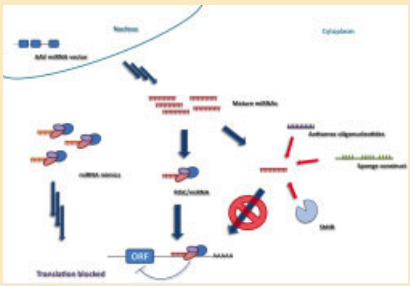
FEATURES

VOLUME 113 • NUMBER 5

ncRNAs as Therapeutic Targets and Diagnostic Tools in Cancer

Roxana S. Redis, Ioana Berindan-Neagoe, Victor I. Pop, and George A. Calin

PUBLISHED ONLINE 28 DECEMBER 2011

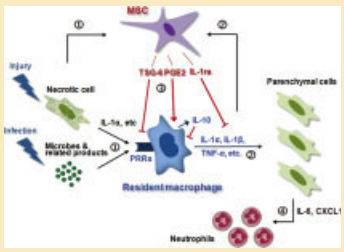


The plethora of studies linking the abnormal expression of miRNAs to all types of cancer has rendered these ncRNAs a leading role in tumor initiation and progression. It is then not surprising that miRNAs have emerged as appealing therapeutic targets and diagnostic tools. In this issue, Redis *et.* review the main findings in this field, starting with the miR-15a/16-1 involvement in CLL (Calin *et al.,* 2002) and finishing with the latest animal models employed for revealing the mechanistic features of the disease. Special focus is set on strategies for targeting miRNAs, which can be achieved either by blocking the expression of oncomiRs with anti-miRNA oligonucleotides, locked nucleic acids or small-molecule inhibitors, or by re-expression of a tumor-suppressor miRNA with miRNA mimics or viral vectors. In the last section of the review, the authors shed light on to the potential use of other non-coding RNAs as therapeutic targets, implying that they will become important therapeutic targets in the near future.

Benefits of MSCs

Darwin J. Prockop and Joo Youn Oh

PUBLISHED ONLINE 29 DECEMBER 2011



For over the past 50 or so years there has been great interest in both the biology and potential therapeutic uses of the stem/progenitor cells from bone marrow referred to as mesenchymal stem or stromal cells (MSCs). The appeal of the cells is that they are relatively easy to isolate and rapidly expand in culture. Also they readily differentiate into several cellular phenotypes, particularly osteoblasts, chondrocytes and adipocytes. Administration of the cells in animal models of a series of human diseases has produced dramatic benefits, but the beneficial effects have been difficult to explain. Recent data demonstrate that the cells only rarely engraft and differentiate in significant numbers in vivo. Instead the beneficial effects are largely explained by the cells responding to signals from injured tissues to up-regulate expression of genes that modulate processes such as excessive inflammatory and immune responses or apoptosis. Some of the beneficial effects can be reproduced by administration of factors the cells are activated to express such as the anti-inflammatory protein TSG-6 or the anti-ROS protein STC-1. Other beneficial effects will require additional study to explain.

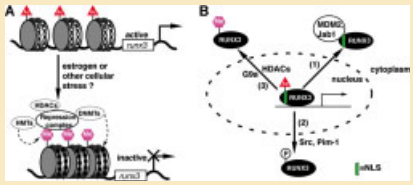
Journal of Cellular Biochemistry

The RUNX3 Tumor Suppressor and Breast Cancer

Lin-Feng Chen

PUBLISHED ONLINE 23 JANUARY 2012

Breast cancer is the leading cause of cancer death in females worldwide and many etiological factors contribute to the development and progression of breast cancer including the inactivation of tumor suppressors. Emerging evidence indicates that RUNX3 is a tumor suppressor in breast cancer. RUNX3 is frequently inactivated in human breast cancer and inactivation of RUNX3 is associated with the initiation and progression of breast cancer. Most important, female *Runx*3$^{+/-}$ mice spontaneously develop ductal carcinoma, and expression of RUNX3 inhibits the tumorigenic potential of breast cancer cells. In this issue, Chen reviews the most recent findings defining the role of RUNX3 as a tumor suppressor in breast cancer. Chen describes how RUNX3 is inactivated in breast cancer at cellular and epigenetic levels and discusses the possible mechanisms underlying the inactivation. Additionally, he discusses how RUNX3 acts as a tumor suppressor in breast cancer by targeting various cellular signaling pathways, including ERα signaling and TGF-β signaling. Finally, Chen explores the therapeutic potential of using RUNX3 for diagnosis and treatment of breast cancer.



When Survival is Challenged, the Immune Cytokine IL-4 Activates Cancer Proliferation

Hernan Roca, Matthew J. Craig, Chi Ying, Zachary S. Varsos, Paul Czarnieski, Ajjai S. Alva, James Hernandez, David Fuller, Stephanie Daignault, Patrick N. Healy, and Kenneth J. Pienta

PUBLISHED ONLINE 15 DECEMBER 2011

Tumor cells take advantage of immune-system cytokines to proliferate and survive in an inhospitable environment. One such cytokine is IL-4, a fundamental molecule of the T-helper-2 or "type-2"-related inflammation. As cancer progresses, the type-2 inflammatory-response increases and, consequently, so does the tumor recruitment of the cells that produce IL-4. In fact, elevated IL-4 has been detected in tumor-infiltrating lymphocytes and other immune-cells in cancer patients. Roca and colleagues analyzed the direct effect of IL-4 on prostate cancer PC3 cells and showed that under nutrient-depletion stress IL-4 can induce cell proliferation. They further investigated the mechanisms of IL-4-induced proliferation and identified the stress-activated kinase JNK as the critical pathway that mediates this response. In the tumor microenvironment, cancer cells face a shortage of nutrients that results in the downregulation of survivin with a consequent decrease in proliferation. The authors demonstrated that under nutrient scarcity, IL-4 stimulates the upregulation of survivin above a critical threshold that is essential for proliferation. Evidence was presented that a similar mechanism could be activated in other cancer cells. This work reveals a program, induced by an immune cytokine, where simultaneous JNK-activation and survivin upregulation can sustain cancer growth even in a stressful nutrient-depleted environment.