |  |
| Exposed as adults at day       |  |
| Exposed to bacteria as embryos |  |

Using the information and the data in the figures above, determine which of the statements are true or which are false.

- A. Exposure to bacteria at the earliest stages of development extends the average lifespan of fruit flies.
- B. Exposure to bacteria at any stage of development can fully restore the lifespan of fruit flies.
- C. The information provided here is sufficient to conclude the possibility that fruit fly lifespan was affected by the egg disinfection technique.
- D. The critical period when the presence of bacteria affects the lifespan of fruit flies occurs between day 2 and 7 of adulthood.

**Question 84**

Males from inbred lines of rats with spontaneous hypertension (SHR) and normal blood pressure (WKY) were separated into 5 groups and received different diets for 10 weeks. The first group of each line received standard food (SF), groups 2, 3, 4 received SF+ a different fatty acid, group 5 received SF+sucrose. In groups 2 – 5, the added component comprised 11% of the energy value of the SF.

| Group | Diet         | Change in body mass<br>( $\Delta$ , %) | Systolic pressure<br>(mm Hg) |                    |
|-------|--------------|----------------------------------------|------------------------------|--------------------|
|       |              |                                        | 0 week                       | 10 weeks           |
| WKY   |              |                                        |                              |                    |
| 1     | SF           | $14.7 \pm 1.3$                         | $122.2 \pm 0.6$              | $123.1 \pm 0.6$    |
| 2     | SF+butter    | $14.9 \pm 2.4$                         | $123.2 \pm 2.0$              | $123.6 \pm 2.2$    |
| 3     | SF+palm oil  | $14.1 \pm 3.2$                         | $123.3 \pm 2.0$              | $123.5 \pm 1.9$    |
| 4     | SF+trans-fat | $14.2 \pm 2.0$                         | $121.3 \pm 2.1$              | $121.9 \pm 1.6$    |
| 5     | SF+sucrose   | $18.7 \pm 1.3$                         | $122.1 \pm 0.9$              | $125.6 \pm 1.3$    |
| SHR   |              |                                        |                              |                    |
| 1     | SF           | $10.1 \pm 0.3$                         | $200.1 \pm 1.8$              | $199.9 \pm 0.8$    |
| 2     | SF+butter    | $20.6 \pm 3.3^{**}$                    | $189.3 \pm 3.6$              | $190.1 \pm 3.9$    |
| 3     | SF+palm oil  | $7.6 \pm 1.6$                          | $204.5 \pm 2.1$              | $204.6 \pm 4.3$    |
| 4     | SF+trans-fat | $10.3 \pm 1.7$                         | $191.1 \pm 1.2$              | $202 \pm 2.0^{**}$ |
| 5     | SF+sucrose   | $10.9 \pm 3.5$                         | $191.3 \pm 4.1$              | $204.7 \pm 3.3^*$  |

**Table 1.** Measurements of body mass and blood pressure of the caudal artery were measured at the start and end of the experiments.

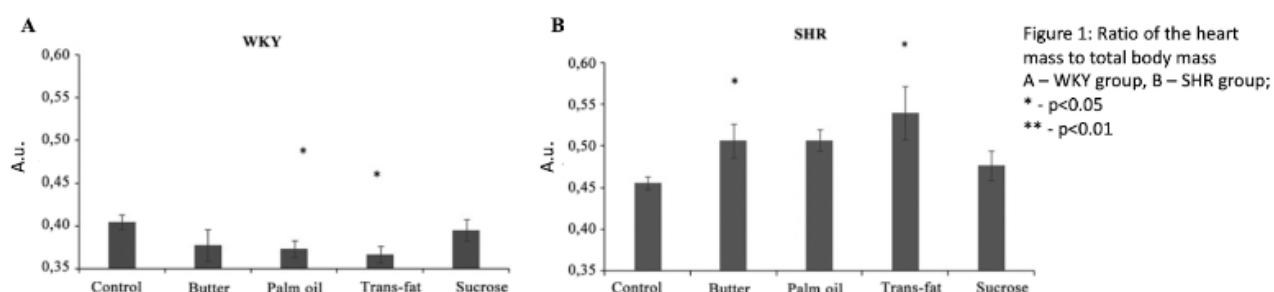


Figure 1. Ratio of the heart mass to total body mass in different dietary regimes.

## Theoretical2



English (Official)

|                                                                                      |  |
|--------------------------------------------------------------------------------------|--|
| Control                                                                              |  |
| Butter                                                                               |  |
| Palm oil                                                                             |  |
| Trans-fat                                                                            |  |
| Sucrose                                                                              |  |
| WKY                                                                                  |  |
| SHR                                                                                  |  |
| Figure 1: Ratio of the heart mass to total body mass<br>A - WKY group, B - SHR group |  |

Using the information and the data in the table and figure above, determine which of the statements are true or which are false.

- A. WKY rats receiving SF+palm oil had increased body mass, higher systolic blood pressure and hypertrophy of the cardiac muscle over that in the control.
- B. In SHR rats receiving SF+butter, increased body mass could contribute to the hypertrophy of the cardiac muscle
- C. In SHR rats, heightened systolic pressure was observed only when trans-fats and sucrose were prevalent in diet
- D. The high content of trans-fats and easily digested carbohydrates in the diet of WKY rats contributed to higher body mass and increased systolic blood pressure



## Theoretical2

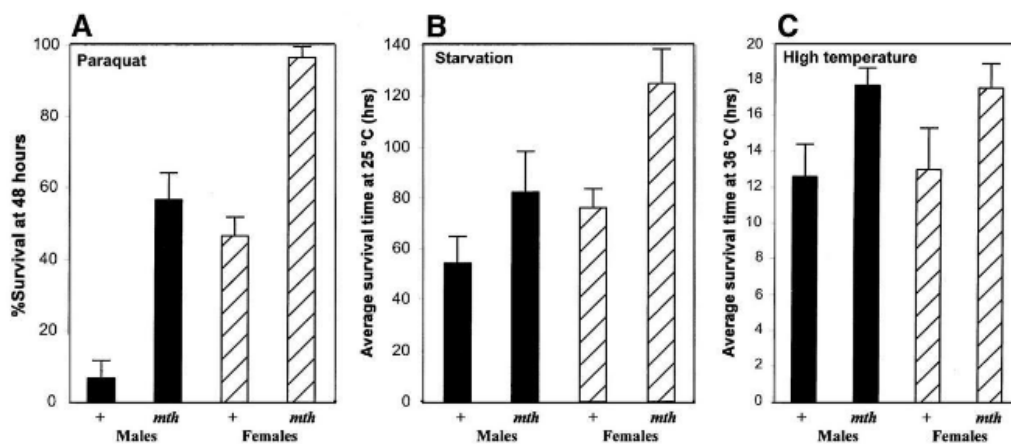


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English (Official)

### Question 85

Researchers used random insertion transposon mutagenesis to disrupt genomic DNA in fruit flies (*D. melanogaster*). One of the isolated mutants, called *mth*, was examined for longevity and stress resistance, compared to the wild type (+) under the influence of paraquat (an inducer of intracellular superoxide anion production), starvation and high temperature. Results of the experiments comparing homozygous *mth* mutants and the wild type (+) are summarized below.



|                                      |  |
|--------------------------------------|--|
| Paraquat                             |  |
| % Survival at 48 hours               |  |
| Average survival time at 25 °C (hrs) |  |
| Average survival time at 35 °C (hrs) |  |
| Males                                |  |
| Females                              |  |

Using the information and the data to determine which of the statements are true or which are false.

