7.013 SECTION PROBLEM STEM CELL SOLUTIONS

PART A.You are studying the differentiation of cells in the hematopoietic (blood-forming) system of humans. The hematopoietic stem cell gives rise to all the different blood cells in the circulatory system.

An abbreviated pathway of blood cell differentiation is shown below. Cells A, B, C, D, and E are stem cells. Cells F, G and H are terminally differentiated. "F" is a red blood cell.

a) What are two characteristics of a stem cell?

1) It is not "end stage" or "terminally differentiated" (not at end of pathway for differentiation).
2) It can make a daughter cell that is the same as itself.

b) Is stem cell A a unipotent stem cell or a pluripotent stem cell? Explain briefly.
Stem cell A is a pluripotent stem cell, it gives rise to many types of differentiated cells. A unipotent stem cell, however, gives rise to one type of differentiated cell.

c) Cell differentiation can be in response to various external factors that stimulate cell differentiation. Red blood cell "F" has lost most of its cellular components, including its nucleus, during differentiation. Blood cell F is required for oxygen transport in humans. The peptide hormone, erythropoietin (EPO), binds to a membrane receptor found on a cell that is a precursor to cell F.

i) Explain why Blood cell F cannot divide to form more of itself.

Since cell F has lost its nucleus, it lacks the genes required for cell division and differentiation and therefore cannot form more of itself.

ii) Which stem cell must EPO act on when production of cell F is required?

EPO acts on stem cell D to stimulate production of cell F.

iii) What is the mechanism of action of EPO?

EPO binds to the membrane receptor on cell D and stimulates an intracellular signalling mechanism that causes stem cell D to produce cell F.

d) Is the cell that is a precursor to F a unipotent or a pluripotent stem cell?

Cell D is a unipotent stem cell.

e) If the precursor to F failed to produce membrane receptors for EPO, what would be the fate of cell D? Would this be a lethal mutation (lethal for the human being)?

Stem cell D would not produce cell F and there would not be cells to transport oxygen within the body.

f) Some athletes train at high altitudes and then race or compete at low altitudes.

i) What happens to their blood composition at high altitudes?

More RBCs are generated to compensate for the lower oxygen content in the air at high altitudes.

ii)What is the advantage(s) of this strategy?

Competing at lower altitudes with an excess of RBCs increases oxygen supply to the muscles.

iii) What is the disadvantage(s) of this strategy?

Higher numbers of RBCs may lead to a blockage in small blood vessels, and thus lead to formation of clots increasing the risk of strokes or heart attacks (Strokes are blockages of blood vessels in the brain.)

PART B

To determine the potency of several cell types (A, B, C, and D) that give rise to the kidney, adrenal glands ovaries or testes, you infect each cell type with a harmless retrovirus that incorporates itself randomly into the genome. This retrovirus can be used as a label to determine that future cells are derived from the original. You introduce these infected/labeled cells into embryos (one infected cell type per embryo), allow them to develop and then look for retroviral presence in the adult kidney, adrenal gland, and ovary or testes.

Embryos with the A cells --> in the animal you detect the virus only in the kidneys.

Embryos with the B cells--> in the animal you detect the virus only in the kidney.

Embryos with the C cells--> in the animal you detect the virus in all tissues tested kidneys, ovary/testes, and the adrenal glands.

Embryos with the D cells --> in the animal you detect the virus only in the testes.

a) Based on this experiment, which of the four cell types have the characteristics of the most pluripotent cell and why?

The cell type C seemed to be able to give rise to all tissues, kidneys, adrenals and gonads, which suggests its pluripotent nature.

b) Knowing that all four different cell types were types of stem cells, which ones could be described as unipotent stem cells and why?

The cell types A, B and D. Because they each give rise to only one cell type.

c) Assuming the group of stem cells (A-D) could be assembled into a linear relationship in term of their origin, which one of the four types could be a precursor of the others?

The precursor must be the one that can become all types, the pluripotent C cell.

d) Stem cells A and B give rise to kidneys. However, further testing has shown that these cells are not identical because they express different genes. What does it imply?

Cell A could be a precursor of B and D or encoding a specific subset of cells within the kidneys, B and D could each give rise to different cell types within the kidney, because it is a complex organ derived from several distinct tissues.

e) It has been found that inbred strains of mice with a certain mutation on the Y chromosome suffer infertility due to incomplete development of their D stem cells in the testes. However, a single injection of D stem cells seems to repopulate the testes and make mice at least partially fertile. Although human physiology and cell composition are almost identical to that of the mice, this form of therapy would not be easily replicated in humans. Explain briefly why.

Unless two people are identical twins (and the Y chromosome mutation arose de novo only in one of them), cell transplants would be rejected by the patients tissues. Inbred mouse strains are almost genetically identical and this is not a problem.