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Carcinogens and protective genes against the cancer

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Abstract

What is a carcinogen? Substances that cause severe gene damage in cells and trigger mechanisms that lead to cancer are called carcinogens. In short, it means "cancer-causing". While some chemicals found in nature can be carcinogens, there are also carcinogens produced by humans. Carcinogens reduce the functions of cancer-preventing genes and cause mutations that damage DNA repair systems. In this proceeding-review study we focus on some of the carcinogens and also the genes that are protective against the cancer.

Introduction

Changes in DNA that cause defects in tumor suppressor proteins and oncoproteins may predispose the patients to develop tumor cells. Growth, development, and intracellular cycle regulatory genes, key oncogenic mutations involve chromosomal sequences and translocations as well as insertions, deletions and base changes [1]. In addition, the destruction of protective genes in DNA repair systems paves the way for possible mutations. Cells that carry mutations that also affect certain cell cycle regulators and accumulate and trigger the development of the cancer. In addition, some DNA repair mechanisms are prone to error [2]. These repair errors contribute to the tumor formation. The fact that cancer cells keep their genetic makeup intact contributes to the formation of an unevenly distributed colony of tumor cells [3]. Therefore, chemotherapy targeting one gene or several genes are ineffective destroying all harmful cells. The ineffectiveness of the method in this way increases the attention drawn to the treatments that prevent blood flow to reach to the tumor site to eventually induce the death of the tumor cells in the region [4].

The tumor-causing abilities of chemical and physical carcinogens depend not only on their capacity to cause DNA damage in cells, but also on the ability or inability of the cells trying to repair this damage [5-7]. Carcinogens defined as chemical carcinogens are divided into two categories as those with direct effect and those with indirect effect, even though they do not have sharp common characteristics and show widespread distribution they are grouped in these two categories [8].

The number of carcinogens that play a direct role is very few, and they are compounds that seek and interact with centers where electrons are high in other compounds [9]. These compounds can chemically interact with nitrogen and oxygen atoms in DNA, disrupting some of the modifiable and normal base pairing patterns in DNA. If these modified nucleotides are not corrected, they cause mismatching of the nucleotides during replication. Some of these types of carcinogens are ethylmethylsulfonate (EMS), dimethyl sulfate (DMS) and mustard gas [10].

Indirectly acting carcinogens are generally non-reactive, often water-insoluble compounds that cause cancer only after reaching the electrophilic centers. Cytochrome found in animals, P450 enzymes are found in the ER of many cells and are particularly abundant in the liver. P450 enzymes normally bind some electron rich center such as hydroxyl groups to non-polar unspecified chemical such as some treatment drugs, rendering them water-soluble and allowing them to be removed from the body. On the other hand, P450 enzymes can convert some inert chemicals into carcinogens. Many chemical carcinogens have a low mutagenic activity before being modified by cellular enzymes [11].

Results

Even in the absence of exogenous carcinogens or mutagens in cells, normal cellular processes can produce large amounts of damaged DNA. DNA damage is due to depurination and alkylation reactions that alter DNA and reactive oxygen derivatives. It is estimated that 20000 changes occur in the DNA of each cell every day, caused by reactive oxygen derivatives and depurination, so DNA repair mechanisms are important defense mechanisms [12].

The usual function of protective genes is to prevent or repair damage to the DNA. There is a link between the loss of DNA repair systems and the likelihood of developing cancer. For example, some cancers are more likely to develop in people who have an inherited mutation in their protein that performs base mismatch or base excision repair [13]. Individuals with xeroderma pigmentosum (XP) or transmitted between generations nonpolyposis colorectal cancer (HNPCC) lacking the necessary DNA repair mechanisms are likely to have mutations in some important genes involved in cell division and proliferation. People with XP are 1000 times more likely to develop skin cancer than those with normal pigments. Seven of the eight known XP genes encode proteins involved in this base excision repair, and when this mechanism is absent, the genes that control the cell cycle in the cells and regulate the vital activities in these processes are mutated. Colorectal cancer genes encode components of mismatch in the DNA repair system. Changes in these components increase the incidence of the colon cancer. The process from benign polyp to cancer progresses much faster than normal cells because cells do not have repair systems, so there is constant mismatch mutagenesis [14].

The DNA polymerase enzyme family of DNA repair mechanisms functions to abolish DNA damage. Nine of these constructs, including DNA polymerase β, can correct errors involving DNA damage and other chemical modifications. These polymerases are also known as lesion bypass polymerases. Each member of this family can repair a different type of damage. These polymerases can tolerate damage because any repair is better than no repair, and lesion bypass polymerases are the last resort when appropriate and ubiquitous polymerases fail to do their job [15]. Thus, they successfully maintain a mutagenic replication function. DNA polymerase β has no error-correcting properties and is highly expressed in some tumors. Perhaps overexpression of this enzyme in the tumor may be necessary for these over-mutated cells to continue dividing. Error-prone repair systems can correct the carcinogenic effect of chemicals or radiation if there is no inherited mutation. There is evidence that DNA mutations in polymerase β are tumor-associated. When two mutant forms of polymerases were sent into the mouse cells, these mice were shown to have a transformed appearance. It was also revealed that foci were formed in mice and these foci were found independently [16].

Protective genes protect the integrity of the chromosome by encoding DNA-repairing enzymes or cause the death of the cell where DNA damage occurred. Changes in the protective genes ensure the survival of the cells that need to die, change in the cell cycle control, and the continuation of mutagenesis in the genome and ultimately the formation of cancer. Inherited DNA repair mechanism disorders detected in some human diseases increase the susceptibility of people to some types of cancer. Cancer cells; similar to the stem cells and germ cells, unlike modified cells, produce telomerase, which prevents the chromosomes from shrinking while DNA makes its own copy, thus preventing the cells from breaking down [17].

Understanding that cancer is a genetic disease led to the development of new approaches to prevent and treat this disease. Today, it is known that carcinogens have an effect on some steps involved in the cell cycle control. By identifying the faults that may have occurred in the components of the checkpoints and repair systems that serve to detect and repair damaged DNA, we can examine the mechanism of cancer in more details. In order for a normal cell to turn into a malignant tumor cell, there are many changes that must occur in the cell. Identifying mutant genes related to cancer can show us at which point we should target the drugs we will use in the treatment [18]. Diagnostic medicine is changing as the possibilities for displaying cellular features increase. Some of the traditional methods used to identify possible tumor cells focus on microscopy of labeled cells, measuring the expression of hundreds of genes, or specific genes that can be good indicators of disease diagnosis and cell growth. Recent DNA microarray analyzes have made it possible to measure the transcription of genes. In the future, techniques that can perform all the important systematic measurements of the cellular stages, such as protein production, change and location, will allow us to get a better portrait of the cell [19]. Therefore, mutations that may occur, such as errors in the DNA repair system are detected, increasing the possibility of preventing cancer with the developed methods and techniques.

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