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Prospective

Oncology Drug Discovery: Planning a Turnaround
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-β 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.

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

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

See commentary, p. 394

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