Molecular Cancer Research

Highlights

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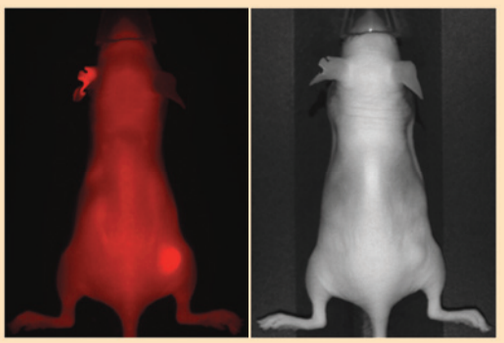
Selected Articles from This Issue



Near-infrared Photoimmunotherapy Targeting PSMA

Nagaya *et al.* Page 1153

Near-infrared photoimmunotherapy (NIR-PIT) is a highly selective cancer therapy that uses an antibody-photoabsorber conjugate (APC) activated by NIR light. NIR-PIT causes minimal damage to non-target tissues and is effective with a variety of antibodies conjugated to the same photoabsorber. Prostate-specific membrane antigen (PSMA) is expressed in more aggressive prostate cancers and is an attractive target for NIR-PIT. Nagaya and colleagues report that NIR-PIT using anti-PSMA Ab-photoabsorber conjugate induced therapeutic effects against a PSMA-expressing prostate cancer in animal models. NIR-PIT could become a new treatment modality for primary and local-recurrent prostate cancer that could be readily translated to humans.

Notch Directs Gene Repression via PRC2

Han *et al.* Page 1173

Aberrant Notch signaling is critical in the initiation and maintenance of the neoplastic phenotype in many human neoplasms. It has long been appreciated that Notch functions as a transcriptional activator and establishes context dependent transcription cascades. What has been missing in the understanding of Notch-mediated transcriptional regulation is how Notch induces gene repression. Han and colleagues provide strong evidence that Notch directly recruits LSD1 and PRC2 to target promoters, which results in transcriptional repression. Not only does this study provide a novel paradigm of Notch signaling but also provides a rationale for developing new therapeutic strategies for Notch-dependent cancers.

Human and Mouse microDNA in Circulation

Kumar *et al.* Page 1197

Prior work reported a large pool of small extrachromosomal circular DNA, microDNA, in normal tissues and cancer cell lines. Kumar and colleagues have now examined whether these circles of DNA, released from cells, can be detected in the blood. MicroDNA are found in the blood, and are released from cancers into the blood. Liquid biopsy is an experimental method being developed to detect cancers by examining the circulating cell-free linear DNA in the blood. These results suggest that circles of DNA are a new pool of circulating DNA that can be specifically examined in liquid biopsies.

H3.3K27M Cooperates with PDGF-B in Brainstem Gliomagenesis

Cordero *et al.* Page 1243

Diffuse intrinsic pontine glioma (DIPG) is an incurable childhood brain cancer whose hallmark mutation is H3K27M. Prior work unraveled that H3K27M inhibits polycomb repressive complex 2 (PRC2), an H3K27 methyltransferase complex. However, the genes downstream of H3K27M that contribute to tumorigenesis are not known. Here, using mouse genetics it is revealed that p16 (CDKN2A) is a target of H3K27M. The mechanism of p16 repression is unclear but involves aberrant histone and DNA methylation at the p16 promoter. Strikingly, the pro-tumorigenic effects of H3K27M were absent in mice with p16/p19 deletion, suggesting that restoring p16 levels is a promising therapeutic strategy.