Solution key - 7.012 Section 16 - 2010

Questions

1. Classify the following as totipotent, pluripotent, bipotent, multipotent, unipotent or differentiated:

- Cells that can differentiate into many cell types. *Pluripotent/multipotent*
- A zygote that is about to start cleavage. *Totipotent (it can form placenta also)*
- Cells isolated from developing brain cortex that produce motor neurons or interneurons when provided with specific growth factors. *Bipotent*
- Human mesenchymal cells that form the hematopoetic, bone, cartilages, muscle and fat cell lineages. *Multipotent/pluripotent*
- Intestinal stem cells that replenish the differentiated intestinal crypt cells. *Unipotent*
- A neuron. *differentiated*

b) Using intestinal cells, you do a pulse chase experiment by first putting the cells in a culture medium containing radioactive dTTP for a short time and then allowing them to grow and divide in medium containing a lot of non-radioactive dTTP.

- What is the rationale for performing this pulse chase experiment?

This experiment would help us to determine (i) the rapid turnover of the labeled cells and (ii) their migration and the fate that they acquire.

- What is the relationship of the rapid turnover of a cell with cell division?

As the cells divide there will be more incorporation of unlabeled thymidine in the DNA with every replication event and this will dilute the labeled thymidine.

2. A patient has a rare recessive genetic disorder due to the loss of a specific gene function. This disease causes a decrease in immune function. The patient receives a bone marrow transplant which is successful in alleviating the symptoms of the disease, such that patient can lead a normal life.

a) Why does the bone marrow transplant relieve the patient's symptoms?

If the bone marrow transplant is successful, the bone marrow cells can proliferate to form the different blood cells that circulate in the patient's body and help them alleviate the signs and symptoms.

b) Your patient marries a man who happens to be carrier for the same genetic disorder. What is the probability that their offspring will inherit the disease if

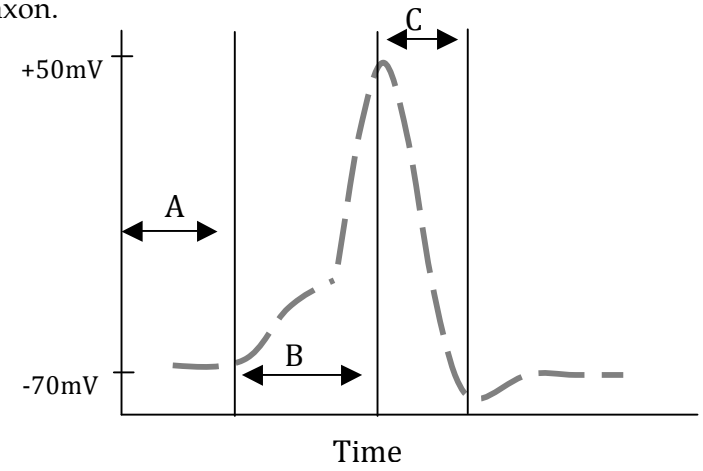
- the couple had a child before the patient had any bone marrow transplant?

The patient is (aa) before the transplant and she marries a carrier (Aa). So the chance that the child will have the disease is (aA, aa, aA, aa) = ½.

- the couple had a child after the patient had a bone marrow transplant, and no longer showed any symptoms of the disorder? Explain your answers.

The probability will remain the same even after bone marrow transplant since the gametes of this patient will still have the "aa" genotype.

3. Shown below is a plot of axonal membrane potential as a function of time, measured at a single position on the axon.



For each of the three time points indicated, fill in the following table. Name the phase of membrane potential that describes the time point, the channels/pumps that are involved, and explain how these channels/pumps maintain that phase.

Time point	Phase	All the ion channel/ Pump involved	Explanation
A	*Resting*	*Na+/K+ pump & open K+ channels*	*Na+/K+ pump creates a difference in concentration for both Na+ and K+ across the cell membrane. The relative concentration of Na+ is high outside as compared to inside and the relative concentration of K+ is low outside as compared to inside the cell. The open K+ channel always allows K+ to flow out of the cell. As K+ moves out of the cell, down its concentration gradient, the inside of the cell becomes negative with respect to the outside of the cell. K+ moves out of the cell until the driving force of the concentration gradient equals the driving force of the electrochemical gradient, which for most cells set the resting membrane potential at -70 mV.*
B	*Depolarization*	*Voltage gated Na+ Channels*	*During the action potential Na+ ions to move into the cells making the inside more positive relative to outside thus depolarizing the membrane.*
C	*Repolarization*	*Voltage gated K+Channels, Na/K pump*	*During action potential it causes the K+ ions to move out of the cells making the inside more negative relative to outside thus repolarizing the membrane.*

4. Dopamine is one of major neurotransmitters in the mammalian brain that regulates mood, cognition and locomotion. Dopamine acts on two types of receptors: the D1 receptor is an inhibitory ligand-gated channel, the D2 receptor activates the G proteins, and is excitatory. The released neurotransmitter is taken back into the presynaptic cell, for re-use.

a) On what part of the neuron are the dopamine receptors localized?
The dopamine receptors are located on post-synaptic membrane.

b) The D1 receptor is inhibitory and transports K+ ions. Would K+ be moved into or out of the postsynaptic cell? Explain the mechanism underlying this inhibitory effect.
At resting membrane potential the concentration of K+ is higher inside the cell compared to outside. The binding of dopamine to its D1 receptor will therefore move K+ ions out of the cell. As a result the membrane potential will be more negative relative to that at the resting state i.e. it is hyperpolarized, and further from threshold potential. Thus the chances of the post-synaptic neuron to fire an action potential will be reduced.

c) The D2 receptor is excitatory, and its ion targets are believed to include Ca2+. Would Ca2+ be moved into or out of the postsynaptic cell? Explain the mechanism underlying this excitatory effect.
The D2 receptors will promote the movement of Ca2+ ions into the cell, since Ca2+ concentration is higher outside the cell than inside. Thus, the inside of the cell becomes more positive relative to the unstimulated state; and the membrane potential will become closer to threshold potential and an action potential.