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Highlighted research articles

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Important news stories affecting the community

NEWS IN DEPTH
Q&A: Christopher Wild on Global Tobacco Use
J&J Partners with Yale to Share Trial Data

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

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REVIEW
Contribution of p53 to Metastasis
E. Powell, D. Piwnica-Worms, and H. Piwnica-Worms

RESEARCH BRIEFS
CD74–NRG1 Fusions in Lung Adenocarcinoma

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

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?
R. Haq
See article, p. 423

Unlikely Suspects Identified in Neuroblastoma Conspiracy
R. Bernards
See article, p. 434

Germline Polymorphisms in RNF31 Regulate Linear Ubiquitination and Oncogenic Signaling
P. Grumati and I. Dikic
See article, p. 480

Prospective
Oncology Drug Discovery: Planning a Turnaround
C. Toniatti, P. Jones, H. Graham, B. Pagliara, and G. Draetta

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Prospective
Oncology Drug Discovery: Planning a Turnaround
C. Toniatti, P. Jones, H. Graham, B. Pagliara, and G. Draetta
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.

**RESEARCH ARTICLES**

**RNA Helicase A Is a Downstream Mediator of KIF1Bβ Tumor-Suppressor Function in Neuroblastoma** .......... 434

**Précis:** Loss of KIF1Bβ in neuroblastoma reduces RNA helicase A nuclear translocation and subsequent XIAP-associated factor 1–dependent neural pruning.

See commentary, p. 392

**Inhibition of KRAS-Driven Tumorigenicity by Interruption of an Autocrine Cytokine Circuit** ............ 452

**Précis:** Activation of autocrine CCL5 and IL-6 signaling by TBK1 and IKKe promotes KRAS-dependent non–small cell lung cancer cell growth.

**Autophagy-Dependent Production of Secreted Factors Facilitates Oncogenic RAS-Driven Invasion** ...... 466
R. Lock, C.M. Kenific, A.M. Leidal, E. Salas, and J. Debnath

**Précis:** IL6 secretion and WNT5A and MMP2 expression are autophagy-dependent and necessary for HRASV12-driven mammary epithelial cell invasion.

**Essential Role of the Linear Ubiquitin Chain Assembly Complex in Lymphoma Revealed by Rare Germline Polymorphisms** .................. 480

**Précis:** Germline polymorphisms that promote linear polyubiquitin chain assembly complex (LUBAC) formation and NF-κB signaling in ABC DLBCL implicate LUBAC as a therapeutic target.

See commentary, p. 394

**ON THE COVER**

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.

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