

## Id1-IGF2-IGF1R-AKT Signaling and Targeted Cancer Therapy

Li et al. \_\_\_\_\_ Page 2651

Id1 induces activation of PI3K/AKT pathway, but the underlying mechanism remains unknown. In this study, Li and colleagues report that Id1 induces the expression and secretion of IGF2 in several cancer types including esophageal cancer. Id1-induced IGF2 could activate the PI3K/AKT pathway by signaling through IGF1R in an autocrine and endocrine manner to promote tumor progression and metastasis. The study also shows that IGF2 and IGF1R are valid targets in esophageal cancer therapy and that a monoclonal antibody targeting IGF1R (cixutumumab), used alone or combined with cytotoxic chemotherapeutic drugs, has potential clinical applications in systemic treatment of esophageal cancer.

## Detecting Plasma Tumor DNA in Early-Stage Breast Cancer

Beaver et al. \_\_\_\_\_ Page 2643

Beaver and colleagues demonstrate the ability to detect DNA mutations in plasma from early-stage breast cancer patients. In a prospective study, blood from 29 patients was obtained prior to surgery and used to detect *PIK3CA* mutations with 93.3% sensitivity and 100% specificity. Five patients had plasma *PIK3CA* mutations after surgery. This study demonstrates the feasibility of detecting plasma tumor DNA in early-stage breast cancer. Importantly, this provides the foundation for future work examining whether persistent plasma tumor DNA postsurgery could identify patients who may benefit from adjuvant therapies versus those that are already cured after surgery.

## Celecoxib Sensitizes Lymphoma B Cells to Apoptosis

Gallouet et al. \_\_\_\_\_ Page 2663

Follicular lymphomas (FL) establish an inflammatory microenvironment, notably driven by COX-2, with a large amount of PGE2 synthesis. To inhibit the crosstalk between the supporting tumor microenvironment and tumor B-cells, Gallouet and colleagues showed that the use of celecoxib, an anti-inflammatory drug, can reduce *in vitro* PGE2 production from FL-patients stromal cells. Moreover, the use of celecoxib and TRAIL, a cytotoxic molecule, can sensitize primary B-cells from FL patients to death. This combination of treatments can therefore target both microenvironment and tumor cells for more efficiency in FL treatments.

## Targeting Cytomegalovirus Antigens for GBM Immunotherapy

Nair et al. \_\_\_\_\_ Page 2684

Although detection of low levels of human cytomegalovirus (CMV) expression in glioblastoma (GBM) has been reported by several groups, the physiologic relevance of this expression remains unclear. Nair and colleagues explored whether the CMV antigen pp65 could serve as an effective tumor rejection antigen in primary GBM. Despite deficits in cellular immunity in patients with GBM, CMV pp65-specific T cells could be reliably activated *in vitro* using pp65 RNA-pulsed autologous dendritic cells. Importantly, CMV-specific T cells were effective in recognizing and killing autologous GBM tumor cells. These studies strongly support the rationale for CMV-targeted immunotherapy in patients with GBM.

# Clinical Cancer Research

## Highlights of This Issue

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