Autophagy Inhibition Improves Chemosensitivity in BRAF^V600E Brain Tumors


Précis: BRAF^V600E-positive pediatric central nervous system tumor cells are autophagy-dependent and can be effectively targeted with combined chloroquine and vemurafenib therapy.

Obligate Progression Precedes Lung Adenocarcinoma Dissemination


Précis: Tumor-cell dissemination is a rate-limiting step in lung cancer metastasis that requires genetic alterations that can be facilitated by p53 loss and is characterized by downregulation of Nkx2-1.

SPSB1 Promotes Breast Cancer Recurrence by Potentiating c-MET Signaling


Précis: Upregulation of SPSB1 enhances the survival of residual tumor cells and mediates tumor recurrence by activating c-MET signaling in aggressive breast cancer subtypes.

See commentary, p. 760

For more News and Research Watch, visit Cancer Discovery online at http://CDnews.aacrjournals.org.

SPSB1 May Have MET Its Match during Breast Cancer Recurrence

Y. Qin and S.S. McAllister

See article, p. 790

BluepRINT for Moderate-to-Low Penetration Cancer Susceptibility Genes Needed: Breast Cancer and Beyond

J. Ngeow and C. Eng

See article, p. 804

A Little pRB Can Lead to Big Problems

P.W. Hinds

See article, p. 840

Targeting Mitochondrial Metabolism by Inhibiting Autophagy in BRAF-Driven Cancers

A.M. Strohecker and E. White

Mini Review

See article, p. 840

罕见突变在RINT1导致携带者的乳腺和Lynch综合征谱系癌症的倾向


Précis: Rare variants in RINT1 are associated with increased risk for breast cancer as well as a spectrum of cancers that are associated with DNA mismatch repair defects.

See commentary, p. 762
Mulcahy Levy and colleagues report that autophagy is increased in BRAFV600E-positive pediatric central nervous system (CNS) tumors, suggesting that BRAF-mutant CNS tumors may be dependent on autophagy. Indeed, inhibition of autophagy was cytotoxic to BRAFV600E-positive CNS tumor cells, and the autophagy inhibitor chloroquine showed synergistic activity with the BRAF inhibitor vemurafenib in BRAF-mutant CNS tumor cells.

The addition of chloroquine to vemurafenib overcame vemurafenib resistance in primary BRAF-mutant pleomorphic xanthoastrocytoma cells, and combined chloroquine and vemurafenib rapidly improved symptoms and led to durable disease stabilization in a patient with vemurafenib-refractory BRAFV600E-positive brainstem ganglioglioma. These findings provide a rationale for combining autophagy inhibitors with BRAF-targeted therapy in patients with BRAF-mutant CNS tumors. For details, please see the article by Mulcahy Levy and colleagues on page 773.