- For both wild type and *mth* populations, female fruit flies tend to be more resilient against all three kinds of stress than corresponding males.
- The survival profile of *mth* mutants against oxidative stress is similar to what we would expect for superoxide-dismutase (enzyme protecting against oxidative stress)-deficient fruit flies.
- mth* mutants are expected to have a longer lifespan, compared to wild-type fruit flies.
- High temperature is more detrimental to wild-type fruit flies than starvation.

## Theoretical2



English (Official)

### Question 86

In 2007, Chinese scientists encountered a giant panda *Ailuropoda melanoleuca*, covered with feces (photo). Scientists installed cameras in the habitat of the great pandas to study this strange case. Chemical analysis of fresh, up-to-5-days-old feces showed that it contained higher amounts of two volatile compounds, beta-caryophyllene (BCP) and beta-caryophyllene oxide (BCPO), compared to feces older than 5 days. Recently, a "cold receptor" TRPM8 has been found in mammalian skin. Experiments on white mice have shown that BCP / BCPOs inhibit the activity of this receptor.



Figure 1. A giant panda covered with feces.

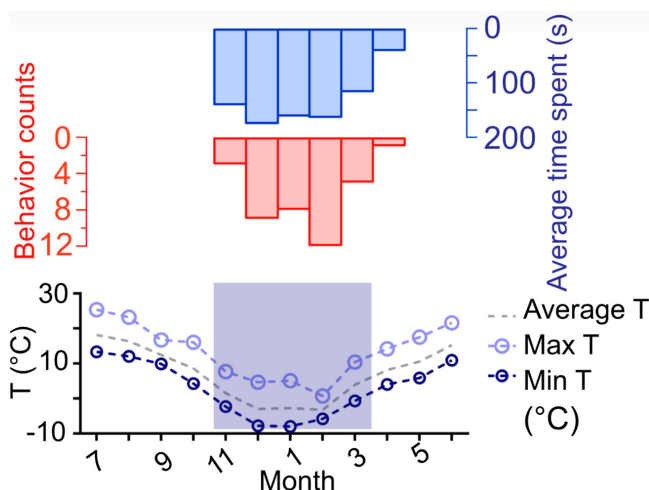


Figure 2: The relationship between behavior (indicated by behavior number and average time spent) and local climate data.

Using the information above, determine which of the statements are true or which are false.

- A. A layer of dried feces can also serve as an insulator and protect from the cold, regardless of its chemical activity on the Panda's body.
- B. There is a non-linear relationship between ambient temperature and probability of a giant panda being covered with fresh feces.
- C. A likely explanation for pandas covering their bodies with fresh feces is to avoid blood-sucking arthropods that grow in their fur.

## Theoretical2



English (Official)

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D. The habit of constantly covering their body with fresh feces can lead to behavior that is detrimental to the health of giant pandas in conditions of prolonged cold.

## Theoretical2



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English (Official)

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### Question 87

To investigate the social behavior among ravens (*Corvus corax*), young individuals were divided into three groups. In Group A, all individuals came from four different families raised by their parents ("parent-raised"). In Group C all individuals came from a mixed population raised by a human ("hand-raised"). In Group B, some individuals came from the human-raised population and some from a raven family ("parent-raised and hand-raised"). The strength of social relationships was measured during various seasons and shown on a graph.

## Theoretical2



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English (Official)

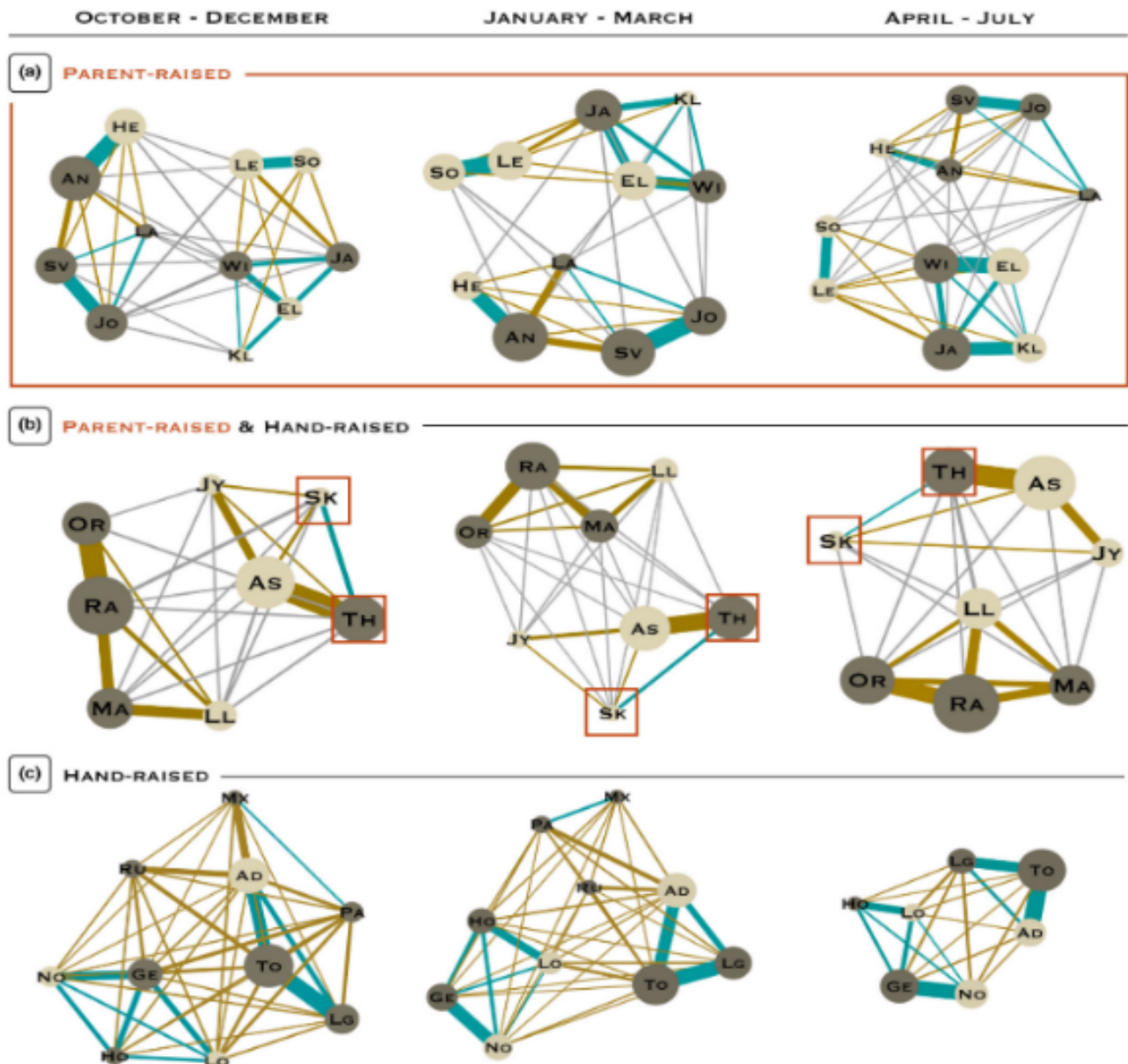


Figure 1. Relationships between individuals (October-July). Male (dark-gray node), female (light-gray node), with bigger nodes for more sociable individuals. Two-letter combinations in the nodes are IDs of individual ravens. In the mixed group B, parent-raised individuals are marked with a red square. The relationship strength ("friendliness") between a pair of individuals corresponds to the thickness of the edge between their nodes, with blue for siblings, brown for individuals raised together from hatching and gray for newly acquainted individuals.

