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Significance of Oncogenes Tumor in Progression and Metastasis

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Description

Cancer is a complex and diverse disease caused by genetic mutations in cells. Oncogenes are genes that have the ability to transform normal cells into cancer cells. Mutations, gene amplification, or overexpression can activate these genes, resulting in uncontrolled cell growth and proliferation. Cancer cells are the driving force behind tumor growth and progression. Cancer is now widely accepted to be caused by the accumulation of genetic alterations in cells. To comprehend the molecular mechanisms of cancer metastasis, it is necessary to identify the genes whose alterations accumulate during cancer progression, as well as the genes whose expression is responsible for cancer cells acquiring metastatic potential. Tumorigenesis is a complex and multistep process in which oncogene and tumor-suppressor gene mutations almost always result in increased proliferation and resistance to cell death. Sustainment of proliferative signals, evasion of growth suppressors, resistance to cell death, replicative immortality, induction of angiogenesis, activation of invasion and metastasis, energy metabolism, evasion of immune destruction, genome instability and mutation, and tumor-promoting inflammation are all hallmarks of most human tumor types.

Molecular analyses of cancer cells in various stages of progression have revealed that alterations in tumor suppressor genes and oncogenes accumulate during tumor progression and correlate with the clinical aggressiveness of cancer. Comparative analyses of gene expression profiles between metastatic and non-metastatic cells have revealed that various genes are differentially expressed in association with the metastatic potential of cancer cells. As the tumor microenvironment actively participates in tumor progression and metastasis rather than acting as a bystander, therapeutic strategies targeting the tumor microenvironment hold great potential. It is known that non-tumor cells are presumably and genetically more stable than tumor cells; thus, therapies targeting the tumor microenvironment are less likely to cause adaptive mutations and rapid metastasis.

Metastasis

Metastasis is the process by which tumor cells escape from primary sites, spread through lymphatic and/or blood circulations, and eventually disseminate to distant sites. The development of metastasis, one of the hallmarks of cancer, accounts for more than 90% of cancer-related deaths. The metastatic cascade is divided into three major processes: invasion, intravasation, and extravasation. The loss of cell-cell adhesion allows malignant tumor cells to dissociate from the primary tumor mass, and changes in cell-matrix interaction allow the cells to invade the surrounding stroma; this is the invasion process. This includes the secretion of substances that degrade the basement membrane and extracellular matrix, as well as the expression or suppression of proteins involved in motility and migration control. Moreover, the tumor must begin angiogenesis because, for tumors smaller than 2 mm in diameter, local diffusion would be sufficient to transfer nutrients to and remove waste products from the tumor site. The dislodged cells then travel through the bloodstream and intravasate, or spread to distant areas, through the blood vessel that is close to the tumor. In the process of tumor "angiogenesis," the interaction between the tumor cell and the stroma is crucial. Once the tumor cell has reached a likely intravasation site, it interacts with the endothelium through biochemical interactions (mediated by carbohydrate locking reactions, which occur weakly but rapidly), develops adhesion to the endothelial cells to form stronger bonds, and thus penetrates the endothelium and the basement membrane; this is the process of extravasation. The new tumor can then spread to this secondary site.

Conclusion

Metastasis is the leading cause of death in cancer patients, and it is a complex problem that requires more than one therapeutic agent to effectively inhibit. Knowledge on barrier function and paracellular permeability may allow one to devise new approaches to controlling trespassing cancer cells and their entry into target tissues and organs.

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