Clinical Cancer Research **Highlights**

October 1, 2014 • Volume 20 • Number 19

Selected Articles from This Issue

Association of PD-1 and Ligands with Response to Anti–PD-1

Taube *et al.* **Page 5064**

The correlation between tumor cell PD-L1 expression in pretreatment surgical pathology specimens and response to anti-PD-1 therapy is an exciting, but preliminary finding. Taube and colleagues expand upon their earlier observations to assess additional histologic and immunoarchitectural features of the pretreatment tumor microenvironment and how they correlate with response to anti-PD1. The presence of immune infiltrates, immune cell subsets, and PD-1, PD-L1 and PD-L2 expression were assessed by immunohistochemistry. Of these, tumor cell PD-L1 expression was the single factor most closely associated with objective response. These findings have both mechanistic and potential biomarker relevance for anti-PD-1 therapy.

The XAGE1 Antibody as a Biomarker for Lung Cancer

Ohue *et al.* **Page 5052**

XAGE1 (GAGED2a) is a cancer/testis (CT) antigen expressed frequently in lung adenocarcinoma, which is the predominant histologic type of lung cancer. Ohue and colleagues investigated the clinical relevance of the XAGE1 (GAGED2a) immune responses in advanced lung adenocarcinoma patients and found that the XAGE1 (GAGED2a) immune response is relevant for better prognosis and that the XAGE1 (GAGED2a) antibody response is a prognostic immune biomarker. On the other hand, XAGE1 (GAGED2a) antigen expression is predictive of a worse prognosis in patients with EGFR-mutated tumors. The protective effect of this naturally occurring immune response supports the concept of immunotherapy.

Anti-CCR4 Monoclonal Antibody for EBV-Associated T/NK LPD

Kanazawa *et al.* **Page 5075**

Epstein-Barr virus (EBV) occasionally leads to T- and natural killer-cell lymphoproliferative diseases (T/NK-LPDs) that are refractory to conventional chemotherapies. Kanazawa and colleagues identified that CC chemokine receptor 4 (CCR4) was expressed on most EBV-positive T- and NK-cell lines. A humanized anti-CCR4 monoclonal antibody, mogamulizumab induced antibody-dependent cellular cytotoxicity activity against CCR4-positive cell lines, and inhibited the growth of EBV-positive NK-cell lymphomas in a murine xenograft model. Furthermore, CCR4 was expressed on EBV-infected cells in 8 of 17 patients with EBV-associated T/NK-LPDs. These finding suggests that mogamulizumab may be a promising therapeutic for patients with EBV-associated T/NK-LPDs.

PIAS3 Expression in Mesothelioma

Dabir *et al.* **Page 5124**

STAT3 is activated in many forms of cancer. Because PIAS3 is a key endogenous inhibitor of STAT3, it is possible that PIAS3 expression could be decreased in malignant tissue and thereby contribute to high STAT3 activation. Indeed, Dabir and colleagues demonstrated this was true in malignant mesothelioma as *PIAS3* transcript levels were among the lowest of all solid tumors and, conversely, high expression of PIAS3 in mesothelioma tumors is predictive of a favorable prognosis. The authors went on to demonstrate that increasing PIAS3 expression in STAT3-driven mesothelioma cells, either by overexpression of exogenous PIAS3, stimulation of endogenous PIAS3 expression by curcumin or incubation with a PIAS3 peptide mimetic, led to decreased cellular STAT3 activation and promoted apoptosis. These results suggest that strategies to reactivate PIAS3 could represent a new therapeutic avenue to inhibit STAT3 activity and induce growth arrest in tumor cells.