Molecular Cancer Research **Highlights**

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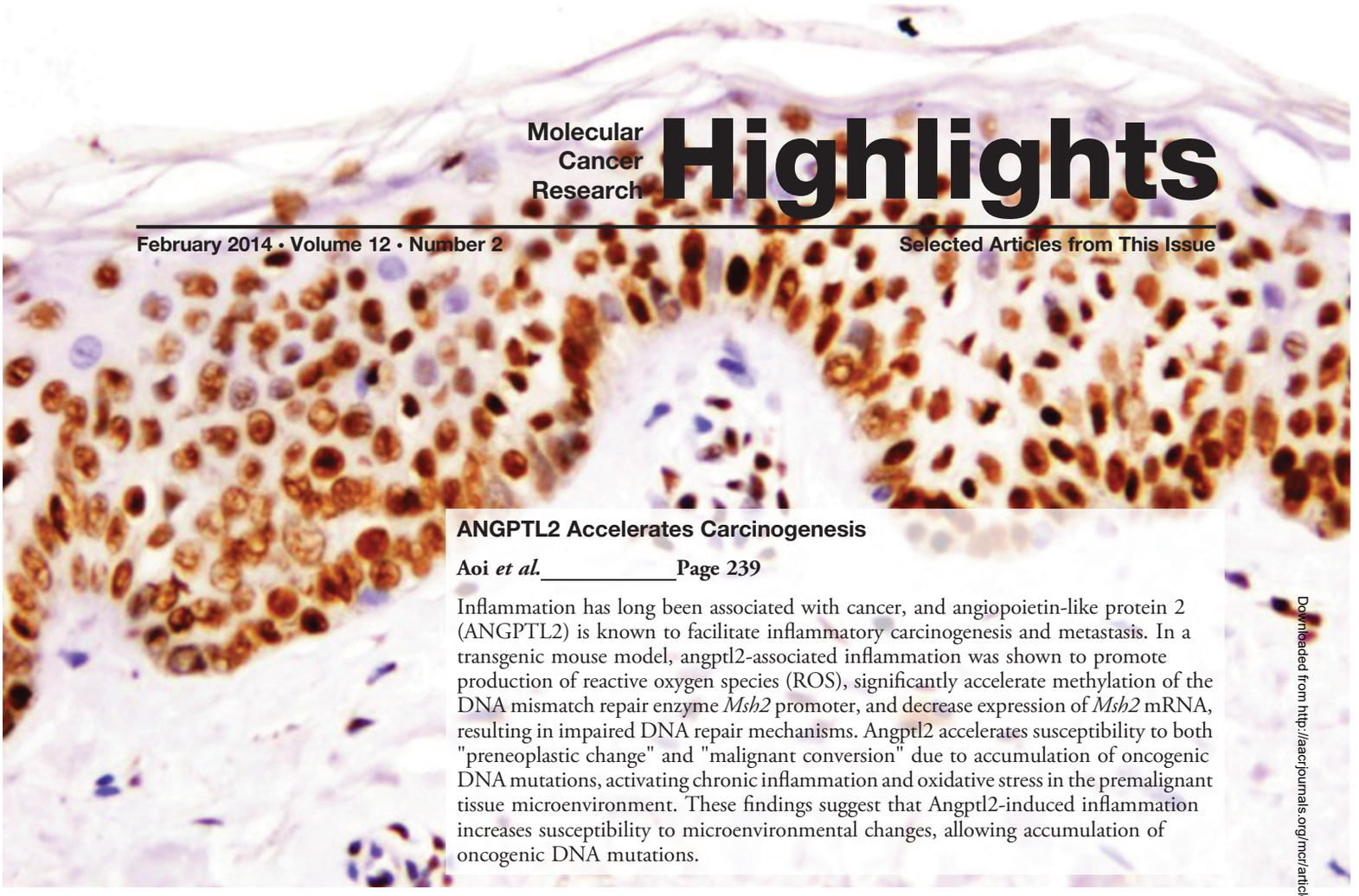
Selected Articles from This Issue



ANGPTL2 Accelerates Carcinogenesis

Aoi *et al.* **Page 239**

Inflammation has long been associated with cancer, and angiopoietin-like protein 2 (ANGPTL2) is known to facilitate inflammatory carcinogenesis and metastasis. In a transgenic mouse model, angptl2-associated inflammation was shown to promote production of reactive oxygen species (ROS), significantly accelerate methylation of the DNA mismatch repair enzyme *Msh2* promoter, and decrease expression of *Msh2* mRNA, resulting in impaired DNA repair mechanisms. Angptl2 accelerates susceptibility to both "preneoplastic change" and "malignant conversion" due to accumulation of oncogenic DNA mutations, activating chronic inflammation and oxidative stress in the premalignant tissue microenvironment. These findings suggest that Angptl2-induced inflammation increases susceptibility to microenvironmental changes, allowing accumulation of oncogenic DNA mutations.

Androgen Receptor Regulation of the 20q13 Amplicon

Labbé *et al.* **Page 184**

From the multitude of contributing factors implicated in prostate cancer, age and family history rank among the highest. However, despite a number of genetic loci linked to hereditary prostate cancer, no *bona fide* susceptibility gene has been identified. In the Rapid Impact article for this issue, Labbé and colleagues report on their study of the 20q13 chromosomal region, which had been previously identified as a hereditary prostate cancer susceptibility locus (HPC20) and is now shown in their study to be frequently coamplified with the androgen receptor (AR) in metastatic prostate cancer. High-resolution mapping uncovered AR recruitment hotspots in the 20q13 region. These findings reveal that AR, a primary driver of disease progression, is intimately involved in gene transcription of a known prostate susceptibility locus.

miR-221 Regulatory Loop in HCC

Fornari *et al.* **Page 203**

The overexpression of miR-221 is a common event in human cancers, with growing evidence supporting its causative role. In this study, Fornari and colleagues identify for the first time the MDM2 oncogene as a direct target of an oncomicroRNA such as miR-221 in cancer tissue. A feed-forward loop sustaining miR-221 aberrant expression was revealed in which miR-221 activates the p53/MDM2 axis by inhibiting MDM2 and, in turn, p53 activation contributes to miR-221 enhanced expression. Moreover, by modulating p53 signaling, miR-221 affects cell-cycle progression and apoptotic response to doxorubicin in hepatocellular carcinoma (HCC)–derived cells, suggesting that miR-221 expression contributes to p53 context-specific response to doxorubicin treatment in HCC.

BMP Differentiates Oligodendroglioma Propagating Cells

Srikanth *et al.* **Page 283**

Little is known about tumor initiating cells in oligodendrogliomas, impeding investigation of critical signaling pathways that could be exploited by targeted therapies. Srikanth and colleagues demonstrate that cells with stem-like characteristics are capable of propagating human oligodendrogliomas. Canonical bone morphogenetic protein (BMP) signaling is intact in these cells and potently diminishes their stemness by inducing astrocytic differentiation. Further analyses revealed sequestration of oligodendrocyte differentiation factors OLIG1/2 by BMP-induced ID proteins as a plausible mechanism. These findings elucidate the molecular pathways underlying the effects of BMP signaling on oligodendroglioma stem-like cells and suggest BMP activation as a potential cancer stem cell–targeted therapy in these tumors.