Molecular Cancer Research

Highlights

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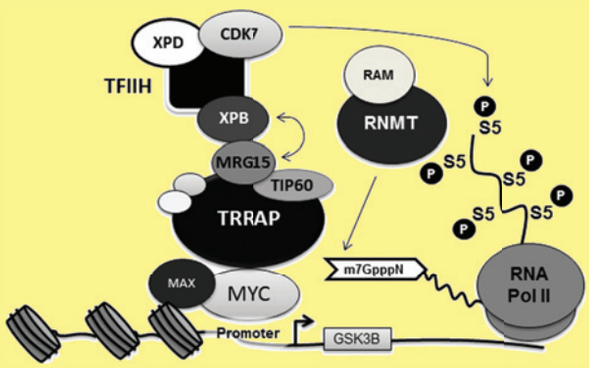
Selected Articles from This Issue



MYC Mediates mRNA Cap Methylation of Wnt Transcripts

Posternak *et al.* Page 213

MYC is a pleiotropic transcription factor that plays an important role in promoting the development and progression of human tumors. In the current study, Posternak and colleagues expand on a global role for MYC in regulating mRNA cap methylation. MYC specifically targets genes involved in Wnt/β-catenin signaling leading to augmented translational capacity and increased Wnt signaling activity. Mechanistically, MYC promotes recruitment of RNA methyltransferase to Wnt signaling gene promoters in part through an interaction between the TRRAP/TIP60 acetyltransferase complex and TFIIH. These data provide additional avenues to pursue in the development of targeted therapies for MYC-driven cancers.

Role of ABCG2 in Prostate Stem Cell Maintenance

Sabnis *et al.* Page 128

Prostate stem cells and prostate cancer stem cells have low or no androgen receptor (AR) expression. The ABC transporter, ABCG2, effluxes dihydrotestosterone (DHT) and is a prostate stem cell marker. Sabnis and colleagues demonstrate that inhibition of the ABCG2-mediated DHT efflux, promotes AR nuclear translocation, activation of AR target genes, and AR-dependent luminal differentiation. ABCG2 inhibition in the presence of DHT reduced the prostate cancer stem cell population and reduced growth rates in the CWR-R1 castration recurrent prostate cancer cell line *in vitro* and *in vivo* xenografts. Thus, ABCG2 inhibition is a possible differentiation therapeutic option in prostate cancer.

ERα-dependent Gene Silencing via DNA Methylation

Ariazi *et al.* Page 152

The estrogen receptor (ER) is well known for its ability to integrate hormonal signals that promote the expression of critical genes involved in breast cancer differentiation, proliferation, and survival. Evidence indicates that ER levels correlate with CpG methylation status suggesting that ER controls expression through pathways that involve DNA methylation. Comprehensive profiling was used to identify ER-silenced genes that could be re-activated using demethylating agents, therapeutic loss of ER, or re-suppressed by gain of ER activity. Importantly, ER-dependent DNA methylation targets were identified in key biological pathways and a subset associated with patient outcomes suggesting the potential for new biomarkers.

Role of AEG-1 in Glioma Stem-like Cell Biology

Hu *et al.* Page 225

Patients with glioblastoma multiforme (GBM), a common malignant brain tumor, display poor survival. Glioma stem-like cells (GSC) enhance GBM escape from chemotherapy and promote tumor relapse. Hu and colleagues demonstrate that astrocyte elevated gene 1 (AEG-1) plays a crucial role in glioma stem cell biology. The expression of AEG-1 is elevated in GBM neurospheres, facilitating β-catenin nuclear translocation and elevating expression of stem cell markers CD133 and SOX2 and activating downstream Wnt signaling genes. Accordingly, this study identifies a novel AEG-1 signaling axis in GSCs and establishes AEG-1 as a therapeutic target for glioblastoma multiforme.