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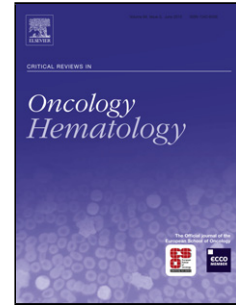
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The stem cell division theory of cancer

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Abstract: All cancer registries constantly show striking differences in cancer incidence by age and among tissues. For example, lung cancer is diagnosed hundreds of times more often at age 70 than at age 20, and lung cancer in nonsmokers occurs thousands of times more frequently than heart cancer in smokers. An analysis of these differences using basic concepts in cell biology indicates that cancer is the end-result of the accumulation of cell divisions in stem cells. In other words, the main determinant of carcinogenesis is the number of cell divisions that the DNA of a stem cell has accumulated in any type of cell from the zygote. Cell division, process by which a cell copies and separates its cellular components to finally split into two cells, is necessary to produce the large number of cells required for living. However, cell division can lead to a variety of cancer-promoting errors, such as mutations and epigenetic mistakes occurring during DNA replication, chromosome aberrations arising during mitosis, errors in the distribution of cell-fate determinants between the daughter cells, and failures to restore physical interactions with other tissue components. Some of these errors are spontaneous, others are promoted by endogenous DNA damage occurring during quiescence, and others are influenced by pathological and environmental factors. The cell divisions required for carcinogenesis are primarily caused by multiple local and systemic physiological signals rather than by errors in the DNA of the cells. As carcinogenesis progresses, the accumulation of DNA errors promotes cell division and eventually triggers cell division under permissive extracellular environments. The accumulation of cell divisions in stem cells drives not only the accumulation of the DNA alterations required for carcinogenesis, but also the formation and growth of the abnormal cell populations that characterize the disease. This model of carcinogenesis provides a new framework for understanding the disease and has important implications for cancer prevention and therapy.

Keywords: cancer etiology, carcinogenesis, cancer prevention, stem cells, cancer stem cells, stem cell environment, cells of origin in cancer, somatic mutation theory of cancer

1. Introduction

Cancer is a disease characterized by the formation and growth of abnormal cell populations that threaten the life of an individual by interfering with vital body functions. Although cancer is known to be ultimately caused by an uncontrolled cell proliferation, the main biological cause of the disease remains poorly understood [1]. An

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