Introduction

FOCUS ON...metastasis suppressors

Cancer patients very often experience spread of tumor cells to secondary locations far-removed from the primary tumor center. In fact more than 90% of cancer deaths are caused by disseminating tumor cells [1]. Research of the last years identified various steps of the metastatic cascade that includes cell invasion, survival in vascular and lymphatic space and colonization and tumor progression in distant organs. These steps are regulated by a class of metastasis effector genes both positively and negatively [2]. Genes that inhibit metastasis but do not affect primary tumor development are called metastasis suppressor genes. This FOCUS ON...assembles a series of mini-reviews providing perspective on some of these genes, on the function of their products and therapeutic efficacy of their targeting.

Jacobs and Sackstein [1] describe how circulating tumor cells use normal leukocyte trafficking to home specific tissues and the role of hematopoietic cell E-/L-selectin (HCELL), a sialofucosylated glycoform of CD44, in tumor cell-endothelium, leukocyte and platelet interaction. Knopke et al. [3] highlight the biological mechanism of action of MAP kinase kinase 4 (MKK4), specifically its valuable use in disrupting tumor cell-microenvironment interactions to elucidate the requirements for metastatic colonization and developing models to allow the study on early steps of dormancy. Tsai and Weissman [4] are dealing with the multiple mechanisms implicated in metastasis suppression by CD82/KAI1, a member of the tetraspanin superfamily of glycoproteins affecting membrane organization, protein interactions and hence cell signaling and intercellular communication. The Nm23 family of metastasis-associated genes particularly the Nm23-H1 anti-metastatic factor is in focus of Saha and Roberts’ contribution [5]. Nm23-H1 has clearly been suggested to play a pivotal role in limiting tumor cell motility and progression induced by several tumor viruses including Epstein-Barr virus, Kaposi-associated herpes virus and human papilloma virus. Finally, Hurst and Welch [6] review functional aspects of the breast cancer metastasis suppressor 1 (BRMS1), the expression of which causes dramatic metastasis suppression in various in vivo model systems. Thereby, BRMS1 associates with chromatin-remodeling complexes, such as Sin3:HDAC known to be powerful epigenetic regulators of gene expression. Furthermore, the authors consider how BRMS1 coordinately regulates expression of the metastasis-associated micro-RNA known as metastamir.

This FOCUS ON...aims at a better understanding of the evolving mechanisms of metastatic regulation and the functions metastasis suppressor proteins exert in this process. The editor greatly thanks the authors for contributing to this exciting mini-review series and both editor and authors hope that this FOCUS ON...will further challenge the metastatic aspect of cancer research.

References


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