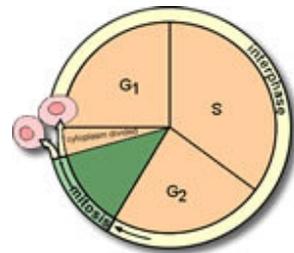


E - Bio Handout

Mitosis and Cancer

I. Multicellular organisms constantly need to make more cells!

- **Each minute** your body needs to make ...*oh*...about **300 MILLION NEW CELLS!** A cell spends a good part of its life in a "**G-phase**" (**growth phase**) working and growing, breaking down sugars, synthesizing proteins, enzymes, and other macromolecules. However, cells inevitably wear out, break down and suffer injuries.
- **In addition**, as organisms grow and change, they need new cells to make more skin tissue, bone tissue, muscle tissue. These new cells can only come from one place: **OTHER CELLS** - through the process of cell division, or mitosis.
- For **multicellular organisms** (like us) **cell division** allows an organism to **grow and develop** from a single cell to trillions of cells, to **repair** and **replace** cells worn out and used up by everyday life, and in some cases, to make specialized cells for reproduction.
 - **Somatic Cells:** (Mitosis) **body cells** of an organism that do all the 'daily' functions of the organism as mentioned above.
 - **Germ Cells:** (Meiosis) **reproductive cells** - eggs and sperm involved in starting the next generation....



II. Cancer: renegade cells escaping the controls on cell division:

1. What is cancer? Cancer is essentially a **disease of mitosis** - the normal 'checkpoints' regulating mitosis are ignored or overridden by the cancer cell. Cancer begins when a single cell is **transformed**, or converted from a normal cell to a cancer cell.

Often this is because of a change in function or a **DNA mutation** that occurs in one of several **genes** that normally function to control growth. **Examples:**
 (1) the **p53 gene**, the "guardian of the genome", usually functions to properly control the cell cycle. However, p53 is mutated in over 50% of all human cancers.
 (2) the **BRCA 1 gene**, the "Breast Cancer Gene" normally functions to suppress tumor formation; but if a gene contains mutations such that BRCA1 does not work properly, tumor formation can begin (**Note:** mutations in this gene do not mean that a person will develop breast cancer, just that they have an increased risk for breast cancer).

Once these crucial **Cell Cycle genes** start behaving abnormally, cancer cells start to proliferate wildly by repeated, uncontrolled mitosis.

2. Tumors - Good Cells gone Bad...? The cancer cells proliferate to form mass of cancer cells called a tumor. As the tumor grows larger, it begins to release proteins from

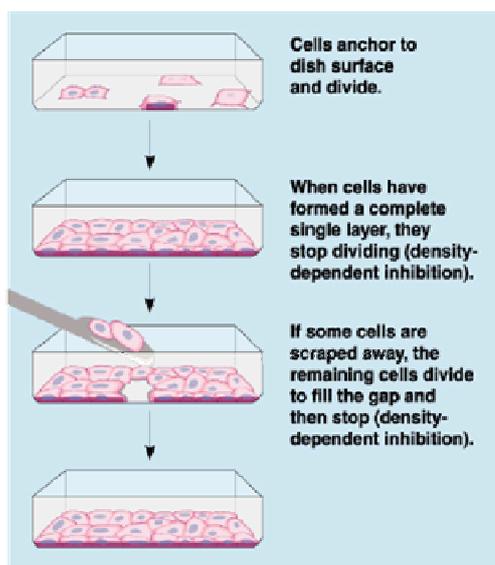
the cell to attract new blood vessel growth (this is called **angiogenesis**). At this point the tumor contains ~ 1 million cells and is about the size of a '**bb**'.

Benign: tumor cells remain at original site. Can be removed surgically or killed by radiation, usually eliminating any further cancer development at that site.

