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### MINI REVIEW

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**Activation of the PD-1 Pathway Contributes to Immune Escape in EGFR-Driven Lung Tumors**


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**Teaching an Old Dog New Tricks: Drug Repositioning in Small Cell Lung Cancer**

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**Personalized Therapy for Acute Myeloid Leukemia**

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### RESEARCH ARTICLES

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**A Systems Biology Approach to Personalizing Therapeutic Combinations**

L.N. Kwong, T.P. Heffernan, and L. Chin

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**Dynamic Interplay of Oncogenes and T Cells Induces PD-L1 in the Tumor Microenvironment**

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### IN THE SPOTLIGHT

**In Focus**

A Systems Biology Approach to Personalizing Therapeutic Combinations

L.N. Kwong, T.P. Heffernan, and L. Chin
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.