Environmental causes of cancer

Cancer is the second most common cause of death in the United States. However, it is a very simple group of diseases in concept: the uncontrolled division of cells. When the division of cells becomes so rapid that the products are not fully functional, it becomes deadly. Most forms of cancer are caused by either the failure of tumor suppressor genes or the development of oncogenes. Tumor suppressor genes are the normal genes which slow down the division of cells. They repair mistakes in the DNA of cells and program the death of cells through apoptosis. Oncogenes, however, are the opposite of suppressor genes. When proto-oncogenes, the healthy cells which determine how often a cell should divide, turn into oncogenes, they no longer provide the correct information for how often the cell should divide. Usually, the cell is permanently activated, producing many unfinished or otherwise impaired cells. Tumor suppressor genes can be compared to the brake pedal in a car – it prevents the car from going too fast. A faulty suppressor gene would prevent the “ car” from stopping. On the contrary, proto-oncogenes are like the gas pedal in a car. Oncogenes can then be represented by the gas pedal being stuck down. In both situations, Body tissue begins to swell, creating a tumor. An important difference between oncogenes and tumor suppressor genes is that cancer develops when they are activated or inactivated, respectively.

The two different cancer-causing genes both play a role during the cell cycle. In the cell cycle, cells go through a series of steps through which it will eventually split into two different cells. While oncogenes make the host cell rush through the cycle, skipping important checks, faulty tumor suppressor genes allow cells to indefinitely reproduce. The cell cycle begins with the G1

(gap 1) phase, in which the cell rests. Cells also get ready to replicate DNA in the S phase later in G1. The S phase is then followed by the G2 (gap 2) phase. After G2, mitosis, or the division of cells occur, followed by the next G1. A cell's journey through the cell cycle is overseen by cyclin-dependent kinase (CDK) proteins. The CDK checkpoints coordinate the timing of cell cycle transitions. From G1 to S, the cell is regulated by cyclins D1, 2, 3, E, and A, while B-type cyclins regulate the G2 to M transition phases. Based on their structural and functional properties, CDK inhibitors are split into two groups. The INK4 proteins mostly function during the middle of the S phase in proliferating cells. These genes might function as tumor suppressors, as suggested by p15 and p16, which frequently contain deletions when observed in the various human tumors they appear in. The second group, the Cip/Kip family, inhibit kinase activities of the preactivated G1 cyclins. Cell cycle arrest can result from Kip genes excessively activating. Most human cancers are acquired, with more than half involving abnormalities in the TP53 gene (which codes for the p53 protein). However, few cancer syndromes are caused by genetically inherited mutations of proto-oncogenes, causing the activation of oncogenes. For example, multiple endocrine neoplasia type 2 is caused by a mutation in the gene RET, developing the uncommon medullary thyroid cancer. It also causes other tumors, including pheochromocytoma and nerve tumors. Cancer caused by both tumor suppressor genes and oncogenes are not usually inherited, but acquired. Acquired changes in many tumor suppressor genes result in the development of sporadic, or non-inherited, cancers. Chromosome rearrangements, gene duplication, or mutation are the most common activators of oncogenes.

Most human cancers are caused by of a complex blend of genetic and environmental factors. While some forms of cancer are evidently related to certain environmental factors, genetics also plays a role, making the substrate acted upon either susceptible or resistant. Lung cancer is more commonly found in smokers than in nonsmokers; however, smokers with high levels of aryl hydrocarbon hydroxylase (an enzyme that metabolizes tobacco smoke's benzo(a)pyrene into highly carcinogenic chemicals) are found to develop lung cancer 30 times more frequently than other smokers. Here, the growth of the tumor is determined by the genetically obtained enzyme that tobacco smoke interacts with. Environmental factors in the development of cancers can be chemical, physical, or biological. Cancer from environmental factors develop in three stages. In the first stage, initiation, the DNA is modified in specific spots, usually by inducing oncogenes. Oncogenes can be activated at this stage as chemical carcinogens are capable of mutating the cell. The second phase, promotion, involves the reversible expansion of the cell, making it the target for prevention. Although promoters are often incapable of causing cancers themselves, they hasten the development of cancers by initiating agents. The last step of cancer development is progression. The tumor becomes invasive, transformed, and is constantly reproducing.

A report in 1775 revealed that people who had constant exposure to coal tar, such as chimney sweeps, had a higher chance of receiving scrotal cancer. The exact cause was found to be benzo(a)pyrene over 140 years later. Most chemical carcinogens are activated by the body's metabolism. Microsomal enzymes, which evolved to detoxify substances, is ironically an example.

Polycyclic hydrocarbons, aromatic amines, or alkylating agents are all chemical compounds which can cause cancer. Chemical carcinogens create adducts, which cause errors in the base sequence of DNA. The damage caused by tobacco, the most common and widespread environmental carcinogen, is constantly increasing because of the resulting number of deaths from cancer and heart or respiratory diseases. Disturbingly, tobacco related cancers can also affect non-smokers who inhale the second hand smoke from others.

Another form of environmental carcinogens are physical carcinogens. Physical carcinogens usually induce cancer through ionizing radiation, ultraviolet radiation, or foreign bodies. Radiation is known to cause DNA mutations and activate oncogenes. Ionizing radiation can be further divided into electromagnetic radiation, from x-rays and gamma rays, and particle radiation. The risk of contracting cancer are mostly dependent on the energy transfer value, dosage, and dose rate. While electromagnetic radiation is weak and has a low energy transfer value (the rate of energy entering the tissue), particle radiation causes more damage because is dense and compacted, having a high energy transfer value. Radiation can cause cancers anywhere on the human body. Natural sources like cosmic rays, terrestrial gamma ray flashes, and radon are the most common sources of radiation exposure, accounting for at least 80%. For example, the sun’s ultraviolet radiation is a common cause of skin cancer. Skin cancers occur more frequently in areas near the equator and other sites exposed to the sun. It was found that people with red hair and certain genetic conditions, like xeroderma pigmentosum, are less able to repair ultraviolet damage and

are therefore more vulnerable to cancers caused by the sun. The ozone layer in the atmosphere and the pigments in our skin both protect us from ultraviolet radiation. Foreign bodies occasionally cause tumors. The composition of the foreign body is less important than its size and shape. The same substance can be more carcinogenic if they are fibrous than if they are powdered, porous, or perforated. The transformation is probably related to errors when connective tissue reacts to the foreign body. The most dangerous foreign body to humans is asbestos, which is a natural mineral fiber often inhaled, causing lung cancer. Other carcinogenic fibers include synthetic vitreous and crystalline fibers.

Biological carcinogens are not often found in humans, but do occur in nature. Information is gathered from tumors caused by viruses in animals, but the reason or method of carcinogenesis is still unclear. Four oncogenic viruses have been found and documented in humans: hepatitis B, Epstein-Barr virus, some papilloma viruses, and HTLV-I. Cancers can also be caused by reoccuring infections. For example, Helicobacter pylori gastritis can lead to gastric mucosa-associated lymphatic tissue lymphoma and to gastric adenocarcinoma. Similar to foreign bodies, parasites can also cause tumors. An example is chronic bladder infection with Schistosoma haematobium, which can develop bilharzial squamous-cell bladder cancer.