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. 909

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

In The Spotlight
Cancer Metastasis: Perivascular Macrophages Under Watch
E. Kadioglu and M. De Palma
See article, p. 932

Targeting a Novel ER/HOXB7 Signaling Loop in Tamoxifen-Resistant Breast Cancer
M.R. Heideman, A. Frei, and N.E. Hynes
See article, p. 944

Mass Cytometry: A High-Throughput Platform to Visualize the Heterogeneity of Acute Myeloid Leukemia
P. Do and J.C. Byrd
See article, p. 988

Adaptive Immune Resistance: How Cancer Protects from Immune Attack
A. Ribas

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Précis: Acquired resistance to EGFR inhibitors can be prevented with dual EGFR and MEK inhibition, which results in prolonged ERK1/2 inhibition and increased apoptosis in EGFR-mutant NSCLC.


Précis: Upregulation of MYC in multiple myeloma cells drives DNA damage via replicative stress and ROS induction, and confers sensitivity to ATR inhibitors and small-molecule inducers of ROS.


Précis: High-dimensional analysis of patient-derived AML cells using mass cytometry identifies changes in immunophenotypic patterns and cell-cycle kinetics that are predictive of AML subtype and chemotherapeutic response.

See commentary, p. 912

On the Cover

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}–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}–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.

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