Autophagy Inhibition Improves Chemosensitivity in BRAFV600E Brain Tumors


Précis: BRAFV600E-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

Rare Mutations in RINT1 Predispose Carriers to Breast and Lynch Syndrome-Spectrum Cancers


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 
$BRAF^{V600E}$-positive pediatric central nervous system (CNS) tumors, sug-
gesting that $BRAF$-mutant CNS tumors may be dependent on autophagy. 
Indeed, inhibition of autophagy was cytotoxic to $BRAF^{V600E}$-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 resis-
tance in primary $BRAF$-mutant pleomorphic xanthoastrocytoma cells, and com-
bined chloroquine and vemurafenib rapidly improved symptoms and led to durable 
disease stabilization in a patient with vemurafenib-refractory $BRAF^{V600E}$-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.