A Genome-Wide Scan Identifies Variants in NFIB Associated with Metastasis in Patients with Osteosarcoma


Précis: The risk variant rs7034162 in NFIB contributes to osteosarcoma metastasis susceptibility.

Real-Time Imaging Reveals Local, Transient Vascular Permeability, and Tumor Cell Intravasation Stimulated by TIE2hi Macrophage-Derived VEGFA


Précis: Hyperpermeability of tumor vasculature is dynamic and restricted to the Tumor MicroEnvironment of Metastasis (TMEM).

See commentary, p. 906

HOXB7 Is an ERα Cofactor in the Activation of HER2 and Multiple ER Target Genes Leading to Endocrine Resistance


Précis: HOXB7 is upregulated by MYC-mediated suppression of miR-196a and enhances expression of ER target genes in tamoxifen-resistant breast cancer cells.

See commentary, p. 909
Tricker, Xu, and colleagues found that combined treatment with the mutant EGFR–selective inhibitor WZ4002 and the MEK inhibitor trametinib delayed the development of acquired resistance in EGFR inhibitor-naïve and EGFR<sup>T790M</sup>-positive lung cancer cells. WZ4002/trametinib treatment prevented ERK1/2 reactivation and increased apoptosis. Combination treatment was also significantly more effective than WZ4002 alone in suppressing tumor regrowth in xenograft models and a genetically engineered mouse model of EGFR<sup>T790M</sup>-mutant lung cancer. Although EGFR and ERK inhibition were maintained in the majority of WZ4002/trametinib-resistant tumor nodules, both AKT and S6 were frequently reactivated, and the addition of an mTOR inhibitor restored WZ4002/trametinib sensitivity in vitro and in vivo. These results highlight the potential clinical utility of initial cotargeting of EGFR and MEK to prevent the emergence of acquired resistance in EGFR-mutant lung cancer. For details, please see the article by Tricker, Xu, and colleagues on page 960.