IN THIS ISSUE
Highlighted research articles ................. 565

NEWS IN BRIEF
Important news stories affecting the community ....... 568

NEWS IN DEPTH
Targeting MCL1, Companies Aim to Unblock Apoptosis ....... 572

RESEARCH WATCH
Selected highlights of recent articles of exceptional significance from the cancer literature ............ 573

ONLINE
For more News and Research Watch, visit Cancer Discovery online at http://cancerdiscovery.aacrjournals.org/CDNews.

REVIEW
Engineering Multidimensional Evolutionary Forces to Combat Cancer ............... 587
C.E. McCoach and T.G. Bivona

RESEARCH BRIEFS
Patient-Driven Discovery, Therapeutic Targeting, and Post-Clinical Validation of a Novel AKT1 Fusion–Driven Cancer ............... 605
Précis: The response to AKT inhibition in a pediatric patient with a LAMTOR1–AKT1 fusion confirms the AKT1 fusion as an oncogenic driver, and subsequent characterization of the fusion suggests potential ways to overcome resistance.

A Stromal Lysolipid–Autotaxin Signaling Axis Promotes Pancreatic Tumor Progression ....... 617
Précis: Lysophosphatidylcholines secreted by activated stromal fibroblasts support pancreatic cancer cell proliferation and migration via autotaxin-mediated production of lysophosphatidic acid.
See commentary, p. 578

IN THE SPOTLIGHT
A FATaL Combination: Fibroblast-Derived Lipids and Cancer-Derived Autotaxin Promote Pancreatic Cancer Growth ................. 578
G. Biffi and D.A. Tuveson
See article, p. 617

Metabolic Checkpoint of Immune Cells in Melanoma Brain Metastases ............ 581
C.A. Egelston and K. Margolin
See article, p. 628

Delivering a STINGing Blow to Small Cell Lung Cancer via Synergistic Inhibition of DNA-Damage Response and Immune-Checkpoint Pathways ................. 584
J.B. Hiatt and D. MacPherson
See article, p. 646
ON THE COVER

Sen and colleagues showed that treatment of human small cell lung cancer (SCLC) cell lines with inhibitors of the DNA damage response (DDR) components CHK1 and PARP resulted in increased expression of PD-L1. Further, inhibition of either CHK1 or PARP in immunocompetent genetically engineered mouse models (GEMM) of SCLC resulted in increased levels of cytosolic DNA, which activates the cGAS–STING innate immune signaling pathway to induce IRF3 activation and subsequently drive IFNβ-mediated increases in PD-L1 expression and T-cell recruitment in SCLC GEMMs. Consistent with these findings, treatment with a CHK1 or PARP inhibitor enhanced the efficacy of anti–PD-L1 therapy and resulted in SCLC tumor regression in vivo. Together, these findings suggest that combined targeting of DDR proteins and immune checkpoint blockade is a potential therapeutic strategy for patients with SCLC. For details, please see the article by Sen and colleagues on page 646.