INTERNATIONAL BIOLOGY OLYMPIAD e. V. IBO

INSTRUCTIONS FOR THE THEORY EXAMINATIONS

PAPER 2: 1.30PM - 4.30PM

Instructions

Each paper comprises 46 questions, which will be completed on a computer.

You MUST answer ALL parts of ALL questions. For multiple-true/false tasks, answer each statement with either 'true' or 'false'. Between none and all of the statements may be true. For calculations, choose the number nearest to the correct answer. You should make your best guess if you are unsure; you will not be penalised for incorrect guesses, but may gain marks.

Each correct answer will score 1 mark. Each incorrect or missing answer will score 0 marks.

You SHOULD attempt the questions IN ORDER, and come back to any that you cannot answer at first. You can flag these by clicking the flag icon, and see your progress by opening the contents pane on the left-hand side. You may find that ideas explored in earlier questions help you answer later questions.

Some figures can be enlarged by clicking on them.

You can change the language you view the papers in by choosing an option from the top right corner.

You will need to use the information given to you in each question creatively, but you will never require advanced technical or specialised knowledge.

You MUST have the following equipment for this exam.

- Approved calculator
- Pen/pencil
- You will be provided with scrap paper. You MUST NOT bring any paper into, or out of, the exam room. A copy of this document will be available on the first page of each exam.

Regulations

You MUST NOT communicate with ANY other candidate at ANY time, whilst you are in the examination room.

You MUST NOT open ANY other windows on your computer.

You MUST NOT access ANY information that could unfairly help you whilst the examination is in progress.

If you require the assistance of a guide you should raise your hand, and remain facing forward until given further instructions.

You MUST NOT attempt to leave your computer station without the assistance of a guide.

If you experience technical problems, you MUST inform a guide IMMEDIATELY.

Good luck!

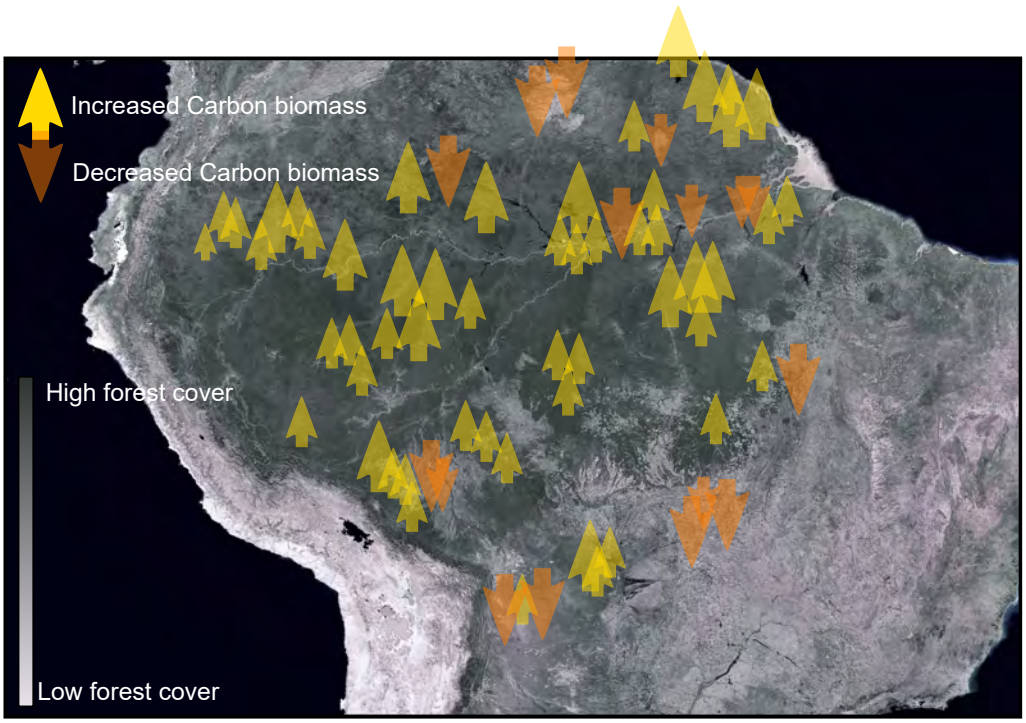
USEFUL SCIENTIFIC DEFINITIONS

WT	In all cases, WT refers to wild-type. Wild-type organisms have not been genetically manipulated, or otherwise chosen for a specific genetic property.
Knockout	Knockout refers to an organism which has had specific gene, which is stated in the question, mutated such that no functional product is produced from it.
Haplotypes	A haplotype is a combination of alleles that occur on the same DNA molecule. For example, if genes A, B, C, D, and E are located on the same chromosome, and each gene has two alleles, this genomic region can have many different haplotypes (AbCdE, abcDE, ABCde etc.). If these genes are strongly genetically linked, some haplotypes will occur in the population more often than expected by chance, i.e. specific alleles of one gene will usually co-occur with specific alleles of the linked genes. Mutations within such a region create new haplotypes, descended from the old. Meiotic crossing over within the region brakes existing haplotypes and randomly recombines alleles thus eliminating the association between alleles over time.
mmHg	Millimeters of mercury. Biologists usually use mmHg as the unit for pressure. mmHg are directly proportional to Pascals and cmH2O, but give rounder numbers in most biological situations.
Partial pressure (PGas)	Partial pressure measures the pressure that a gas would exert on its surroundings if only that gas was present. Partial pressures are noted as Pgas (e.g. Po2 = partial pressure of oxygen). For example, the total pressure of atmospheric air, at sea-level, is 760 mmHg, and oxygen makes up 21 % of all the molecules in atmospheric air. Therefore the partial pressure of oxygen in atmospheric air is Po2 = 0.21 x 760 = 160 mmHg. The partial pressure of a gas in solution, is the partial pressure that the gas would have in air which is in equilibrium with the solution. For example, the partial pressure of oxygen in a glass of water exposed to atmospheric air for a long time will also be 160 mmHg. Hence, partial pressures are used by biologists to predict the rate and direction of gas transfer and equilibrium conditions. Partial pressures are NOT directly proportional to the concentration of the gas in a solution. Concentration depends on partial pressure, solubility, temperature etc.
Expression	Many DNA genes are transcribed to produce RNA, which is translated to produce a polypeptide. This folds, and may be modified, to give a functional protein. Unless stated otherwise, the expression level of a gene describes how much functional protein it is generating through the combined action of these processes. Therefore, if expression is increased, more functional protein is being produced. This does not necessarily mean there is increased amounts of protein (it may be degraded quickly). The functional product may also need further steps to become activated.
Arrows	In scientific diagrams, arrows are taken to mean leads to, activates, becomes, or simply a label.
Flat-headed arrows	In scientific diagrams, flat-headed arrows are taken to mean inhibits, blocks, reduces.

ADAPTING TO THE ENVIRONMENT

AMAZON BIOMASS

Forests sink more than 30% of anthropogenic CO_2, but the way they handle atmospheric CO_2 is changing. This map shows the change in total fixed carbon mass in the Amazon over the last decade. The Amazon rainforest is responding to climate change similarly to most rainforests.



	True	False
Excluding deforestation, rainforests have shown a net increase in carbon biomass in recent years.	X	
Increasing UV input, due to a thinning ozone layer, can increase carbon fixation.		X
Increasing atmospheric CO_2 concentration can increase carbon fixation.	X	
Small increases in temperature increases the rate of photosynthetic enzymes.	X	

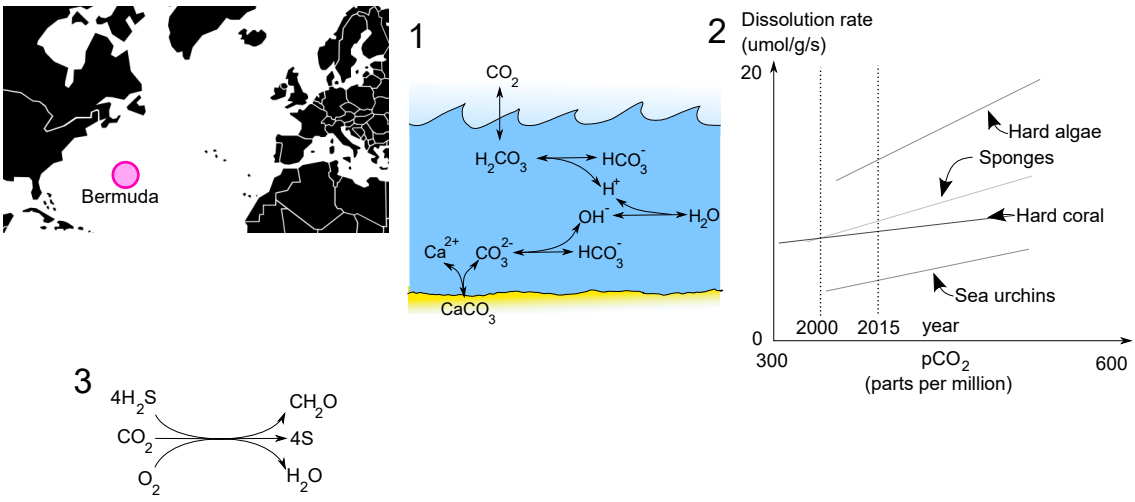
Explanation:
This question was inspired by Dimitar Epihov of The University of Sheffield.

This simple question assesses understanding of limiting factors for enzymatic photosynthesis.

- Most arrows point upwards.
- UV is not a useful wavelength for chlorophyll, and damages most plants.
- RUBISCO is notoriously inefficient, and increasing CO2 improves activity by raising substrate availability.
- Photosynthetic enzymes work faster at higher temperature. (http://rstb.royalsocietypublishing.org/content/363/1498/1811)

BERMUDAN CORAL

Oceans also sink more than 30% of anthropogenic carbon dioxide, which dissolves to form an acid that alters calcium carbonate solubility (1). Many marine invertebrates have calcium carbonate skeletons, which form marine sediments and reefs. The British island of Bermuda is a hub for studying coral reefs and sea trenches, so the effect of CO_2 on Bermudan sediments in seawater was measured (2). Five thousand metres below the reefs, marine bacteria fix CO_2 to grow (3).



	True	False
Anthropogenic carbon dioxide damages invertebrate skeletons.	X	
The structure of the Bermudan barrier reef is under threat due to changes in seawater chemistry.		X
The growth of invertebrates contributes to the oceans' ability to sink carbon.	X	
Bacteria at hydrothermal vents use modified photosynthetic enzymes to fix carbon.		X

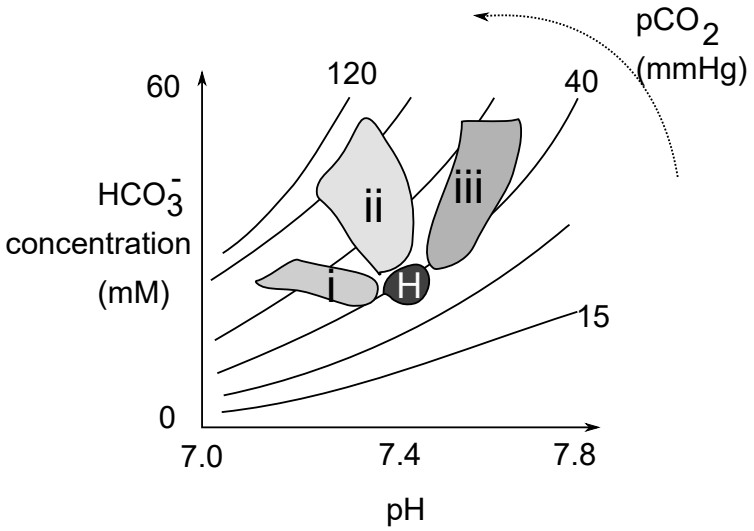
Explanation:
This question was inspired by Laetitia Gunton of the Royal Society of Biology.

The question assesses understanding of chemical equilibria and inorganic chemistry in biology.

- Forms an acid which can react with CaCO3 (1), to increase dissolution rate (2).
- Reef building corals show a very minor change in rate over the last decades (2). There must be reasonably good integrity to withstand hurricanes, tides etc, so a tiny change in dissulution rate unlikely to cause collapse.
- Invetebrate carbonate skeletons consumes Co2 fixed by producers, and forms sedimentary rock.
- No light is available; O2 is consumed, not generated; a reducing agent is consumed, not generated etc.

ACIDOSIS

Blood pH must be tightly controlled. To achieve this, the lungs excrete CO_2 from the body and the kidneys alter blood HCO_3^- levels. The blood chemistry of healthy people (H) and people with diseases i, ii, and iii was analysed, and falls in the ranges shown.



	True	False
Disease i makes blood too acidic.	X	
Disease ii involves increased gas exchange in the lungs.		X
Disease ii involves harmful changes in kidney function.		X
Vomiting can induce the phenotype seen in iii.	X	

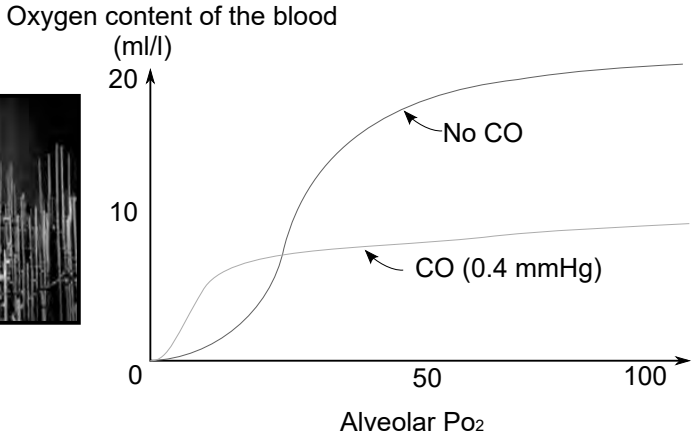
Explanation:

This question explores understanding of pH further, in a different context. Candidates need to think carefully about the cause and response to deviations in homeostasis.

- pH is lower than healthy people.
- Blood is tending towards being too acidic. Basic HCO3- is high, indicating kidneys are attempting to correct the situation. CO2 is high, which is driving the acidity. Therefore gas exchange in the lungs is impaired.
- See above
- Blood is tending towards alkali. CO2 is high, indicating the lungs are attempting to correct the situation. HCO3- is high, suggesting that the kidneys are producing too much, or that stomach acid has been lost (a net loss of H+ from the body), and replacing it has favoured an increase of HCO3- in the blood. (see equilibria from previous question).

CARBON MONOXIDE POISONING

Sir John Kendrew (1917-1997) published the structure of haem-proteins, revealing how oxygen is transported in the blood.
Carbon monoxide is a poisonous gas which can enter the blood via the lungs and alters oxygen transport. In normal air, Po_2 = 100 mmHg in the lungs. After addition of CO, so Pco = 0.4 mmHg, there are equal molar amounts of CO and O_2 in the blood.



	True	False
Carbon monoxide increases the affinity ('tightness of binding') of haemoglobin for oxygen.	X	
0.4 mmHg of carbon monoxide reduces the solubility of oxygen in plasma.		X
Carbon monoxide reduces the amount of functional heamoglobin in the blood in physiological conditions.	X	

Explanation:
This question was inspired by Kieran Toms of the University of Cambridge.

This question assesses understanding of binding kinetics and equilibria from a more quantitative perspective.

- At low PO2, more oxygen is carried (curve is shifted leftwards).
- The small upwards slope after Hb saturation is unchanged.
- The maximum capacity of Hb to bind oxygen is reduced (curve shifted downwards), and oxygen cannot out-compete CO.

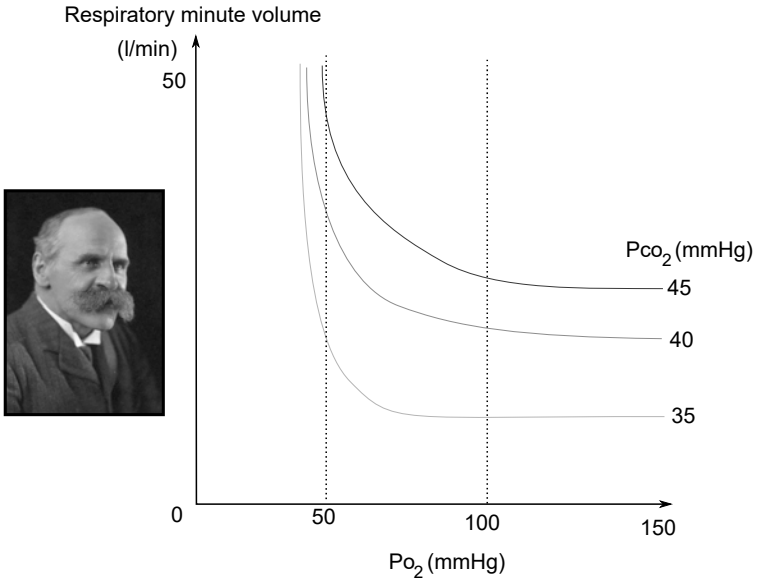
	50 x greater	100 x greater	150 x greater	200 x greater	250 x greater
Choose the nearest relative affinity to the correct answer.					X

Explanation:

- 100 mmHg / 0.4 mmHg = 250x affinity.

ALVEOLAR GASES

John Haldane (1892-1962) discovered many mechanisms which control gas exchange and breathing.
The effect of altering the pressure of oxygen or carbon dioxide in air sacs (alveoli) within human lungs on the volume of air breathed every minute was recorded.
Alveolar air, at sea level, usually has Po_2 = 100 mmHg, Pco_2 = 40 mmHg.



