IN THIS ISSUE
Highlighted research articles 1494

NEWS IN BRIEF
Important news stories affecting the community 1498

RESEARCH WATCH
Selected highlights of recent articles of exceptional significance from the cancer literature 1503

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

VIEWS
In The Spotlight
Molecular Characterization of Malignant Mesothelioma: Time for New Targets? 1508
C. Aggarwal and S.M. Albelda
See article, p. 1548

Unleashing Blocked Apoptosis in Cancer Cells: New MCL1 Inhibitors Find Their Groove 1511
B. Leber, J. Kale, and D.W. Andrews
See article, p. 1566
See article, p. 1582
See article, p. 1598

TET2 Deficiency Sets the Stage for B-cell Lymphoma 1515
J.R. Shingleton and S.S. Dave
See article, p. 1632

REVIEW
The Clinical Impact of the Genomic Landscape of Mismatch Repair–Deficient Cancers 1518
G. Germano, N. Amirouchene-Angelozzi, G. Rosso, and A. Bardelli

RESEARCH BRIEFS
Landscape of Acquired Resistance to Osimertinib in EGFR-Mutant NSCLC and Clinical Validation of Combined EGFR and RET Inhibition with Osimertinib and BLU-667 for Acquired RET Fusion 1529
Précis: RET fusions were detected in patients with EGFR-mutant NSCLC who developed resistance to EGFR inhibition, and targeting RET in combination with EGFR inhibition produced responses in two patients.

Isoform Switching as a Mechanism of Acquired Resistance to Mutant Isocitrate Dehydrogenase Inhibition 1540
Précis: IDH1- or IDH2-mutant acute myeloid leukemia and solid tumors can develop resistance to isoform-selective IDH inhibition through mutation of the other IDH isoform.

Integrative Molecular Characterization of Malignant Pleural Mesothelioma 1548
Précis: Comprehensive, multiparameter genomic analyses of malignant pleural mesothelioma characterize a near-haploid molecular subtype, define prognostic molecular subsets, and identify high expression of VISTA in the epithelioid subtype.
See commentary, p. 1508

Research.
A Novel MCL1 Inhibitor Combined with Venetoclax Rescues Venetoclax-Resistant Acute Myelogenous Leukemia ............1566


Précis: An identified MCL1 inhibitor induced apoptosis in AML cells and was safely combined with BCL2 inhibition to overcome BCL2 inhibitor resistance and enhance antitumor activity in mouse models of AML.

See commentary, p. 1511

AMG 176, a Selective MCL1 Inhibitor, Is Effective in Hematologic Cancer Models Alone and in Combination with Established Therapies ...............1582


Précis: Drug discovery and optimization yielded the selective MCL1 inhibitor AMG 176, which induced apoptosis in cells from hematologic malignancies in vitro and in vivo and could be combined with other therapies.

See commentary, p. 1511

Exploiting MCL1 Dependency with Combination MEK + MCL1 Inhibitors Leads to Induction of Apoptosis and Tumor Regression in KRAS-Mutant Non–Small Cell Lung Cancer ............1598


Précis: Dual inhibition of MCL1 and MEK induces apoptosis and tumor regression in KRAS-mutant models of NSCLC, and BCL-xl inhibition may enhance sensitivity to MCL1 inhibition.

See commentary, p. 1511

Deletion 6q Drives T-cell Leukemia Progression by Ribosome Modulation ...............1614


Précis: SYNCRIP and SNHG5 haploinsufficiency increases leukemic-initiating cell activity and drives del(6q) T-ALL progression by reducing the translation efficiency of transcripts involved in mitochondrial respiration.

Correction

Correction: In Vivo E2F Reporting Reveals Efficacious Schedules of MEK1/2–CDK4/6 Targeting and mTOR–S6 Resistance Mechanisms . . . . . . . . . . . . . . .1654


AC icon indicates AuthorChoice

For more information please visit http://www.aacrjournals.org
The cover features three related studies investigating inhibitors of the antiapoptotic BCL2 family protein MCL1. Ramsey and colleagues used fragment-based methods and structure-based design to discover VU661013, a potent, selective small-molecule MCL1 inhibitor that synergized with BCL2 inhibition in models of acute myeloid leukemia. Caenepeel and colleagues identified an orally bioavailable selective MCL1 inhibitor, AMG 176, that triggered apoptosis in hematologic malignancies. Nangia, Siddiqui, and colleagues found that dual inhibition of MCL1 and MEK suppressed the growth of KRAS-mutant lung tumors. Collectively, these findings indicate that MCL1 inhibitors may be beneficial alone or in combination therapies to treat patients with a variety of malignancies. For details, please see the articles by Ramsey and colleagues on page 1566, Caenepeel and colleagues on page 1582, and Nangia, Siddiqui, and colleagues on page 1598.