## Theoretical2



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English (Official)

|                  |  |
|------------------|--|
| October-December |  |
| January-March    |  |
| April-July       |  |
| Parent-Raised    |  |
| Hand-Raised      |  |

Using the information and the figures above, determine which of the statements are true or which are false.

- A. To develop a stronger relationship with a sibling, individuals have to receive parental guidance.
- B. Siblings will always stay closer together than with non-relatives if raised by parents.
- C. Even after being introduced to each other, previously unacquainted individuals never created close relationships.
- D. Individual sociability always stays the same throughout development.

## Theoretical2



English (Official)

### Question 88

Researchers developed two groups of common pigeons, *Columba livia*, "free choice" and "random union". In the first group, all the pigeons, both females and males, were released into a single cage, where they were able to freely court and form pairs. In the second, "random union" group, each of multiple cages was filled with one male and one female together, until they began to court and form pairs, after which the pairs were released into a common cage. In the "free choice" group, the courtship process took significantly longer than in the "random union" group. However, the pairs of the "free choice" group started to breed earlier and laid more fertilized eggs. In both groups, the attractiveness of different individuals for the opposite sex (both males and females) was very different. In the "free choice" group, the couples formed from individuals with similar levels of attractiveness (both partners had high, medium or low attractiveness), while in "random union" group this pairing pattern was not present..

Using the information above, determine which of the statements are true or which are false.

- A. The only explanation for the pairing pattern observed in the "free-choice" group is that the birds were aiming to pair with a similarly attractive individual.
- B. The reproductive rate in the "random union" group of common pigeons is due to the possibility of forming pairs of males and females of the matching level of attractiveness.
- C. The freedom to choose a partner increases the reproductive capacity of common pigeons.
- D. Results of this experiment suggest that over time the population of common pigeon will be selected for more attractive traits.

### Question 89

During the breeding season, *Notophthalmus viridescens* newts form groups. A mature female produces pheromones, and has a full abdomen of eggs and actively seeks a mate. Males also secrete pheromones, exhibit coloured spots, display courtship behavior in the form of wiggling movements, and compete specifically for larger females. During amplexus, the male clasps the female's body with his hind limbs for up to three hours (Figure 1), during which time he exhibits various behaviors, such as cheek rubbing, tail vibration and forelimb rubbing. Rival males could occasionally try to dislodge the mating male during amplexus. Following amplexus, the male deposits his sperm packet on the bottom of the pond. Females use their cloacas to collect the sperm packets. Rival males can also release sperm packets close to the mating pair and these could be collected by the female as well. Fertilized eggs are laid over the following few weeks.



Figure 1. Amplexus of *Notophthalmus viridescens* newts: the male is on top.

Using the information above, determine which of the statements are true or which are false.

- A. Male-male contests can occur both through the competition over larger-bodied females and during amplexus.
- B. A male uses both olfactory and tactile cues to both attract the female and also stimulate her during amplexus.
- C. Females actively seek larger-bodied males to ensure their own reproductive success.
- D. There are apparently no mechanisms for sperm competition to occur in this newt species.



## Theoretical2



English (Official)

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### Question 90

The South American (French Guiana) cane toad (*Rhinella marina*) was introduced to Australia about 90 years ago to control the cane beetle (*Dermolepida albobirtum*) populations. To study the adaptive features of the species under the new conditions, the phenomena of cannibalism and the duration of early larval stage (non-feeding) were studied.

In the first experiment, the late-stage tadpoles of native South American and invasive Australian populations were released into two separate aquariums, each divided by a maze. One part of each aquarium contained clean water and the other part had newly hatched larvae of the same source population (Figures A, B).

In the second experiment, tadpoles and larvae of the respective populations were placed together in two separate aquaria and the proportion of cannibalism was recorded for each population (Figure C).