	True	False
Increasing blood acidity (lowering pH) increases breathing rate.	X	
Breathing rate is determined by the oxygen content of blood in normal conditions.		X
At high altitude (atmospheric pressure < 50 % of sea level), falling carbon dioxide pressure in the blood has a greater impact on breathing than falling oxygen pressure.		X
Total blood oxygen content changes negligibly when alveolar oxygen pressure is increased from 50 mmHg to 150 mmHg.	X	

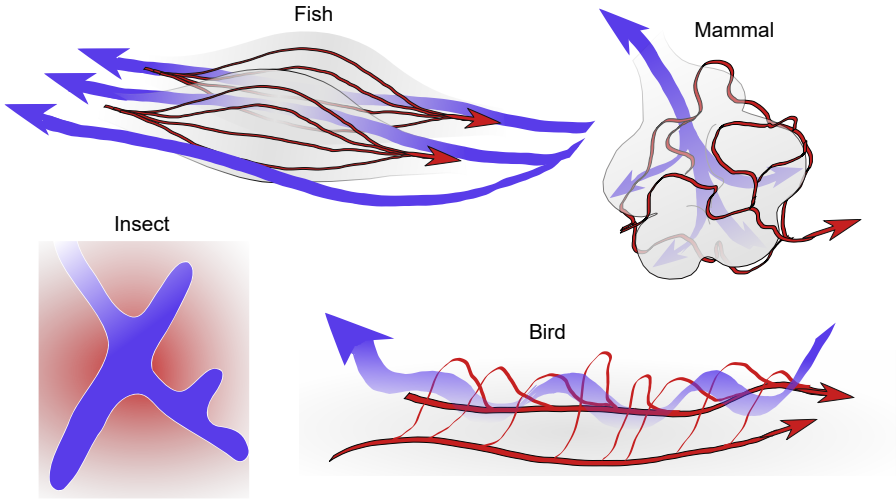
Explanation:
This question was inspired by Kieran Toms of the University of Cambridge.

Candidates will explore how breathing rate is given the oxygen saturation curve of heamoglobin presented previously.

- Increases Pco2 in blood (which is in equilibrium with Pco2 in alveloli)
- There is only a moderate change in breathing rate if O2 varies about it's normal value, of 100 mmHg, between 75 mmHg to 150 mmHg. However, a 5 mmHg change in pCO2 about the normal value can half or double rate. Therefore, the amount of CO2 in blood determines breathing rate.
- Po2 will fall to <50 mmHg, which will increase breathing rate. Increased breathing rate will blow off CO2, so falling Pco2 will break the increase. The steepness of the lines, and the fact they converge, demonstrates the O2 effect dominates.
- Explains why CO2 is used to regulate breathing in normal conditions, and keep O2 well into the safe zone, where Hb is not at risk of rapid desaturation. The curves in this question are directly influenced by those of the previous question.

ANIMAL RESPIRATORY SYSTEMS

The gas exchange surfaces, and the direction of respiratory-medium and blood flow, of different animals are sketched. Mammals and birds must use respiratory muscles to drive air to these surfaces, as shown.



	True	False
Mammals require passive diffusion to exchange gases.	X	
Mammals extract a greater proportion of the air's oxygen than fish extract from water.		X
Air must reach within micrometers of active insect cells.	X	
Bird lungs exchange gas with air for a greater proportion of a breathing cycle than mammals.	X	

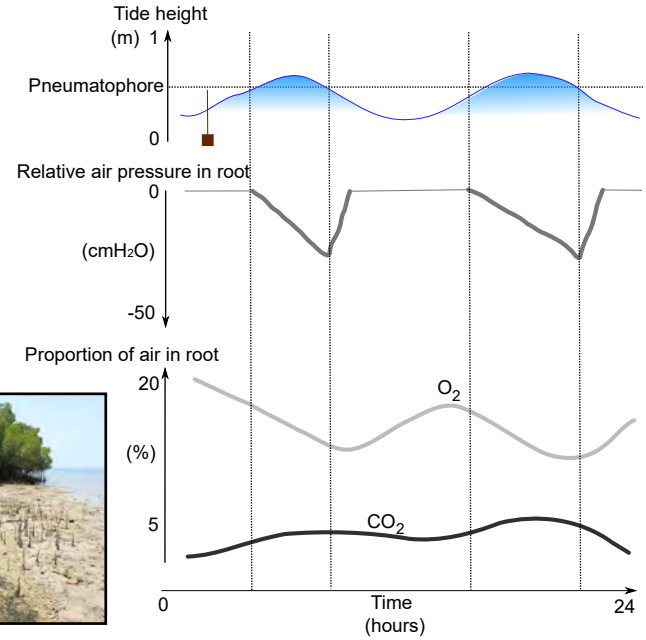
Explanation:

This simple question assesses understanding of gas exchange and lung anatomy.

- All animals require gases to diffuse across the exchange surface, because they are not actively pumped.
- Mammalian alvelar blood and gas can only ever reach euilibrium, whereas countercurrent flow in a fish maintains a concentration gradient until almost all the O2 is extracted from the water.
- Blood (heamolymph) is not actively pumped, therefore gas must diffuse to cells from air, therefore air must be close to cells (diffusion in gas is vastly faster than diffusion in solution).
- Bird lungs always take new gas into lungs (see figure), mammals breath out for half the cycle (see figure) having reached equilibrium.

AIR ROOTS

Mangrove trees grow in intertidal flats, and can have vertical roots (pneumatophores) which act like snorkels for the submerged roots. The mechanism through which they facilitate gas exchange was investigated by recording gas pressures, relative to atmospheric air, as pneumatophores are covered and uncovered by the tide.



	True	False
Air is sucked into roots when pneumatophores are revealed by falling tides.	X	
Respiration in the roots contributes to the air pressure changes in the roots.	X	
Pneumatophores supply CO_2 for photosynthesis.		X
Respiration rate in the roots slows when pneumatophores are submerged.		X

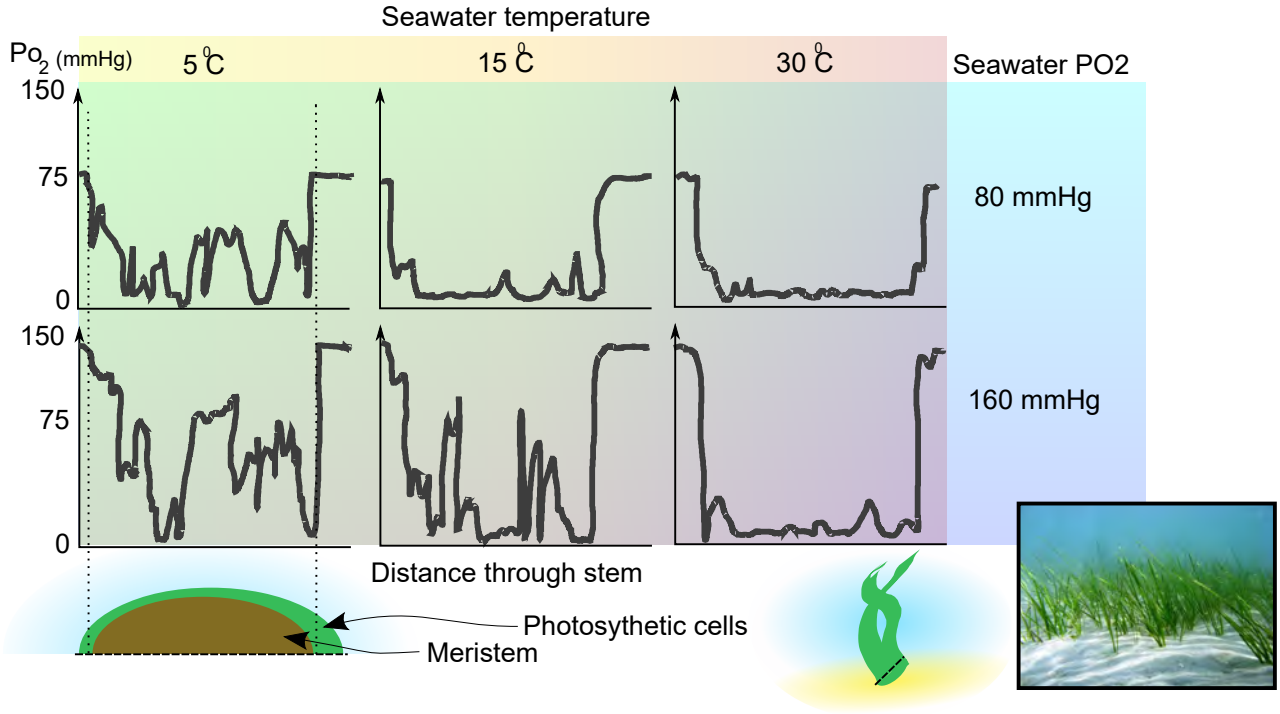
Explanation:
This question was inspired by Adeline Colussi of the Swiss Olympiad and University of Cambridge.

Active gas exchange in plants is also considered. Candidates need to understand the importance of pressure.

- Pressure in roots is negative whilst covered, then restored to 0 as revealed, suggesting suction is built, then air enters.
- O2 is consumed (more than CO2 builds up because it remains dissolved) which contributes to a decline in overall gas pressure.
- They act on the roots, and CO2 actually falls when they're uncovered.
- O2 declines at a relatively constant rate

MERISTEM OXYGEN

Seagrass grows rapidly from a meristem at its base. However, weak growth and death of entire seagrass meadows, have become common in recent years. The oxygen partial pressure along the diameter of a seagrass stem was recorded at different seawater temperatures and oxygen saturations.
Atmospheric Po_2 is usually = 160 mmHg.



	True	False
Rising seawater temperatures could explain the loss of seagrass meadows.	X	
These experiments were performed in the dark.	X	
The meristem has a faster metabolic rate than surrounding tissue.	X	
There is more CO_2 in the meristem at 30 °C, than at 5 °C.	X	
The meristem will receive more oxygen in rough ocean conditions than calm ocean conditions.	X	

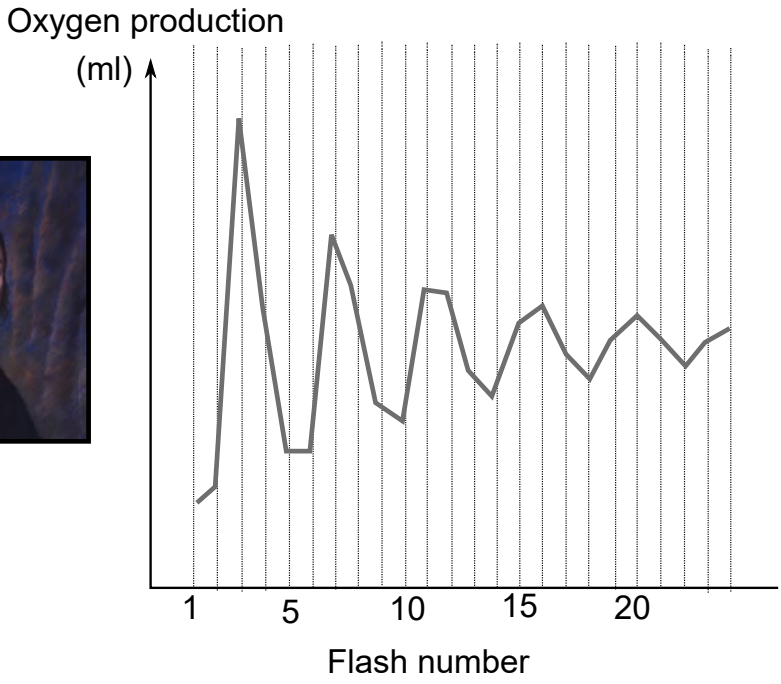
Explanation:
This question was inspired by Morten Eskildsen of the Danish Olympiad.

The effect of gas exchange, metabolism, and environmental factors on Oxygen availability are brought together in this question.

- Oxygen is depleted at high temperatures.
- The photosynthetic cells do not have higher O2 than the surrounding water (actually, slightly lower)
- Oxygen is lower here, indicating increased consumption.
- We're looking at measures of Po2, not [O2], hence changes are not due to low O2 solubility at high temperature, but an interaction between the meristem and temperature consuming O2 at high temperature. Likely faster enzyme action > faster respiration.
- Assuming atmospheric PO2 is fixed at sealevel, the Po2 of water around seagrass depends on how quickly it diffuses to it, compared to how quickly seagrass consumes it. Rough conditions speed this up.

PHOTOSYNTHETIC OXYGEN

Joseph Priestley (1733-1804) discovered that plants consume CO_2. In this process they produce elemental oxygen, which he also discovered. In chloroplasts, the oxygen-evolving complex loses single electrons when exposed to light. After a specific number of electrons are lost, the complex regains electrons from water to produce oxygen, in a cycle. Consecutive pulses of light were flashed at a solution of chloroplasts, and the amount of oxygen produced from each flash was recorded.



	True	False
2 light pulses are sufficient to complete the oxygen-evolving cycle.		X
A maximum of 4 electrons is lost by the complex.	X	
At the beginning of the experiment, most complexes had already lost 1 electron.	X	
More oxygen is evolved for the same light exposure at the end of the experiment.		X

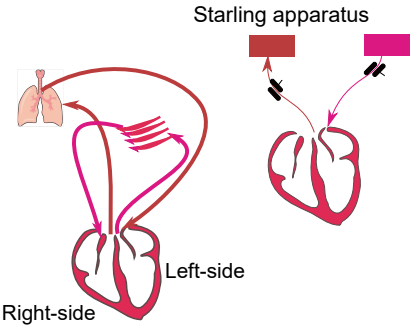
Explanation:

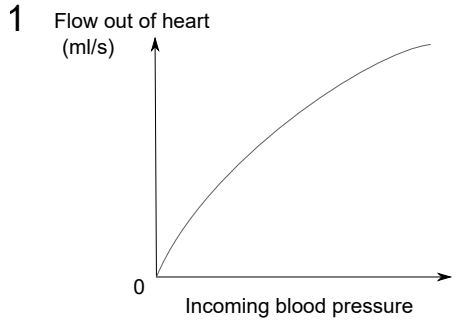
This question explores the molecular chemistry of photosynthesis.

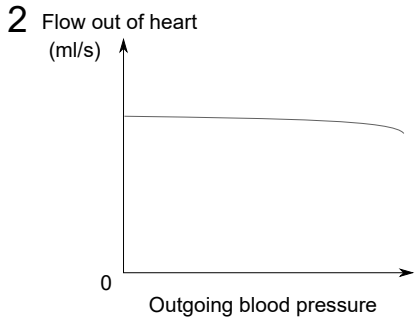
- Oxygen is evolved every 4th flash (wavelength peak-to-peak).
- See above
- Three flashes were sufficient to generate the first spike in oxygen evolution.
- The pulses get smaller (because the OECs gradually loose synchronisation, as flashes don't stimulate 100 % of them), but the mean per flash (centre-line) does not drift.

FRANK-STARLING LAW

William Harvey (1578-1657) discovered that the heart pumps blood around the body in a circuit. Ernest Starling (1866-1927) discovered many of the fundamental properties of the circulatory system, including how cardiac output (the amount of blood pumped in a given time) is controlled. Starling completely removed a beating heart from the body, and attached it to an apparatus that allowed him to alter the pressure of incoming 'venous' (1) or outgoing 'arterial' blood (2). He then measured cardiac output.
Both the left and right-sides of the heart gave similar results.







	True	False
Responses to exercise include toning (contraction of smooth muscle) of the veins.	X	
If outflow from the right-side of the heart increases, nervous or hormonal coordination is required for outflow from the left-side of the heart to match it.		X
The energy required for the heart to beat increases as venous blood pressure increases.	X	
In the early stages of heart failure, cardiac output can be maintained if blood volume is increased.	X	

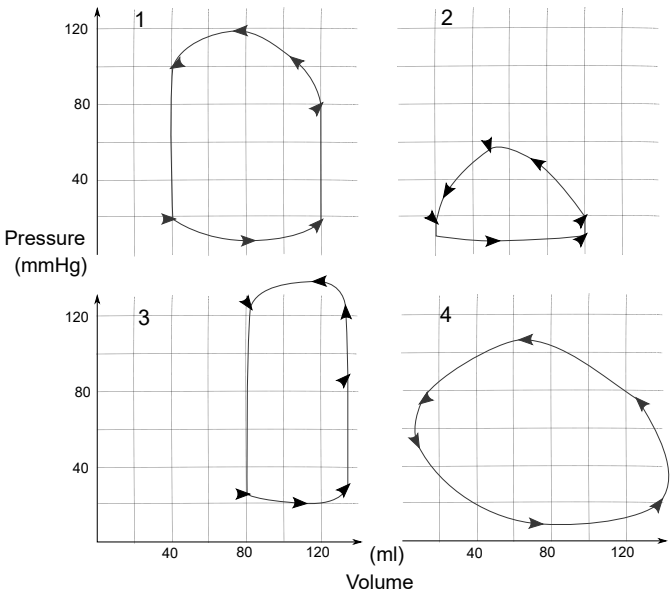
Explanation:

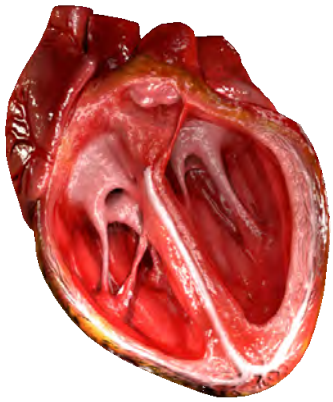
This question explores how cardiac output is controlled. (The implication in most textbooks that heart rate and stroke volume is actively increased to cause an increase output is misleading, given that the heart cannot suck blood through veins, since they would collapse). As alluded to in the stem, and shown in the data, the heart can only pump blood that the veins deliver to it, and will adjust to pump all of that blood.

- This is infact the primary aim of all global responses to exercise. Toned veins channel blood quickly to the heart, raising incoming blood pressure. This is seen to have a steep effect on cardiac output.
- If right heart outflow increases, then blood will build up in the left heart more quickly. Can see from graph, this increases cardiac output as above. This measurement is from an isolated heart. (The lungs hold only 2-3 beats worth of blood, and only a tiny imbalnce in cardiac outputs would cause oedema, or collapse the low pressure pulmonary vesseles. No mechanism, other than starling's, is sufficiently rapid or accurate to balance them.
- Increased venous blood pressure leads to increased cardiac output. If the heart is pumping more blood each beat, it will require more energy.
- Kidney activity determines blood volume. Blood volume determines the pressure of venous blood. This determines cardiac output. Arterial blood pressure is dependent on cardiac output. Therefore, the physiological response to heart failure is to boost water retention, to drive more blood to the heart, to force it to pump more. This explains the swollen ankles, and other water-retention symptoms in elderly people.

