Genetics and Cancer Activity

The cell cycle is controlled by a combination of positive and negative regulators.

**Proto-oncogenes** include positive regulator genes that produce factors that stimulate the cell cycle. Proto-oncogenes can be mutated to become oncogenes. Most proto-oncogenes found to date produce factors that stimulate the cell cycle too much. Whereas a proto-oncogene product is like a gas pedal that can be pushed or relaxed, an oncogene product is like a gas pedal that is stuck to the floor.

1. Look at the figure to the right. At the cellular level are mutations in proto-oncogenes generally dominant-acting or recessive-acting? Explain

**Tumor suppressor genes** include negative regulatory genes that produce factors that inhibit cell division under normal conditions. Many tumor suppressor gene products are like the brakes for cell division. When you think of the protein products of mutant tumor suppressor genes, think of having a car brake that is defective.

2. Look at the figure on the right. At the cellular level are mutations in tumor suppressor genes dominant-acting or recessive-acting? Explain

3. The normal function of gene P is to kill cells that show signs of chromosome damage. Mutant forms of gene P are found to be involved in cancer. Is gene P likely to be a proto-oncogene or a tumor suppressor gene? Why?

4. The normal function of gene M is to signal for cells to divide when the body needs to heal a wound. Mutant forms of gene M have been found to be involved in cancer. Is gene M likely to be a proto-oncogene or a tumor suppressor gene? Why?
The breast cancer 1 (BRCA1) gene has been implicated in breast cancer.

Below is a pedigree of a family showing the incidence of breast cancer with a particular BRCA1\(^-\) allele. BRCA1\(^+\)/BRCA1\(^-\) females who have this particular allele of BRCA1\(^-\) have a high chance of developing early onset breast cancer.

There are no BRCA1\(^+\)/BRCA1\(^-\) individuals in this family.

BRCA1\(^-\) mutations usually cause breast cancer in females but not in males; one member in generation I is heterozygous for the mutant allele; individuals II-1 and II-5 are BRCA1\(^+\)/BRCA1\(^+\).

5. What are the possible modes of inheritance (X-linked, Autosomal, Mitochondrial, or Y-linked; dominant/recessive) in this family and why? Explain your answer.

6. Write the genotype next to each person in the pedigree above.

7. If a man has a BRCA1 mutation (remember, there are no BRCA1\(^+\)/BRCA1\(^-\) individuals in this family), what is the chance he will pass the mutation on to his daughter? What about his son?
Patients with inherited forms of breast cancer inherit one normal allele and one mutant allele of a gene (ex. BRCA1⁺/BRCA1⁻). Then, subsequent somatic changes lead to a cell with no functional BRCA1 alleles. This cell then divides to make a tumor.

For example, a new somatic mutation can occur in the functional BRCA1⁺ allele in a population of diving cells.

**Woman: BRCA1⁺/BRCA1⁻ Heterozygote**

Or chromosomal errors (such as mitotic nondisjunction) can leave an individual with only the BRCA1⁻ allele in a cell. A cell without any normal BRCA1 alleles can begin to divide uncontrollably, leading to cancer.

8. A woman is BRCA1⁺/BRCA1⁻. If you could analyze 10 of her non-cancerous somatic cells, how many wild-type and how many mutant copies of BRCA1 would you expect to find in each cell?

9. If you analyzed 10 of her tumor cells, how many wild-type copies of BRCA1 would you expect to find in each cell?

10. A man is BRCA1⁺/BRCA1⁻ but does not have breast cancer. If you could analyze 10 of his sperm cells, how many wild-type and how many mutant copies of BRCA1 would you expect to find in each cell?
11. The BRCA1 gene is a tumor suppressor gene. At the cellular level, are mutations in tumor suppressor genes dominant acting or recessive acting (look at question 2)?

12. Look back at the pedigree. At the organismal level, does the BRCA1 allele behave as a dominant or recessive allele?

13. Explain the paradox to your answers in question 11 and question 12.