

Tumor Suppressor Genes and Oncogenes

(Biochemistry/Molecular Biology Small Group)

OBJECTIVES

- Describe the differences between tumor suppressor genes and oncogenes, and give three examples of each.
- Map key cell cycle proteins and regulatory signaling pathways to the stages of the cell cycle.
- Describe the concepts of Knudson's two hit hypothesis and multi-step carcinogenesis.
- Compare and contrast, at a molecular genetic level, cancers that occur in early childhood (eg. Rb) vs. those that occur in adults (eg. colorectal cancer).
- For inherited cancers, explain the difference between the phenotypic pattern of inheritance versus the effect of the mutation at the cellular level.
- Compare and contrast sporadic and inherited forms of retinoblastoma.
- Describe the basic management of patients affected with or at risk for developing familial retinoblastoma.

Professionalism

- Demonstrates respect for others' contributions, time and values.

Interpersonal & Communication Skills

- Synthesizes and summarizes information for the benefit of the learners.
- Identifies and solves problems using intelligent interpretation of data

REQUIRED READING

Students should read the following lecture syllabus sections before attending the small group discussion:

- Cell Proliferation and its Regulation
- Tumor Suppressor Genes and Oncogenes: Genes that Prevent and Cause Cancer.

OPTIONAL READING (papers available through UC-elinks)

- GeneReview on Retinoblastoma on the NCBI GeneTests website: <http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=gene&part=retinoblastoma>
- Classon, M. and Harlow, E. The Retinoblastoma Tumour Suppressor in Development and Cancer. *Nature Reviews: Cancer*. **2**, 910-917 (2002).
- Humphries, A. and Wright, N.A. Colonic crypt organization and tumorigenesis. *Nature Reviews: Cancer*. **8**, 415-424 (2008).
- Deshpande A. and Hinds P.W. The Retinoblastoma Protein in Osteoblast Differentiation and Osteosarcoma. *Current Molecular Medicine*. **6**, 809-817 (2006).

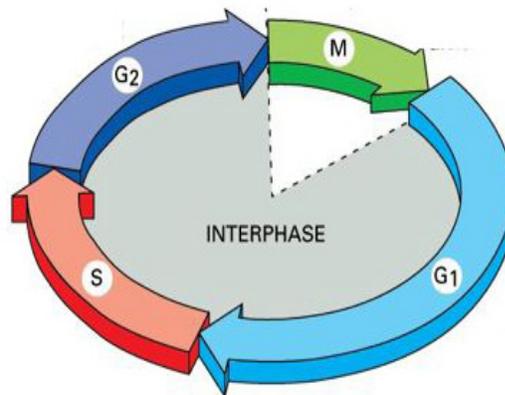
QUESTION 1

As scientists study the DNA changes seen in cancer cells, we have learned that certain genes are altered in many adult tumors. Among the genes that are commonly affected are genes encoding p53, cyclin D, Rb, p16, K-ras, myc, and an EGF receptor (her2/neu). We have also learned that certain types of alterations are associated with each of these genes. For example, some of them are commonly activated while others are often inactivated.

a) What effect do each of the above gene products have on the cell cycle? (Fill in table and use the schematic of the cell cycle to indicate where each gene product functions.)

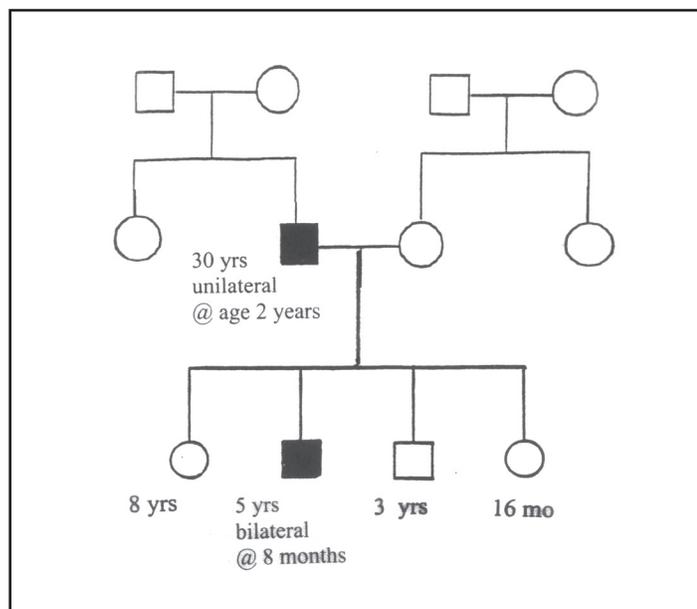
b) Which of the genes named above are likely to be activated in cancers and which are likely to be inactivated? What mechanisms are involved in activating or inactivating these genes?

	Oncogenes	Tumor Suppressor Genes
Effect on Cell Proliferation		
Examples		
Mutation Type (Dominant vs. Recessive)		
Effect on Function of Gene Product		
Effect on Apoptosis		
Activated or Inactivated in Cancer		



QUESTION 3

Nathan is a 5-year-old boy who you are seeing in the pediatric clinic for a regular check up. According to his mother, Nathan had a “blur” in both eyes since birth. At 2 months of age, his eyes would “wander off.” At 8 months of age, his pediatrician noted poor red reflex in his eyes. He was subsequently referred to a pediatric ophthalmologist. He was diagnosed with bilateral retinoblastoma at the age of 8 months. He was treated by enucleation of his right eye and cryotherapy of the tumor region in his left eye, and the vision in his left eye was saved. He is currently in good health. Nathan has 3 siblings (see pedigree below): an older sister age 8 years, a younger brother age 3 years, and a baby sister age 16 months. None of Nathan’s siblings have shown any signs or symptoms of retinoblastoma. Nathan’s father was diagnosed with unilateral retinoblastoma at the age of 2 years, and was successfully treated with radiation in the affected eye. Nathan’s mother is in good health, and there is no other immediate family history of retinoblastoma or other cancers.



- a) Based on what you know about the genetics of retinoblastoma, is the father’s case likely to be sporadic or inherited? Why?

- b) Besides retinoblastoma, what other types of cancers are patients who inherit *RBI* mutations at risk for developing? Considering the molecular mechanism leading to retinoblastoma, hypothesize why this might be?
- c) Is there still a risk of developing retinoblastoma or other cancers in any family members? What management do you suggest for Nathan's father? For Nathan? For Nathan's siblings?