Cancer—an aberration of development

Lecture Key points

Cancer illustrates how basic science can help us understand and ultimately treat human disease.

All cancers ultimately have a genetic basis as they result from mutations in human genes, either inherited or somatic.

Cancer cells exhibit behaviors found in normal cells during development, differentiation, and homeostasis but they combine these in unfortunate ways and without normal regulatory cues that keep them in check.

Cancer metastasis involves acquisition of a new set of cell behaviors.

Cancer evolves these properties in a multistep process through the process of natural selection.

Two broad categories of mutations drive cancer—mutational activation of oncogenes, whose protein products normally promote proliferation, and mutational inactivation of tumor suppressors, whose protein products normally inhibit proliferation.

Many oncogenes encode components of cell signaling pathways.

Oncogenes mutations are rare mutations causing constitutive activity and are thus genetically dominant.

Targeted therapies that block signaling are creating new forms of cancer treatment.

Rb provides an example of how a tumor suppressor can normally inhibit cell proliferation.

Tumor suppressor mutations are loss of function and thus genetically recessive.

SAMPLE Learning objectives

After this lecture you should be able to:

Compare properties of cancer cells with those shared by normal cells during embryonic or postembryonic development.

Explain why cancer development takes a long time, in terms of the number of mutations in an advanced tumor.

Contrast the type of cancer-causing mutations that are found in oncogenes with those in tumor suppressor genes, in terms of effect on protein function and genetic properties.

Illustrate the normal roles of proto-oncogenes in cell signaling and cell behavior.

Describe the cell biological roles of some of the genes that contribute to metastasis.
Explain the genetics and cell biology of tumor suppressors, using Rb as an example

Contrast tumor suppressors like Rb with those like p53 that act as “guardians of the genome”

**Guided Reading Q’s**

Read Alberts 712-721+724 and answer the following questions about cancer.

1) List two key properties of cancer cells

2) Define metastases

3) What is the normal mutational error rate WITHOUT exposure to carcinogens? Given this, why doesn’t cancer arise MORE OFTEN?

4) Describe the role of evolution by natural selection in the development of cancer?

5) How many copies of each gene are present in the human genome? __________

6) What is the normal role of a proto-oncogene? How many copies of an oncogene must be mutated and is/are these mutations loss-of function or gain of function?

7) What is the normal role of a tumor suppressor gene? How many copies of a tumor suppressor gene must be mutated and is/are these mutations loss-of function or gain of function?

8) What are three ways a proto-oncogene can be “activated”?

9) How do mutations in APC contribute to familial colon cancer—i.e., in what sequence do the two mutations occur?

10) Provide three examples of how understanding basic cell mechanisms has led to new treatments?