PRESSURE-VOLUME LOOPS

The pressure and volume of beating ventricles can be measured as they change with time.
Recordings (1) and (2) are from the same resting, healthy heart, beating at 60 beats per minute (bpm).
At maximum cardiac output of 28.8 l/min, the maximum ventricular volume doubles, and the minimum ventricular volume halves.
Recordings (3) and (4) are from different diseased hearts.





	2 l/min	5 l/min	6 l/min	7 l/min	10 l/min
Choose the nearest output to the correct answer.		X			

Explanation:

- 60*(120-40) = 4800 ml / min

	100 bpm	125 bpm	150 bpm	175 bpm	200 bpm
Choose the nearest rate to the correct answer.		X			

Explanation:

- Double volume is 120*2 = 240 ml. Half is 40/2 = 20 ml. Hence SV becomes 240 - 20 = 220 ml. 28800 / 200 = 131 bpm

	True	False
Recording 1 is of the right-side of the heart, recording 2 is of the left-side of the heart.		X
Recording 3 indicates an aortic (arterial) obstruction.	X	
Recording 4 indicates leaky heart valves.	X	

Explanation:

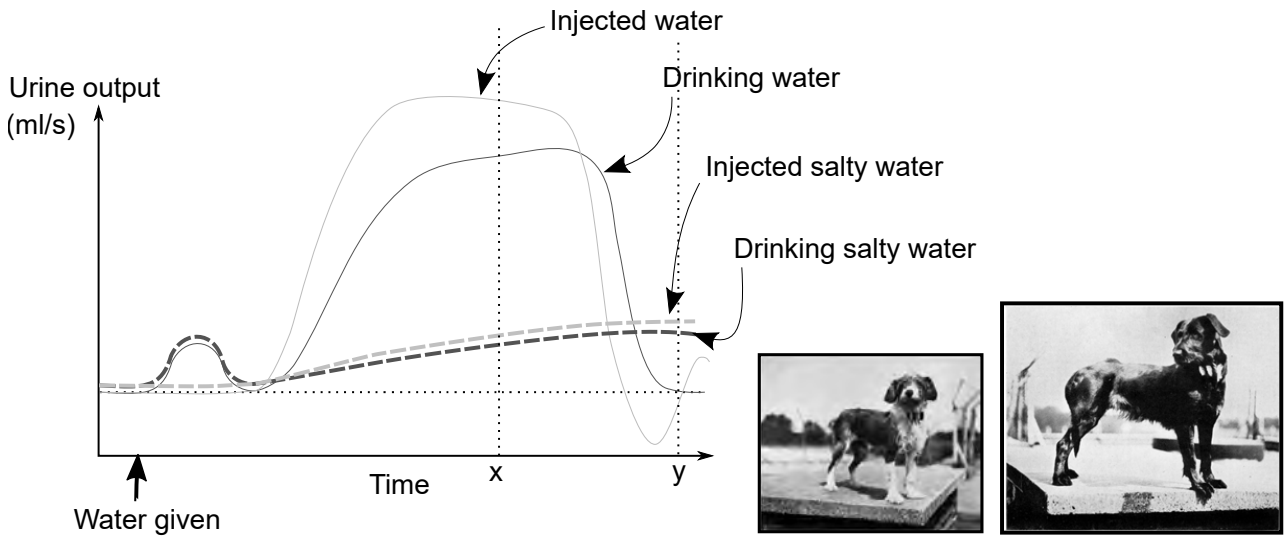
This question was inspired by Kieran Toms and Becky Peel of the University of Cambridge.

The physics of an individual heartbeat in different circumstances is explored. Cadidates are assessed on understanding of the different sides of the circulation and the anatomy of the heart.

- They both come from the same heart, and as expected, show the same volume change each beat. (1) generates a much higher pressure, so is pumping to the body, rather than the lungs.
- The stroke volume is slightly decreased, but the heart operates at a larger volume (to generate more forceful contractions via Starling's mechanism). The pressure generated is higher than usual. This is consistent with a heart struggling to pump against an afterload, such as a plaque, clot, or rigid vessels.
- The heart is unable to generate pressure without changing in volume, indicating leaks.

BLOOD OSMOLARITY

Ernest Verney (1894-1967) explained the regulation of urine production. At the indicated time, dogs (Canis lupus familiaris) were given equal volumes of fresh water, or salty water of the same concentration (osmolarity) as blood, orally or through jugular injection. The volume of urine generated was measured with a catheter.



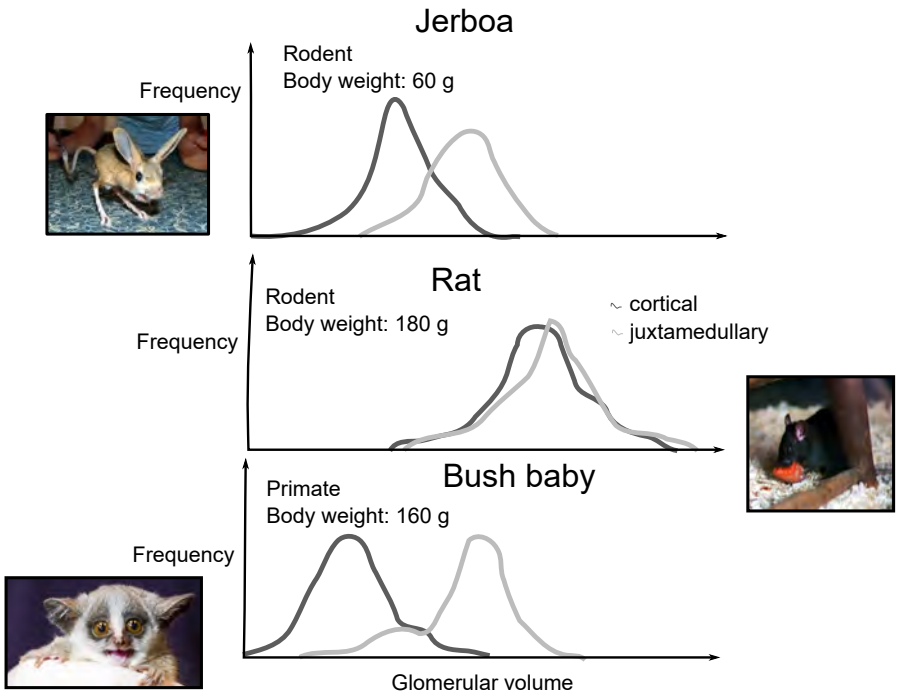
	True	False
Blood volume is adjusted more quickly than blood osmolarity.		X
Blood osmolarity receptors are the dominant regulators of urine production.	X	
Receptors in the gastrointestinal tract regulate the kidneys.	X	
Urine at time X has a higher osmolarity than urine at time Y.		X

Explanation:
This question considers regulation of the circulatory system in the long term. Candidates need to consider the influence of different factors, sensors and responses.

- Compare salty water to fresh. Urine output changes slowly, to a lower degree, and for a longer time. (osmolarity swings cause quick death, volume disrupts ardiac output so blood pressure, which can be buffered for a time by vessel constriction/relaxation).
- Osmolarity as above. Compare injection to drinking - the common effect on the blood produces the biggest spike.
- There is a small spike after drinking, not driven by osmolarity, or changes to the blood. This is an anticipatory response before fluid is absorbed.
- After fesh water input, dilute urine is produced to remove it, and this is corrected by Y. After isosmotic input, the urine will remain isosmotic.

ANIMAL NEPHRONS

In kidneys, glomeruli are sieves which filter plasma into nephrons. Nephrons modify this fluid, and reabsorb or excrete it. The volumes of individual glomeruli, leading to two types of nephron, were measured in different animals. In all species, juxtamedullary nephrons are much fewer in number than cortical nephrons, but produce more concentrated urine.



	True	False
Glomerular volume is proportional to body size.		X
Bush Babies (Galagidae) live in arid habitats.	X	
Jerboa (Dipodidae) and Bush baby nephron volume distribution has evolved convergently (not inherited from a common ancestor).	X	
In rats (Rattus), the majority of urine is derived from juxtamedullary nephrons.		X

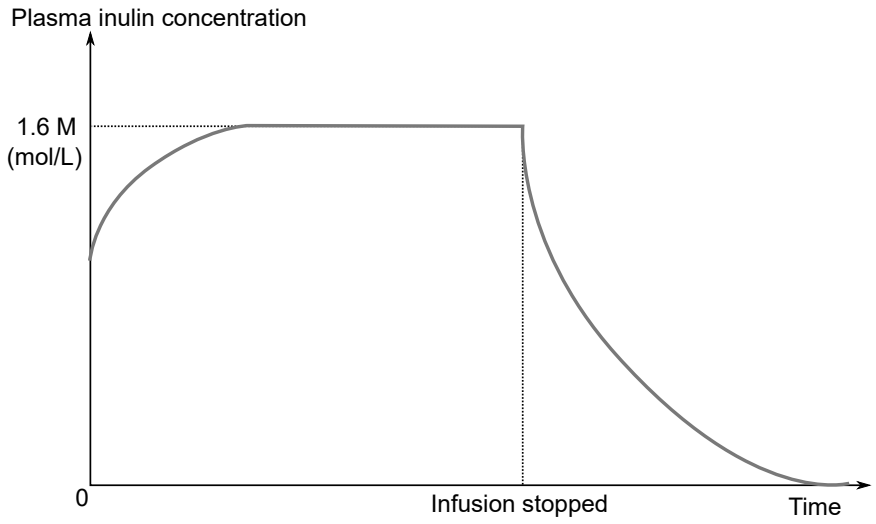
Explanation:
This question was inspired by Rekha Vartak of India.

The role of kidney anatomy in maintaining blood volume/osmolarity in different environments is explored.

- .Compare Bush baby to Jerboa.
- Have comparitively large juxtamedullary nephrons to produce more concentrated urine, to conserve water.
- They are very distantly related, and the closer rat has a different distribution. Correlates well with habitat, not clade.
- Cortical nephrons dominate in all species.

RENAL FILTRATION

Inulins are inert polysaccharides which cannot cross cell membranes. Inulins were infused into a human vein at a constant rate of 0.2 moles per minute. After infusion is stopped, a total of 25 moles of inulins were collected in the urine.



	True	False
Rate of inulin secretion is proportional to its concentration in blood.	X	
A drug which freely passes through cell membranes will be lost in urine at a faster rate than inulins, when at the same concentration in blood.		X

Explanation:
This question was inspired by Mats Carlberg of Sweden, and Kieran Toms of the University of Cambridge.

The importance of kidney anatomy on the secretion of different substances is explored. More about filtration in glomeruli.

- Exponential decline after infusion stops. The definition of exponential is the rate of change is proportional to the amount.
- As filtrate is concentrated into urine along the nephron, its volume decreases. This causes inulin to become more concentrated in the urine, but something else would diffuse out, back into the body. Thus it would be secreted more slowly.

	25 ml/min	50 ml/min	75 ml/min	100 ml/min	125 ml/min
Choose the volume closest to the correct answer.					X

Explanation:

- Rate of addition and removal equal when 0.2 Moles given every minute and concentration is 1.6 moles/litre. Hence, 0.2/1.6 = 0.125 l/min.

	8 l	16 l	24 l	32 l	40 l
Choose the volume closest to the correct answer.		X			

Explanation:

- 25 moles is distributed in a volume which gives a final concentration of 1.6M. 25/1.6 = 15.6 l.

SALT MARSHES

Most of the best farmland, including the English fens, is low lying and threatened by rising sea levels. Spartina patens and Typha angustifolia are marsh plants. To investigate the effect of seawater exposure on these species, they were planted in saltwater marshes and freshwater marshes, with and without neighboring plants (1), or in greenhouses at six salt concentrations (2).

1

	Average biomass (g/cm^2)			
	Spartina patens		Typha angustifolia	
Neighbours	Salt	Fresh	Salt	Fresh
+	8	3	0	18
-	10	20	0	33

2

		Salinity (parts per thousand)	0	20	40	60	80	100
Maximum biomass (g/cm^2)	Spartina patens		77	40	29	17	9	0
	Typha angustifolia		80	20	10	0	0	0

	True	False
Spartina patens is more salt-tolerant than Typha angustifolia.	X	
Spartina patens physiology is better adapted for saltwater exposure than freshwater exposure.		X
Spartina patens will become more common as sea-levels rise.	X	
The distribution of Typha angustifolia in habitats with graded salinity is determined by competition.		X

Explanation:
This question was inspired by Quyen Nguyen Van of the Vietnamese Olympiad.

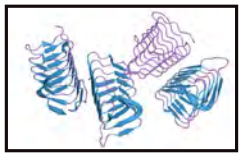
The ability of plants to regulate osmolarity in different environments is also explored.

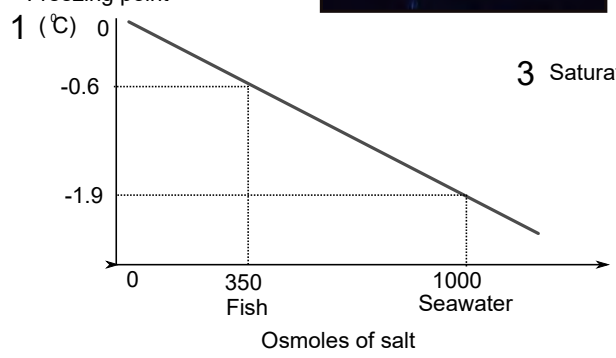
- It mass is higher in salt march, and it survives higher salt concentration.
- Without competion, it has a higher mass in low salt conditions.
- It is better able to outcompete other plants that cannot tolerate salt, and so in a natural environment, has a higher growth in salty conditions.
- It is able to grow with competition in fresh water, but cannot survive moderate salt. Therefore, it is restricted by abiotic, rather than biotic factors.

ANTARCTIC FISH

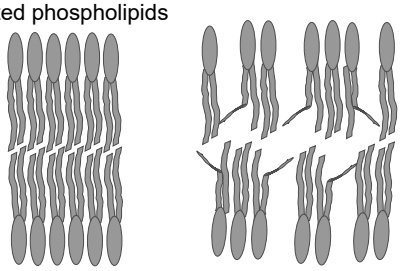
The Royal Research Ship Sir David Attenborough and submarine Boaty McBoatface will explore British Antarctica. Life here exists below the freezing temperature of usual fish, which is determined by their osmolarity (1). Salt accounts for the majority of blood's osmolarity. Antarctic fish are therefore prone to freezing, which usually occurs by the expansion of pre-existing ice crystals in the water. Some Antarctic fish reduce their freezing point by > 2 ^{o}C by secreting antifreeze proteins into the blood (2). Additionally, Antarctic fish must have an appropriate cell membrane chemistry, to prevent their membranes from becoming too rigid at low temperatures (3).

2





3 Saturated phospholipids



Unsaturated phospholipids

	True	False
Fish staying at great depth under floating ice shelves need to produce antifreeze proteins.		X
The anti-freeze proteins function mainly by increasing the osmolarity of the fish.		X
Antarctic fish have increased expression of phospholipid desaturases.	X	
Antarctic fish have better temperature sensors and dynamic responses to temperature than temperate fish.		X

Explanation:

The impact of osmolarity on temperature tolerance, and other methods to tolerate cold is explored. Candidates' understanding of physical chemistry in biology is assessed.

- Away from existing ice crystals, the fish exist in a supercooled state.
- To account for a >2C drop in freezing temperature, their osmolarity would have to increase many fold. Instead they bind small ice crystals, and somehow stop their expansion.
- Saturated lipids pack tightly, with lots of intermolecular interaction, which causes them to become rigid at low temperature. Desaturases change the shape, to loosen the intermolecular bonds. (Butter versus spreads).
- Temperatures at the poles are stable and always very cold. Seasons, weather, currents etc, can result in wild swings elsewhere, so these fish are able to sense and respond to temperature, instead of consituitively adapting to cold.

CYANOBACTERIA EVOLUTION

Scientists are uncertain how Natural Selection shapes genome size, gene number, physiological flexibility and other important features in response to environmental pressures. Ecological and genetic characteristics of four species of marine cyanobacteria are listed in the table. Prochlorococcus are the most abundant cyanobacteria on earth. The Prochlorococcus lineage evolved from Synechococcus.

	Synechococcus	Prochlorococcus eNATL	Prochlorococcus eMED4	Prochlorococcus eMIT
Depth at which found	Very deep	Deep	Shallow	Shallow
Region in which found	Global	Global	Poles	Equator
Ability to tolerate low nutrient conditions	Cannot tolerate	Can tolerate	Can tolerate	Can tolerate
Ability to tolerate high light exposure	Cannot tolerate	Cannot tolerate	Can tolerate	Can tolerate
Ability to tolerate high temperatures	Cannot tolerate	Cannot tolerate	Cannot tolerate	Can tolerate
Genome size (mB)	2.4	1.87	1.66	1.71
Number of genes in genome	2700	2100	1900	1700

	True	False
A species requires more genes to specialise to a new habitat.		X
Prochlorococcus species can tolerate low nutrient conditions because they have more genes with which they can utilise their environment.		X
Intense equatorial sunshine drove the evolution of light tolerance.		X
Measuring genome size can be used to estimate the number of genes Prochloroccous has.		X

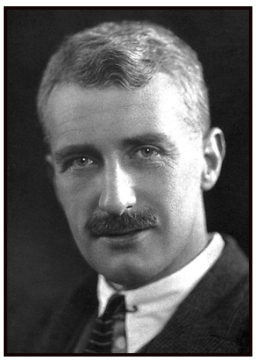
Explanation:
The genetic features that allow organisms to tolerate different environments is explored.

- Species tend to loose genes they no longer use as they specialise.
- Have fewer genes.
- Correlates better with living in shallow water.
- The three Prochloroccus have no correlation between genome size and gene number, within the species.

REPRODUCTION & EVOLUTION

ORGANISM SCALING

Archibald Hill (1886-1971) invented the field of biophysics, which can use simple geometric equations to predict how the anatomy of large and small animals differs.
(1) Organisms exchange substances across a surface area. These substances are used to supply a volume of tissue.
(2) The maximum force a muscle can generate is proportional to the number of muscle fibres contracting in parallel.
(3) The maximum force a column can withstand is proportional to its cross-sectional area.



