# Cancer

**A**. What is it?

- A **cancer** is an uncontrolled, independent proliferation of robust, healthy cells.

    * In some the rate is fast; in others, slow; but in all cancers the cells never stop dividing. This distinguishes cancers - **malign tumors** or **malignancies** - from benign growths like moles where their cells eventually stop dividing.

    * Cancers are **clones**. No matter how many trillions of cells are present in the cancer, they are all descended from a single ancestral cell.

    * Cancers begin as a **primary tumor**. At some point, however, cells break away from the primary tumor and - traveling in blood and lymph - establish **metastases** in other locations of the body. Metastasis is what usually kills the patient.

    * Cancer cells are usually less differentiated than the cells of the tissue where they arose. Many people feel that this reflects a process of "de-differentiation", but I doubt it.

    * Rather, cancers arise in precursor cells of the tissue; cells that are normally in a period of rapid mitosis and not yet fully differentiated.

- 1971 "The War on Cancer" ... huge amount of gov't resources.
    * today, 560,000/yr die, 28% of all deaths
        ** children: 2000 deaths/yr
        ** males: 295,000/yr, lung, prostate, colorectal
        ** females: 266,000/yr, lung, breast, colorectal

- types: 4 major categories:

1. **Carcinoma** - most common, solid tumors of skin & derivatives
    * skin, esophageal, respir. tree (pharyngeal, laryngeal, bronchial), lungs, bladder, dig. organs, genetalia (most = germinal epithelial layers)

    * of all cancers, 50% involve breast, lung, prostate, colorectal; 40% spread among the rest.

2. **Sarcoma** - rarest - <2%, dense tissues. Bone, muscle, cartilagenous, fat (VERY rare!!).

3. **Leukemia** - 4% WBC or bone marrow.

4. **Lymphomas** - 4%, WBC, spleen, lymph nodes.

**B**. Causes of Cancer.

- Cancers are caused by several factors....often, more than 1 factor causes a single case of cancer. Here are summaries of 2 large influences: changes in genetic material and viruses.

1. Genetics: anything that damages DNA; that is anything that is **mutagenic**
   * radiation that can penetrate to the nucleus and interact with DNA
   * chemicals that can penetrate to the nucleus and damage DNA. Chemicals that cause cancer are called carcinogens.

   - Cancer cells contain several (6-8) mutated genes.

   * **Sporatic** = 80% of ID'd cases, occurring @ random w/in population. 2 normal genes are inherited for either a suppressor or protoonca gene (see later section on types of genes involved). 1st mutation = somatic, then a later somatic mutation ("**two-hit**").

      ** But still a "genetics" problem: the mutation of a somatic. Individual is a **"Compound Heterozygote**".

   * **Familial** = 20% of cases. Recessive... a somatic heterozygote for a supressor or an oncogene. When normal cell mutates, get cancer ... "**one-hit**" hypothesis so it looks dominant. But ... it has to happen in the spot where the tumor could happen ... often, simply "sloughed off".

      - Many different forms..here are some common examples (but doesn't include many common types! This is all I could give without a genetics lesson!):

   a) Genes that stimulate **angiogenesis**. Tumors, like any tissue, need a blood supply to bring food and oxygen and to take away wastes. So as it grows, a developing cancer must be able to stimulate the growth of new, normal, blood

vessels into itself. This is done by the release of angiogenesis stimulants, e.g., **vascular endothelial growth factor (VEGF)**, perhaps as an additional effect of mutated oncogenes or tumor suppressor genes.

b) **Metastasis genes**: genes that enable cells of the tumor to separate from the primary tumor and migrate to other parts of the body. These can be:

* mutations in genes whose products normally keep the cells of a tissue adhering to one another.

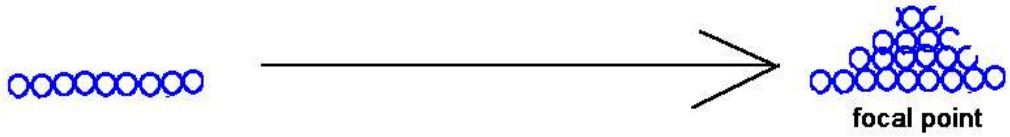
* mutations in genes whose products normally keep the cells adhering to their substrate.

c) **Oncogenes** ("oncos" = "mass"; see later). "Protoonca" = "Precancerous". Their mutated or over-expressed products stimulate mitosis even though normal growth signals are absent. Directly cause cancer if mutated.

