

Section 17 – Solution key

Questions:

1. Why is cancer predominantly a disease of old age? What about the usual cause of cancer makes it more common in older people?

Cancer is caused by multiple mutations inside the same cell. The chances of a single cell acquiring multiple mutations increase as the person ages.

2. Why are the mutations that cause cancer generally not passed on to one's offspring? Why are almost all cancers sporadic as opposed to familial/inherited?)

Most of these mutations are the mutations in the somatic cells and not the germline cells.

3. Describe the basic principal behind the standard Ames test. How is this different from modified Ames test?

The standard Ames test is used to assess the mutagenic potential of chemical compounds. The test uses several strains of the bacterium that carry mutations in genes involved in histidine synthesis, so that they require histidine for growth. The variable being tested is the mutagen's ability to cause a reversion to growth on a histidine-free medium. In the modified Ames test the rat liver extract is added to test chemical to simulate the effect of metabolism. Some compounds, like benzopyrene, are not mutagenic themselves but their metabolic products are mutagenic. The mutagenicity of a substance is proportional to the number of bacterial colonies observed.

4. What does it mean that a tumor is almost always clonal (or monoclonal)?

Cancer originates due to multiple mutations in a single cell. Once this cell becomes cancerous it multiplies uncontrollably to form descendent cells that are the clones of this cell. Therefore it is regarded as clonal.

5. Why is it that cancer cells containing mutations in genes encoding ECM (extracellular matrix) proteins are more dangerous than cancer cells with normal ECM genes?

These cells cannot attach to the matrix and are free to migrate and metastasize.

6. Weinberg's famous experiment: Ras was the first oncogene to be discovered. Ras is part of a cell signaling pathway. The input for this pathway is an extracellular protein growth factor, and the output is to induce transcription of genes necessary for the cell cycle to occur. Ras is a GTPase that is active in the GTP-bound form but inactive in the GDP-bound form. Ras was discovered in the Weinberg lab via the following experiment. Human tumor DNA was cut into pieces, and each different piece was put into a different mouse cell. The mouse cells were then grown in Petri plates. Only the mouse cell that took up the mutant allele of the oncogene could grow and divide enough to form a colony of cells.

a) Do you think that the mouse cells had their own versions of Ras before the experiment began? If yes, do you think that the mouse versions of Ras were wild-type or mutant?

Yes, they had wild-type versions of Ras gene before the experiment was done.

b) In this experiment, it seems that there was only one mutation necessary to make the mouse cells over-proliferate. We know, however, that cancer results from an accumulation of mutations. Why then did this experiment work?

A cell line is already immortalized and is therefore predisposed to transformation unlike the wild-type cells. Hence a single mutation is enough to transform it to a cancerous cell line.

c) If a patient had a tumor that was caused in part by mutations in Ras, do you think it would be a good therapeutic decision to treat the cancer patient with a drug that targets and inhibits Ras?

Most likely, yes, since oncogenic mutation is a gain-of-function mutation.

d) Do you think it would be a good therapeutic decision to provide this cancer patient with a wild-type copy of the Ras gene?

No, since adding a wild-type copy of Ras gene cannot suppress the phenotype caused by the gain-of-function mutation.

e) Do you think that this experimental technique would work to identify tumor suppressor genes? Why or why not?

No, it would not work. A mutation in a tumor suppressor gene is a homozygous loss-of-function mutation. Therefore introducing a mutated copy of the tumor suppressor gene into the cells that have two wild-type copies of the same gene will not work (the effect of wild-type allele is dominant to the mutated allele).

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