	True	False
Increasing an organism's mass 8 times approximately halves its surface area to volume ratio.	X	
Diffusion rates are more likely to be inadequately low for large animals than small animals.	X	
Larger animals can carry heavier objects, compared to their body weight, than small animals.		X
A cat's (Felis silvestris catus) bones are disproportionately thick, as a ratio of their body size, when viewed alongside an elephant's (Elephantidae) skeleton.		X

Explanation:
This question was inspired by Becky Peel of the University of Cambridge.

Candidates ability to apply basic maths to biological problems is assessed.

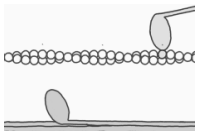
- S proportional to l^2. V proportional to l^3 . Hence, S/V is proportional to l^{-1}. M is proportional to V. Hence, S/V is proportional to $m^{-⅓}$.

  0.5 = 8^(-1/3)

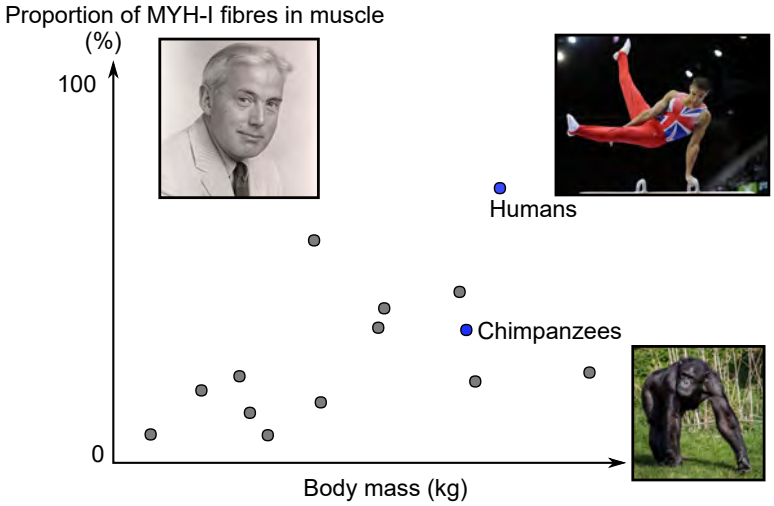
- See surface area:volume (the derivation was hard, so appropriate to award 2 marks based on it)
- Muscle force proportional to muscle area which is l^2. Body mass proportional to V is propotional to l^3. Therefore body mass increases more rapidly than strength, with size.
- As for muscles, Elephants weight puts more force on their bones than is made up for by their increased cross section.

MUSCLE ANATOMY

Hugh Huxley (1924-2013) proposed the sliding filament theory of muscle contraction. Myosin can bind actin filaments, then change conformation, tugging on actin. Skeletal muscle myosin can only generate tension on actin by this change of conformation, and releases actin immediately once it is complete. During each cycle of binding, myosin hydrolyses one ATP molecule.



Myosin is found as two alternative forms; MYH-I or MYH-II. Individual muscle fibres either contain MYH-I, or MYH-II, but individual muscles contained a mix of fibre-types. The mix of fibre-types in different mammal species (dots) was measured. MYH-II cycles more quickly than MYH-I.



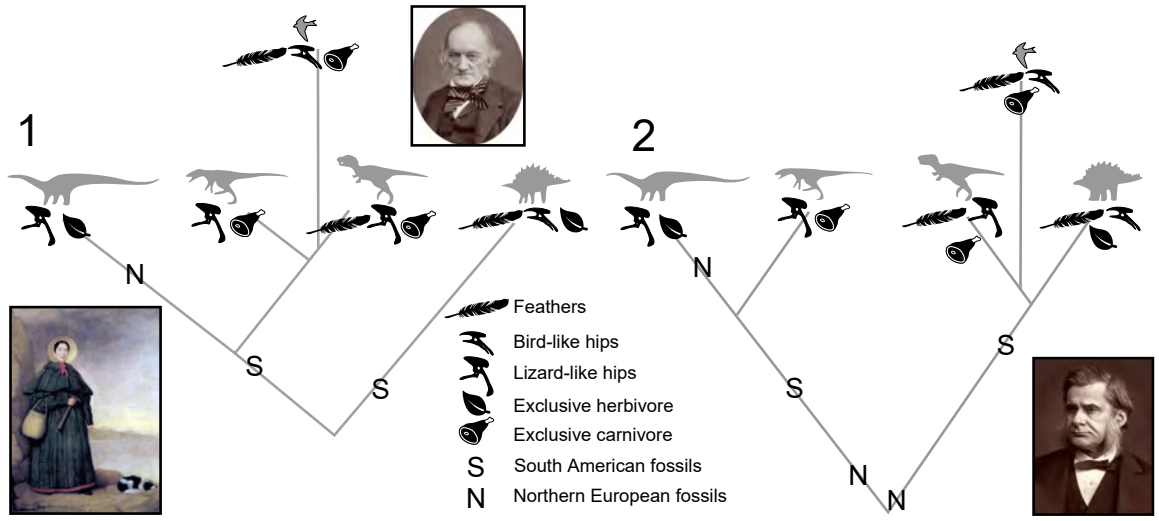
	True	False
Human muscles contract more quickly than chimp (Pan) muscles when opposed by the same load.		X
A muscle fibre generates more force when it is shortening rapidly, compared to when its shortening is resisted by a load.		X
Chimps generate a greater proportion of the ATP in their muscles aerobically, compared to humans.		X
The most recent common ancestor of humans and chimps is likely to have had muscles more similar to humans' than chimps'.		X
A tensed muscle that is not shortening, does not consume ATP.		X

Explanation:
This complex question requires candidates to extrapolate several aspect of physiology and ecology from a simple biochemical mechanism. Ability to relate biochemistry to its consequences is assessed.

- More human fibers are MYHI than in chimpanzees, which contract slower.
- Myosin can only generate force in the brief period it is bound and changing conformation. In quickly sliding fliaments, this change is completed quicker, and a greater proportion of myosin is not bound, but cycling back into position. Imagine pulling a heavy load - you go slower and take little steps to spend more time with your feet on the ground.
- MYHII cycoles rapidly, and therefore consumes ATP more rapidly, so relies on anaerobic glycolysis to a greater extent, meaning Chimps are less efficient and quickly fatigue.
- Humans are an outlier - the only species known that has a predominance of MYHI fibers. Reflects humans incredible ability in endurance activities. The ancestral condition is therefore similar to chimps.
- Can only generate tension by changing conformation to tug on actin. Therefore, myosin runs on the spot. Hence muscle fatigues. even when not moving, if loaded.

DINOSAURS

Mary Anning (1799-1847) developed the concept of prehistoric life, by collecting fossils. Richard Owen (1804-1892) coined the term dinosaurs, whilst Thomas Huxley (1825-1895) used fossils to show birds (Aves) evolved from, and are, dinosaurs (Dinosauria). Until last year, scientists believed the dinosaur phylogeny was as shown in (1). In 2017, British scientists analysed many more fossils and produced a new tree (2) based on hundreds of characteristics, including those shown. For birds, the characters are representative of ancestral birds.



	Phylogeny (1)	Phylogeny (2)
Some sauropods (Sauropoda; the group farthest left in each tree) were feathered.	X	
Bird-like hips evolved multiple times (convergence)	X	
Exclusive carnivory evolved multiple times.		X
The earliest dinosaurs evolved in the Southern hemisphere.	X	

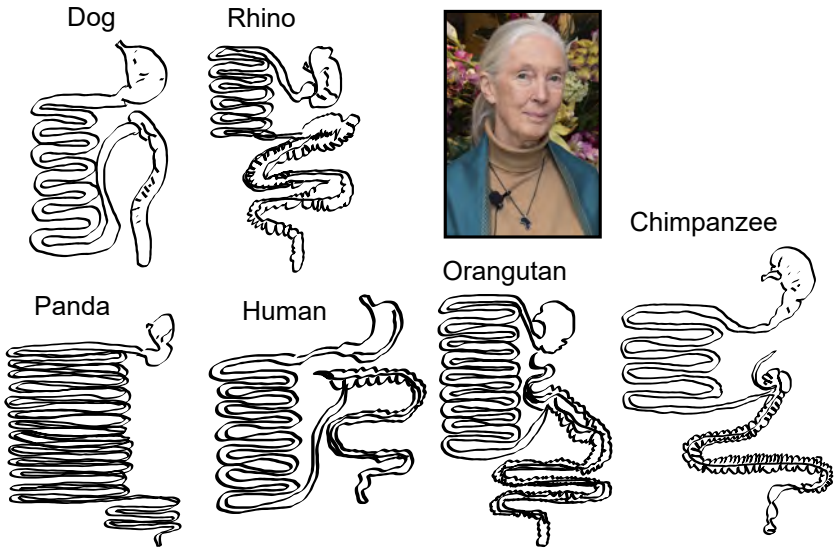
Explanation:

The question assesses understanding of phylogenies and homologous versus convergent traits. The idea of using Occam's razor to formulate a theory is explored.

- Stegosaurus, Tyrannosaurus and birds have been found with feathers, therefore, it's likely that all dinosaurs possess them under the current phylogeny.
- Tyrannosaurs, with lizard like hips, is more closely related to chickens than stegosaurus (with bird hips) in the current phylogeny.
- Both major groups within the new phylogeny contain exclusive herbivores, and exclusive carnivores. (It is suggested ancestral dinosaurs were omnivores).
- Fossils closest to the root of the tree were found in south america. Extra fossils have since been analysed that are more basal, and found in Britain.

DIGESTIVE SYSTEMS

Dame Jane Goodall (1934-present) discovered that great apes (Hominidae) use tools, to access more nutritious food, and hunt for meat. Bears (Ursidae) exhibit similar behaviour, but giant pandas (Ailuropoda melanoleuca) only eat bamboo. These different animals have gut anatomies which reflect their diets, as shown. Sketches have been enlarged to similar sizes to allow comparison. Dogs (Canis lupus) represent a typical carnivore, Rhinos (Rhinocerotidae) a typical herbivore.



	True	False
Humans invest more energy in digestion to acquire nutrients than chimpanzees (Pan) do.		X
Chimpanzees eat more meat and fruits than orangutans (Pongo).	X	
Giant panda digestive systems extract most of the nutrients present in Bamboo.		X
Food passes more rapidly through orangutans than through humans.		X

Explanation:

This question also explores comparative anatomy. Understanding of digestion is assessed.

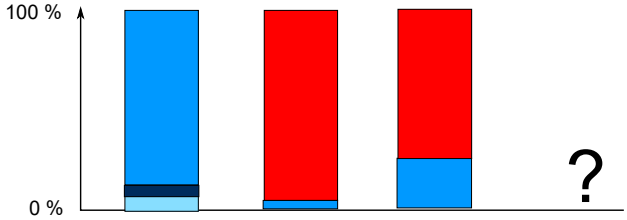
- Carnivores have a high quality, low digestion diet. Herbivores have a low quality, intensively digested diet. Comparing the Dog to the Rhino, the most striking differences are the large, highly folded hind gut, and more complex stomach, of the Rhino. THe Chimpanzee has a larger, more folded hindgut, and folded stomach, compared to human.
- The Orangutan gut looks typically herbiverous, indicating a low quality diet.
- The panda gut has non of the features expected of a herbivore (and looks much like other bears' which eat a highly nutritious diet). Therefore, they only extract a small proportion of the limited energy available in Bamboo.
- The more complex gut, with appendix etc., holds and ferments low quality food to release energy.

PREHISTORIC BRITONS

Stonehenge was built in the late Neolithic (Stone age; ~ 3000 BC) on what was Europe's most important trade route, between Cornwall and the Eastern Mediterranean. In the Early Bronze age (~ 2500 BC), the Beaker phenomenon swept across Europe, and many peoples began producing characteristic pottery (1). To discover whether British people bought and made Beaker pots, or Britain was invaded by a people that did, remains from different sites were genome sequenced. The average proportion of alleles originating from different populations (colours) in the genomes of Neolithic, Beaker and Late Bronze Age individuals was compared (2). Rs4988235(T) is an allele of the gene for the enzyme lactase which causes it to be produced into adulthood. Its frequency in British people through time was measured (3). Lactose is a sugar in milk.

1

2 Average proportion of allels from different populations



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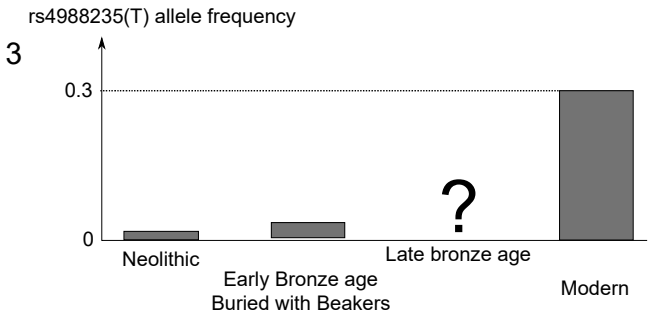


	True	False
A large proportion of Beaker people in Britain were native British people.		X
Beaker people in Britain mostly replaced non-Beaker people.	X	
From this data, it can be concluded that modern Britons are very genetically distinct from bronze age Britons.		X

Explanation:
This question also requires different hypotheses to be tested by comparing shared traits (DNA in this case). Different causes of molecular evolution are explored.

- They are almost all more closely related to a group that is not related to neolithic Britons.
- Very few people related to the neolithic groups remain.
- Just because rs4988235 is at a higher frequency, nothing about the rest of the genome can be concluded.

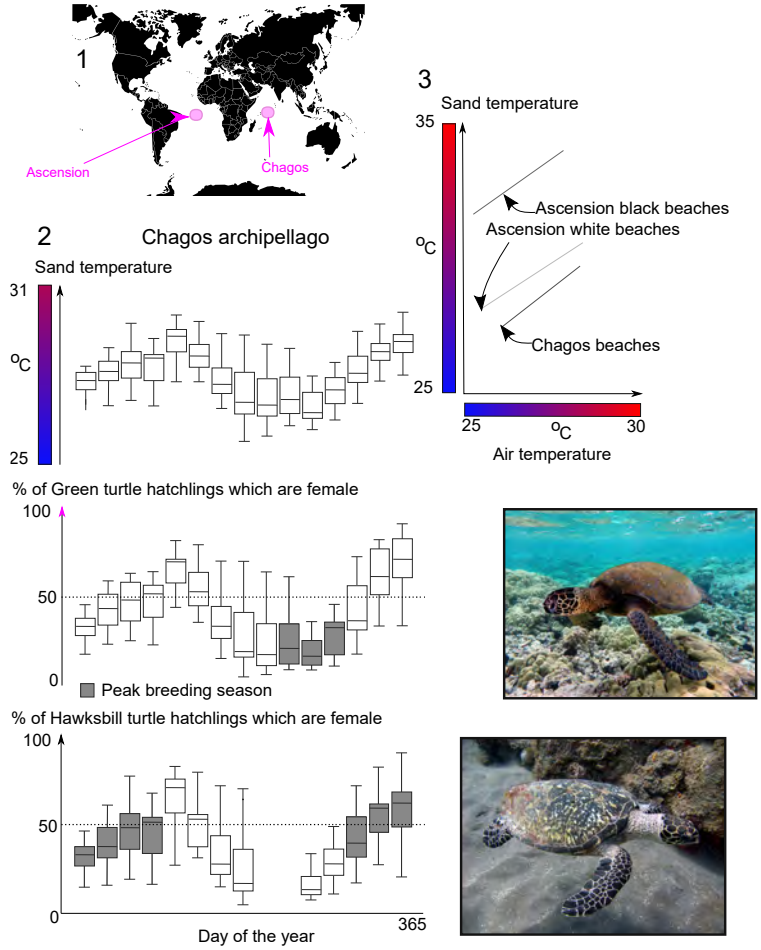
	0.1	0.2	0.3	0.4	0.5
Choose the nearest proportion to the correct answer.					X

Explanation:

- Is dominant because just need some enzyme to digest milk. Hardy weinberg eqm = 1-(0.7*0.7) = 0.51

TURTLES

British Territories in the Atlantic, Indian, Mediterranean and Pacific Oceans are vast new marine reserves which Green turtles (Chelonia mydas) and Hawksbill turtles (Eretmochelys imbricata) inhabit (1). Sex determination in turtles depends on the temperature of the nest, as shown for Chagos Archipelago hatchlings (2). Sand temperature in turn depends on the nest site (3). The majority of breeding occurs in peak breeding season, but a scarcity of males reduces breeding rates.



	True	False
Ascension produces an excess of female turtles.	X	
The Chagos Archipelago produces a roughly balanced sex ratio of Hawksbill hatchlings.	X	
Chagos island turtle breeding will be less disrupted by global warming, than Ascension island turtle breeding.	X	
Conservationists should protect heavily shaded nest beaches as a priority.	X	

Explanation:
This complex question requires candidates to evaluate the interaction of development and geography, and understand several correlations presented in different ways.

- (3) shows Ascension tends to have hotter sand, and (2) shows this gives rise to more females.
- During peak breeding season, hatchlings are ~50 % female, and deviations cancel.
- (3) Slopes are similar, but Chagos is lower, so female dominance won't become as detrimental, as quickly. Absolute value as well as change needs to be considered.
- Dark beaches are hotter because they absorb more sunlight. Shading beaches can cool them, to maintain balanced sex ratios in a warming climate.

TESTES HISTOLOGY

Robert Hooke (1635-1703) popularised microscopy in his famous book Micrographia, and invented the term 'cells'. Analysing the size and shape of cells indicates their identity, whilst the appearance of their nucleus can indicate how transcriptionally active a cell is, or whether it is dividing. Specific junctions between cells allow internal substances to be transferred between them, or external substances to be trapped behind them. Testes have a distinct appearance under electron microscopes, as shown. Germ cells (which could pass their genetic material to the next generation) may undergo meiosis, and gradually adopt a morphology specialised for motility: these mature sperm are released into the centre of fluid filled tubes, in a process that happens in continuous waves.

