IFNα Enhances T-Cell Killing of Solid Cancers

Rossi et al.  Page 2341

Trop-2 is highly expressed in diverse epithelial cancers with limited presence on normal tissues. Here, Rossi and colleagues report redirected T-cell therapy targeting Trop-2 on solid tumors with a trivalent bispecific antibody (bsAb). Studies with human blood and animal models showed that interferon-α enhanced T-cell mediated antitumor activity significantly, without causing increased cytokine production that is often associated with adverse side effects. Additionally, this group discovered that following association of T cells with target cells, Trop-2, and possibly other tumor cell proteins, was translocated to the cell surface of T cells. This target/T-cell phenomenon mediated by bsAb warrants further investigation.

Overcoming Vemurafenib Resistance in Melanoma by CDK4/6 Inhibitor LY2835219

Yadav et al.  Page 2253

MAPK reactivation through BRAF spliced variants, NRAS mutation, and RTK activation is the major resistant mechanism to BRAF inhibition in melanoma. In this study, Yadav and colleagues studied in vivo and in vitro melanoma models of acquired resistance to vemurafenib, and described that reactivation of MAPK and overexpression of cyclin D1 were common features across the resistant models. Treatment with LY2835219, a CDK4/6 selective inhibitor, was sufficient to induce growth regression in vemurafenib-resistant tumors and enhanced apoptosis in vemurafenib-resistant cells, suggesting that targeting cyclin-D1/CDK4 signaling by LY2835219 could be an effective strategy to overcome MAPK-mediated resistance to BRAF inhibitors.

Targeting Endoglin in Pancreatic Cancer: A Double-Speared Approach

Pal et al.  Page 2264

Endoglin has emerged as an attractive target for antiangiogenic therapy in various cancers. Only a few studies explored the effect of targeting tumor cell–specific endoglin. Pal and colleagues have analyzed the effects of targeting tumor cell–specific endoglin in pancreatic cancer. Their results indicate that endoglin-targeted antiangiogenic therapy in pancreatic cancer may offer an additional advantage by targeting the tumor cells as well. Moreover, inhibition of endoglin also contributed to drug sensitivity, making it ideal for combination therapies in case of chemotherapy-resistant tumors. Overall, their data suggests endoglin-targeted therapy could be a double-speared approach for pancreatic cancer treatment.

A Zebrafish Chemical Screen for Antilymphatic Compounds

Astin et al.  Page 2450

Lymphangiogenesis in tumors is an integral step in the metastatic spread of cancer cells and there is a need to identify novel antilymphangiogenic agents. Astin and colleagues used a zebrafish-based chemical screen to identify compounds that have antilymphatic activity in both zebrafish and mouse models of lymphangiogenesis. One compound, kaempferol, a natural product found in plants, was shown to inhibit VEGF signaling and was able to reduce the density of tumoral lymphatics and lymph node metastases in a breast cancer xenograft model. These findings reveal that zebrafish are a viable platform for the identification and development of mammalian antilymphatic compounds.
Molecular Cancer Therapeutics

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