**Molecular Cancer Research**

**Highlights**

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**Selected Articles from This Issue**

**p53 Loss Compromises Response to WEE1 Inhibition**

Diab et al. • Page 1115

TP53 is the most commonly mutated gene in solid tumors, and loss of p53 function is strongly correlated with resistance to chemotherapy in head and neck cancer. In this study, Diab and colleagues demonstrate that inhibition of WEE1, a kinase involved in regulating cell cycle transition during S phase and mitosis, has increased efficacy in p53-deficient cells due to incomplete resolution of DNA damage and stalled replication forks. These lesions are carried over across more than one round of cell division, thereby magnifying the effects of genotoxic therapy.

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**Targeting MCAM Reduces Bone Metastasis in Prostate Cancer**

Zoni et al. • Page 1049

Prostate cancer represents an increasing clinical burden, and metastatic prostate cancer has thus far proven incurable. Metastatic prostate cancer primarily localizes to the bones, inducing osteopathy and bone-related adverse events in patients. Here, Zoni and colleagues demonstrate greatly reduced incidences of bone metastatic lesions by blocking MCAM. Ablation of MCAM or blockade with an MCAM-specific monoclonal antibody reduced interactions between prostate cancer cells and osteoblasts in vitro, and significantly reduced the formation of osteolytic lesions as well as overall tumor growth in vivo. Taken together, these data support the potential utility of targeting MCAM to slow or prevent prostate cancer bone metastasis.

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**PAI1 Drives TNBC Cytoskeletal Reorganization and Glycolysis**

Humphries et al. • Page 1142

Cancer cell motility is a key factor in disease progression, and expression of plasminogen activator inhibitor 1 (PAI1) is associated with increased cellular migration and poor prognosis. Here, Humphries and colleagues demonstrate that increased PAI1 expression reprograms cellular energetics, increasing reliance on glycolysis and inducing mitochondrial fission, cytoskeletal rearrangement, and invasiveness both in vitro and in vivo. Targeting this pathway may present a novel means of blocking cell migration and tumor progression.

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**Molecular Characterization of Prostate Cancer Using MSI**

Randall et al. • Page 1155

For decades, prostate cancer diagnosis and prognosis have been largely based on Gleason scoring, a histologic grading scale of the disruption of prostate architecture as the disease increases in severity. While effective, the scale is somewhat subjective and can be difficult to apply to the limited tissue samples obtained from biopsy. Here, Randall and colleagues detail a mass spectrometry imaging workflow based on lipid and metabolite abundance that tightly correlate with increasing Gleason score. The data suggest that lipidomics and metabolomics could represent a higher-fidelity, faster means of scoring prostate cancer aggressiveness to support diagnostic efforts in the clinic.
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