CONTRIBUTION OF p53 TO METASTASIS

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

CD74–NRG1 FUSSIONS 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.

SEE COMMENTARY, P. 390

IN THE SPOTLIGHT

METABOLIC DYSREGULATION IN MELANOMA: CAUSE OR CONSEQUENCE?

R. Haq

UNLIKELY SUSPECTS IDENTIFIED IN NEUROBLASTOMA CONSPIRACY

R. Bernards

GERMLINE POLYMORPHISMS IN RNF31 REGULATE LINEAR UBIQUITINATION AND ONCOGENIC SIGNALING

P. Grumati and I. Dikic

PROSPECTIVE

ONCOLOGY DRUG DISCOVERY: PLANNING A TURNOVER

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.

ON THE COVER
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