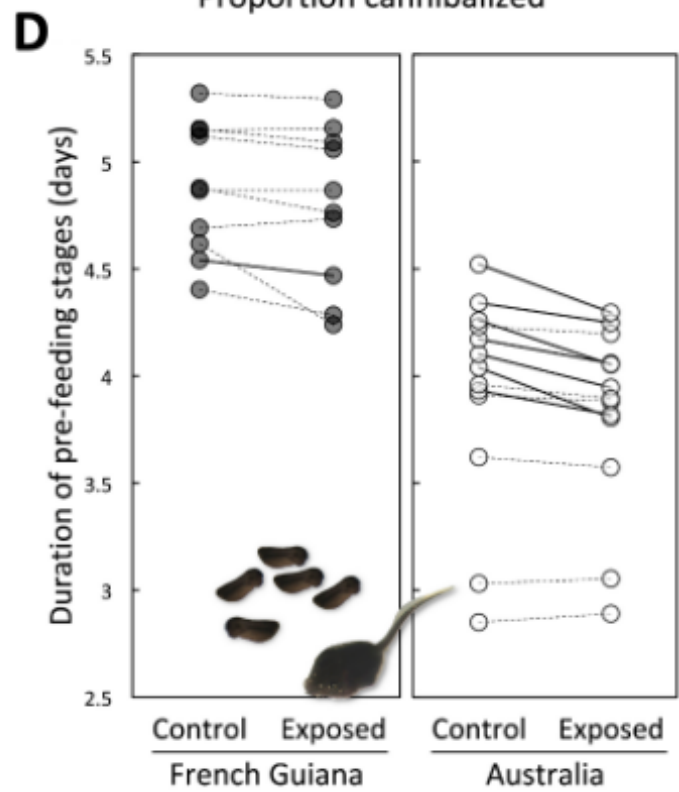
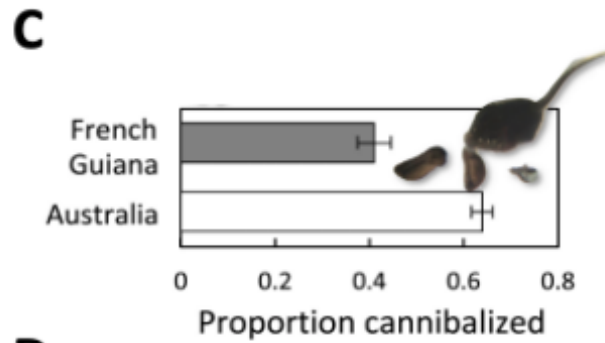
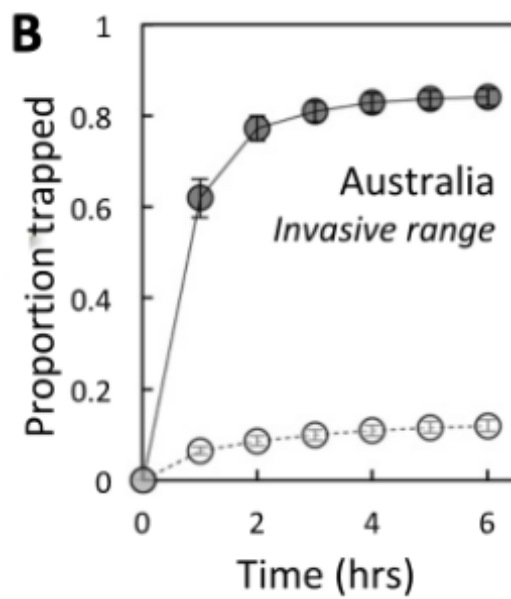
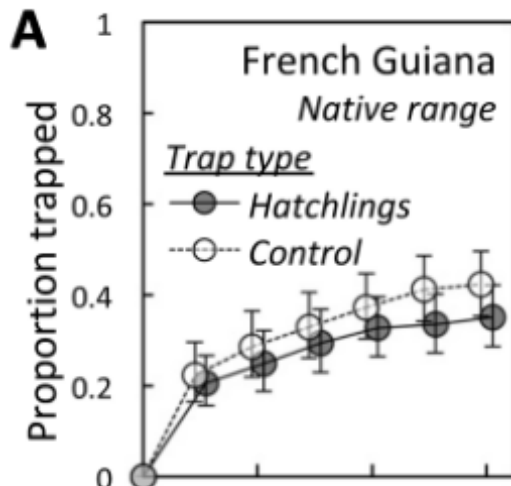
In the third experiment to study the duration of the early larval stage (non-feeding), the larvae of each population were divided into two groups. One was kept in clean water and the other in an aquarium containing late-stage tadpoles of the same population (Figure D).

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## Theoretical2



English (Official)

|                                       |  |
|---------------------------------------|--|
| French Guiana                         |  |
| Native range                          |  |
| Trap type                             |  |
| Hatchlings                            |  |
| Control                               |  |
| Proportion trapped                    |  |
| Invasive range                        |  |
| Proportion cannibalized               |  |
| Exposed                               |  |
| Duration of pre-feeding stages (days) |  |

Figure: A, B - Graphs of movement of tadpoles in the aquarium (A - South American, B - Australian). Horizontal axis - time, vertical axis - the proportion of tadpoles. White circles - tadpoles swimming towards clean water, black circles - tadpoles swimming towards larvae. C - the proportion of larvae cannibalized; D - Duration of the pre-feeding stages determined in separate aquariums, one with clean water (control), the other with late-stage larvae (experimental). Solid lines-  $P < 0.05$

Using the information and the figures above, determine which of the statements are true or which are false.

A. South American tadpoles prefer clean water.

B. Cannibalism has been reported more frequently in the Australian toad population than in the South American population, becoming a stable form of feeding behavior.

C. In the Australian population, the early larval stage has been significantly reduced in duration, which can be seen as an adaptation to avoid cannibalism.

D. A decrease in the duration of the early larval stage was observed in the experimental groups of both South American and Australian toads.

## Theoretical2



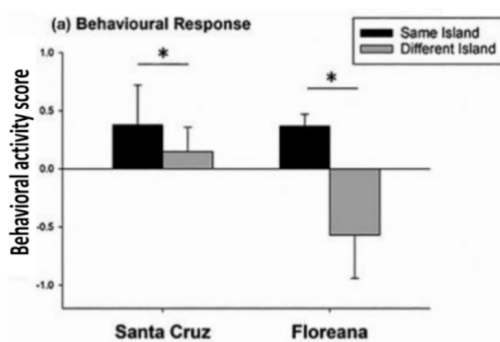
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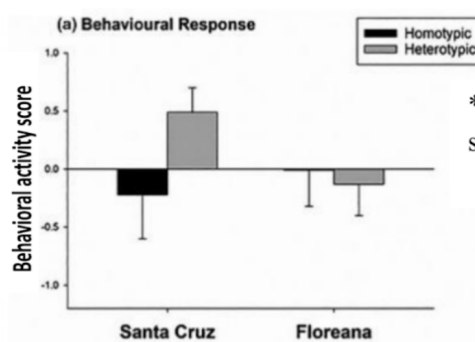
### Question 91

Researchers noted that males of small tree finches (*Camarhynchus parvulus*) sing by repeating one specific syllable over and over. They also found that 4 unique syllables occur among males collected from Santa Cruz island, 3 unique syllables occur among males from Floreana island, and 3 additional syllables are common among both. To make quantitative measurements, they decided to summarize the behavioral activity of every individual in response to a song by a numerical score (behavioral activity scores are on the Y-axis in the plots below). In the first experiment, researchers subjected an individual from each population to a song recording from its native or foreign island. In the second experiment, they subjected each individual to a song recording containing its own syllable (homotypic) or a different syllable (heterotypic).

**(1) Geographic Origin of the Intruder Song**



**(2) Syllable Type of the Intruder Song**



\* - denotes statistically significant difference

|                                              |  |
|----------------------------------------------|--|
| Geographic origin of the intruder song       |  |
| Syllable type of the intruder song           |  |
| Behavioral activity score                    |  |
| Santa Cruz                                   |  |
| Floreana                                     |  |
| Same Island                                  |  |
| Different Island                             |  |
| Behavioural Response                         |  |
| Homotypic                                    |  |
| Heterotypic                                  |  |
| denotes statistically significant difference |  |

Using the information and the figures above, determine whether the following statements are true or false.

- Male finches can recognize intruders from another population by their song.
- Male finches change their behavior significantly when they hear a song with unfamiliar syllables.

## Theoretical2



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C. The first figure shows that male finches acquire their defining syllables genetically.

D. The second figure shows that the presence of common syllables between Santa Cruz and Floreana populations is a result of evolutionary convergence.