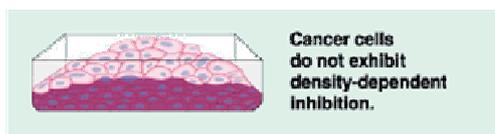
Malignant: some tumor cells send out signals that tell the body to produce a new blood vessel at the tumor site. These cells not only have their own food and oxygen supply, they also have an avenue for **escape** to a new part of the body - through the new blood vessel and into bloodstream. Cells that break away from the tumor begin to spread to surrounding tissues (via the bloodstream or lymph) and start new tumors = **metastasis**. Usually surgery is performed to remove the tumor, followed by radiation and chemotherapy.

3. Unusual features of Cancer Cells.

(1) Cancer cells are frequently "**immortal**": whereas normal cells divide about 50 times and then die, cancer cells can go on dividing indefinitely if supplied with nutrients (A common laboratory cell line, HeLa cells, was originally isolated from a tumor in 1951 and is still growing).



(a)



(b)

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(2) Cancer cells ignore the usual **density-dependent inhibition of growth** in cell culture (or in body tissues), multiplying after contact with other cells are made, piling up until all nutrients are exhausted. **Density-dependent inhibition is a control mechanism** when cells reach a certain density they will stop reproducing. If some cells die the density becomes less and the cells will reproduce to regain the same density and then normally stop.

(3) Cancer cells may also have an abnormal **cell surface**; instead of "sticking" to its neighboring cells, cancer cells tend to "round up" and break attachments to its neighbors cells, allowing for metastasis.

(4) Cancer cells often have unusual **numbers** of chromosomes or mutations in chromosomes. **Aging**, exposure to **toxins** (like components of tobacco tar), **mutagens** (like ultraviolet light) all cause mutations in genes and cancer; but normal errors in DNA replication can lead transformation of the cell if they occur in a crucial gene.

Stopping cancer cell growth:

Chemo Drugs that stop DNA synthesis/ replication:

- Adriamycin and Cytosine prevent DNA from unwinding properly,
- 5FU inhibits incorporation of T nucleotides
- Methotrexate and 5-MP prevent cells from making nucleotides
- ARA-C is a C nucleotide "mimic" that gets incorporated and stops further DNA synthesis
- *No DNA replication, no new cancer cells!*

Chemo drugs Taxol and Vincristine, both natural products from plants, work by **inhibiting spindle fiber formation and disrupting mitosis**. *No mitosis, no new cancer cells*

Common Chemotherapy Drugs

You probably know someone, maybe a friend or family member, who has been diagnosed with cancer. If the cancer is found to be **benign**, usually the recommended course of treatment is removal of the tumor, followed by **radiation therapy** to destroy any remaining cancer cells at the site of the original tumor. If pathologists determine that the cancer cells are **malignant** (have traveled to the **lymph nodes**, or have cellular characteristics that suggest malignancy), a recommended course of treatment **chemotherapy**, sometimes called "chemo" - a slang term meaning "drug therapy with chemicals".

Most chemo drugs are known as "**anti-neoplastics**". [anti-nee-oh-PLAS-tics.] - neoplastics being cancer cells. Most antineoplastics work by **stopping cell division in one or another stage of the cell cycle**. They cause cell death in any dividing cell, and since most human cells are not dividing all the time, they preferentially kill cancer cells. But any human cell types which divide frequently are also killed: cells in the gastrointestinal tract, the bone marrow, and hair follicles. These are reversible processes and will symptoms will disappear when the drug is discontinued. (But the cancer cells will be hopefully killed by then).

Cancer Growth Animation Worksheet

View the cancer growth animation either by clicking on the link found in the Bio 12 animation webpage or using the following url:

http://www.pbs.org/wgbh/nova/cancer/grow_flash.html

Answer the following questions from the animation

1. What type of cancer is studied in the animation and where does it form?
2. How many cells are in the human body?
3. Identify two things that can cause mutation?
4. Why do normal cells usually reproduce?
5. What is angiogenesis?
6. What is metastasis?