IN THIS ISSUE

Highlighted research articles .................................. 377

NEWS IN BRIEF

Important news stories affecting the community .................. 380

Q&A: Christopher Wild on Global Tobacco Use ................. 383

J&J Partners with Yale to Share Trial Data ........................ 384

RESEARCH WATCH

Selected highlights of recent articles of exceptional significance from the cancer literature .................. 385

ONLINE

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

REVIEW

Contribution of p53 to Metastasis ............................... 405

E. Powell, D. Piwnica-Worms, and H. Piwnica-Worms

RESEARCH BRIEFS

CD74–NRG1 Fusions in Lung Adenocarcinoma ............... 415


Précis: CD74-NRG1 fusions are observed in invasive mucinous lung adenocarcinomas and drive cell transformation via activation of ERBB3–PI3K–AKT signaling.

Response of BRAF-Mutant Melanoma to BRAF Inhibition Is Mediated by a Network of Transcriptional Regulators of Glycolysis ................................. 423


Précis: MYC, HIF1α, and MONDOA act downstream of BRAF to regulate glycolysis and mediate melanoma cell sensitivity to BRAF inhibition by vemurafenib.

In The Spotlight

Metabolic Dysregulation in Melanoma: Cause or Consequence? .................. 390

R. Haq

See article, p. 423

Unlikely Suspects Identified in Neuroblastoma Conspiracy .... 392

R. Bernards

See article, p. 434

Germline Polymorphisms in RNF31 Regulate Linear Ubiquitination and Oncogenic Signaling .................. 394

P. Grumati and I. Dikic

See article, p. 480

Prospective

Oncology Drug Discovery: Planning a Turnaround .............. 397

C. Toniatti, P. Jones, H. Graham, B. Pagliara, and G. Draetta

Q&A: Christopher Wild on Global Tobacco Use ................. 383

J&J Partners with Yale to Share Trial Data ........................ 384

Selected highlights of recent articles of exceptional significance from the cancer literature .................. 385

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R. Haq

See article, p. 423

Unlikely Suspects Identified in Neuroblastoma Conspiracy .... 392

R. Bernards

See article, p. 434

Germline Polymorphisms in RNF31 Regulate Linear Ubiquitination and Oncogenic Signaling .................. 394

P. Grumati and I. Dikic

See article, p. 480

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Fernandez-Cuesta and colleagues identified recurrent fusions between CD74 and the exons encoding the EGF-like domain of the neuron-specific neuregulin 1 (NRG1) III-β3 isoform in invasive mucinous lung adenocarcinomas that lack common kinase driver mutations. The CD74–NRG1 fusion generates a membrane-bound protein that exposes the EGF-like domain of NRG1 on the extracellular surface, which creates a ligand for ERBB2–ERBB3 heterodimers and promotes oncogenic transformation by activating the PI3K–AKT pathway downstream of ERBB3. These findings implicate CD74–NRG1 as an oncogenic driver in lung adenocarcinomas and suggest that the ERBB3–PI3K–AKT pathway may be a therapeutic target in the invasive mucinous subtype, which currently lacks effective treatments. For details, please see the article by Fernandez-Cuesta and colleagues on page 415.