## Theoretical2



English (Official)

### Question 92

In their seminal paper from 1973, J.M. Smith and G.R. Price used computer modeling to investigate intraspecific animal interactions. They assumed two mechanisms by which animals can inflict damage: soft, also known as "conventional" (e.g. snakes wrestling) and hard, also known as "dangerous" (e.g. snakes biting each other). They assigned positive rewards for the early retreat (accounting for saved resources) or winning (accounting for obtained resources) and negative rewards for receiving damage. Simulations were performed for various matches of stereotyped behaviors ("Mouse", "Hawk", "Bully", "Retaliator", and "Prober-Retaliator"). Averages of final rewards for each match are summarized below, with more positive values indicative of a more favorable outcome for the individual with that behavior type. For example, a "Bully" gets 80.0 points in a match against a "Mouse", while the "Mouse" gets 19.5 points in a match against the "Bully".

|                     | "Mouse" | "Hawk" | "Bully" | "Retaliator" | "Prober-Retaliator" |
|---------------------|---------|--------|---------|--------------|---------------------|
| "Mouse"             | 29.0    | 19.5   | 19.5    | 29.0         | 17.2                |
| "Hawk"              | 80      | -19.5  | 74.6    | -18.1        | -18.9               |
| "Bully"             | 80      | 4.9    | 41.5    | 11.9         | 11.2                |
| "Retaliator"        | 29.0    | -22.3  | 57.1    | 29.0         | 23.1                |
| "Prober-Retaliator" | 56.7    | -20.1  | 59.4    | 26.9         | 21.9                |

Assuming that in a mixed population, all fights occur between randomly chosen pairs, determine whether the following statements are true or false.

- A. In a population with 90% "hawks" and 10% of "mice", "mice" would eventually go extinct.
- B. A population composed of "retaliators" and "mice" would most likely have a stable composition from generation to generation.
- C. If a population is comprised of 99.9% "mice", then "mouse" is surely an evolutionarily stable strategy
- D. If a population comprises 99.9% "retaliators", then "retaliator" is surely an evolutionarily stable strategy.

## Theoretical2



English (Official)

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### Question 93

In his book "The Origin of Species", Darwin recognized that the relationships between castes of social insects in the colony can present complications for his theory of natural selection.

By considering the modern understanding of insect evolution, determine whether the following statements are true or false.

- A. Worker ants are the most numerous members of the colony as they have achieved greatest reproductive success.
- B. Worker ants phenotypically resemble their parents, as they carry parental genes.
- C. As widespread sterility in some insect colonies leads to decreased reproductive success for some individuals, it must have come about due to genetic drift.
- D. The colony's evolutionary fitness depends on the queen's reproductive success.

## Theoretical2

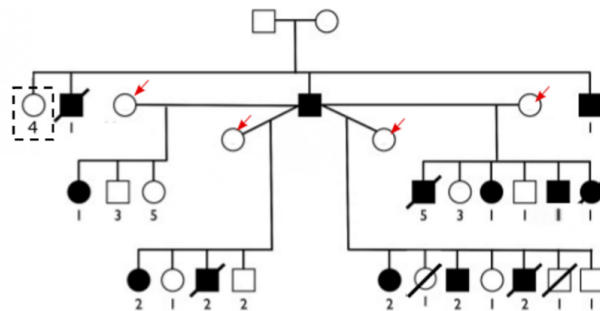


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English (Official)

### Question 94

Below is a canine pedigree of a common monogenetically inherited disease. Squares and circles represent males and females respectively, and black and white colors indicate the presence or absence of the trait respectively. The numbers indicate the number of dogs in each category and the diagonal lines crossing over squares/circles indicates a deceased dog.



Using the information and pedigree, determine whether the following statements are true or false.

- All the females indicated with red arrows are heterozygous for the trait.
- The trait could be autosomal recessive.
- The trait could be X-linked recessive.
- The genotypes of all four females in F1 (marked with dotted box) must be the same.



## Theoretical2



English (Official)

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### Question 95

Familial Mediterranean Fever (FMF) is a genetic disorder commonly associated with Eastern Mediterranean populations. A genetic segregation analysis of some of the Armenian populations showed that the frequency of the underlying autosomal recessive allele is roughly 0.073.

Using this data, and assuming Hardy-Weinberg equilibrium determine whether the following statements are true or false. In your calculations, round the final answers to the nearest integer.

- A. On average, approximately 1 in 188 individuals in this population has FMF.
- B. In a random sample of 100 people from this population, we can expect approximately 7 carriers.
- C. In a random sample of 63 married couples from this population, we can expect 8 couples, where at least one partner is a carrier.
- D. The child of a carrier and a non-symptomatic individual of unknown genotype from this population has a 1 in 29 probability of having the disease.

## Theoretical2

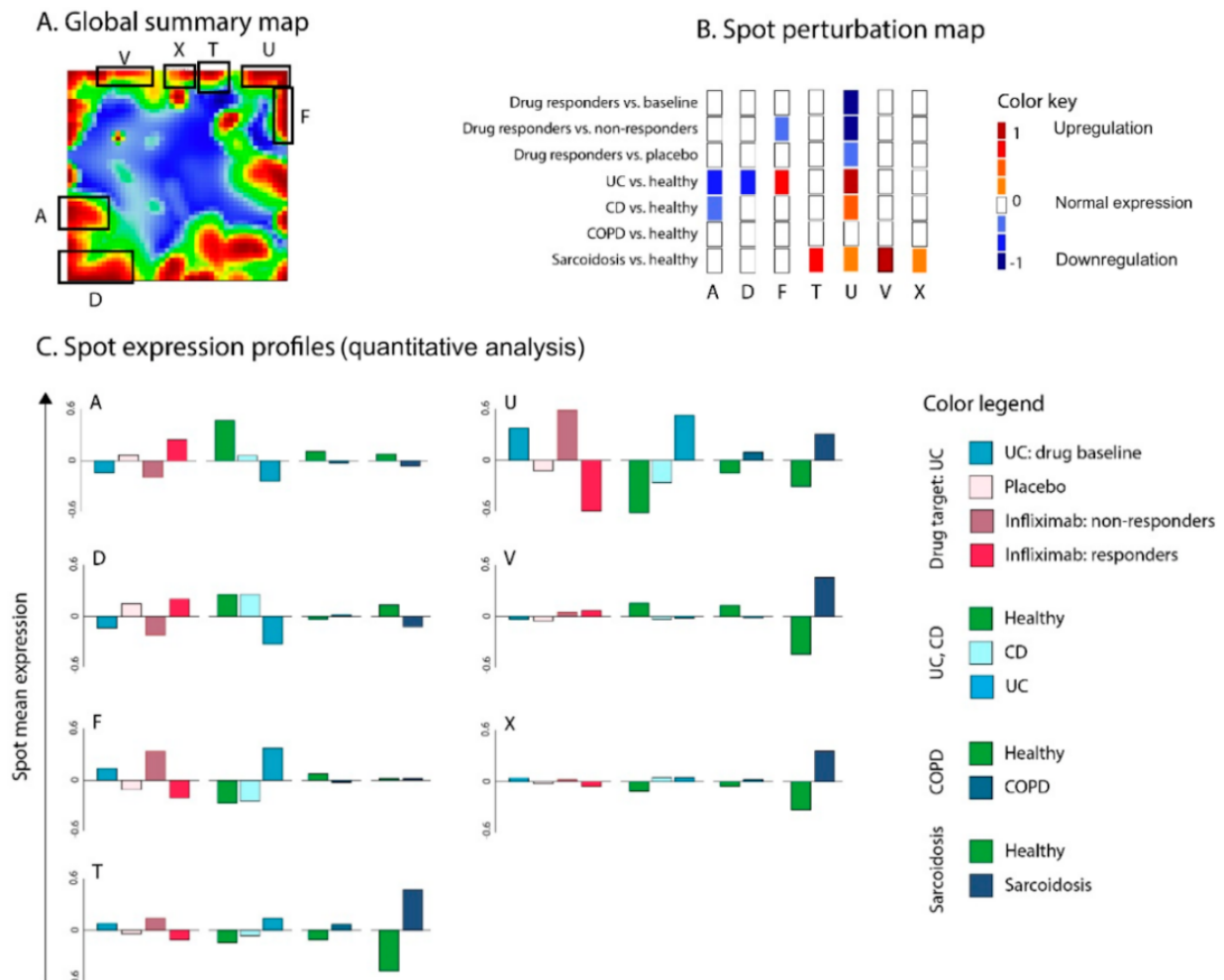


English (Official)

