Clinical Cancer Research **Highlights**

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Selected Articles from This Issue

NSCLC with Concomitant EGFR Mutations and ALK Rearrangements

Yang *et al.* **Page 1383**

EGFR-mutations and *ALK* rearrangements could co-exist in non-small cell lung cancer (NSCLC). To explore the predictive biomarkers in *EGFR*/*ALK* co-altered tumors, Yang and colleagues, investigated molecular alterations of *EGFR* and *ALK* in a 977-case Chinese cohort and correlated phospho-EGFR and phospho-ALK with responses to EGFR-TKIs and crizotinib. Tumors with such co-alterations could have diverse responses to first-line EGFR TKIs, which were associated with phospho-EGFR levels. Elevated phospho-ALK levels correlated the efficacy of subsequent crizotinib treatment. This study showed the potential utility of receptors phosphorylation status to predict the treatment by EGFR-TKI or crizotinib in *EGFR*/*ALK* co-altered NSCLC.

Inhibition of DNA Repair in Glioblastoma

Rodrigo *et al.* **Page 1235**

Glioblastomas are highly fatal brain tumors that are extremely radioresistant. This study identifies NVP-BEZ235 (a dual PI3K/mTOR inhibitor) as a potent inhibitor of key DNA repair enzymes, DNA-PKcs and ATM, *in vivo*. Treatment with this drug blocks the repair of radiation-induced DNA damage in tumors, resulting in remarkable radiosensitization and prolonging survival of brain-tumor bearing mice. Based on the results presented, blocking DNA repair with potent and bioavailable inhibitors of DNA-PKcs and ATM appears to be a feasible option for improving GBM therapy in the future.

Nexrutine Inhibits Pancreatic Cancer Via Stat3/NFκB

Gong *et al.* **Page 1259**

Gong and colleagues demonstrate an important activity of the natural compound, Nexrutine on inflammation-associated carcinogenesis and inhibition of fibrosis. The study elaborates on the noteworthy signaling axis among STAT3, NFκB, COX-2 and EP4. The authors show that STAT3 negatively regulates NFκB activation. Suppression of this crosstalk inhibits COX-2 transcriptional activity and subdues prostaglandins. The immediate outcome of this study can influence current modalities for pancreatic cancer treatment through the combinatorial use of Nexrutine as a dual inhibitor of NFκB and STAT3. It also has clinical implications for other inflammation and fibrosis-associated cancers.

Vaccine Responses After Adoptive T-cell Transfers in Myeloma

Rapoport *et al.* **Page 1355**

Relapse of myeloma after autologous stem cell transplantation (ASCT) is frequent. Posttransplant immunotherapy using adoptive T-cell transfers and tumor antigen vaccines may improve clinical responses if a high frequency of tumor antigen-directed immune responses can be generated. Rapoport and colleagues show that adoptive transfer of costimulated autologous T cells which are primed and boosted by a MAGE-A3 Trojan peptide vaccine combined with the TLR-3 agonist and novel vaccine adjuvant Poly-ICLC induces vaccine-directed cellular immune responses in 76% of patients after ASCT. A high frequency of vaccine-directed antibody responses also occurred but only in the presence of montanide.

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