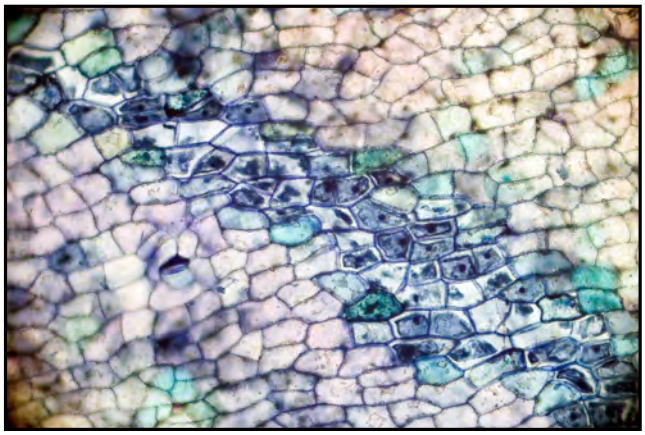
	True	False
Cell i helps prevent autoimmunity against testes-specific antigens.		X
Cell ii is a diploid (has two copies of each chromosome) germ-line cell.	X	
Cell iii facilitates transport of sex hormones (testosterone).	X	
Cell iv is using unique histones (DNA-binding proteins) to super-compact DNA.		X

Explanation:
This question assesses understanding of micro-anatomy and how it influences function in the context of meiosis.

- There are no impermeable junctions between these cells. Actually, the extensive tight junctions between sertoli cells sequester developing spermatids from immune cells.
- It sits at the start of the developing spermatid progression, but is on the somatic side of the tight junctions, so must be diploid. If it wasn't, immune cells would recognise the absence of some cell surface alleles, and destroy it.
- Is an endothelial cell of a capillary. A red blood cell can be seen squeezing through the vessel lumen.
- This cell shows chromosomes sorting out, and an enlarging nucleus in the process of meiosis. Only mature spermatids need to super-compact DNA for efficient swimming.

FLOWER SCENTS

Flowers produce volatile fragrances from their petals to attract pollinators, but only once they have become fertile. Some volatile molecules diffuse through petal-cell (pictured) membranes into the air.
The ABC superfamily of transmembrane transporters use ATP to pump substances out of cells. These include multi-drug resistance pumps that export many foreign chemicals from bacterial, plant and cancer cells. To investigate whether ABC transporters pump some volatile fragrances into the air, scientists generated several testable hypotheses.



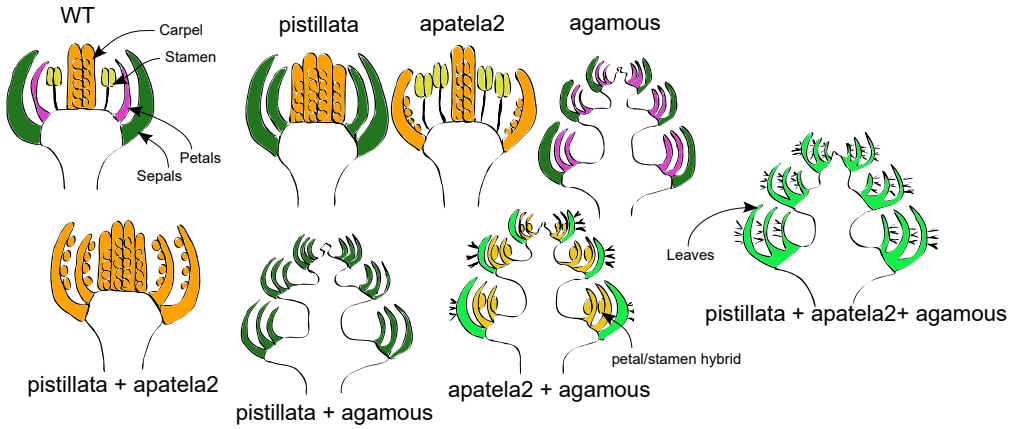
	True	False
An ABC transporter which is most highly expressed in budding flowers, compared to open flowers, is the one involved in fragrance emission.		X
Plant strains which express ABC transporters at high levels in their flowers are more fragrant, compared to strains which express ABC transporters at low levels in their flowers.	X	
There is a higher concentration of volatile fragrances inside petal cells when ABC transporters are blocked.	X	
Altering ABC transporter function has a greater effect on the emission of small volatile molecules, than large volatile molecules.		X

Explanation:
This question assesses understanding of active and passive transport in the context of plant physiology.

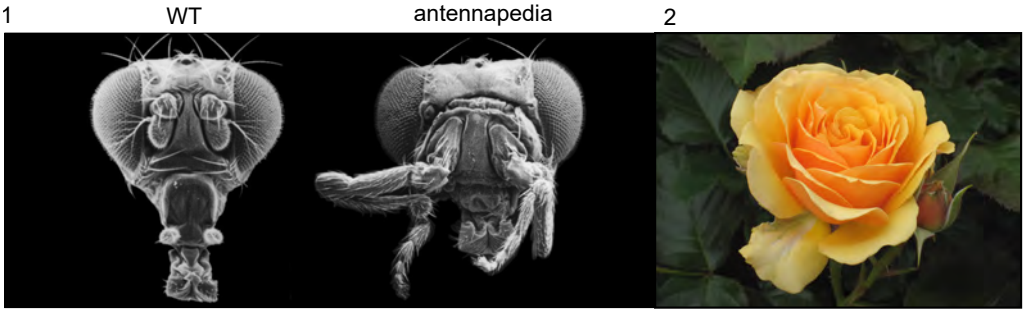
- Expect a strong upregulation once flower becomes fertile. i.e. when it opens compared to when it buds.
- Will pump more fragrance into air.
- Causes a build up because they're not pumped out and diffusion is slower than active transport.
- Small molecules will diffuse through membranes more easily.

ABC MODEL OF FLOWERING

Arabidopsis flowers are formed incorrectly when the pistillata, apatela2 or agamous genes are knocked-out, as shown. Genes which determine the identity of parts of an organism are called homeotic selectors (or HOX genes in animals). HOX genes expressed more posteriorly (towards the anus) tend to repress those expressed more anteriorly (towards the head).



(1) shows a WT fruit fly (Drosophila melanogaster) head, and one which has the antennapedia mutation. (2) shows a typical decorative rose with an agamous phenotype.



	True	False
Homeotic selector genes tend to have small and simple promoters compared to other genes.		X
PISTILLATA expression is necessary for cells to determine they should become part of a flower.		X
Expression of AGAMOUS causes floral meristems to stop growing after four whorls.	X	
The antennapedia mutation is a loss of function, or knock-out, mutation.		X
All these genes are first expressed once a cell is specialising/differentiating into its final role.		X

Explanation:
This question was inspired by Dimitar Epihov of The University of Sheffield, and Remie Janssen of the Dutch Olympiad.

This question explores how the expression of master developmental regulators in specific locations defines organs. The ability to observe phenotypes and hypothesise an explanation is assessed.

- To define a location, they must integrate information about their precise x, y and z positions, and this must be done robustly, since they must be expressed in exactly the right place.
- Without pistilla, an attempt at making floral organs still occurs. Another regulator initiates the flowering program.
- Without agamous, many extra whorls or organs appear.
- Legs are expressed posteriorly to antennae. Therefore the HOX gene dictating the presence of legs must normally be absent from the head, or it would repress the anterior HOX genes. Therefore this HOX must be turned on in an inappropriate position, leading to the repression of antennae HOXs and formation of legs.
- It is seen from the flowers and flies that whole structures, comprising many celly types, form when these genes are altered, therefore they must first act early in development.

COURTING FLIES

Sexual orientation in Drosophila matings (male with female, versus male with female, versus female with female) can be controlled by the gene fruitless. Fruitless mRNA is cut (spliced) in multiple ways to give two forms, FRUITLESS-A and FRUITLESS-B.
The sexual development and sexual orientation of WT and fruitless knockout flies, and flies which express either FRUITLESS-A or FRUITLESS-B, were studied.

Genotype of fly	Male		Female	
	Appearance of fly	Fly mates with	Appearance of fly	Fly mates with
WT	Male	Females	Female	Males
fruitless knockout	Male	Males and females	Female	Males
FRUITLESS-A only	Male	Females	Female	Females
FRUITLESS-B only	Male	Males	Female	Male

	True	False
Fruitless controls the development of appearance in flies.		X
FRUITLESS-A causes flies to court females.	X	
FRUITLESS-B has a role in determining the sexual orientation of female flies.		X
FRUITLESS-A and FRUITLESS-B perform the same role in male and female flies.		X

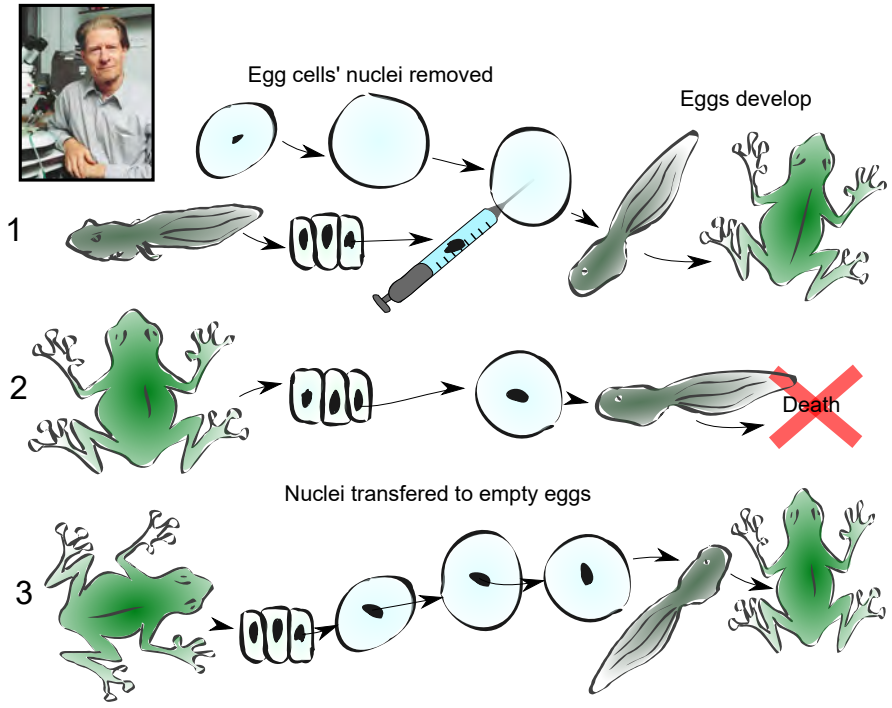
Explanation:
This question was inspired by Kevin Moffat of Warwick University.

This time, the expression of different isoforms of an mRNA in controlling behaviour is explored.

- Appearance is unaffected
- If only A is present, Females are courted by both sexes.
- Females are fine in knockouts.
- Fruitless A is needed in males to make them exclusively attracted to females, but not in females.

MASTER DEVELOPMENTAL REGULATORS

Sir John Gurdon (1933-present) took differentiated cells from tadpoles (1) or frogs (2, 3), and transferred their nuclei to enucleated eggs. These eggs were allowed to develop (1, 2), or the nuclei were passaged through more enucleated eggs (3). He was able to artificially clone animals (Xenopus laevis) for the first time.



	True	False
Gurdon proved adult cells contain all the DNA required by the fetus.	X	
Cytoplasmic factors are sufficient to regulate cell type.	X	
The most powerful (irreversible) regulators of cell type are turned on early in development.		X
Factors which determine cell type can take a long time to act on some genes.	X	

Explanation:
These nobel prize winning experiments are used to explore how potency is controlled as cells adopt a fate.

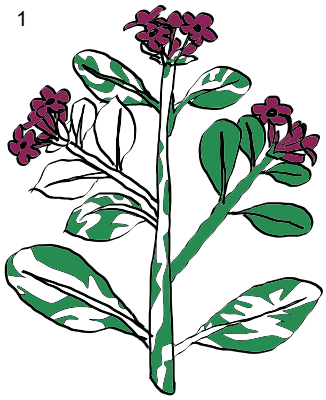
- Famously. The adult cell can generate another adult.
- Putting a skin nucleus in egg cytoplasm reprograms it into an egg.
- (2) versus (1) Earlier cells are easier to reprogram (and need to adopt more different fates).
- (3) versus (2). Prolongues exposure to egg factors is needed to fully reprogram the adult cell.

VARIEGATED PLANTS

Four o'clock plants (Mirabilis jalapa) can have a mix of white and green patches on their leaves, so they appear variegated - a picture showing the different colours of branches possible, but not necessarily the usual pattern of these branches, is shown (1). Variegated plants were grown, and flowers on green, white or variegated branches were fertilised by pollen from green, white or variegated branches. The progeny had the following phenotypes.

Phenotype of branch bearing seed	Phenotype of branch bearing pollen	Phenotype of offspring plant
White	White	White
White	Green	White
White	Variegated	White
Green	White	Green
Green	Green	Green
Green	Variegated	Green
Variegated	White	White, green, or variegated
Variegated	Green	White, green, or variegated
Variegated	Variegated	White, green, or variegated

1



	True	False
Chloroplasts can be transmitted through pollen during Four o'clock plant reproduction.		X
During cell division as a plant grows, each daughter cell has the same composition of alleles.		X
Egg cells in a variegated flower can contain different chloroplasts with distinct genomes.	X	
Older branches of a variegated four o'clock plant are more likely to be all white, or all green, than younger branches.		X

Explanation:
This question was inspired by Dimitar Epihov of The University of Sheffield.

The question explores how genetic material is segregated in different organelles, mitosis and meiosis.

- The progeny phenotype is only affected by the maternal flower.
- Chloroplasts are assorted randomly, so drift occurs, and eventually all white, or all green cells appear.
- Some green, some white > variegated offspring.
- Newer branches are produced from cells which have divided more times, so are more likely to have become all white, or all green.

IVF

Sir Robert Edwards (1925-2013) invented in vitro fertilisation (IVF) and Sir Douglas Turnbull developed '3 parent IVF': the nuclear DNA of a mother and father are transferred into an enucleated oocyte from a second female. The ethicist Baroness Mary Warnock (1924-present) has enabled the UK to pioneer the safest and most advanced reproductive medicines, to combat genetic diseases such as Leigh syndrome.
Leigh syndrome is caused by mutations to the mitochondrial gene COX2. Mitochondrial DNA (mtDNA) in the muscles typically has the following distributions.

Sample	% of mtDNA which is WT	% of mtDNA which is COX2 mutant
Healthy mother of healthy child	100	0
Healthy mother of Leigh's child	30-50	50-70
Healthy child	100	0
Leigh's child	<20	>80

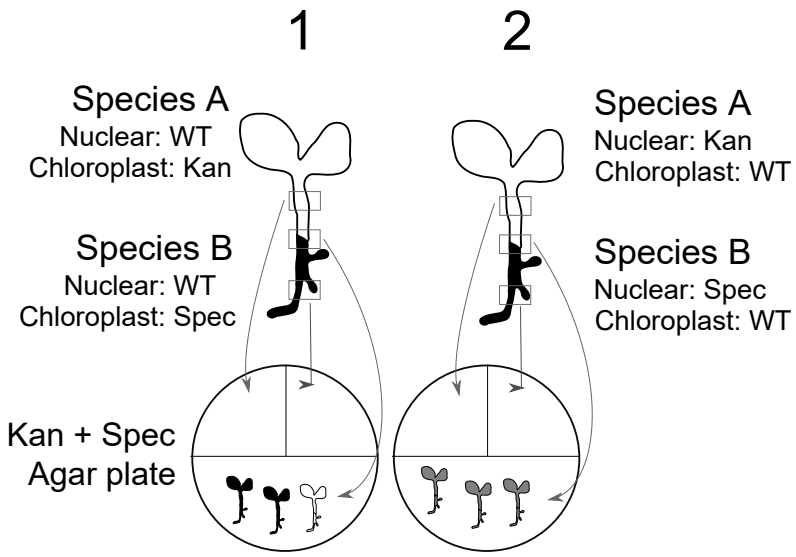
	True	False
30% of fully functional mitochondria is sufficient to prevent Leigh's disease.	X	
The father of a Leigh's child should be screened for COX2 mutant mtDNA.		X
If only a small amount of cytoplasm is accidently transferred with the nuclear DNA, the three-parent IVF child is safe from Leigh syndrome.		X
Rapidly dividing tissues are typically more affected by mtDNA mutations than slowly dividing tissues.	X	
Sampling a cell from an early IVF embryo could determine whether the foetus will develop Leigh syndrome when implanted.		X

Explanation:
This question builds on the previous one to explore mitochondrial disease. Candidates' understanding of how biological knowledge influences medical ethics is assessed.

- Healthy mother can have only 30% healthy DNA
- Mitochondria are not passed down the paternal line
- As in previous question, these data are explained by random sorting of cells. Therefore, even one defective mitochondria could come to dominate the adult tissues of the baby.
- More likely to have a high proportion of mutant DNA, as above. (Hence bone marrow is often severely effected).
- The distribution of mtDNA in one cell is not informative of the rest.

GRAFTING

In nature, different plant species can graft together. An experiment was done where shoots from species A were grafted onto roots of species B. Plant chloroplast and nuclear genomes were independently transformed with different antibiotic resistance genes (Kan and Spec). Single cells from the shoot, root, and graft junction were excised, then grown on agar with antibiotics. Surviving cells are grown into adult plants. Plants phenotype is denoted by its colour.



