Exp Oncol 2009
31, 1, 2



Experimental ONCOLOGY

# CANCER STEM CELLS

According to modern concepts stem cells represent a key link not only in embryogenesis and postembryonic period of the development, but they are also a source for neoplastic development. 150 years ago R. Virchow in the well-known concept has assumed the possibility that cancer originates from the limited population of cells. Today the cancer stem cells model of tumors draws the increasing attention of researchers. In classical stochastic model, all neoplastic cells possess tumorigenic potential. In contrast, the concept of cancer stem cells assumes, that in solid tumor only a small amount of cells (about 1%) is tumorigenic. The elaboration of methods affecting directly cancer stem cells can be the best form of cancer therapy. Being clonal in the origin, solid tumors are histologically heterogeneous, comprising both cancer and host tumor-associated cells, the cells of inflammatory infiltrates and vascular structures. Usually, stroma makes up a considerable part of a malignant tumor.

The following types of stem cells are known: embryonic, fetal, adult, and cancer stem cells. The latter are defined, as the population of cells capable of self-renewal, with limited differentiation, giving tumor growth upon transplantation to NOD/SCID mice with the expressed immunodeficiency. The evidence suggesting the existence of stem cells were first obtained in human leukemia, and later mammary cancer, ovarian, brain tumors, retinoblastoma, melanoma, osteogenic tumors, prostate cancer. The fraction of cancer stem cells was found out in a number of cancer cell lines. There are several hypotheses on the origin of cancer stem cells. First, cancer stem cells may originate from normal stem cells of corresponding tissue which are long-living and possess high efficiency of DNA repair as a result of repeated mutations and a selective expression of genes. For instance, now it is considered that stem cells of acute myeloid leukemia are derived from normal polipotent hematopoietic stem cells. According to other assumption, cancer stem cells are derived from unipotent progenitors that reacquire the properties of stem cells to self-maintenance. In favour of this hypothesis is the fact that development of a blast crisis of chronic myeloid leukemia involves the committed cells of granulocyte-macrophage lineage. It must not be ruled out also, that some tumors arise from more mature cells acquiring the properties of cancer stem cells upon their dedifferentiation. One more variant is possible also. In some gastric cancers the cells of marrow origin are transformed into cancer stem cells in a gastric mucosa as a result of *Helicobacter pylori* associated chronic infection. This hypothesis can be extended to other tumors of epithelial nature, associated with chronic inflammation, including ovarian, esophageal and colorectal tumors. The horizontal gene transfer by phagocytosis of fragmente DNA from apoptotic cells can lead to acquiring of properties of cancer stem cells by cell-recipients. For instance, the cells of invasive glioma are highly phagocytic. The human embryonic stem cells may also be tumorigenic. Upon transplantation *in vivo* of human undifferentiated embryonic stem cells to mice, teratomas grow which can become malignant named teratocarcinomas.

Cancer stem cells are surrounded by other cells making their microenvironment within the given tissue named “a niche”. Functions of diverse systems of cancer stem cells, including ability to self-renewal, differentiation, ability to adhesion, division and a survival, are controlled, maintained and stimulated by extracellular signals from the niche as well as by intrinsic genetic programs within the cancer stem cells. The changes of a niche as a result of an infection, inflammations, exposure to chemical agents or radiation can activate the proliferation of stem cells, initiating tumoral process. The analysis of structural and functional pattern of the niche of cancer stem cells can shed light on character of signals of the niche and specify areas of the further research.

Resistance mechanisms of cancer stem cells includes also high level of expression of transporter molecules which are removed by therapeutic agents. It is necessary to yield new insights into different mechanisms allowing the cell avoiding the influence of therapeutic agents. That will help to open new ways of molecular biomedical investigations. It is necessary also to study biological properties, the cellular mechanisms of reprogramming, to isolate preparatively the cancer stem cells from tumors and to identify their new markers, for developing of the targeted methods of therapy. Having blocked the processes providing ability of vital functions of cancer stem cells of tumors, and having interrupted interaction ways between them and their environment, we, probably, also will manage the influence of development of tumoral process.

***Editor-in-Chief of Experimental Oncology***
***V.F. Chekhun***