Molecular Cancer Research

Highlights

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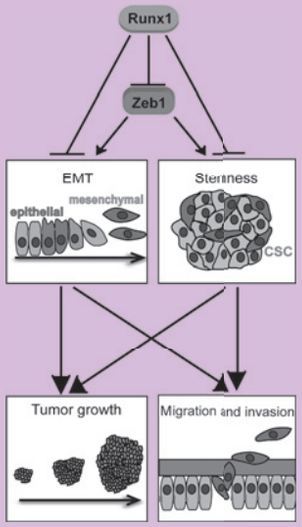
Selected Articles from This Issue



RUNX1 Inhibits Breast Cancer Stem Cells

Hong *et al.*_____Page 1952

The transcription factor RUNX1, represses the breast cancer stem cell (BCSC) phenotype and suppresses tumor growth *in vivo*. BCSCs sorted from pre-malignant breast cancer cells exhibit decreased RUNX1 levels, while ectopic expression of RUNX1 suppresses tumorsphere formation and reduces the BCSC population. Ectopic expression of RUNX1 reduces breast cancer cell migration, invasion, and *in vivo* tumor growth. RUNX1 suppresses tumor growth by repressing cancer stem cell activity and directly inhibiting Zeb1 expression. Clinical findings reveal the highest RUNX1 levels in normal mammary epithelial cells and low RUNX1 expression in tumors is associated with poor patient survival.

Z4 Complex Member in NUT Carcinoma

Shiota *et al.*_____Page 1826

NUT Carcinoma (NC) is a rare, distinctly aggressive subtype of squamous carcinoma driven by NUT-fusion oncoproteins, most commonly BRD4-NUT, and there is currently no effective therapy. The current Rapid Impact, discovers a novel NUT fusion, ZNF592-NUT, from a young patient with NC arising in pelvic bone. In the more typical context of BRD4-NUT-driven NC, it was determined that ZNF592, along with its known "Z4" complex interactors (ZNF532 and ZMYND8) associate with BRD4-NUT and are required to sustain NC, but not non-NC, growth and viability. This study establishes the oncogenic role of Z4 units in NUT carcinoma, offering potential new targeted therapeutic strategies.

USP6 in IFN-Mediated Apoptosis of Ewing Sarcoma

Henrich *et al.*_____Page 1834

Ubiquitin-specific protease 6 (USP6) is the key pathogenic agent in several benign tumors, however its role in malignant entities has not been examined. Henrich and colleagues describe a role for USP6 in Ewing sarcoma (ES), a highly lethal pediatric bone cancer. While USP6 does not enhance ES transformation, it is associated with an interferon (IFN) response in both cultured ES cells and clinical specimens. Further, USP6 renders ES cells exquisitely sensitive to exogenous IFNs, with Type I IFN inducing apoptosis specifically in USP6-positive ES cells through induction of the pro-apoptotic ligand TRAIL. These findings raise the possibility of using USP6 as a biomarker for IFN treatment of ES.

FLYWCH1/β-Catenin Axis Regulates Cell Migration

Muhammad *et al.*_____Page 1977

β-catenin suppressors tightly regulate the transcriptional activity of the activated Wnt/β-catenin pathway during both normal development and cancer. Here, a novel β-catenin transcription suppressor with a FLYWCH/Zn-finger DNA-binding domain, called "FLYWCH1" is identified. The FLYWCH1 protein directly binds to nuclear β-catenin and rearranges its transcriptional activity to selectively block the expression of specific target genes associated with colorectal cancer cell-cell adhesion and migration. This study, for the first time, characterizes and describes a possible anti-metastasis and tumor suppressive role of FLYWCH1 in the context of the Wnt/β-catenin pathway.