Notes Pg 358

The Molecular Biology of Cancer

* Certain genes regulate cell growth and division — mutations lead to cancer
* May be spontaneous, or environmental influences such as chemical carcinogens, xrays, viruses
* Oncogene- cancer causing genes
* Protooncgene- normal cellular gene
* Oncogenes are formed by either movement of DNA w/in genome, amplification of a proto-oncogene, and point mutation
* Malignant cells are frequently found to contain chromosomes that have broken and rejoined incorrectly, translocating fragments from one chromosome to another
* Amplification increases the # of copies of the gene in the cell.
* Point mutation changes the gene’s protein product to one that is more active or more resistant to degradation than the normal protein.
* Tumor-suppressor genes make protein products that inhibit cell division, the proteins normally help prevent uncontrolled cell growth. If these genes are not expressed, excessive growth will lead to cancer
* Some tumor suppressor proteins normally repair damaged DNA, this prevents cancer causing mutations
* Other tumor suppressor genes control adhesion of cells to each other or to ECmatrix, in cancer there will not be proper cell anchorage

Oncogene proteins and faulty tumor suppressor proteins interfere with normal signaling pathways

* Ras protein is a protooncogene found in 30% of human cancers
* P53 protein is a tumor suppressor found in 50% of human cancers
* Ras protein relays a growth signal from a growth factor receptor on the plasma membrane to protein kinases, this leads to synthesis of protein that stimulates the cell cycle
* Ras oncogenes have a point mutation that leads to hyperactive verstion of ras protein, leads to excessive cell division
* P53 gene is expressed when damage to the cell’s DNA gives a signal. P53 then activates p21 to halt cell cycle to allow time for the cell to repair the DNA; if irrepairable p53 activates suicide genes to cause cell death by apoptosis. If p53 is missing, cancer may ensue.

Multiple mutations underlie the development of cancer

* + Cancer results from an accumulation of mutations, so the older we are, the more likely we are to get cancer.
  + Colorectal cancer: first sign is a polyp- small benign growth in the colon lining. Cells look normal but divide too frequently
  + Development of a malignant tumor is paralleled by a gradual accumulation of mutations that activate oncogenes and knock out tumor suppressor genes
  + For cell to be cancerous: appearance of at least one oncogene, and mutation or loss of several tumor-suppressor genes.

(Tsupp genes are recessive, so both alleles must block tumor suppression, but oncogenes behave as dominant alleles) and in many tumors the gene for ***telomerase*** is activated. This enzyme prevents erosion of the ends of the chromosomes, thus removing a natural limit on the number of times the cells can divide.

* + Retroviruses cause some types of leukemia, hepatitis viruses can cause liver cancer, wart viruses cause cancer of the cervix
  + Viruses integrate their genetic material into DNA, retrovirus may donate an oncogene to the cell
  + Cancer runs in some families because their genomes are similar to each other’s and may be more likely to develop cancer genes
  + Breast cancer is second most common type of cancer in U.S.
  + BRCA 1 and 2 are genes involved in breast cancer. Mutations in either gene increase risk for developing breast cancer, both are tumor supressor genes, because their wildtype alleles suppress breast cancer
  + The study of these and other genes associated with inherited cancer may lead to new methods for early diagnosis and treatment of all cancers

Pg 221 Cancer cells have escaped from cell-cycle controls

* Cancer cells do not respond normally to body’s control mechanisms. They divide excessively and can kill the organism. Normal cells exhibit density dependent inhibition but cancer cells do not stop dividing
* In culture cancer cells will divide indefinitely if they are given nutrients. Cells from Henrietta Lacks are still dividing in culture since 1951
* Problem begins when single cell undergoes transformation, and if it escapes body’s immune system, it will form a tumor, a mass of abnormal cells within normal tissue.
* Tumor is benign if it remains in one site, lump can be removed by surgery.
* Tumor is malignant if it can impair the functions of organs. This is cancer.
* Cancer cells may have unusual number of chromosomes, metabolism may be deranged, lose attachments to neighboring cells and extracellular matrix
* Cancer cells may separate from original tumor, enter blood and lymph vessels, proliferate to form more tumors, called ***metastasis***
* Treatments include highenergy radiation and chemotherapy
* Cellular transformation always involves alternation of genes that somehow influence the cellcycle control system.