Cancer

The oldest description of cancer were written in Egypt as early as 3000 BC as part of an ancient Egyptian textbook on surgery.

The word "cancer" comes from the Greek work carcinos, which means crab. Hippocrates used this term to describe the disease because the projections of a cancer invading nearby tissues. During the 16th century, when the theory of bodily humors prevailed, it was believed cancer was caused by excess black bile buildup; But this was discarded early when no black bile was found. After invention of the microscope, evidence accumulated that cancer was the result of uncontrolled cell division but the cause was still unknown.

Learning Objectives

1. Describe the distinguishing features of a cancer
2. Discuss the mechanism by which cancers evolve
3. Explain what is meant by "metastasis" and the mechanisms by which it occurs
4. Explain the difference between the "grade" and the "stage" of a cancer
5. Discuss risk factors for cancer and strategies for prevention
6. Define the following terms:
    - Cell differentiation
    - Benign tumor
    - Malignant tumor
    - Dysplasia
    - Carcinogen
    - Proto-oncogene and onogene
    - Tumor-suppessor gene (anti-oncogene)
    - Apoptosis

Cancer Biology

Cancer is the result of a long process that begins when one of the cells in organs or tissue becomes damaged or altered in a way that causes it to break free from normal controls that allow cells to work in harmony. Cancer cells with divide via mitosis even if they do not receive the appropriate signals. This can lead to a mass of cells, or a tumor.

The nucleus of a cell contains the genetic information, within the chromosomes. Certain genes make products that lead cells to reproduce. The genes responsible for making cells divide are called **proto-oncogenes.** Changes in normal genes lead to the production of proto-oncogenes,

making cells divide faster. There are also genes that stop the division of cells, known as **tumor-suppressor genes** (AKA anti-oncogenes). We have two of these genes (one from each parent), so if one tumor-suppressor gene is damaged, usually the other is able to stop the cell from behaving abnormally.

The process by which tumors cause the body to provide the cell with nutrients is call **angiogenesis.** The tumor sends out messages that say "feed me" and the nearby blood vessels send over new extensions that deliver food and oxygen. The blood vessels also act as a passageway for movement of tumor cells. The movement of tumor cells to other parts of the body is called **metastatis.** 90% of cancer deaths occur when the tumor spreads to different parts of the body.

One way the development of cancer is prevented is the death of defective cells. If the body is unable to replace or repair the damaged, stressed, or worn-out cells it commits cellular suicide, or **apoptosis.** This leads to the breakdown and death of the cell. It is estimated over 50 billion cells undergo apoptosis each day in adults, and is carefully regulated through complex mechanisms. Cancer cells lose this critical capability and lead to buildup of abnormal cells. Cancer cells can also develop resistance to drug or chemotherapy treatment in the same way bacteria might.

Cell Differentiation

A major difference between cells in a growing embryo and those in an adult is that most of an adult's are differentiated (they have become specialized in structure and function). Muscle cells are elongated and contain an abundance of contractile proteins, whereas pancreas cells are specialized for secretion of digestive enzymes.

The cells in the earliest stages of an embryo are totipotent, meaning they have the capacity to divide and give rise to any of the specialized cells in the body. In contrast, in an adult the replacement if shed or worn out cells takes place by division of somatic stem cells (also called adult stem cells), which are not fully differentiated but can give rise to only a limited array of cells.

For example, stem cells in the bone marrow (hematopoetic steam cells) and divide and give rise to progenitor cells that can differentiate into cellular elements of blood and immune system, including red blood cells, lymphocytes, platelets and more. Bone marrow stromal stem cells (mesenchymal stem cells or skelatal stem cells) can generate bone, cartilage and fat cells.

When stem cells are called upon to generate a particular type of cell, they undergo asymmetric cell division in which one of the child cells has a finite capacity for cell division and begins to differentiate and the other sibling cell remains a stem cell with unlimited proliferative ability.

New cells are born through the division of an existing cell into two through mitosis. The need for new cells continues through our entire life, but is greatest in early life. A fertilized egg divides into two cells, which splits to 4, 8, 16, 32, 64, etc... In a fully grown adult the rate of cell proliferation is much less, and under normal circumstances only takes place when signals indicate cells need to be replaced.

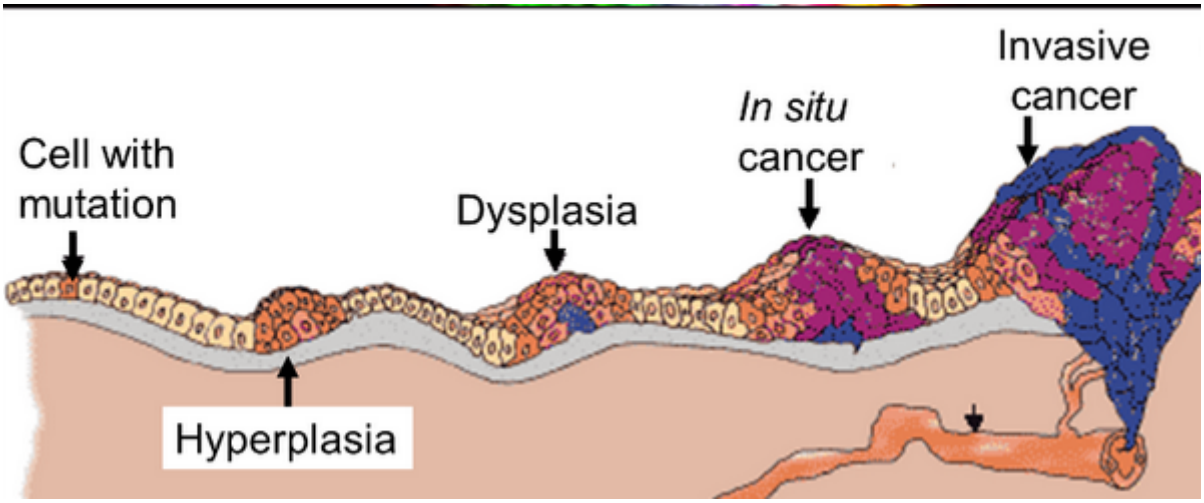
Cell differentiation is not completely understood, but involves the activation or inactivation of certain genes in response to the cell's interaction with neighboring cells and with its extracellular matrix (ECM). Receptors on the cell will bind to specific molecular elements in the ECM and this binding activates the intracellular signal transduction pathways that turn certain genes on or off. As a result some genes can be expressed in a given cell, and others cannot. Some cells, like sketelal and muscle cells, become terminally differentiated meaning their ability to proliferate is permanently lost, though they can continue to perform their functions.