### Question 96

Identifying new applications for approved drugs outside of the scope of their original medical indication is an important strategy in modern pharmaceuticals. This strategy is often based on transcriptome analysis. It is assumed that upon administration, the drug causes significant changes in the expression of a particular gene set or sets. These changes characterize the effect of the drug. If the targeted gene set is also associated with a disease (e.g., the gene set is overexpressed during the disease and underexpressed upon drug administration), the studied drug may be a candidate for the disease treatment.

The drug Infliximab's effect on Crohn's disease (CD), chronic obstructive pulmonary disease (COPD), sarcoidosis and ulcerative colitis (UC) has been studied using the transcriptome-based approach. Infliximab is an immunosuppressive agent used to treat CD and UC. Gene expression data was obtained from the colonic biopsy samples of CD patients, Infliximab or placebo-treated UC patients, as well as from lung tissue of COPD and sarcoidosis patients. The results of the analysis are summarized in the Figure 1 below. Figure 1A shows the summary heatmap of the transcriptome. Gene sets with the same expression patterns form spots on the heatmap (A, D, etc.). Colors red to blue (from warm to cold) indicate the expression level from upregulation (overexpressed) to downregulation (underexpressed), correspondingly. Figure 1B shows the expression of spots (A, D, etc.) in the test specimens relative to the control (healthy, placebo, or before Infliximab administration). Figure 1C shows quantitative analysis of spot expression profiles.



**Figure 1.** Evaluation of Infliximab's effect on UC, CD, COPD, and sarcoidosis. (A) Global transcriptome summary heatmap with identified potentially therapeutically relevant gene clusters - spots (A, D, F, T, U, V, X). (B) Drug- and disease-spot perturbation heatmap. (C) Quantitative analysis of spot expression profiles.

## Theoretical2



English (Official)

|                                                  |  |
|--------------------------------------------------|--|
| CD vs. healthy                                   |  |
| Color key                                        |  |
| COPD                                             |  |
| COPD vs. healthy                                 |  |
| Downregulation                                   |  |
| Drug responders vs. baseline                     |  |
| Drug responders vs. non responders               |  |
| Drug responders vs. placebo                      |  |
| Drug target: UC                                  |  |
| Global summary map                               |  |
| Healthy                                          |  |
| Infliximab: non-responders                       |  |
| Infliximab: responders                           |  |
| Normal expression                                |  |
| Placebo                                          |  |
| Sarcoidosis                                      |  |
| Sarcoidosis vs. healthy                          |  |
| Spot expression profiles (quantitative analysis) |  |
| Spot mean expression                             |  |
| Spot perturbation map                            |  |
| UC vs. healthy                                   |  |
| UC, CD                                           |  |
| UC: drug baseline                                |  |
| Upregulation                                     |  |

Based on these results, determine whether the following statements are true or false.

- A. Spot U's expression, which was upregulated in UC, CD, and sarcoidosis, can be antagonistically targeted by Infliximab.
- B. Spot F, which was upregulated in UC, is associated with response to infliximab.
- C. Expression perturbation in each of the studied spots is associated with at least one disease from the experiment.
- D. UC is characterized by downregulation of spots A and D.

## Theoretical2

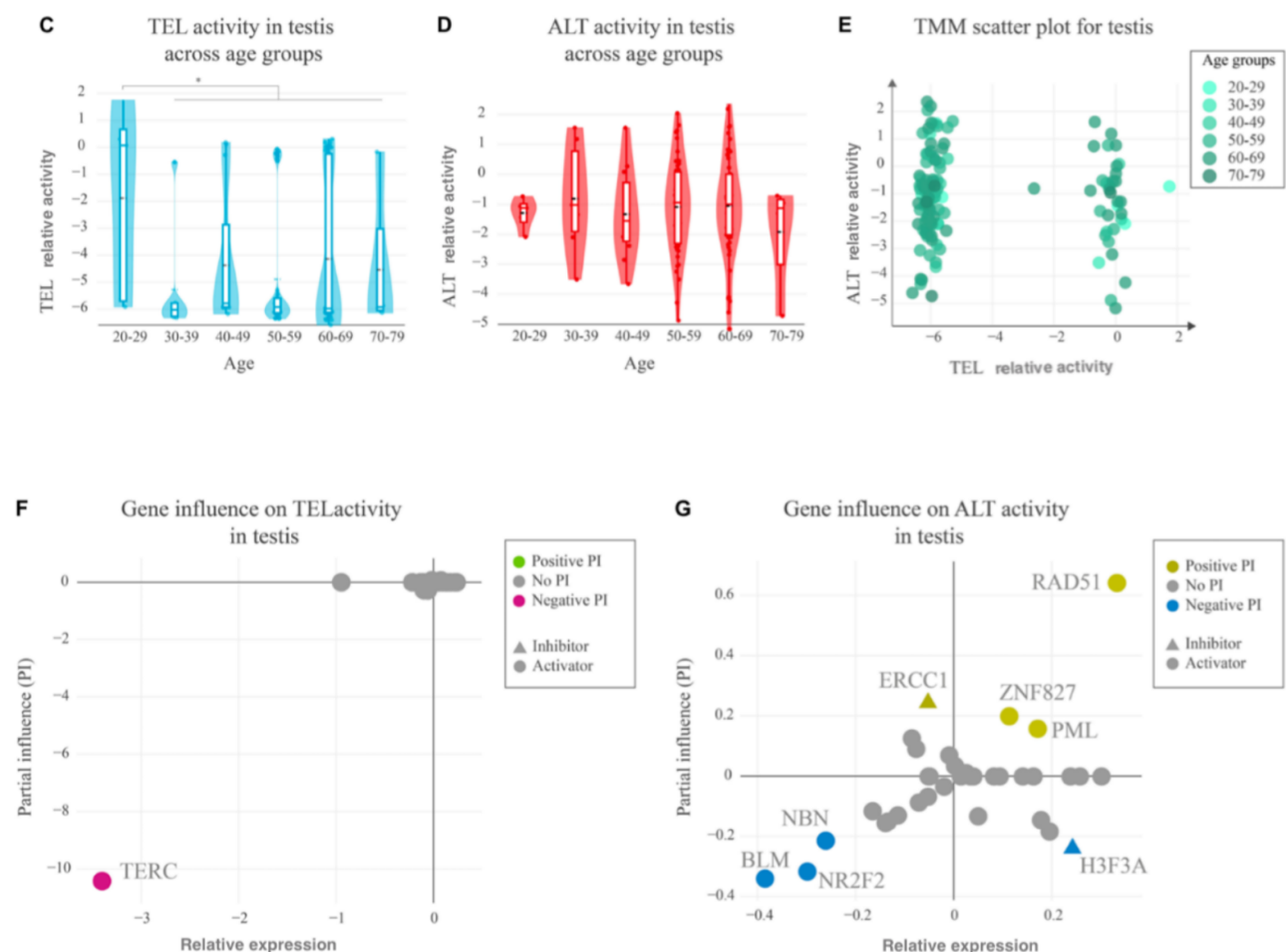


English (Official)

