Molecular Cancer Research **Highlights**

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Selected Articles from This Issue

AKR1B10, a Target of p53, Is Downregulated in Colon Cancer

Ohashi *et al.* **Page 1554**

Regulation of metabolism is a novel tumor-suppressive function of p53. Here, Ohashi and colleagues reveal how the inactivation of p53 inhibits cell death in colon cancer. With the use of genomic analyses, the metabolic enzyme aldo-keto reductase family 1, member B10 (*AKR1B10*) was identified as a direct transcriptional target of p53. Knockdown of the AKR1B10 transcript significantly suppressed p53-induced apoptosis in colorectal cancer cells. Furthermore, low expression of AKR1B10 in colon cancers was clinically correlated with poor prognosis. These results demonstrate that the downregulation of AKR1B10, which causes the inhibition of p53-induced apoptosis, contributes to the survival rate of patients with colon cancer.

Stabilization of Pim-3 by TCTP

Zhang *et al.* **Page 1508**

Pim-3, a proto-oncogene with serine/threonine kinase activity, is aberrantly expressed in cancerous tissues and is known to play a critical role in tumor development and progression. In order to identify potential novel regulators of Pim-3, Zhang and colleagues performed a yeast two-hybrid screen using a human HeLa matchmaker cDNA library and revealed that translationally controlled tumor protein (TCTP/*TPT1*) specifically interacts with and enhances Pim-3 protein stability by blocking its ubiquitin–proteasome-mediated degradation, thereby promoting tumor growth *in vitro* and *in vivo*. These findings recognize the TCTP/Pim-3 pathway as a new therapeutic target in human pancreatic cancer.

miR-103 and miR-107 Inhibit Homologous Recombination

Huang *et al.* **Page 1564**

Error-free repair of DNA double-strand breaks by homologous recombination is essential for maintaining genomic stability and promoting resistance to DNA-damaging chemotherapies, but its regulation by microRNAs is poorly characterized. Huang and colleagues used a cell-based screening approach to identify miR-103 and miR-107 as potent inhibitors of homologous recombination. Mechanistically, miR-103 and miR-107 directly targeted RAD51 and RAD51D to mediate chemosensitivity to cisplatin and PARP inhibitors and are implicated in the endogenous regulation of RAD51D in several tumor subtypes. These findings not only demonstrate that miR-103 and miR-107 promote genomic instability and chemosensitivity but also show their utility as therapeutic agents for the chemosensitization of tumors.

Angiogenesis Genes Induce FGF-mediated Resistance in HNSCC

Gyanchandani *et al.* **Page 1585**

Increased resistance to antiangiogenic therapies underscores the need for relevant preclinical models to gain insight into the mechanisms that drive refractoriness. Gyanchandani and colleagues developed a novel head and neck squamous cell carcinoma (HNSCC) xenograft model of acquired resistance to the VEGF inhibitor bevacizumab and uncovered an FGF signaling network in resistant tumors. Increased expression of FGF2 was regulated by overexpression of angiogenesis-related genes, including *PLCG2*, *FZD4*, *CX3CL1*, and *CCL5*, via increased ERK signaling. Inhibition of FGFR in resistant tumors led to restoration of sensitivity to bevacizumab, suggesting that cotargeting of VEGF and FGF overcomes resistance to antiangiogenic therapy in HNSCC.

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