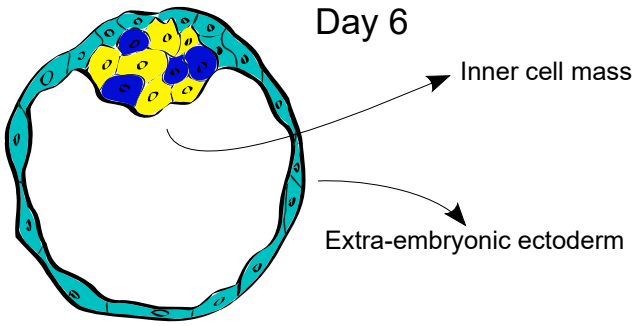
	True	False
Chloroplasts can travel the complete length of the plant.		X
Genomes can be transferred between species.	X	
Plants which grow on the agar plates from (1) can cross with their parents.	X	
Plants which grow on the agar plates from (2) can cross with their parents.		X

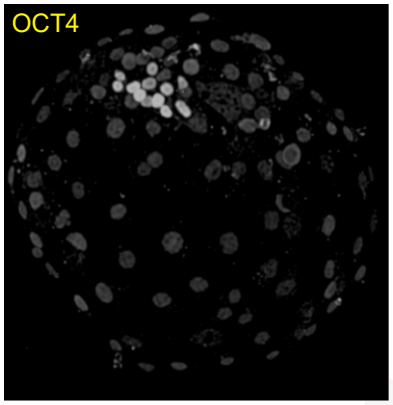
Explanation:
Reference: http://www.pnas.org/content/109/7/2434.full and DOI: 10.1038/nature13291

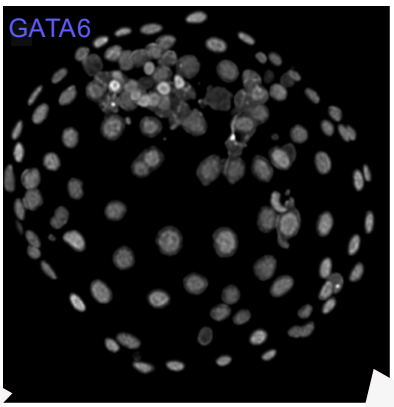
- False. Plant parts from the above and below the graft junction do not grow, so chloroplasts have not moved.
- True, to grow nuclei must have grown in (2).
- True. Mixed chloroplast genomes do not make a new species.
- No. When the nuclei move the genomes are combined, creating a new species. This is seen through the intermediate phenotype. Tetraploids cannot cross with their progenitors as it leads to 3n.

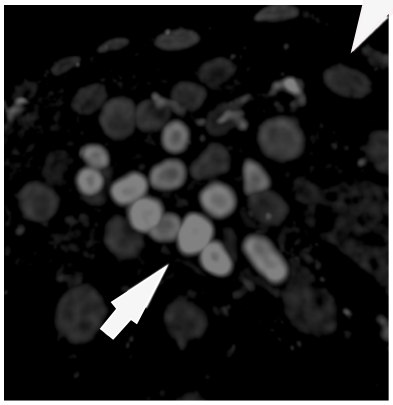
HUMAN EMBRYOLOGY

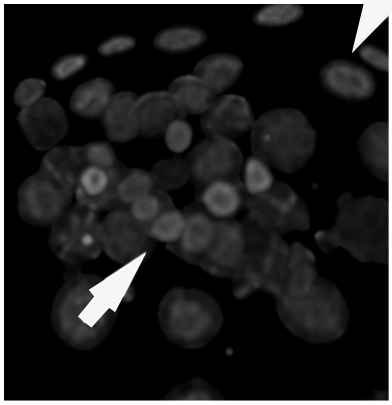
Sir Martin Evans (1941-present) was the first person to culture Embryonic Stem Cells (ESCs)(from a mouse). It is now known that the following transcription factors:
- OCT4 determines ESCs to become epiblast,
- GATA6 determines ESCs to become extra-embryonic endoderm,
-CDX2 determines ESCs to become epiblast.
In all previously known animal studies, OCT4 and GATA6 are found only in the inner cell mass, and block the transcription of one-another, until cells adopt one fate. Additionally, no known animal cells express all three markers at the same time. However, closely related species can have quite different embryos. Hence, in 2016 English scientists grew human embryos in Vitro for a record breaking 14 days, and stained them for these transcription factors. Arrows mark the same point on each image.



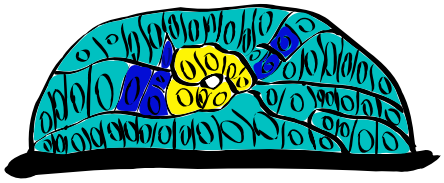




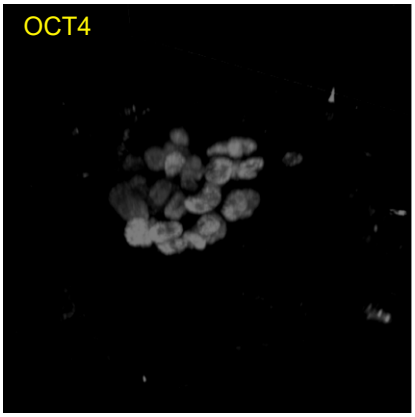


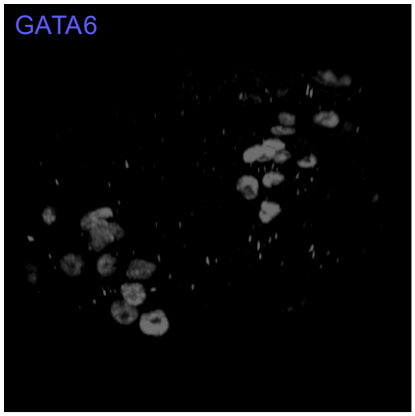


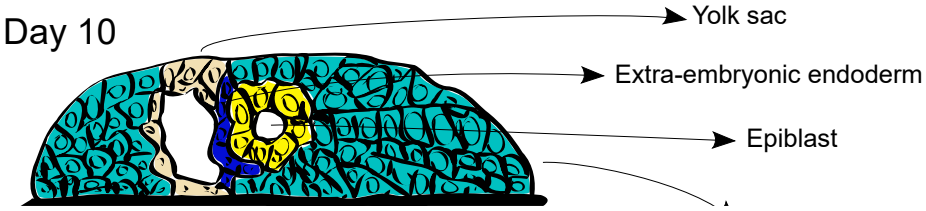
Day 8



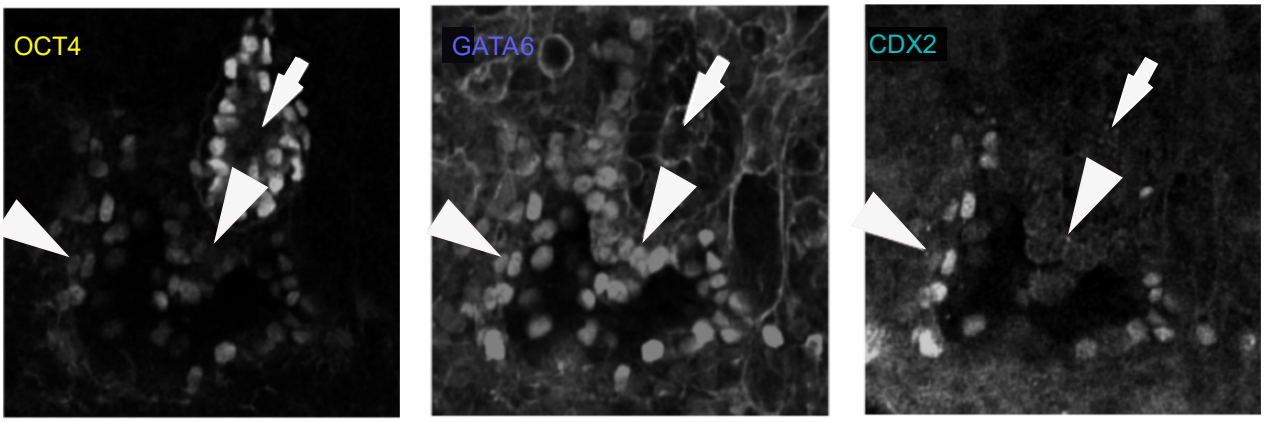
Implants onto artificial uterus







Extra-embryonic ectoderm



	True	False
OCT4 and GATA6 repress one-another to differentiate the inner cell mass in humans.	X	
OCT4 is not found outside the inner cell mass in humans.		X
Human yolk sac cells are typical of previously known animal yolk sac cells.		X
Cells expressing OCT4 may adhere more strongly to one another, than to other cell types.	X	
It can be concluded from these images that a population of GATA6 expressing cells switch their fate after day 8.		X

Explanation:
This complex question ties together ideas of micro-anatomy, cell identity and gene expression. Candidates observational skill is assessed.

- At day 6, there is some overlap between cells expressing high levels of each, but by day 8, they have mostly sorted into exclusive cell types. This is consitent with a stochastic initial expression, followed by one coming to dominate the other in any given cell.
- There are many green cells in the extra-embryonic ectoderm, some brightly so.
- At day 10: Note the ring of green cells, which corresponds to the hollow epiblast. This has a line of red cells to its left, bordering another cavity. There is a line of blue cells marking the other side of this cavity - these are the yolk sac cells. It can be seen that these stain positively for blue, red and green markers. The stem indicates that this is not true of any known animal.
- The OCT4 expressing cells go from being intersperesed throughout the ICM, to being in a clump. This could be because cells change the amount of OCT4 they express with time, or because they stick to one another tightly, which causes them to clump. (In reality, both mechanisms appear to be used, with differential adhesion being the most important).
- At day 8, GATA6 expressing red cells are found either side of the epiblast. By Day 10, they are found only to the left of the epiblast. They could switch their fate, but they could migrate. Students need to realise the limitations of interpreting fixed images.

DOMESTICATION

Plants have a plastic developmental body plan, built up of simple units. Brassica oleracea is the progenitor for many domesticated Brassica crops. During domestication of each crop different units were selected.

Brassica oleracea

Brussel sprouts

Cauliflower

Kale

Kohlrabi

Broccoli

	Shoot apical meristem	Root apical meristem	Leaf	Axillary meristem	Internode
Brussel sprouts				X	
Cauliflower	X				
Kale			X		
Kohlrabi					X
Broccoli	X				

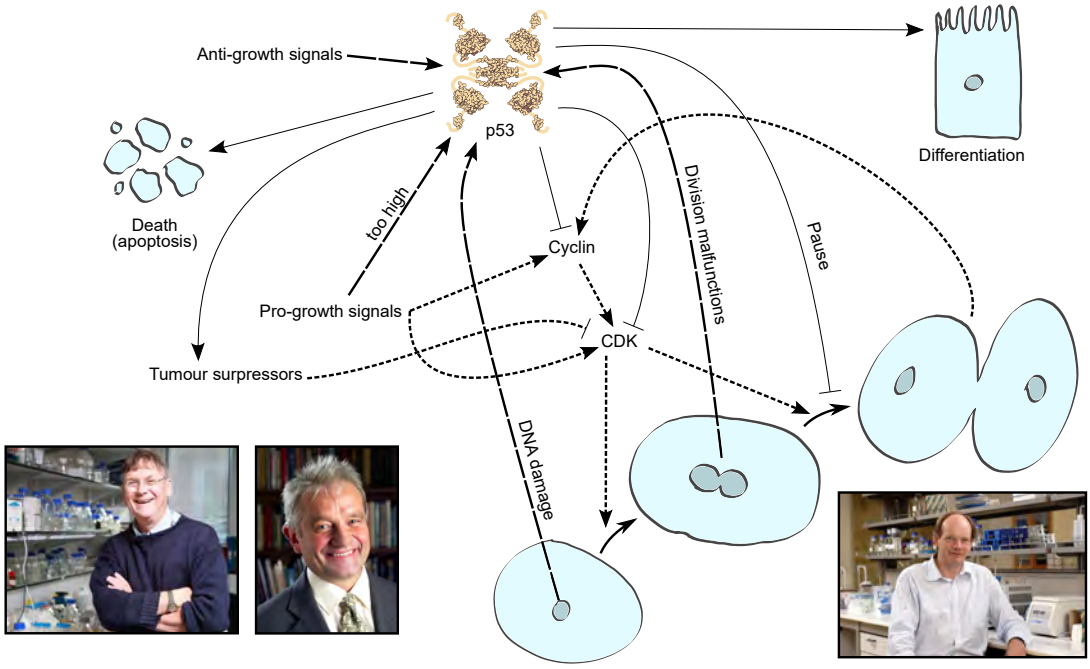
Explanation:
A simple question on basic plant anatomy and considering domestication of crops.

-
-
-
-
-

DISEASE & DECAY

THE CELL CYCLE

The major ways by which the cell-cycle is regulated in all eukaryotes were discovered by British scientists. In humans, Cyclins (discovered by Sir Tim Hunt; 1943-present) are transcribed at specific cell-cycle stages, and bind cyclin-dependent kinases (CDK; discovered by Sir Paul Nurse; 1949-present), to coordinate division. Protein-53 (p53; discovered by Sir David Lane; 1952-present) is activated by a huge array of post-translational modifications, which allows it to exert diverse effects. p53 can exert these effects even when its activity is reduced by half, but each p53 monomer is only active when bound to three other functional p53 monomers in a homotetramer. p53 is mutated in the majority of cancers ever sequenced.



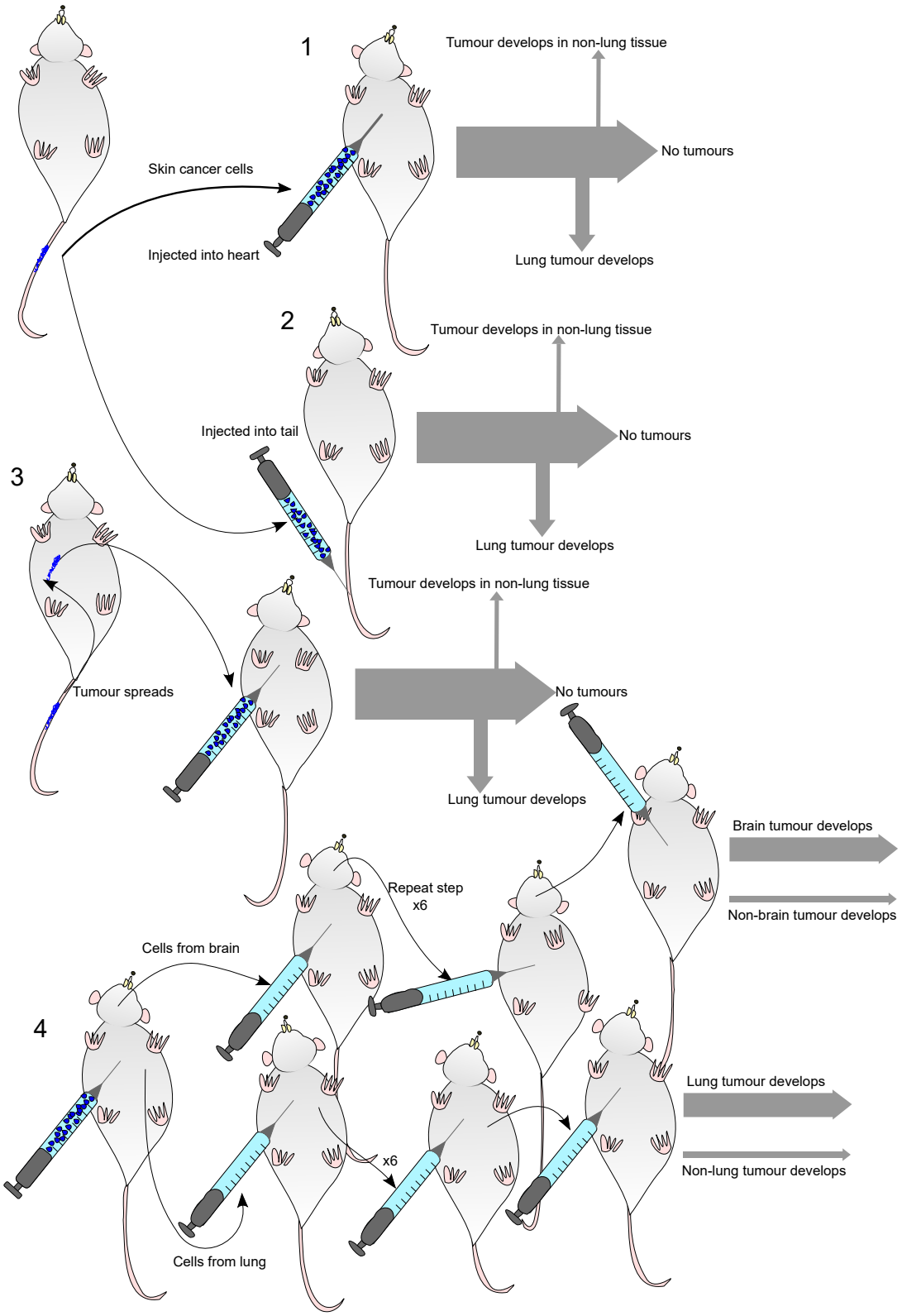
	True	False
Tumours which have lost p53 activity have higher mutation rates than tumours which have p53 activity.	X	
Single celled organisms, such as yeast (Saccharomyces), possess equally powerful regulators like p53.		X
Treatments which deliver more p53 to cells, would reduce the division of healthy cells.		X
Both alleles of p53 are usually mutated in cancer.		X
P53 knockout mice (Mus musculus) show an overgrowth of bone-marrow cells.	X	

Explanation:
This question requires creativity to explore the cell cycle, and consider how the mechanism of action of proteins affects disease.

- DNA damage and other division malfunctions activate P53, which can prevent proliferation of damaged cells, or give time to repair damage.
- There is no selective advantage for a single celled organism to apoptose, or enter a permanent state of cell cycle arrest. P53's main role appears to be as 'The guardian of the genome' in cancer-prone multicellular organisms.
- P53 is activated post-tranlationally. Therefore more protein does not alter the rate of division, until problems arise.
- Activity needs to be reduced by more than half, but, since tetrameres are formed, 15/16 ths of all terameres are disrupted by one faulty allele.
- P53 is needed to drive stem cells to differentiate, and exit the cell cycle.

METASTASIS

Different types of primary tumours give rise to secondary tumours at different rates, and in characteristic places. (The primary organ is where the primary tumour occurs, the secondary organ is where the secondary tumour develops). To understand why, healthy mice (Mus musculus) were injected with cells from skin cancers which spontaneously developed in different mice: Arrow thickness = relative proportion of mice exhibiting the symptom.
(1) Cells from the primary tumour were injected into the heart.
(2) Cells from the primary tumour were injected into the tail vein.
(3) Cells from a secondary tumour were injected into the heart.
In (1, 2 & 3) cancer cells were recovered from the lymph of 100% of the injected mice within hours.
In (4), cells from primary tumours were injected into the heart, and cells recovered from homogenised brain or lung were serially passed through fresh mice.


