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

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


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

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


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