Molecular Cancer Research

Highlights

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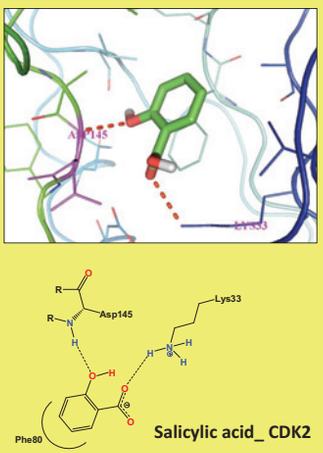
Selected Articles from This Issue



Aspirin and Salicylic Acid Down-regulate Cyclin A2/CDK2

Dachineni *et al.* Page 241

The evidence that aspirin prevents cancer is compelling; however, the underlying mechanism leading to its anti-cancer effect is enigmatic. In this research article, cyclin A2 and CDK2 are demonstrated to be novel targets of aspirin and its primary metabolite, salicylic acid. Both therapeutic agents caused down-regulation of cyclin A2 and CDK2, at the protein and mRNAs levels, in a diverse panel of cancer cells and resulted in a reduction in CDK2 activity. Importantly, it is also demonstrated that CDK2 is a novel salicylic acid binding protein. These results show that the anti-cancer effects of aspirin occur through down-regulation of cell cycle regulatory proteins.

Targeting the Adaptive Hypoxic Response in Multiple Myeloma

Mysore *et al.* Page 253

Multiple myeloma resides in a hypoxic environment and shows signs of an induced hypoxic response that contributes to tumorigenesis and tumor drug resistance. Targeting this adaptive hypoxic response would have important ramifications for treating this disease. To test this, Mysore and colleagues used a Pyrrole-Imidazole polyamide that can displace a major regulator of hypoxic response, HIF1, from its DNA-binding site. Evidence shows that the polyamide suppressed growth of multiple myeloma xenografts in mice and inhibited the hypoxic response *in vitro* and *in vivo*; thus, revealing the therapeutic utility of these molecules in the treatment of multiple myeloma.

KRAS Regulated miR-31 Modulates Invasion Migration

Kent *et al.* Page 267

Pancreatic cancer is a deadly and highly metastatic disease frequently harboring activating mutations in the *KRAS* oncogene. MicroRNAs (miRs) are important regulators of gene expression with an established role in cancer pathogenesis. Here, miR-31 is identified as a transcriptional target of the RAS-MAPK signaling pathway. The miR-31 host gene promoter is activated by the transcription factor ELK1. Enforced expression of miR-31 enhanced invasion-migration of pancreatic cancer cells via down regulation of the miR-31 target RASA1 and activation of RHOA. These results implicate miR-31 as a novel effector in the RAS-transformation program and demonstrate a mechanism for the metastatic behavior of pancreatic cancer.

Cancer-associated Fibroblasts Regulate Collagen Cross-linking

Pankova *et al.* Page 287

Cancer-associated fibroblasts (CAFs) are a vital cellular component of the tumor microenvironment (TME) and are a recognized source of intratumoral collagen. This study is important because it shows that CAFs not only produce collagen but also regulate the types of cross-links that form between collagen strands and contribute to the biomechanical properties of tumor stroma. Mechanistically, this activity of CAFs was mediated by lysyl hydroxylase 2 (PLOD2/LH2), which strengthens the growing body of evidence that targeting LH2 has the potential to suppress the growth and metastasis of tumors in patients.

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