1
Tumour develops in non-lung tissue
No tumours
Skin cancer cells
Injected into heart
Lung tumour develops
2
Tumour develops in non-lung tissue
Injected into tail
No tumours
Lung tumour develops
3
Tumour develops in non-lung tissue
Tumour spreads
No tumours
Lung tumour develops
Brain tumour develops
Non-brain tumour develops
Repeat step
x6
Cells from brain
4
Lung tumour develops
x6
Non-lung tumour develops
Cells from lung

	True	False
The pattern of secondary tumours can be accurately predicted simply by how close different organs are to the primary tumour.		X
Crossing the blood vessel wall, in the secondary organ, is the limiting step in the formation of secondary tumours from circulating cancer cells.		X
Cells of a new secondary tumour evolve over time to thrive in the secondary organ.	X	
Cancer evolves as it spreads to seed new secondary tumours more efficiently.		X

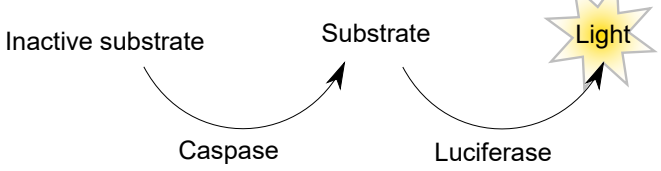
Explanation:
This question, also about cancer, explores how it evolves.

- (This has some role in predicting the distribution of a subset of secondary tumours in patients). (1) versus (3) - tumour favours lungs wherever injected.
- Cancer is recovered from the lymph in the majority of animals, but tumours develop in a small minority.
- (4) tumour usually favours lung, but by only selecting cells from brain, can evolve a population that favours the brain.
- (1) versus (2). Secondary tumour no more likely to seed further tumours than primary.

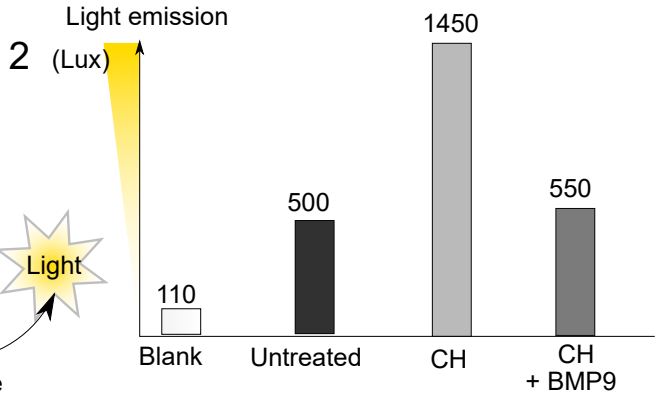
APOPTOSIS

Sir Alastair Currie (1921-1994), Sir John Sulston (1942-present) and colleagues discovered how cells can commit controlled suicide (apoptosis).
Apoptosis is executed by Caspase enzymes. Cyclohexamide (CH), which inhibits ribosomes, was used to induce apoptosis in cells treated with the hormone bone morphogenetic protein-9 (BMP9). To measure the number of apoptotic cells after treatment, inactive luciferase substrate, and the light-emitting enzyme luciferase, were added.

1



2



	-80 %	-70 %	- 60 %	- 50 %	- 40 %
Choose the nearest change to the correct answer.		X			

Explanation:

- Must subtract blanks, and compare 0 ng/ml to 5 ng/ml. Therefore = ((1450-110)-(550-110))/(1450-110) = 0.67164179 reduction. All readings were to 2 sig fig. Hence 0.67. Therefore -67%.

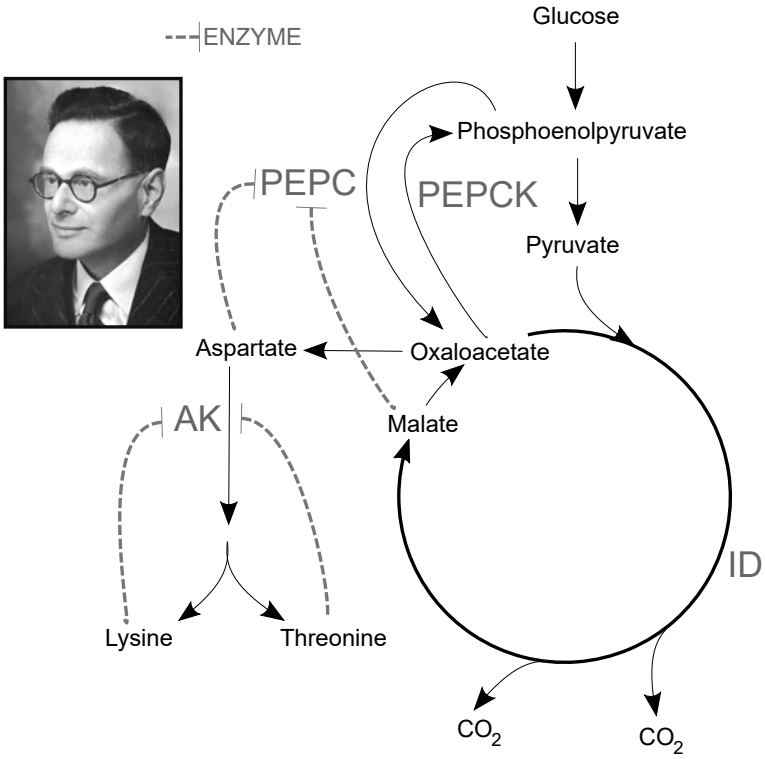
	True	False
BMP9 treatment causes an increase in apoptosis.		X
A large excess of both inactive substrate and luciferase is required to give a linear luminescence signal in response to caspase activity.	X	
Caspase gene expression is increased during apoptosis.		X

Explanation:
This simple question assesses basic data handling, and also considers how enzymes are regulated.

- Luminescence is lower, indicating reduced caspase activity
- At high caspase activities, luciferase activity may start to become limiting
- Must be activated post-translationally, because the drugs (cyclohexamide) blocks translation.

KREBS CYCLE

Sir Hans Krebs (1900-1981) uncovered the major biochemical pathway of mitochondria.
The Krebs cycle was artificially modified in a free prokaryote to maximise lysine production.



	True	False
Blocking the final step of threonine synthesis leads to an unregulated increase in lysine synthesis.		X
Increasing ID activity increases lysine synthesis.		X
Making PEPC insensitive to malate/aspartate increases lysine synthesis.	X	
Increasing PEPCK activity increases lysine synthesis.		X

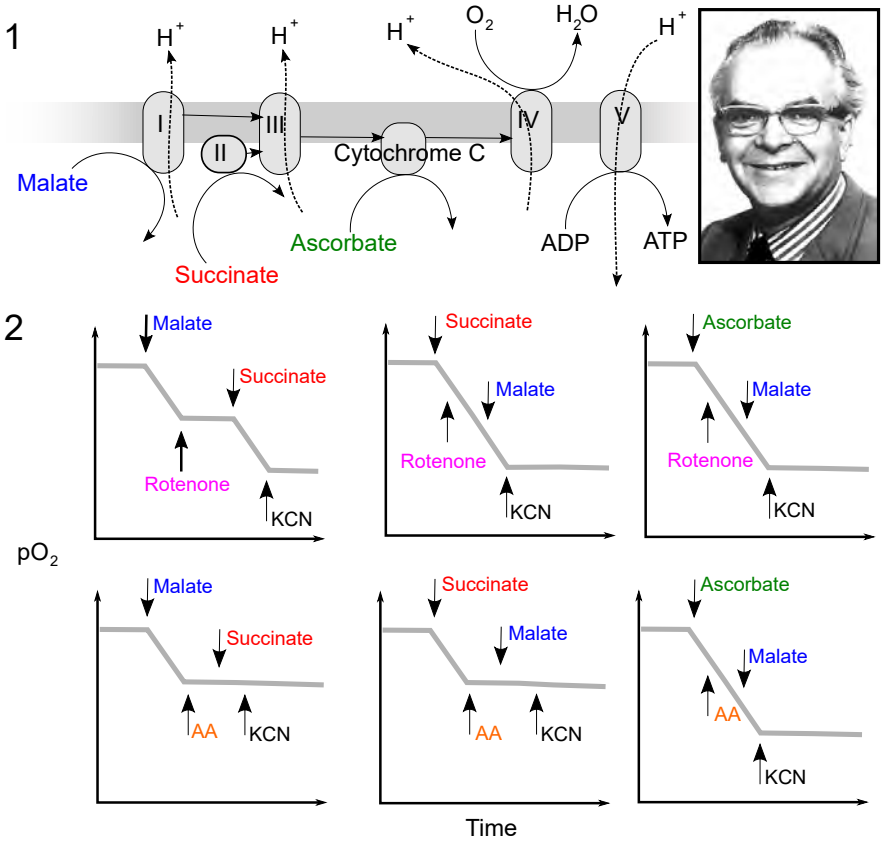
Explanation:
This question was inspired by Mats Carlberg of Sweden.

This question explores how long metabolic pathways are regulated.

- Lysine inhibits its own synthesis.
- Carbon is lost in the krebs cycle, reducing the availability of carbon backbones to synthesise lysine.
- Increases oxaloacetate production, which can be converted to Lysine.
- Gluconeogenesis removes carbon backbones which could be used to synthesise Lysine.

ELECTRON TRANSPORT CHAIN

Peter Mitchell (1920-1992) discovered how mitochondria produce ATP.
Electrons are harvested from succinate, malate and ascorbate (vitamin C), and drawn onto oxygen. Complexes I-IV sequentially harness their energy to pump protons across mitochondrial inner membranes (1).
The oxygen saturation of a suspension of mitochondria, treated with substrates and the poisons potassium cyanide (KCN), rotenone or antimycin A (AA) at the indicated points, was measured over time (2).



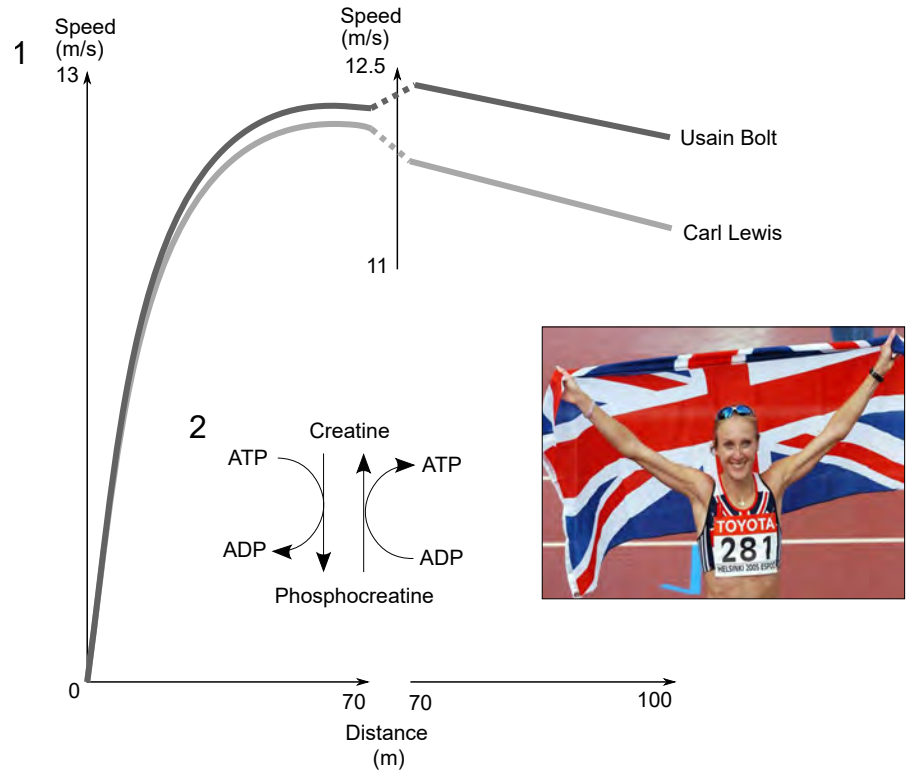
	True	False
Rotenone inhibits complex I.	X	
Antimycin A inhibits cytochrome C.		X
Cyanide poisoning can be treated with malate.		X
Oxygen consumption is increased by poisons which introduce pores to mitochondrial membranes.	X	

Explanation:
This question was inspired by Dia Ghose and Josh Dickerson of the University of Cambridge.

- Blocks malate metabolism, nothing else.
- Blocks malate and succinate, not ascorbate.
- Does not reactivate oxygen consumption.
- Dissapates proton gradient, so electron transfer chain speeds up.

ELITE RUNNERS

In the last few games, team GB has used sport science to finish second in Olympic and Paralympic medal tables.
The running velocity of different gold-medal 100m sprinters is presented (1).
Phosphocreatine, which is present in the cytoplasm of muscle, buffers ATP levels in a one-step reaction (2).
Glycolysis generates a few ATP by converting glucose to pyruvate. Mitochondria generate dozens of ATP by converting pyruvate to CO_2.



	True	False
Faster sprinters metabolise more muscle glycogen to CO_2 than slower sprinters.		X
The kinetics of their glycolytic enzymes are an essential determinant of which medals these sprinters win.	X	
Creatine, as a dietary supplement, would enhance the performance of Usain Bolt (Jamaica's 100 and 200 m winner) more than Paula Radcliffe (Britain's record breaking marathon runner).	X	
Glycolysis becomes the main energy source of these sprinters after ~ 70 meters.	X	

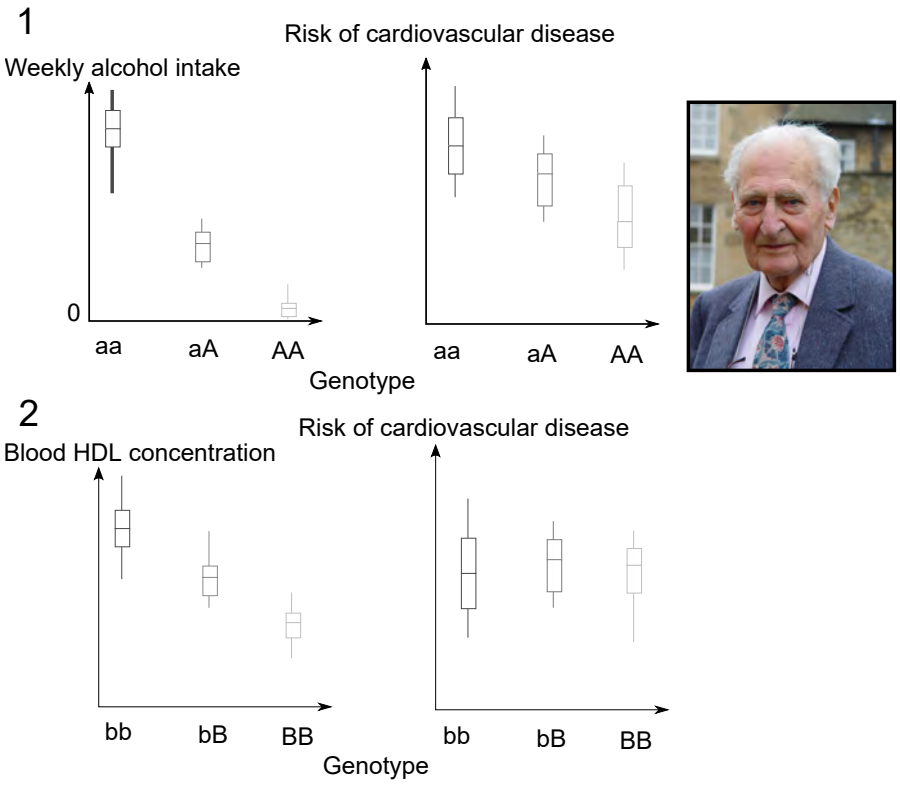
Explanation:
This question was inspired by Dimitar Epihov of The University of Sheffield.

The end result of the simultaneous action of the different metabolic pathways is explored.

- Aerobic respiration is not useful.
- Strongly determines rate of ATP generation in latter half of the sprint, and therefore the rate of their deceleration.
- Buffers a small amount of ATP, so is briefly useful in a sprint, but negligable in an endurance race which consumes more energy overall.
- at this point, there is a marked halt in acceleration, and a small decelration, indicating energy is no longer being generated from pre-existing ATP, or P-Cr, but by glycolysis.

MENDELIAN RANDOMISATION

Sir Richard Doll (1912-2005) invented statistical methods to prove smoking causes human disease. Mendelian randomisation was invented to investigate more subtle behaviours, such as the health impacts of alcohol (1) and high density lipoproteins (HDLs; 'good' cholesterol) (2). An underlying genotype, inferred to cause a behaviour, is identified, and its correlation with disease is assessed. White British people were recruited for this study.



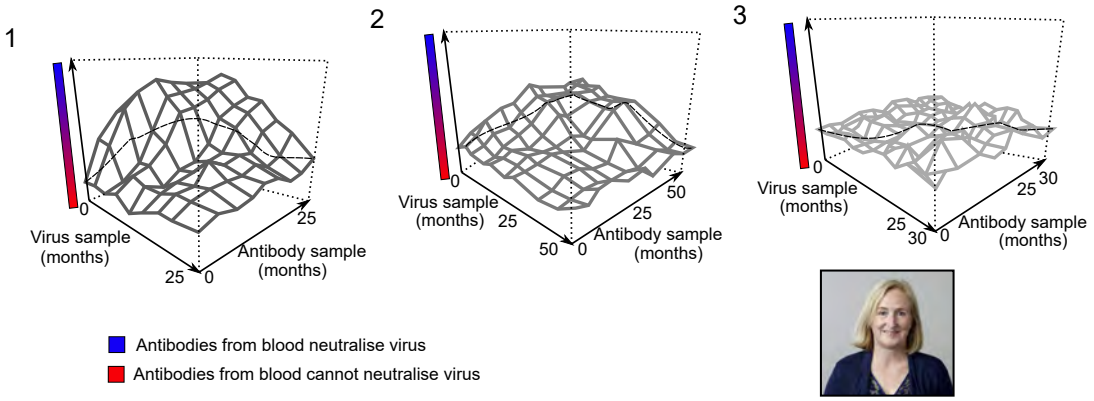
	True	False
Compared to not drinking any alcohol, consuming small amounts of alcohol is beneficial to health.		X
Drugs which raise HDL are expected to reduce cardiovascular disease.		X
If people with the genotype aa, who happen to consume no alcohol for religious reasons, have a high risk of cardiovascular disease, it should be concluded alcohol contributes to disease directly.		X
If the allele a is found to be more common in Scotland, and A in Wales, the conclusions of a UK wide study will be strengthened.		X

Explanation:
This question assesses understanding of correlation versus causation, and environment-genotype interaction.

