FEATURES

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piRNAs and Piwis in Cancer Epigenetics

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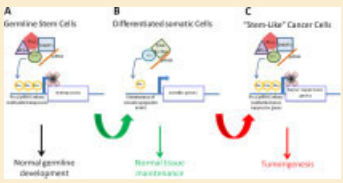
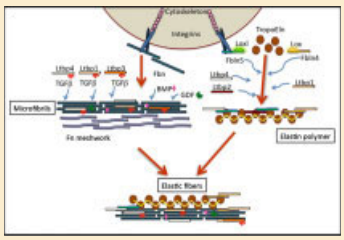


Piwi proteins are known to be critical for stem cell maintenance during development, especially in the germline, where they associate exclusively with a class of small RNAs called piwi-interacting RNAs (piRNA). Together, Piwi and piRNAs maintain genomic integrity by silencing transposon repeats through DNA methylation. Recently several groups have uncovered that Piwi family members and piRNAs are expressed in human cancers. The exact role that Piwis and piRNAs might play in tumorigenesis remains undetermined, however the importance of epigenetic regulation has been well studied in cancers and DNA methylation remains an important epigenetic regulatory mechanism that is perturbed during the tumorigenic process. This review provides a context for the recent studies that have identified Piwis and piRNAs outside the germline and in a cancer context. Moreover, this review offers a potential model by which Piwi expression may contribute to tumorigenesis.

LTBPs: Master Regulators of TGF-β

Vesna Todorovic and Daniel B. Rifkin



TGF-β is an extraordinarily potent cytokine that regulates processes as varied as cell cycle progression, T cell differentiation and extracellular matrix maintenance. Abnormalities in TGF-β action affect development and tissue homeostasis, causing numerous pathologies including cancer, fibrosis and autoimmune disease. Thus, TGF-β action must be tightly controlled at many levels, including secretion and storage in the extracellular space. Mature TGF-β is secreted as part of a latent complex consisting of the growth factor, its propeptide and a separate gene product covalently bound to the propeptide called the latent TGF-β binding protein (LTBP). Todorovic and Rifkin have reviewed the published work describing the central role of LTBPs in modulating TGF-β functions, starting from the cytokine's folding and secretion, through its extracellular targeting and activation. The authors additionally describe how loss of individual LTBP isoforms (LTBP1-4) affects development and function of different organs in mice and humans. As expected, most of these phenotypes are the result of altered TGF-β activity. However, some LTBP-related pathologies stem from processes not directly dependent on TGF-β action, such as elastogenesis. Recent advancements in understanding of LTBP biology, as described in this review, have revealed the multifaceted nature of these proteins as they have been promoted from TGF-β chaperones to master regulators of this complex cytokine.

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