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<th>MINI REVIEW</th>
<th>What a Tangled Web We Weave: Emerging Resistance Mechanisms to Inhibition of the Phosphoinositide 3-Kinase Pathway</th>
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### ONLINE
For more News and Research Watch, visit Cancer Discovery online at http://CDnews.aacrjournals.org.
Akbay and colleagues found that EGFR activation in non–small cell lung cancer (NSCLC) resulted in an immunosuppressive microenvironment characterized by upregulation of programmed cell death 1 (PD-1) and its ligand PD-L1, reduction of CD8+ cytotoxic T cells, and induction of tumor-promoting cytokines. PD-1 blockade suppressed EGFR-driven NSCLC growth via increased T-cell infiltration and improved cytotoxic T-cell function, as well as reduced expression of immunosuppressive cytokines. PD-L1 induction in human NSCLC cells was dependent on EGFR activation, as treatment with EGFR kinase inhibitors decreased PD-L1 levels. These results define a non–cell-autonomous role of oncogenic EGFR in promoting immune evasion in lung cancer and suggest that dual inhibition of EGFR and PD-1 may be effective in EGFR-mutant NSCLC. For details, please see the article by Akbay and colleagues on page 1355.

Individually Systems Medicine Strategy to Tailor Treatments for Patients with Chemorefractory Acute Myeloid Leukemia

A Chimeric RNA Characteristic of Rhabdomyosarcoma in Normal Myogenesis Process

H. Yuan, F. Qin, M. Movassagh, H. Park, W. Golden, Z. Xie, P. Zhang, J. Sklar, and H. Li

Précis: A PAX3–FOXO1 chimeric RNA identical to the gene fusion expressed in alveolar rhabdomyosarcoma is transiently expressed in normal cells during skeletal muscle differentiation.

Discovery of a Mutant-Selective Covalent Inhibitor of EGFR that Overcomes T790M-Mediated Resistance in NSCLC


Précis: CO-1686 specifically and irreversibly inhibits mutant EGFR proteins including EGFR(T790M) while sparing wild-type EGFR activity.