M220 Lecture 24

Persistent (Chronic) Viral Type Infections (continued)

Prions are self-replicating proteins with no detectable nucleic acids and are also suspected agents of some of the slow viral type diseases. The disease called scrapie which occurs in sheep and the disease called kuru in humans are two disease processes that fit into this category. Mad cow disease (bovine spongiform encephalopathy) is a persistent infection caused by prions. Humans can contract this infectious agent in contaminated beef and end up with a serious and fatal dementia called variant Creutzfeldt–Jakob disease (CJD).

Cancer

A tumor is any abnormal growth. A benign tumor is an abnormal growth that is self-limiting, generally slow growing, non-invasive and tends to be localized in an area. Benign cells do display contact inhibition. Benign tumors can still be fairly large. Malignant tumors are generally rapid growers, autonomous (not under normal control of body cells) and invasive. These malignant cells will show a loss of contact inhibition. Primary malignant tumors give rise to secondary tumors as cells can slough off and invade other locations. This process of spreading is called metastasis and can result in multiple foci of tumor growth.

Changes Observed in Cancer (transformed) Cells

1. Changes in cell chemistry including possible alterations in acid/base balance and the production of abnormal protein kinases.
2. Chromosomal abnormalities including fragmentation are seen in cancer cells.
3. Metabolism is accelerated and cancer cells divide with great frequency. Cancer cells under microscopic examination are captured in the process of mitotic division much more than normal cells.
4. Cancer cells display antigens that distinguish them from normal cells. TSTA or tumor-specific transplantation antigen is displayed on tumor cell surfaces. T antigens are found in the nuclei of tumor cells.
5. Cancer cells do not display contact inhibition tendencies.
6. Cancer cells will look very different from normal cells. Tissue and organ morphologies become altered. For example cancer cells appear more round than their normal counterparts. In general, cancer cells are said to be less differentiated.

Cancer Types

1. Sarcoma—cancer derived from connective tissue.
2. Carcinoma—cancer derived from epithelial tissue.
   a. Adenocarcinoma—cancer derived from glandular epithelial tissue
3. Leukemia—cancer derived from white blood cells.
4. Lymphoma—solid tumor of white cell origin.
Factors Responsible for Transforming Normal Cells to Cancer Cells

1. Physical Agents
   a. Ionizing radiation-UV, X-rays, gamma rays etc. Most of these affect DNA.
   b. Irritants or abrasives-asbestos, fiberglass etc.

2. Chemical Agents-these chemical agents are called carcinogens. Benzpyrene is an environmental carcinogen found in jet fuel exhaust, cigarette smoke and charcoal broiled meats. DES or diethylstilbestrol used for an array of indications including menopausal symptoms was linked to cervical and other cancers in women whose mothers took DES. Saccharin used as an artificial sweetener is a probable carcinogen. Estrogen used in hormone replacement therapy can be carcinogenic. Aflatoxin produced by Aspergillus flavus is associated with liver cancer. The list goes on.

3. Genetic Mechanisms
   a. Mutations-can be spontaneous or triggered by a physical or chemical mutagenic agent. Changes in DNA can cause division control mechanisms to go wrong. Cells will continue to divide in an abnormal fashion.
   b. Oncogenes-genes present in the genome that upon abnormal activation can transform a normal cell into a cancerous cell. Oncogenes in their normally functioning form are called proto-oncogenes and will code for proteins that help to regulate cell growth and differentiation. Mutagenic agents and viruses may play roles in oncogene activation.

4. Decreased Immune State-cells that are in the process of transforming into a cancer cell, or fully transformed cells can be destroyed on a regular basis by the immune system. An immune system that is not fully functioning may allow these "bad" cells to proliferate out of control.

5. Nutritional State-complete intake of necessary nutrients will maintain homeostatic balance and good health. Some foods such as the cruciferous vegetables can act as anti-oxidants which will help to maintain cell membrane structure by inhibiting the oxidation of certain fatty acids. This is an example of a beneficial source of nutrition. This may play a role in decreasing the incidence of cancer. Other nutrients such as animal fats may play a role in increasing certain cancers such as colon cancer.

6. Stress-chronic and excessive levels of stress are generally considered unhealthy.

7. Viruses-oncogenesis can be induced by viruses. In 1908 Ellerman and Bang determined that cell free filtrates (no bacteria or other cells) from chickens with chicken leukemia could be transferred to healthy chickens and cause leukemia. In 1911 a cancer of connective tissue in chickens named a Rous sarcoma could also be transferred to healthy chickens. It was discovered later that most stocks of Rous sarcoma virus contains another virus. The Rous sarcoma virus is defective and requires a helper virus to form infective units. Several leukemia viruses have been discovered. FLV (feline leukemia virus), BLV (bovine leukemia virus), MLV (murine leukemia virus), ALV (avian leukemia virus). In 1957 a polyoma virus in mice was shown to cause multiple types of cancer in different places. In 1961 a virus known as SV (simian virus) 40 was injected into hamsters and caused cancer. Was this a situation where the wrong host (hamster rather than monkey) produced the cancer? SV 40 was also found as a contaminant in early polio vaccines. What were the ramifications of this?