Clinical Cancer Research **Highlights**

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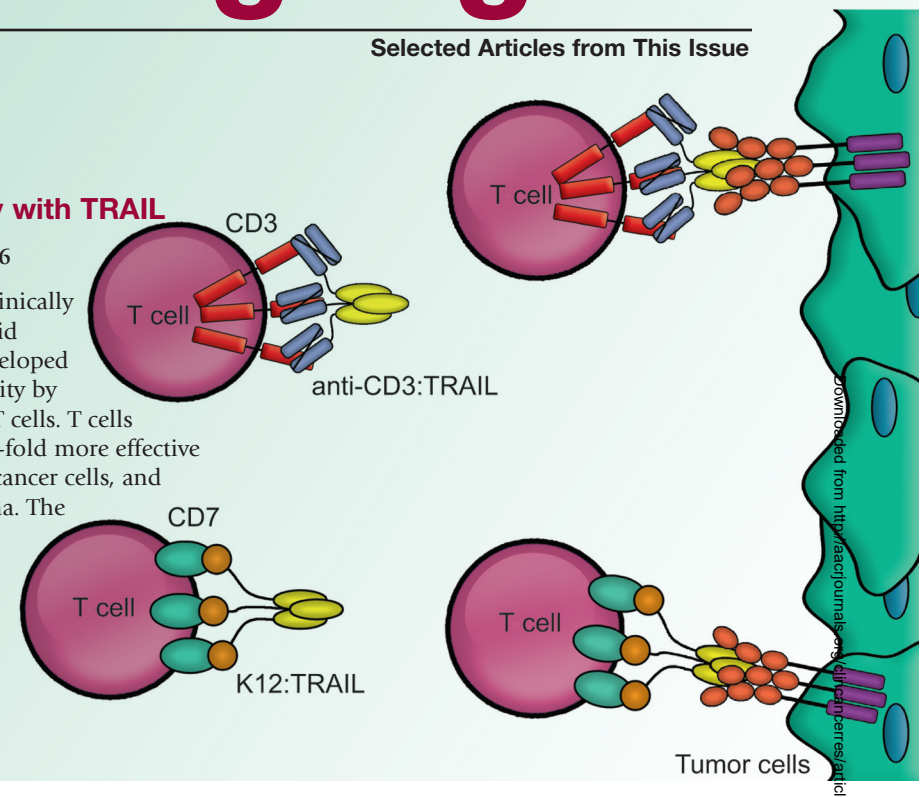
Selected Articles from This Issue

Enhancing T-Cell Tumoricidal Activity with TRAIL

de Bruyn *et al.* _____**Page 5626**

Adoptive T-cell therapy generally fails to trigger clinically relevant anticancer immunity in patients with solid tumors. In this issue de Bruyn and colleagues developed a novel strategy to augment antitumor T-cell activity by selectively delivering TRAIL to the cell surface of T cells. T cells armed with TRAIL in this manner were up to 500-fold more effective against cancer cell lines, primary patient-derived cancer cells, and in a xenograft model of advanced colon carcinoma. The reported approach may easily be integrated into current adoptive T-cell strategies and thus may be useful for optimizing adoptive T cell therapy in patients suffering from solid cancers.



p53-Dependent Downregulation of *TCL1*

Voltan *et al.* _____**Page 5649**

The oncogene *TCL1* plays a key role in promoting leukemic transformation in B chronic lymphocytic leukemia (B-CLL). Voltan and colleagues show, with primary cells from patients with B-CLL and in B leukemic cell lines with different p53 status, that activation of p53 represses the transcription of *TCL1*. They obtained these results through *ex vivo* analysis of the effect of Nutlin-3, a nongenotoxic activator of the p53 pathway, on *TCL1* regulation, and the results were confirmed by p53 knockdown and *TCL1* overexpression experiments. The data suggest that *TCL1* downregulation is an important mediator of Nutlin-3 cytotoxicity and that therapeutic strategies should be further explored to improve its antileukemic activity.

Metronomic Topotecan and Pazopanib in Pediatric Solid Tumors

Kumar *et al.* _____**Page 5656**

The antitumor and antiangiogenic activity of oral low-dose metronomic topotecan in combination with oral pazopanib has been established in pediatric neuroblastoma, rhabdomyosarcoma, and osteosarcoma mouse models. The activity of this regimen across multiple pediatric tumor types, including metastatic models, creates an opening for development of pediatric clinical trials that incorporate this oral maintenance regimen. The hope is that this strategy will lead to control of minimal residual disease and increase survival in children with these aggressive tumors.

Custirsen Plus Docetaxel or Mitoxantrone in Metastatic CRPC

Saad *et al.* _____**Page 5765**

Clusterin (CLU) is a stress-activated cytoprotective chaperone upregulated by a variety of anticancer therapies that confers treatment resistance when it is overexpressed. Preclinical studies have shown that CLU suppression resensitizes docetaxel-refractory cancer cells to docetaxel. This clinical trial provides evidence that a combination of the CLU inhibitor custirsen with chemotherapy is feasible in patients with progressive metastatic castrate-resistant prostate cancer (CRPC) after first-line docetaxel therapy. In addition, because anticancer activity and pain responses were higher than expected, the results show some evidence of enhanced docetaxel activity as well. Moreover, these results reaffirm that custirsen decreases levels of serum CLU, and for the first time identify correlations between serum CLU and survival.