



Recombinant Human Erythropoietin Increases Breast Cancer Metastasis

Hedley *et al.* _____ Page 6151

Administration of recombinant human erythropoietin (rHuEPO) has largely replaced blood transfusion in patients with cancer-induced anemia. Potential detrimental effects of this approach, such as thromboembolic risks and potential tumor response leading to enhanced disease progression, have become points of discussion and concern. Hedley and colleagues present data demonstrating potentiating effects on metastasis and reduction of chemotherapeutic efficacy in secondary sites by rHuEPO. This study begins to uncover the underlying functional explanation for the adverse events and decreased survival that have been observed in erythropoietin-treated metastatic breast cancer patients undergoing chemotherapy.

ALDH1A1 CTL Recognition of Cancer-Initiating Cells

Visus *et al.* _____ Page 6174

Cancer-initiating cells (CIC) are being readily identified by elevated levels of aldehyde dehydrogenase (ALDH), namely ALDH1A1, a tumor-associated antigen recognized by HLA class I-restricted CD8⁺ T cells. Pertinent to developing immunotherapy for targeting CICs, Visus and colleagues demonstrate that ALDH^{bright} cells are sensitive to cytolysis by ALDH1A1-specific CTLs *in vitro* and *in vivo*. In preclinical models of human tumor xenografts growing in immunodeficient mice, adoptive therapy with ALDH1A1-specific CD8⁺ T cells targeted ALDH^{bright} cells and inhibited xenograft growth and metastasis or prolonged survival. These results highlight ALDH1A1 as a target of T cell-based immunotherapy to eliminate CICs.

Dual Inhibition of EGFR and HER2 in Prostate Cancer

Chen *et al.* _____ Page 6218

Androgen withdrawal therapy (AWT) is considered the standard of care for patients with metastatic prostate cancer, but resistance to this therapy develops within 2 to 3 years after treatment. Chen and colleagues show that during AWT, increased levels of the receptor tyrosine kinases HER2 and ErbB3, members of the epidermal growth factor receptor (EGFR) family, result in a significant ErbB-dependent survival advantage that allows progression to castration-resistant prostate cancer. However, dual EGFR/HER2 inhibition, which also inhibits their dimerization partner, ErbB3, induced apoptosis in cells undergoing AWT. These results indicate that administration of dual EGFR/HER2 inhibitors together with AWT may impede the onset of castration-resistant prostate cancer.

MicroRNA Expression in Microsatellite Instability Colorectal Cancer

Balaguer *et al.* _____ Page 6239

MicroRNAs (miRNAs) have critical functions across various biologic processes and can be potentially used as cancer biomarkers. Colorectal cancer is a heterogeneous disease, and the identification of various types of colorectal cancer with histopathologic methods alone is challenging. In this study, Balaguer and colleagues used miRNA expression profiling for molecular classification of hereditary and sporadic forms of colorectal cancer. Their data show that miRNA expression profiling not only distinguished between tumor and normal tissues, but more importantly, a subset of miRNAs successfully discriminated among Lynch syndrome, sporadic microsatellite-unstable, and microsatellite-stable colorectal cancers. These findings could have tremendous clinical and translational relevance in the diagnosis, prognosis, and treatment strategy for patients with different subtypes of colorectal cancer.