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Research Highlight

α_2 integrin as regulator of metastatic potential

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Regulation of cellular events is a complex process that involves several factors in their specific interactions and interplays. However, within this complexity exist also signs of specificity and changes in single protein could significantly influence the properties and responses of cells.

Recently, Ramirez and colleagues[1] provided innovative results that emphasize the important and selective role of one specific protein, α_2 integrin, in the complex process of tumor metastasis. This protein, as a part of heterodimeric $\alpha2\beta1$ integrin, was identified as a metastasis suppressor in both breast and prostate cancer.

Tumor metastasis is a process by which tumor cells spread from original source tissue to distant sites within the body, and it is not a single event but requires a series of steps. The known key cellular events required for metastasis include invasion of the surrounding stromal tissue, intravasation, evasion of programmed cell death, arrest within the vasculature at a distant site, extravasation, and establishment and growth within a new microenvironment[2]. However, despite intensive research focused on the process of tumor progression and metastasis, the molecular factors involved and mechanisms that determine and drive the dynamic process of cancer metastasis are not fully elucidated. For a better understanding of the biological processes that underline metastasis is essential to identify individual systems that play a key role in these processes.

The study of Ramirez and colleagues[1] represents a valuable contribution to the identification of specific factors that play the key role in tumor invasion. Their data provide important information for identification of potential molecular mechanisms involved in metastatic responses. They highlight the power of a single protein, α_2 integrin, in modulation of tumor invasion and identify also the key mechanistic steps involved in stimulation of metastatic cascade in consequence of loss of $\alpha2\beta1$ integrin expression. The principal model used for the study of processes of breast cancer initiation and progression was a clinically relevant model of tumor-prone genetically engineered animals that spontaneously develop metastasis [mouse mammary tumor virus-Neu (MMTV-Neu) model]. The selective role of α_2 integrin, as a part of heterodimer $\alpha2\beta1$, in breast cancer progression was explored using animals with deleted gene for this protein. Other experimental approaches validated the observed role of the α_2 integrin as a metastasis suppressor also in subtypes of human cancer.

Massive metastatic progression of breast cancer is direct causality of patient death. Therefore, the research focused on regulatory points of metastatic cascade is of great importance. In this respect, recent findings suggest direct links among integrins and tumor metastasis[3]. The integrins are family of extracellular matrix receptors and their actions could be related to altered activation of matrix metalloproteinases[4]. Functions of matrix metalloproteinases were described to be related to intracellular signaling pathways that include some kinase cascades such as ERK[4] and Rho[5]. Detailed description of regulatory sequence determining specific role of α_2 integrin, metalloproteinases and protein kinases in formation of metastasis needs to be studied in future.

Results of Ramirez and colleagues' study further expand our knowledge about the importance of α_2 integrin in cancer progression, and could be explored in improvement of specific diagnosis of breast cancer metastatic potential. Finally, α_2 integrin has to be considered as a potential therapeutic target in the treatment of this disease.

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