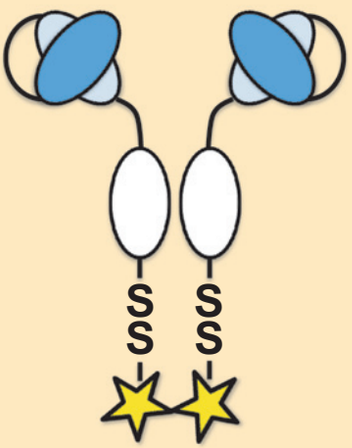
Molecular Cancer Therapeutics **Highlights**

July 2014 • Volume 13 • Number 7

Selected Articles from This Issue



Potent Combinational Antibody-Based Delivery of Interleukin-2 and Cytotoxics

Gutbrodt *et al.* **Page 1772**

Antibody-mediated pharmacodelivery of potent payloads represents a rapidly growing strategy in the field of cancer therapeutics. In this study, Gutbrodt and colleagues report the combination of antibody–drug conjugates (ADC) and interleukin-2–based immunocytokines targeting the alternatively-spliced extradomain A (EDA) of fibronectin. The combination promoted complete tumor eradications and conferred protective immunity in a syngeneic immunocompetent mouse model of leukemia, demonstrating, for the first time, that ADCs and immunocytokines can synergize. Since the EDA of fibronectin is commonly expressed in the majority of human solid tumors, lymphomas, and acute leukemias, the combination of these armed antibodies may have potential therapeutic applications in cancer.

Metronomic Docetaxel in PRINT Nanoparticles and EZH2 Silencing in Ovarian Cancer

Gharpure *et al.* **Page 1750**

Metronomic chemotherapy has recently been recognized to have better therapeutic ratio compared to conventional therapeutic approaches. However, its efficacy in combination with an antiangiogenic treatment has not been well studied. Here, Gharpure and colleagues used metronomic docetaxel incorporated in PLGA-PRINT nanoparticles in combination with EZH2 siRNA (murine sequence) incorporated in chitosan nanoparticles. In ovarian cancer mouse models, the combination therapy effectively reduced tumor burden via reduced angiogenesis and proliferation and increased apoptosis. These results suggest that this combination therapy holds great potential for ovarian cancer therapy.

HER3 Inhibitor MM-121 Enhances Cetuximab Potency in HNSCC

Jiang *et al.* **Page 1826**

Intrinsic or compensatory HER3 signaling may contribute to resistance to the EGFR monoclonal antibody cetuximab in head and neck squamous cell carcinoma (HNSCC). Here, Jiang and colleagues investigated the therapeutic benefit of combining MM-121/SAR256212, an anti-HER3 monoclonal antibody, with cetuximab in HNSCC models. The results revealed that the combination of cetuximab and MM-121 enhanced antitumor activity both *in vitro* and *in vivo* through simultaneously inhibiting the activation of HER3 and EGFR and consequently the downstream PI3K/AKT and ERK pathways. This study provides a rationale for clinical application of HER3 inhibitor with EGFR-targeted therapies in HNSCC.

Lethal Synergism of Dual BRAF and CK2 Iinhibition

Parker *et al.* **Page 1894**

Therapeutic targeting of mutant BRAF suppresses pro-growth signaling of the MAPK pathway. Parker and colleagues used a mass spectrometry screen of phosphoproteins to uncover previously unknown responses of BRAF inhibition. Bioinformatics was used to predict kinase families most likely responsible for regulating these changes. The authors showed that the upregulation of protein kinase CK2 family substrates was a consequence of blocking mutant BRAF, and further demonstrated antiproliferative synergy through the combinational blockade of BRAF and CK2 in BRAF-mutant melanomas and thyroid cancer cells. This highlights the potential of dual CK2/BRAF inhibition as a novel therapeutic strategy for cancers with BRAF mutation.