MAX Inactivation in Small Cell Lung Cancer Disrupts MYC–SWI/SNF Programs and Is Synthetic Lethal with BRG1. . . . . . . . . . . . . . . . . . . . . .292

Précis: MAX is a tumor suppressor recurrently altered in SCLC that is regulated by the SWI/SNF protein BRG1, and BRG1 depletion is selectively toxic in MAX-deficient cells.

See commentary, p. 273

An In Vivo Functional Screen Identifies ST6GalNAc2 Sialyltransferase as a Breast Cancer Metastasis Suppressor . . . . . . . . . . . . . .304


See commentary, p. 275

RapidCaP, a Novel GEM Model for Metastatic Prostate Cancer Analysis and Therapy, Reveals Myc as a Driver of Pten-Mutant Metastasis . . . . . . . . . . .318

Précis: RapidCap is a GEM model of prostate cancer that exhibits features typical of human disease and identifies MYC as a spontaneous metastatic driver.
Romero and colleagues identified recurrent inactivating deletions within MYC-associated factor X (MAX) in small cell lung cancer (SCLC) cell lines and tumors that were mutually exclusive with MYC amplification, inactivation of MAX dimerization protein (MGA), and mutations in BRG1 (also known as SMARCA4), which encodes an ATPase subunit of the SWI/SNF chromatin remodeling complex, suggesting that these genetic alterations drive SCLC through disruption of a common pathway. Indeed, BRG1 directly regulated MAX expression, and MAX upregulated MYC target genes in a BRG1-dependent manner. Moreover, BRG1 depletion selectively inhibited the growth of MAX-deficient SCLC cells, suggesting that a synthetic lethal relationship exists between these two proteins and raising the possibility that BRG1 may be a therapeutic target in SCLC. For details, please see the article by Romero and colleagues on page 292.

Précis: Unlike AKT inhibitors, PI3K inhibitors rapidly induce cancer cell death because they also inhibit activation of wild-type RAS and downstream RAF–MEK–ERK signaling.

Précis: Intratumor methylation heterogeneity coevolves with genetic alterations and is associated with high-risk, poor prognostic markers in a subset of CLL tumors.

Précis: ABT-199 shows on-target activity against AML cells that correlates with BCL-2 expression and can be predicted by mitochondrial BH3 profiling.

See commentary, p. 278