

ADVANCES IN STUDIES ON INVASIVE TUMOR GROWTH AND METASTASIS

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There is an accumulation of mutations and changes in the expression of protooncogenes and tumor suppression genes during multistep carcinogenesis. This leads to an acquisition by tumor cells of not only a growth phenotype, as a result of the disturbed control of proliferation and apoptosis, but also of invasive phenotype, characteristic for malignant tumor cells. The tumor cells expressing the invasive phenotype infiltrate the basal membrane of vessels, tissues, and organs and are able to initiate secondary growth in distant places. Acquisition of the invasive phenotype and realization of the program of malignant tumor growth are the consequences of genetic instability with subsequent heterogeneity of the population of cancer cells.

Only some cancer cells may survive, evading normal homeostatic mechanisms. The clonal or polyclonal expansion of the surviving tumor cells is responsible for progressive growth. These tumor cells express beneficial traits for survival as a new species – the cancer cells are able to avoid differentiation, replicative senescence, and to achieve “immortality”.

At present, studies are focused on identification of the genes, the alterations in expression of which are related to invasive tumor growth and acquisition of metastatic potential. The invasive tumor cells produce molecules which enable them to spread into the surrounding peritumoral tissues. Moreover, these cells are able to utilize the physiological functions and components of their microenvironment to realize their invasive phenotype. The invasive tumor cells interact with fibroblasts, endothelial cells and immunocytes, utilizing the growth factors, adhesive molecules, enzymes and nutritional factors secreted by the components of the extracellular matrix. These interactions enable the invasive cancer cells to migrate, enter the blood vessels, survive in the blood stream, leave the vessels and initiate growth as metastases, the development and growth of which depends on the induction of new vessels – angiogenesis.

A better understanding of the biology of invasive growth and the mechanisms of metastatic potential indicate new targets for antitumor therapy, which should complete conventional treatment, aiming to eliminate the majority of if not all cancer cells.