Ex. of Normal Cell Division: The outer layer of skin (eipdermis) is about 12 cells thick. Cells in its lowermost basal layer divide just fast enough to replinish shed cells. Division of a basal cell produces one cell that remains in the basal layer and retains the capacity to divide. The other migrates out of the basal layer and loses the capacity to divide, thus the number of dividing cells in the basal layer stays roughly the same.

Ex. of Abnormal Cell Division: The transition to skin cancer begins when the normal balance between cell division and cell loss is disrupted. Basal cells divide faster than needed leading to an increasing number of dividing cells. This creates a growing mass of a tissue called a "tumor" or "neoplasm". The organization of the tissue gradually becomes more disrupted.

Benign Tumors (skin moles, lipomas) are abnormal growths that are no longer under normal regulation, but grow slowly, resemble normal cells,and still have surface recognition proteins that bind them together and keep them from invading or metastasizing.

Evolution of a Cancer



Atrophy: Reduction in cell mess

Hypertrophy: Enlargement of cell size

Hyperplasia is an increase in the number of cells in a tissue with normal cell morphology and normal cell to cell interaction

Dysplasia is a pre-cancerous state characterized by increased cell proliferation with high abnormal and variable appearance to the cells. Cell to cell interactions are diminished, and the architecture of the tissue is less organized. Dysplasia is potentially reversible and doesn't always progress to cancer, but indicates a pre-cancerous state with high probability of evolving to cancer and considered "per-malignant".

Carcinoma "in situ" literally means cancer in place. These cells have transitioned to being cancerous. In situ cancer may remain contained indefinitely, but additional mutations may occur that enable it to invade neighboring tissue and shed cells into the blood or lymph.

Metastatis is the movement or spreading of cancer cells from one tissue to another and their prolideraation at the new site. Cancer cells usually spread through the bloodstream or lymphatic system. The tumor mass can also spread locally, compress other structures and damage surrounding tissues.

Characteristics of Cancer Cells:

- Self-sufficiency in growth signals; an autonomous drive to proliferate - pathological mitosis - by virtue of the activation of oncogenes such as ras or myc.
- Insensitivity to growth-inhibitory signals; they inactivate tumor suppressors.
- Evasion of programmed cell death (apoptosis); suppression and inactivation of genes and pathways that normally enable cells to die.

Cancer Risk Factors

Radiation

Non-ionizing - low frequency, long wavelength energy which is not energetic enough too penetrate deeply or create free radicals.It only penetrates single-celled organisms and the superfical cell layers of multicellular organisms. However, it can damage DNA in superfical cells and cause mutations. UV rays from the sun and tanning salons accounts for 50-90% of all skin cancers. Ex. radio signals, microwaves, power lines, heat lamps, etc.

Ionizing - Proton, neutrons, x-rays, and gamma rays have highly energetic wavelengths enabling them to deeply penetrate tissues. Lead shields block this form of radiation. DNA can be damaged by a direct hit, but it more often indirectly damages DNA by stripping away electrons when they strike a molecule, thereby creating a highly reactive free radical. The resulting free radical can damage other molecules by stealing electrons or breaking phosphate bonds in DNA, thus giving it a cumulative mutagenic effect. Ex. Nuclear fallout, radioactive chemicals, Radon, etc.

Chemicals

A chemical carcinogen is any discrete chemical compound which has been shown to cause cancer. These can enter the body through absorption, ingestion, or inhalation. Some of these include

formaldehyde, chloroform, asbestos, and arsenic. Tabaco smoke contains over 60 carcinogens.

Heterocyclic amines (HCAs) & Polycyclic Armoatic Hydrocarbons (PAHs) are a family of carcinogenic chemicals formed in cooking muscles meats (beef, pork, fowl and fish). Eggs and tofu are not associated. HCAs form when amino acids and creatine (a chemical found in muscles) react at high cooking temperatures.

Viruses

Viruses are estimated to cause 15-20% of all cancers. The host's genetic susceptibility, mutations, exposure and immune system deficiencies are also factors. Oncoviruses (cancer-causing viruses) include Epstein-Barr virus, hep B and C, HPV, and herpes. AIDs also indirectly increases risk of cancer due to impared immune function.

Consumption and Heredity

High BMI is associated with increased risk of colon, breast, kidney, esophagus, stomach, pancreas, gallbladder and liver cancer. Fat tissues produce excess amounts of estrogen, high levels are associated with some cancers. Obese people often have increased levels of insulin in their blood, which may promote the development of certain tumors. Fat cells may have a direct or indirect effect on tumor growth regulators.

Alcohol intake is associated with an increased risk of cancer of the mouth esophagus, pharynx, colon, and liver.

Most cancers are sporatic, and have to hereditary predisposition. However, there are some which can be hereditary such as Retinoblastoma, breast cancer, and colon cancer.

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