- An oncogene is a gene that when mutated or expressed at abnormally-high levels contributes to converting a normal cell into a cancer cell.

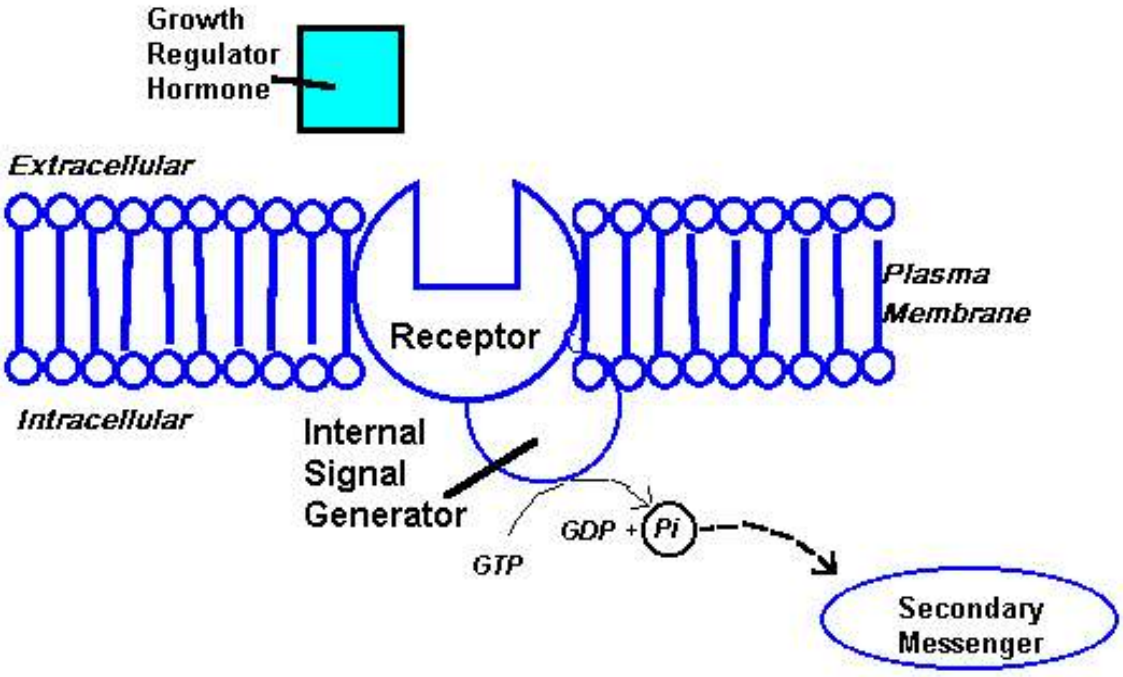
* we don't know what their product was before they were "oncogenes" ... The product of oncogenes = Growth Regulators (hormones), Receptors, or Secondary Messengers (G-protein) ...see below!

- Cancer cells are cells that are engaged in uncontrolled mitosis. Normally, cells show **Contact Inhibition** (if touch, they stop growing). Cancer cells lack this trait; form a **Focus Point**.




* **hyperplasia** (increased growth of normal cells) then changes to **dysplasia** (continued growth w/ changes in cell and nuclear structures, forming a **polyp**).

- Much of this is controlled hormonally. Normal Pathways of hormone action:




2. Viruses and Cancer . Many viruses have been studied that reliably cause cancer when laboratory animals are infected with them. What about humans? The evidence obviously is indirect but some likely culprits are **retroviruses** using **insertion mutagenesis** (activating an onccogene):

* two papilloma viruses that infect the reproductive organs

** Of the several human papilloma viruses (HPV) that infect humans, two have been implicated as a risk factor for cervical cancer. Once inside the cells of its host, one of these synthesize a protein, E7, which binds to the Rb protein preventing it from binding to the host transcription factor E2F.

* the **hepatitis B** and **hepatitis C** viruses, which infect the liver and are closely associated with liver cancer (probably because of the chronic inflammation they produce)

* some **herpes viruses** such as the **Epstein-Barr virus.**

- but note! Clearly viral infection only contributes to the development of cancer.

* many people are infected by these viruses and do not develop cancer. When cancers do arise in infected people, they still follow our rule of clonality. Many cells have been infected, but only one (usually) develops into a tumor.

* again it appears that only if an infected cell is unlucky enough to suffer several other types of damage will it develop into a tumor.