BREAKING ADVANCES

2131 Highlights from Recent Cancer Literature

REVIEWS

2133 DNA Damage in Cancer Therapeutics: A Boon or a Curse?
Anchit Khanna

2139 Classifying Cancers Based on T-cell Infiltration and PD-1
Michele W.L. Teng, Shin Foong Ngiov, Antoni Ribas, and Mark J. Smyth

PRIORITY REPORTS

2146 Therapeutically Targetable ALK Mutations in Leukemia
Précis: These findings suggest a rationale for personalized treatment of certain leukemia patients with ALK kinase inhibitors, with immediate implications for clinical evaluation.

2151 Tumor-Induced Pressure in the Bone Microenvironment Causes Osteocytes to Promote the Growth of Prostate Cancer Bone Metastases
Joseph L. Sottnik, Jinlu Dai, Honglai Zhang, Brittany Campbell, and Evan T. Keller
Précis: This study illuminates the critical contribution of physical forces to tumor cell growth in the tumor microenvironment, identifying osteocytes as critical mediators of the effect of this force in the bone metastatic niche.

2159 Mechanistic Rationale to Target PTEN-Deficient Tumor Cells with Inhibitors of the DNA Damage Response Kinase ATM
Nuala McCabe, Conor Hanna, Steven M. Walker, David Gonda, Jie Li, Katarina Wikstrom, Kieran I. Savage, Karl T. Butterworth, Clark Chen, D. Paul Harkin, Kevin M. Prise, and Richard D. Kennedy
Précis: These results offer a preclinical mechanistic rationale for clinical evaluation of ATM inhibitors for treatment of PTEN-deficient tumors.

MICROENVIRONMENT AND IMMUNOLOGY

2166 Effective Eradication of Glioblastoma Stem Cells by Local Application of an AC133/CD133-Specific T-cell--Engaging Antibody and CD8 T Cells
Shruthi Prasad, Simone Gaedicke, Marcia Machain, Gerhard Mittler, Friederike Braun, Michael Hettich, Elke Firtz, Kerstin Klingner, Julia Schuler, Dagmar Wider, Ralph M. Wäsch, Christel Herold-Mende, Ursula Eßasser-Beile, and Gabriele Niedermann
Précis: In combination with a T-cell microinfusion into the brain, a novel bispecific antibody that delivers T cells to glioma stem-like cells mediates strong antitumor effects.

2177 Full-Length Semaphorin-3C Is an Inhibitor of Tumor Lymphangiogenesis and Metastasis
Yelena Mumblat, Ofra Kessler, Neta Ilan, and Gera Neufeld
Précis: An antibody-based strategy to block the development of new lymph vessels into tumors, as well as the metastasis of tumor cells into lymph nodes, suggests the antibody may offer generalized therapeutic potential to treat any solid tumor.

2187 JAK Inhibition Impairs NK Cell Function in Myeloproliferative Neoplasms
Kathrin Schönberg, Janna Rudolph, Maria Vonnahme, Sowmya Parampalli, Yajnanarayana, Isabelle Cornez, Maryam Hejazi, Angela R. Manser, Markus Uhrberg, Walter Verbeek, Steffen Koschmieder, Tim H. Brummendorf, Peter Brossart, Annkristin Heine, and Dominik Wolf
Précis: Findings indicate that the approved JAK kinase inhibitor Jakafi (Incyte) significantly depletes natural killer cells in patients, possibly explaining the higher rates of infection reported with drug treatment in either approved or experimental settings where this drug is being tested.

2200 CTLA-4+ Regulatory T Cells Increased in Cetuximab-Treated Head and Neck Cancer Patients Suppress NK Cell Cytotoxicity and Correlate with Poor Prognosis
Précis: These findings suggest that the response to anti-EGFR therapy could be improved by the addition of anti-CTLA-4 therapy, with immediate implications for clinical translation.
LETTER TO THE EDITOR

2400 Drug Combination Studies and Their Synergy Quantification Using the Chou–Talalay Method—Letter
John C. Ashton

CORRECTION

2401 Correction: HOXB7, a Homeodomain Protein, Is Overexpressed in Breast Cancer and Confers Epithelial–Mesenchymal Transition

ABOUT THE COVER

Some lupus autoantibodies penetrate into live cells, and the potential to use these cell-penetrating antibodies against cancer is an emerging concept. An optimized lupus anti-DNA antibody construct, 3E10 di-scFv, has now been shown to localize into cell nuclei and to selectively cause accumulation of DNA damage in and kill cancer cells with certain defects in DNA repair and therefore has potential in targeted cancer therapy. In this image the fluorescent signal demonstrates nuclear localization by the optimized lupus antibody construct in DLD1 colon cancer cells that were immunostained after treatment with 3E10 di-scFv. For details, see article by Noble and colleagues on page 2285.