### Question 97

There are two mechanisms of telomere lengthening in a cell: the telomerase-dependent (TEL) pathway and the alternative telomere-lengthening (ALT) pathway. The activity of the TEL and ALT pathways has been studied in a number of healthy human tissues based on the expression of the genes involved in those pathways (see Figure). A pathway is considered active if the relative activity value is greater than 0.

Gene effect is measured by the **Partial Influence (PI)** metric. If PI is greater than 0, the gene activates the pathway; if less than 0, it suppresses the pathway; if 0, it does not affect the pathway activity. The greater the absolute value of PI, the greater the effect of that gene on pathway activation. **Relative** expression is the natural logarithm of the expression of a gene in a sample divided by the mean of the expression of that gene in all samples.



**Figure.** The relative activity values of the TEL and ALT pathways in testis (C-E) across age groups. Gene influence on TEL/ALT activity in testis (F-G).

## Theoretical2



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|                                          |  |
|------------------------------------------|--|
| Activator                                |  |
| Age                                      |  |
| Age groups                               |  |
| ALT activity in testis across age groups |  |
| ALT relative activity                    |  |
| Gene influence on ALT activity in testis |  |
| Gene influence on TELactivity in testis  |  |
| Inhibitor                                |  |
| Negative PI                              |  |
| No PI                                    |  |
| Partial influence (PI)                   |  |
| Positive PI                              |  |
| Relative expression                      |  |
| TEL activity in testis across age groups |  |
| TEL relative activity                    |  |
| TMM scatter plot for testis              |  |

Using this information and analysis, determine whether the following statements are true or false.

- A. RAD51 is the most critical factor resulting in activation of the ALT in testis.
- B. TERC decreases the activation of the TEL pathway in testis
- C. The relative activity values of the TEL pathway are clearly divided into two age groups
- D. TEL pathway activity predominates at a younger age, while the ALT pathway is more important in older age

## Theoretical2

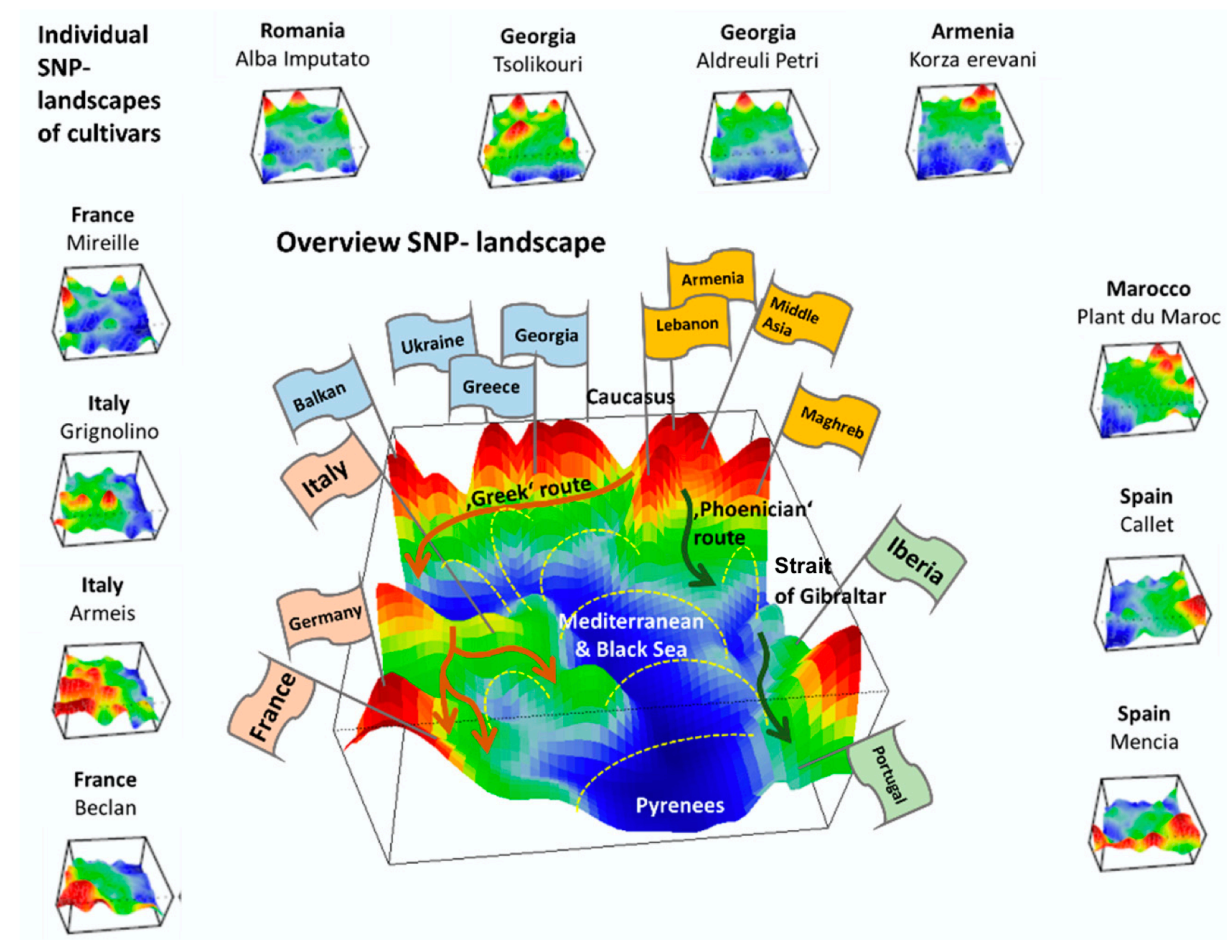


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English (Official)

### Question 98

The evolution of grape species is closely connected to the historical and cultural development of humans. Archaeological research shows that the cultivation of grapes began 8000 - 10000 years ago in the Middle East and South Caucasus. To understand the genetic diversity and evolution of grapes, single nucleotide polymorphisms (SNPs) of about 800 cultivars have been studied. As a result, a genomic map for each cultivar was obtained, and the distribution of point mutations indicated on them (Figure). The closer the mutations are located to each other on the map, the more likely they are to be found together in a genome. The red "mountains" on the map indicate a high probability of mutations in that area, and the blue "plains" a low probability. The summary map shows the variety of mutations found across cultivars. The map is annotated with the names of geographical areas, found to be associated with the mutation groups. Further phylogenetic analysis of cultivars revealed two geographical routes of crop evolution: northern (from the Caucasus to the Balkans to Western Europe) and southern (through Palestine, Maghreb to the Iberian Peninsula). These paths are shown with arrows on the map.



