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### RESEARCH BRIEFS

**Autophagy Inhibition Improves Chemosensitivity in BRAF V600E Brain Tumors** .................. 773

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

### RESEARCH ARTICLES

**Obligate Progression Precedes Lung Adenocarcinoma Dissemination** .................. 781

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** .................. 790

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** .... 804

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 \( \text{BRAF}^{\text{V600E}} \)-positive pediatric central nervous system (CNS) tumors, suggesting that \( \text{BRAF} \)-mutant CNS tumors may be dependent on autophagy. Indeed, inhibition of autophagy was cytotoxic to \( \text{BRAF}^{\text{V600E}} \)-positive CNS tumor cells, and the autophagy inhibitor chloroquine showed synergistic activity with the \( \text{BRAF} \) inhibitor vemurafenib in \( \text{BRAF} \)-mutant CNS tumor cells. The addition of chloroquine to vemurafenib overcame vemurafenib resistance in primary \( \text{BRAF} \)-mutant pleomorphic xanthoastrocytoma cells, and combined chloroquine and vemurafenib rapidly improved symptoms and led to durable disease stabilization in a patient with vemurafenib-refractory \( \text{BRAF}^{\text{V600E}} \)-positive brainstem ganglioglioma. These findings provide a rationale for combining autophagy inhibitors with \( \text{BRAF} \)-targeted therapy in patients with \( \text{BRAF} \)-mutant CNS tumors. For details, please see the article by Mulcahy Levy and colleagues on page 773.