

**Exam 1**  
**BC 368**  
**Spring 2015**  
**Answer Key**

1. C
2. E
3. C
4. D
5. E
6. A
7. D
8. C
9. B
10. A

11. See King et al. (2014) Nature Communications; DOI: 10.1038/ncomms6631

a) Clearly, his DNA must be compared to *something*. It is unlikely that there are any comparison samples of Richard himself because he died so long ago. The absence of living descendants makes it difficult to obtain a comparison sample. (Note that normal PCR-STR will be useless in this case if modern relatives are used for comparison. After this many generations, there will be too little similarity for comparison.)

b) Amplification at the amelogenin gene gives PCR products that vary in size depending on whether the gene is on the x- or the y-chromosome. Therefore, the presence of two different sized products means that the remains came from a male.

c) The skeleton is an exact mitochondrial DNA match to the descendant from female lineage 1 and has only a single difference to the descendant from female lineage 2. There are many positions that differ from the reference, showing that this is not a common sequence. It is highly likely that the remains are those of Richard, and the single base difference comes from a mutation in the last 500 years.

d) Tracing lineage through the male line is more problematic than through the female line because of “false paternity events” that can occur in any of the intervening generations. Therefore, even though these data do not support the hypothesis that these remains are those of Richard, because the y-chromosome is passed down from father to son intact, the fact that they do not match can be explained by a false paternity event in the last 500 years.

12. a) At temperatures below the apparent gel-to-liquid-crystalline phase transition temperature ( $T_m$ ), the anisotropy *decreases* with an increase in the amount of cholesterol incorporated in the membrane. Thus, incorporation of cholesterol in DPPC membranes decreases the rigidity of the resulting bilayers below the  $T_m$ , which suggests that the membranes become more fluid below the  $T_m$ . On the other hand, at temperatures above the  $T_m$ , the anisotropy *increases* with an increase in the amount of cholesterol incorporated in the membrane. Thus, the incorporation of the cholesterol into DPPC membranes increases the rigidity of the resulting bilayers above the  $T_m$ , which suggests that the membranes become less fluid above the  $T_m$ . This is exactly what we said would happen in class. Cholesterol interferes with close packing of the lipid tails in the gel state, increasing fluidity, and its rigid ring structure decreases mobility in the liquid crystalline state, decreasing fluidity.

b) The anisotropy *increases* with increased cholesterol in the gel phase of the membrane matrix, suggesting decreased fluidity. This should be unexpected to you because it's the opposite of what occurred in a). Because of the cationic structure of these lipids, the interaction between the lipid monomers should be considerably weaker than in the DPPC case because of unfavorable electrostatic repulsion at the level of the head group in membranes. Note that for the pure

cationic lipid membranes, the initial anisotropy values are considerably lower than in DPPC bilayers. Acting as filler molecules, cholesterol reduces the inter-monomer lipid head group repulsion in these cationic lipid assemblies. Above the  $T_m$ , the effect of cholesterol is the same as in a).

13. For  $\text{Na}^+$  transport into the cell:

$$\begin{aligned}\Delta G^{\circ} &= RT \ln [\text{Na}^+]_{\text{in}}/[\text{Na}^+]_{\text{out}} + ZF\Delta\Psi \\ &= (8.315 \text{ J/mol-K}) * 310\text{K} * \ln 10/140 + (1) * (96,500 \text{ J/V-mol}) (-0.060 \text{ V}) \\ &= -6.8 \text{ kJ/mol} - 5.8 \text{ kJ/mol} = -12.6 \text{ kJ/mol}\end{aligned}$$

For  $\text{H}^+$  transport out of the cell:

$$\begin{aligned}\Delta G^{\circ} &= RT \ln [\text{H}^+]_{\text{out}}/[\text{H}^+]_{\text{in}} + ZF\Delta\Psi \\ &= (8.315 \text{ J/mol-K}) * 310\text{K} * \ln \{x/1 \times 10^{-7}\} + (1) * (96,500 \text{ J/V-mol}) (+0.060 \text{ V}) \\ &= 2.6 \text{ kJ/mol} * \ln \{x/1 \times 10^{-7}\} + 5.8 \text{ kJ/mol}\end{aligned}$$

Set these equal and opposite to find out when they break even.

$$12.6 \text{ kJ/mol} = 2.6 \text{ kJ/mol} * \ln \{x/1 \times 10^{-7}\} + 5.8 \text{ kJ/mol}$$

$$\text{Solve for } x: \quad 2.6 = \ln \{x/1 \times 10^{-7}\} \quad x = 1.38 \times 10^{-6} \text{ M} \quad \text{pH} = 5.9$$

Note that you could also have recognized that this is an electroneutral process and left out the membrane potential term for both ions, since they cancel. You would have ended up with the same final number.