**Figure.** Genomic maps of grape cultivars

Based on the results, indicate whether the following statements are true or false.

A. The results support the archaeological theory that the cultivation of grapes began in the South Caucasus (Georgia, Armenia) and Barber Mahik (Eastern Anatolia, Northern Lebanon and Syria).

## Theoretical2



English (Official)

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- B. The main reason for dichotomous branching in the evolution of grape cultivars is the Mediterranean Sea, which is the biggest barrier to genetic exchange.
- C. The Pyrenees is a greater barrier for plant genetic exchange than the Strait of Gibraltar.
- D. Genetic differences in Spanish Mencia and French Mireille cultivars can be explained by sympatric speciation.





### Question 99

Newfoundland was originally only inhabited by one species of hare, the arctic white hare *Lepus arcticus* (up to 70 cm in length and up to 7.0 kg). It has previously been found both in open fields and in the woods of Newfoundland, feeding on grasses, various parts of trees and shrubs. Around 100 years ago, the small white hare *Lepus americanus*, (up to 52 cm in length and up to 1.55 kg) was introduced to the island. *Lepus arcticus* currently inhabits only open areas and *Lepus americanus* inhabits only forested areas. The forested areas are also inhabited by a predator of hares - the Canada lynx *Lynx canadensis*.



*Lepus arcticus*



*Lepus americanus*

## Theoretical2



English (Official)



*Lynx canadensis*

Using the information and images indicate whether the following statements are true or false.

- A. *Lepus americanus* has pushed *Lepus arcticus* out of the wooded area because it is physically stronger and more adapted to living in a wooded area.
- B. *Lepus arcticus* feeds only on herbs, and *Lepus americanus* only on bark and branches of trees.
- C. Living in the open fields, *Lepus arcticus* avoids becoming prey to *Lynx canadensis*.
- D. *Lepus arcticus* later moved out of wooded areas to avoid being predated on by *Lynx canadensis*.

## Theoretical2



IBO  
33<sup>rd</sup> 2022  
ARMENIA

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### Question 100

One of the modern environmental problems is the spread of invasive alien species, the success of which is due to the adaptive properties of these species. Temperature is one of the most important environmental factors for species. The experiment examined the cold resistance of *Melanoides granifera* mollusc, a representative of the tropical fauna, to low temperatures. The molluscs were initially kept at low temperatures for 8 h or 168 h, then transferred to 18°C or 20°C conditions for acclimation (Figure 1). The lowest temperature threshold for survival was investigated.

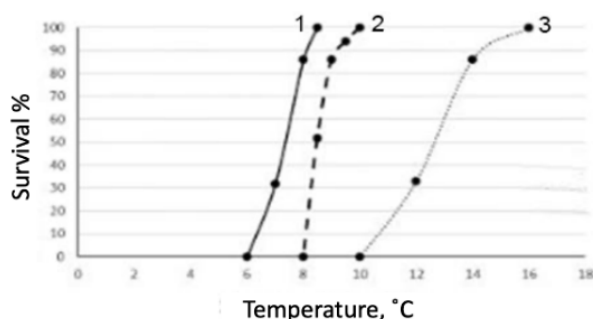


Figure 1: The survival of molluscs *Melanoides granifera* after acclimation, as a function of the temperature of cold exposure. Curve 1: survival after 8 hours cold exposure and acclimation in 18°C, curve 2: survival after 8 hours cold exposure and acclimation in +20°C, curve 3: survival after 168 hours cold exposure and acclimation in +20°C.

Using the information and the figure, indicate whether the following statements are true or false.

- A. The survival of *Melanoides granifera* depends on the acclimation temperature and the duration of initial exposure to low temperatures.
- B. Reducing the acclimation temperature by 2°C leads to an increase in the cold resistance of the mollusc.
- C. Prolonged exposure to initial low temperatures increases the cold resistance of the mollusc.
- D. If the mollusc has a good ability for spreading, it can spread from tropical areas to a temperate zone with temperatures below 10°C and become a successful invasive species.

## THEORETICAL 2

| Q  | A | B | C | D |  | Q   | A | B | C | D |
|----|---|---|---|---|--|-----|---|---|---|---|
| 51 | ✓ | X | X | ✓ |  | 76  | X | X | ✓ | ✓ |
| 52 | X | X | ✓ | ✓ |  | 77  | ✓ | X | X | ✓ |
| 53 | X | ✓ | ✓ | X |  | 78  | ✓ | ✓ | ✓ | X |
| 54 | ✓ | X | ✓ | X |  | 79  | ✓ | X | ✓ | X |
| 55 | X | X | X | ✓ |  | 80  | ✓ | ✓ | X | ✓ |
| 56 | ✓ | ✓ | ✓ | ✓ |  | 81  | ✓ | X | X | ✓ |
| 57 | X | ✓ | ✓ | X |  | 82  | X | ✓ | ✓ | X |
| 58 | ✓ | X | ✓ | X |  | 83  | ✓ | ✓ | X | ✓ |
| 59 | X | ✓ | ✓ | X |  | 84  | X | ✓ | ✓ | X |
| 60 | ✓ | ✓ | X | X |  | 85  | X | X | ✓ | ✓ |
| 61 | ✓ | X | ✓ | ✓ |  | 86  | X | ✓ | X | ✓ |
| 62 | ✓ | X | X | ✓ |  | 87  | X | X | ✓ | X |
| 63 | ✓ | X | X | ✓ |  | 88  | X | X | ✓ | X |
| 64 | ✓ | X | X | ✓ |  | 89  | ✓ | ✓ | X | X |
| 65 | ✓ | X | ✓ | ✓ |  | 90  | X | ✓ | ✓ | X |
| 66 | ✓ | ✓ | ✓ | ✓ |  | 91  | ✓ | X | X | X |
| 67 | ✓ | X | ✓ | X |  | 92  | X | ✓ | X | ✓ |
| 68 | X | X | ✓ | X |  | 93  | X | X | X | ✓ |
| 69 | ✓ | ✓ | ✓ | X |  | 94  | ✓ | ✓ | ✓ | X |
| 70 | ✓ | X | X | X |  | 95  | ✓ | X | X | ✓ |
| 71 | ✓ | ✓ | X | ✓ |  | 96  | ✓ | ✓ | ✓ | ✓ |
| 72 | ✓ | X | ✓ | ✓ |  | 97  | ✓ | ✓ | X | X |
| 73 | ✓ | X | ✓ | X |  | 98  | ✓ | ✓ | ✓ | X |
| 74 | X | ✓ | ✓ | ✓ |  | 99  | X | X | ✓ | X |
| 75 | ✓ | X | ✓ | ✓ |  | 100 | ✓ | ✓ | X | X |