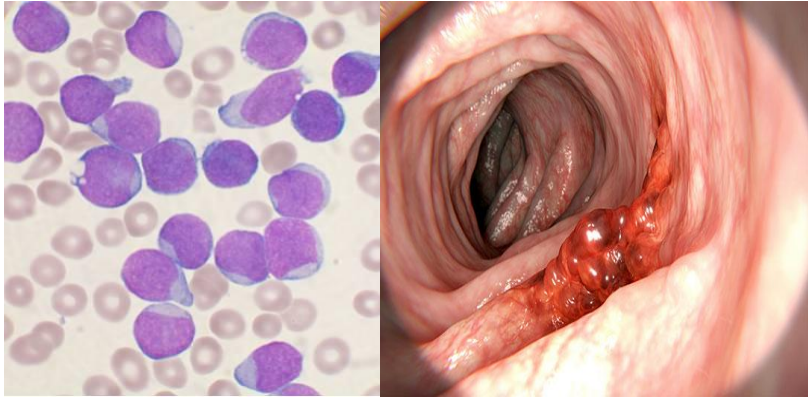


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THEORIES OF CARCINOGENESIS

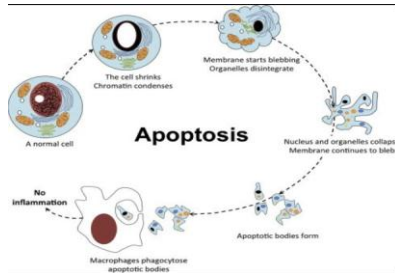
Cancer is a broad term. It describes the disease that results when cellular changes cause the uncontrolled growth and division of cells. Some types of cancer cause rapid cell growth, while others cause cells to grow and divide at a slower rate. Certain forms of cancer result in visible growths called tumors, while others, such as leukemia, do not.



Wright's stained bone marrow aspirate smear from a person with precursor B-cell acute lymphoblastic leukemia.

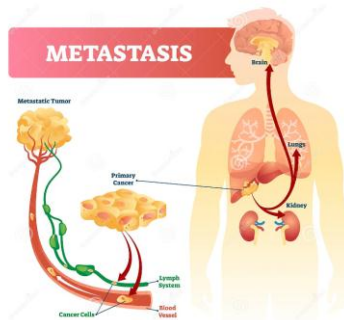
Computer model of cancer tumor

Most of the body's cells have specific functions and fixed lifespans. While it may sound like a bad thing, cell death is part of a natural and beneficial phenomenon called apoptosis. A cell receives instructions to die so that the body can replace it with a newer cell that functions better.



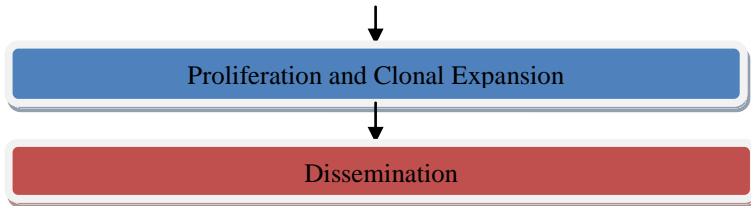
Stages of Apoptosis

Cancerous cells lack the components that instruct them to stop dividing and to die. As a result, they build up in the body, using oxygen and nutrients that would usually nourish other cells. Cancerous cells can form tumors, impair the immune system and cause other changes that prevent the body from functioning regularly. Cancer cells generally have very low adhesion, so they easily break away from the tumor and spread throughout the body, becoming the basis for secondary tumors. This process is called metastasis. The figure below shows one of the ways of metastasis.



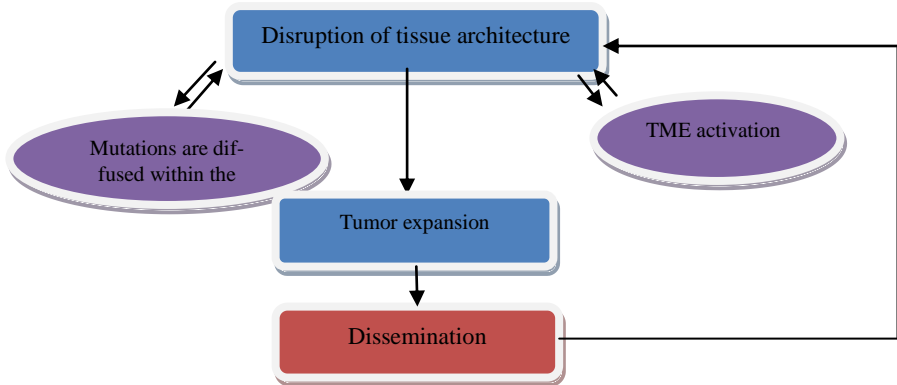
Today there are two main theories of carcinogenesis: Somatic mutation theory (SMT) and Tissue organization field theory (TOFT). For 50 years, the theory of SMT has been leading. It is based on the assumption that cancer develops from a single somatic cell, which "collected" a variety of DNA mutations, and these mutations appear in genes that control the cell cycle and proliferation.

Mutations / genetic rearrangements in the cell



The default state of the cell is quiescence, and a genetic event in the cell triggers a unidirectional, irreversible and deterministic process that leads to tumor expansion and dissemination

A younger alternative theory of TOFT is based on the fact that carcinogenesis is a problem of the incorrect organization of tissues.



In the tissue organization field theory the default state of the cell is proliferation, and a disruption of the tissue architecture leads to the diffusion of various mutations within the tumor and to the activation of the tumor microenvironment (TME). Through feedback mechanisms, this leads to further disruption of the tissue architecture, which promotes tumor expansion and dissemination.

Due to the lack of evidence for the first two theories, a third theory is also distinguished - the result of their merger. It says that the problem lies in cell mutations and in the anomalies of tissue organization.