Molecular Cancer Research Highlights

April 2012 • Volume 10 • Number 4

Selected Articles from This Issue

Werner Deficiency Impairs MYC-Induced Tumorigenesis

Moser *et al.* _____ Page 535

The MYC oncogene family is amplified and aberrantly expressed in many cancers. Despite MYC's unquestioned relevance to human cancer and decades of research, there are no therapies that target MYC. Here, Moser and colleagues showed that WRN, a DNA helicase involved in DNA repair and ageing, is required for proliferation of MYC-overexpressing cancer cells but not normal cells. Blocking WRN expression or function causes regression of MYC-associated lung cancers and increases survival of mice with MYC-driven lymphomas. As WRN is a nonessential, but druggable gene, targeting its enzymatic activity could be effective treatment for MYC-associated cancers.

Prostate Stroma Facilitates Prostate Cancer Bone Metastasis

Li *et al.* _____ **Page 494**

Nearly 70% of prostate cancer patients have lost expression of TGF-β type II receptor in the stroma, contributing to cancer progression. Li and colleagues evaluated whether TβRII loss in the primary environment affected prostate cancer bone metastasis, and found that TβRII expression was lost in prostate cancer cancer-associated fibroblasts in bone metastatic tissues. Using conditional stromal *Tgfbr2* knockout mice, they showed that loss of TβRII in prostatic fibroblasts contributes to cell adhesion, and early establishment and subsequent bone lesion development through upregulation of CXCL16 and CXCL1. Thus, changes in the primary tumor microenvironment can be predictive of and therapeutic targets for prostate cancer metastasis.

miRNA Profiling in Colorectal Cancer

Reid *et al.* _____ **Page 504**

Altered expression of miRNAs is associated with various human cancers, including colorectal cancer (CRC). Reid and colleagues analyzed miRNA profiles of 40 CRCs and their paired normal tissues and searched for putative targets of the differentially expressed miRNAs in gene expression datasets of normal and tumor samples. They identified 121 genes involved in key pathways of CRC progression, adding a novel layer of regulation in the Vogelstein multistep model of CRC pathogenesis. One pair, miR-1 and MET, was studied and miR-1 emerged to have a tumor suppressor function in CRC by directly downregulating MET oncogene.

Xenoestrogens Engage EZH2 to Increase Tumorigenesis

Greathouse *et al.* _____ **Page 546**

Early life environmental exposures can increase risk for cancer later in life. For developmental exposures to endocrine disruptors, such as environmental xenoestrogens, reprogramming of the epigenome is thought to underlie this increased cancer risk. Greathouse and colleagues showed that the histone methyltransferase EZH2 is a target for xenoestrogens that induce this type of developmental reprogramming. They showed that activation of PI3K/AKT signaling by xenoestrogens phosphorylates and inactivates the methyltransferase EZH2. As a result, levels of the repressive H3K27 epigenetic methyl mark are reduced, reprogramming genes to become hyperresponsive to estrogen and promoting the development of hormone-dependent tumors. These data emphasize the importance of a life-course approach to identifying environmental causes of cancer, and provide a direct mechanism by which early life environmental exposures can disrupt the epigenome and increase susceptibility to tumorigenesis later in life.

Molecular Cancer Research

Highlights of This Issue

Mol Cancer Res 2012;10:483.