- There is no evidence that aA's, which drink a small amount, have a lower risk than AA's, which do not drink at all.
- Gene B is correlated with HDL levels, but not cardiovascular disease. (HDLs are regarded to mark a healthy lifestyle, not be a direct contributor to cardiovascular disease, unlike LDLs).
- These people are natural controls. If they have a risk equivalent to AAs, then the study's conclusions are valid. If their risk is high, it indicates the aa genotype is correlated to alcohol consumption, but also something else which is actually responsible for increasing the risk of cardiovascular disease.
- The study would be confounded because the genotypes would correlate with numerous cultural factors, as well as alcohol consumption, which might be affecting cardiovascular health.

REDQUEEN HIV

Dame Amanda Fisher discovered many properties of the HIV.
HIV has two states. It can remain dormant within cells or can be active, replicating and producing viral proteins. In 2016, the National Health Service announced a new treatment, which awakens dormant HIV and kills active HIV. Many recipients are preliminarily cured.
Three patients (1, 2, & 3) contracted HIV at time 0, and remained untreated. Each month, blood samples were taken from each patient. Antibodies and virus were separately extracted from the samples. Antibodies from each timepoint were mixed with viruses from each timepoint, and the infectiousness of the antibody-treated virus was measured.



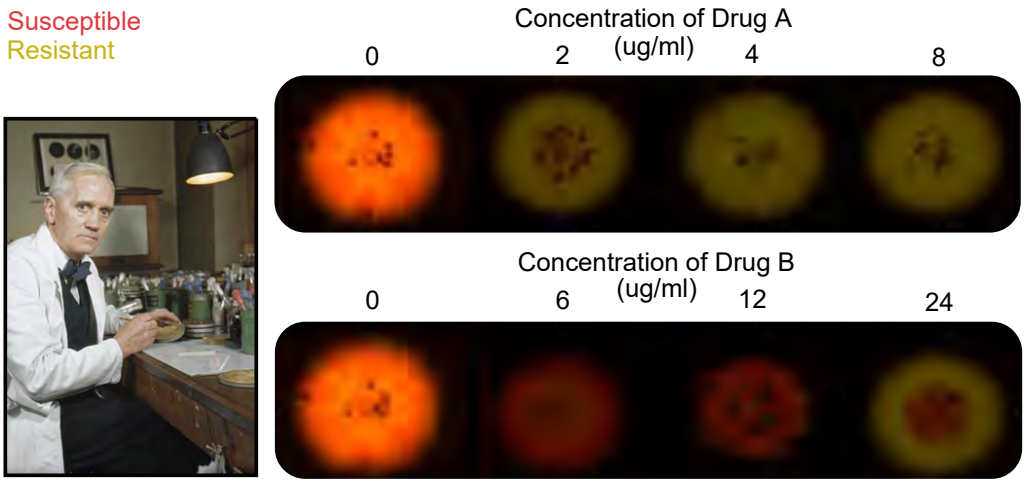
	True	False
In the first month of infection, patients suppress circulating HIV.		X
Patients' antibodies will be more effective against awakened dormant virus, than currently active virus.	X	
Patient 2 developed AIDS last.	X	
The virus evolved most rapidly in patient 3.		X
The immune system is better at targeting cells infected with inactive virus than active virus.		X

Explanation:

- First blood sample is innefective against all virus.
- Blood is always more effective against older virus than contemporary virus.
- Blood activity didn't collapse until ~ month 50
- Patient 3 was a non-responder, so there was never immunological selection to drive evolution of virus within the host.
- Needs foreign proteins to be expressed.

ANTIBIOTIC RESISTANCE

Sir Alexander Fleming (1881-1955) discovered antibiotics, but humanity's biggest killers are now mostly resistant to them.
In one pathogen, antibiotics are degraded either by intracellular enzymes, or by enzymes released into the surrounding environment. A strain susceptible to antibiotics was labelled red, and a resistant strain was labelled yellow. Equal amounts of susceptible and resistant bacteria were mixed and seeded as a dense lawn on plates. These were treated with drug A or B at different concentrations, and grown for a period of time. The colour of the remaining cells was photographed.



	True	False
This species of bacteria expresses the target of Drug B.	X	
When there is no drug, the plates will become increasingly yellow, and less red, with time.		X
Resistance to Drug A involves an extracellular enzyme.		X
Plasmids carrying genes for antibiotic resistance are more likely to spread when resistance uses extracellular enzymes, than when it uses intracellular enzymes.		X

Explanation:
This question was inspired by Scarlet Harris of the University of Oxford.

This simple question explores mechanisms of antibiotic resistance, and their evolutionary dynamics.

- Red can only grow inside of yellow, so the drug must be effective.
- The red bacteria do not have the cost of the antibiotic production and so will outgrow yellow.
- Red dies out, so the drug must not have been broken down, so it is not extracellular.
- Extracellular enzymes work for both strains at once so are less likely to be shared than intracellular enzymes which are required for survival. i.e. a higher selection pressure.

PRIONS

John Griffith (1928-1972) explained the biology of prion diseases. Prions are proteins which have folded incorrectly into a more stable form. When a prion comes into contact with its correctly folded counterpart, it catalyses this protein to also re-fold into a prion. Prion build-ups, which resist proteolysis, damage the brain, and in the 1990s millions of cattle (Bos taurus) in the UK had to be destroyed to prevent prions from spreading.

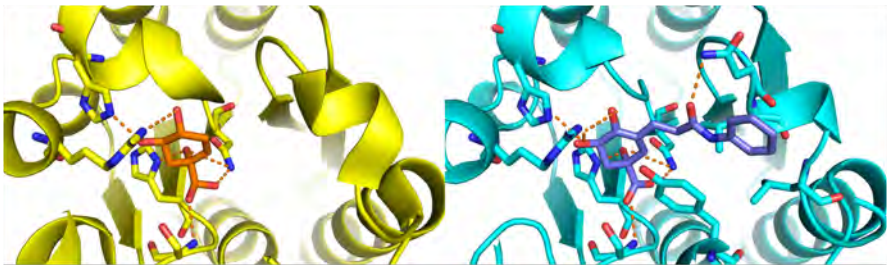
	True	False
At the start of disease, prions accumulate exponentially.	X	
Animal prion diseases may spread to humans.	X	
Cattle with some genetic variants may be protected from prion diseases.	X	
Banning animal protein supplements in livestock diets is an effective way to reduce prion diseases.	X	

Explanation:
This question explores universal disease dynamics using a non-living agent.

- Logic.
- Some animal proteins may be similar enough to human ones to affect them too.
- Some cattle's proteins may be a different shape so the stable prion cannot bind it, or is less likely to misfold in the first place.
- Prions could be eaten in the diet and so spread from cattle to cattle, as not digested by proteases. Stopping canabalism will stop spread, and isolate cases.

TUBERCULOSIS DRUGS

The UK runs the biggest collaborations to screen for new antibiotics for tuberculosis. Molecules X and Y were found, which binds to the active site of a Mycobacterium tuberculosis enzyme. Dashed lines indicate hydrogen bonds.
Molecule Z was also found to inhibit the enzyme, by binding a site other than the active site.



X Y

	True	False
Molecule X binds to the enzyme's active site reversibly.	X	
Molecule Y could have been found in a screen for molecules which increase the temperature at which the enzyme denatures.	X	
Molecule X binds to the active site more tightly than molecule Y.		X
Molecule Z is a better drug candidate if the substrate concentration is usually very high.	X	

Explanation:
This question was inspired by Robert Starley of the University of Cambridge, and Nanuka Gvazava.

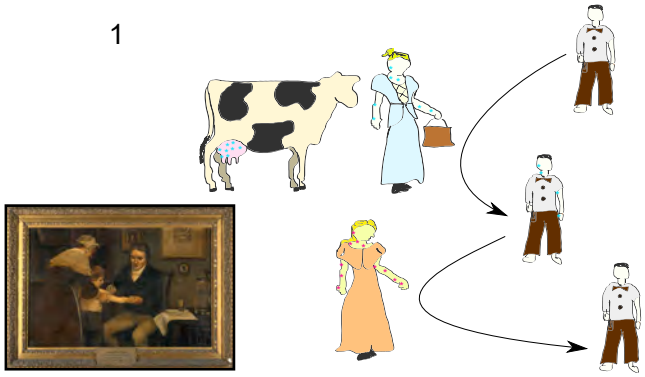
Enzyme properties are analysed in a precise way. DOI:10.1042/BJ20110002

- Small molecule, only has H-bonds, no covalent ones.
- Y fits snugly into the enzyme, forming interactions, enzyme, logically increasing denaturing temperature.
- Y has more H bonds than X (as well as pi-pi stacking and hydrophobic interactions).
- If substrate concentration is very high the active site may be always in use and X outcompeted, molecule Z does not bind the active site.

VACCINATION AND EPIDEMIOLOGY

Edward Jenner (1749-1823), the inventor of immunology, pioneered modern vaccination. Jenner noticed milkmaids exposed to cowpox did not catch smallpox. Jenner injected pus from a cowpox infection (top), into a boy, who became mildly ill. Jenner later injected the boy with pus from a smallpox victim (bottom), and the boy did not become ill (1). Smallpox was usually spread through the respiratory tract, was highly contagious, and quite deadly, but, due to vaccination, is now the only human pathogen to have been driven extinct.

1

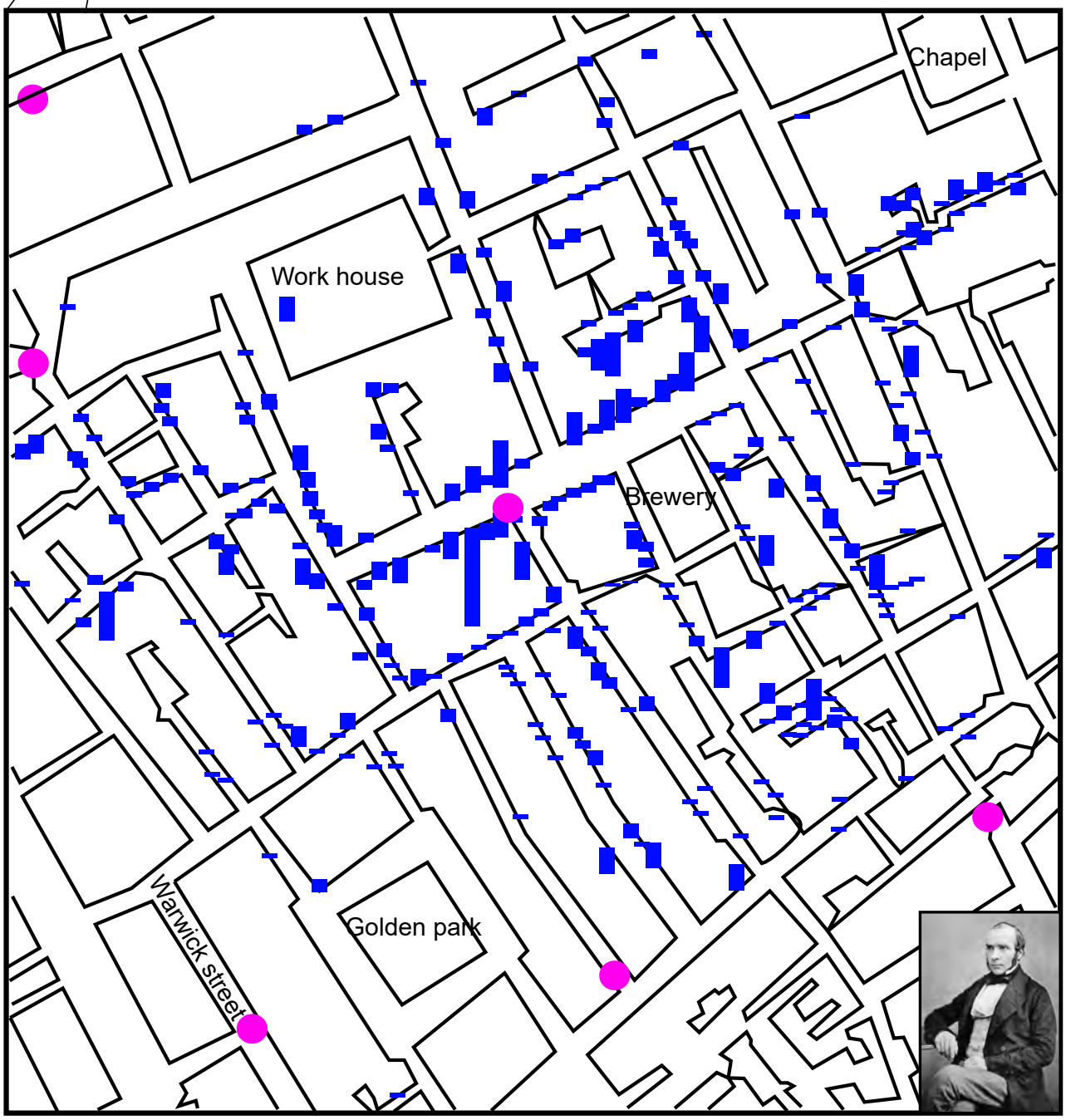


John Snow (1813-1858) invented epidemiology. Snow mapped the occurrence of cases in Victorian London during the first Cholera pandemic, and saved many lives (2). In 1961, the current seventh global Cholera pandemic began in Indonesia.

2

1 cholera case

Water pump



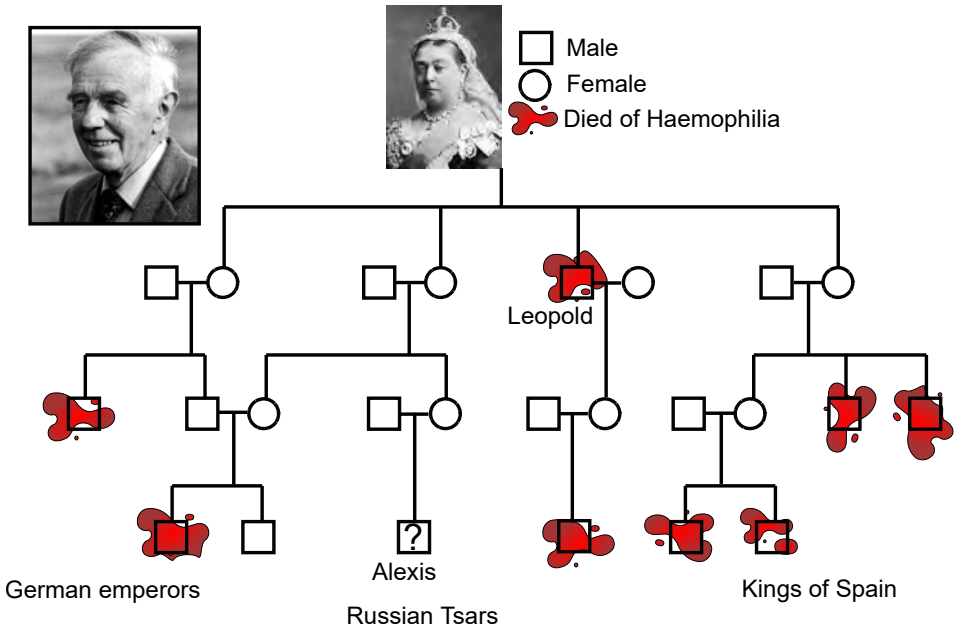
	True	False
Smallpox and Cowpox share some amino-acid sequences on their surface.	X	
People often contracted smallpox more than once.		X
Snow ended the Cholera outbreak by removing the handle from the Warwick Street water pump.		X
Smallpox remains viable outside of the host for longer than Cholera.		X
Smallpox lingers in isolated communities longer than Cholera.		X

Explanation:
This question ties together understanding of immunology and epidemiology. Candidates must consider the evolutionary dynamics of different diseases.

- Yes, they must as antibodies against cowpox worked against smallpox.
- Antibodies once made will stop reinfection, which is what allows the vaccination to work.
- The WarwickStreet pump did not contain Chloera, as seen from the map.
- Is given that smallpox is respiratory and highly contagious, which is a hallmark of shortlived, directly transmitted diseases. Cholera is observed to pass through the environment, in food or water, meaning it must be hardy.
- Smallpox has high virulence and morbidity, and elicits strong immunity, so it rapidly infects, kills, or immunises all its hosts, then dies out. Cholera persists in the environment for a long time.

HAEMOPHILIA

Robert Macfarlane (1907-1987) explained the biochemistry of blood clotting, and discovered the cause of haemophilia B, which causes fatal bleeding.
Queen Victoria's son, Prince Leopold, was the first European noble to develop haemophilia B, but it quickly devastated European royal lines. An incomplete family tree is shown.



	0 %	12 %	25 %	50%	100 %
Choose the nearest probability to the correct answer.			X		

Explanation:

- Alexis' grandmother must possess the mutation to have passed it on to the grandchildren of the german emperors (it cannot have come from their unaffected father). Therefore, there is a 50 % chance Alexis' mother received the affected X. And a 50% chance that Alexis received this X from his mother (he must inherit X from his mother). Therefore, a 0.5*0.5 = 25%.

	True	False
In this family, haemophilia B could have originated from a new (de novo) mutation during meiosis in Queen Victoria's oocytes.		X
Clotting factor activity is reduced by more than half in these haemophiliacs.	X	

Explanation:
This question was inspired by Andrew Treharne of the Royal Society of Biology.

This simple question assesses understanding of monogenic inheritance.

- Victoria passed heamophillia to multiole children, so the mutation must be present in many of her immature oocytes. (Likely it occurred in one of the gametes that lead to her, or during mitosis in her early germ-line cells).
- Explains why it is recessive, not haploinsufficient.