14. a) The amount of exchanger goes up with the training program. The muscle is therefore able to extrude more  $\text{H}^+$  into surrounding tissue, allowing it to avoid a drop in pH that inactivates PFK-1. Glycolysis can continue for longer.

b) Depolarization results in opening of voltage-gated  $\text{K}^+$  channels, which cause  $\text{K}^+$  to exit the cell, down its electrochemical gradient.

c) The  $\text{Na}^+\text{-K}^+$  pump re-establishes the normal potassium ion concentrations in the muscle cell. It looks like the pump is working better after the training program because the increase in extracellular  $\text{K}^+$  is not as great during these runs to exhaustion. It is likely that this pump has been up-regulated like the exchanger. (Note that leak channels do not re-establish concentrations as they allow ion flow energetically downhill only.)

15. a) Gq pathway

b) phospholipase C

c)  $\text{IP}_3$

d)  $\text{IP}_3$  binds to calcium channels in the sarcoplasmic reticulum, opening them so that  $\text{Ca}^{2+}$  flows down its electrochemical gradient and enters the cytoplasm

e) Gs pathway

f) protein kinase A

g) aquaporin

h) Different binding affinities of the receptors ( $V_1$  and  $V_2$ ).  $V_1$  must have a higher  $K_m$ .

16. a) Yes. Glucagon works through a Gs pathway in liver cells to activate PKA, which activates glycogen phosphorylase b kinase, which activates glycogen phosphorylase, which catalyzes glycogen breakdown. The net result is release of glucose through GLUT2 into the bloodstream.

b) Yes. Insulin works through a RTK pathway in liver cells to promote glycogen synthesis, which keeps the glucose gradient high, promoting glucose uptake. Note that GLUT2 transporters are not sequestered like the GLUT4 transporters of skeletal muscle and adipose tissue, but if your answer included these transporters, you did not lose points.

c) The Gs-coupled-receptor is a monomer, so Fab is as effective as the whole antibody. All it takes is one antigen-binding site to activate the receptor. On the other hand, the insulin receptor is a receptor tyrosine kinase, meaning that it is a dimer. It is likely that both monomers must have signal bound in order for activation to occur. Because each antibody has two antigen-binding sites, Ab either bind to both monomers or cross-link different receptors and cause them to cluster on the cell surface. Clustering would allow the individual kinase domains of the receptors to phosphorylate adjacent receptors in the cluster. Fab can only bind to one of the monomers, and the odds are slim that another Fab will come in and bind to the other monomer.

17. Your patient appears to have some kind of glycogen storage disease, but not one of the more serious ones. The protruding abdomen in his youth suggests that glycogen breakdown in the liver is impaired. Muscle weakness further suggests that the problem is also found in the muscle. The patient's symptoms are somewhat mild and do not appear to be life threatening.

Only the last three enzymes would affect the liver's ability to break down glycogen and maintain blood sugar. A defect in glucose 6-phosphatase would not affect the muscles, since muscles do not have this enzyme. It would also cause larger problems for the patient. A mutation in glycogen phosphorylase would cause liver enlargement, but there would be no response to glucagon. The best answer is a defect in debranching enzyme in both the liver and muscle.

18. a)  $\Delta G^\circ = -30.5 \text{ kJ/mol} + 43 \text{ kJ/mol} = + 12.5 \text{ kJ/mol}$

The reaction is unfavorable under standard conditions because  $\Delta G^\circ > 0$ .

Note that you flip the sign of the phosphocreatine reaction because it is being phosphorylated, not hydrolyzed.

b)  $\Delta G = \Delta G^\circ + RT \ln \left\{ \frac{[\text{ADP}][\text{phosphocreatine}]}{[\text{ATP}][\text{creatine}]} \right\}$

$$\Delta G = +12.5 \text{ kJ/mol} + 8.315 \text{ J/mol-K} (310 \text{ K}) (\ln \{0.001\}0.001 / \{0.01\}0.030)$$

$$\Delta G = -2.2 \text{ kJ/mol}$$

Yes!