BREAKING ADVANCES

4543 Highlights from Recent Cancer Literature

OBITUARY

4545 Angela M.H. Brodie, PhD, FAACR: In Memoriam (1934–2017)
V. Craig Jordan

SPECIAL REPORT

4548 Charting the Future of Cancer Health Disparities Research: A Position Statement from the American Association for Cancer Research, the American Cancer Society, the American Society of Clinical Oncology, and the National Cancer Institute
Blase N. Polite, Lucile L. Adams-Campbell, Otis W. Brawley, Nina Bickell, John M. Carethers, Christopher R. Flowers, Margaret Foti, Scarlett Lin Gomez, Jennifer J. Griggs, Christopher S. Lathan, Christopher I. Li, J. Leonard Lichtenfeld, Worta McCaskill-Stevens, and Electra D. Paskett

REVIEW

4556 Epithelial-to-Mesenchymal and Mesenchymal-to-Epithelial Transition in Mesenchymal Tumors: A Paradox in Sarcomas?
Giuseppina Sannino, Aruna Marchetto, Thomas Kirchner, and Thomas G.P. Grünewald

PRIORITY REPORT

4562 Acquired Immune Resistance Follows Complete Tumor Regression without Loss of Target Antigens or IFNγ Signaling
Marco Donia, Katja Harbst, Marit van Buuren, Pia Kvinnsborg, Mattias F. Lindberg, Rikke Andersen, Manja Idorn, Shamaila Munir Ahmad, Eva Ellebæk, Anja Mueller, Paolo Fagone, Ferdinando Nicoletti, Massimo Libra, Martin Lauss, Sine Reker Hadrup, Henrik Schmidt, Mads Hald Andersen, Per thor Straten, Jonas A. Nilsson, Toni N. Schumacher, Barbara Seliger, Göran Jönsson, and Inge Marie Svane
Précis: These findings indicate that acquired resistance to T-cell–based immunotherapy that can occur in patients is not due to loss of target antigens or IFNγ signaling, which appear to remain intact, but rather to other mechanisms yet to be identified.

MOLECULAR AND CELLULAR PATHOBIOLOGY

4567 APOBEC3A and APOBEC3B Activities Render Cancer Cells Susceptible to ATR Inhibition
Rémi Buisson, Michael S. Lawrence, Cyril H. Benes, and Lee Zou
Précis: These results define a DNA replication stress in cancer cells driven by mRNA editing APOBEC cytosine deaminases that may guide therapeutic opportunities via inhibitors of the DNA repair kinase ATR.

4579 Cytosine Deaminase APOBEC3A Sensitizes Leukemia Cells to Inhibition of the DNA Replication Checkpoint
Abby M. Green, Konstantin Budagyan, Katharina E. Hayer, Morgann A. Reed, Milan R. Savani, Gerald B. Wertheim, and Matthew D. Weitzman
Précis: The cytosine deaminase APOBEC3A is highly expressed in a subset of acute myeloid leukemias, where it may be a candidate biomarker for the response to DNA replication checkpoint inhibitors.

TUMOR AND STEM CELL BIOLOGY

4589 Glycerol-3-phosphate Acyltransferase 1 Promotes Tumor Cell Migration and Poor Survival in Ovarian Carcinoma
Rosemarie Marchan, Bettina Böttner, Jörg Lambert, Karolina Edlund, Iris Glaser, Meinolf Blaskewicz, Gregor Leonhardt, Lisa Marienhoff, Darius Kashta, Moritz Anfr, Carsten Watzl, Katrin Madjar, Marianna Grinberg, Eugen Rempel, Roland Hergenröder, Silvia Selinski, Jörg Rahmehführer, Michaela S. Lesjak, Joanna D. Stewart, Cristina Cadenas, and Jan G. Hengstler
Précis: These findings suggest that enzymes downstream of glycerophosphocholine affect cell migration, likely via their influence on lysophosphatidic acid, a pro-oncogenic signaling lipid, with potential implications for cancer prognosis and therapy.

4602 TP53INP1 Downregulation Activates a p73-Dependent DUSP10/ERK Signaling Pathway to Promote Metastasis of Hepatocellular Carcinoma
Kai-Yu Ng, Lok-Hoi Chan, Stella Chai, Man Tong, Xin-Yuan Guan, Nikhil P Lee, Yunfei Yuan, Dan Xie, Terence K Lee, Nelson J Dusetti, Alice Carrier, and Stephanie Ma
Précis: This study shows how common downregulation of a stress response gene in liver cancer promotes metastatic progression, also providing a mechanistic rationale for new therapeutic approaches in this setting.
PRMT1-Mediated Translation Regulation Is a Crucial Vulnerability of Cancer
Jessie Hao-Ru Hsu, Benjamin Hubbell-Engler, Guillaume Adelmant, Jialiang Huang, Cailin E. Joyce, Francisca Vazquez, Barbara A. Weir, Philip Montgomery, Avid Tshemiak, Andrew O. Giacomelli, Jennifer A. Perry, Jennifer Towbridge, Yuko Fujiwara, Glenn S. Cowley, Huafeng Xie, Woonjin Kim, Carl D. Novina, William C. Hahn, Jarrod A. Marto, and Stuart H. Orkin

Précis: These findings provide a rationale for targeting the arginine methyltransferase Prmt1, a regulator of protein translation, as a strategy to eradicate cancer cells, which commonly display unique translation-dependent requirements.

WEEl Kinase Inhibitor AZD1775 Has Preclinical Efficacy in LKB1-Deficient Non–Small Cell Lung Cancer
Amanda L. Richer, Jacqueline M. Cala, Kelley O’Brien, Yashit M. Carson, Landon J. Inge, and Timothy C. Whitsett

Précis: These findings provide a preclinical proof of concept for the use of a G2-M checkpoint inhibitor to effectively treat a particularly aggressive subgroup of lung adenocarcinomas.

Identification of Interacting Stromal Axes in Triple-Negative Breast Cancer
Sadiq M. I. Saleh, Nicholas Bertos, Tina Gruosso, Mathieu Gigoux, Margarita Souleimanova, Hong Zhao, Atilla Omervoglu, Michael T. Hallett, and Morag Park

Précis: This study shows how a signature of immune and desmoplasmic stromal markers in an aggressive form of breast cancer can produce a simple ontology for gauging tumor heterogeneity and informing prognosis.

Targeting Adenosine in BRAF-Mutant Melanoma Reduces Tumor Growth and Metastasis
Arabella Young, Shin Foong Ngioj, Jason Madore, Julia Reinhardt, Jennifer Landsberg, Arash Chitsazan, Jai Rautela, Tobias Bald, Deborah S. Barkauskas, Elizabeth Ahern, Nicholas D. Huntington, Dirk Schadendorf, Georgina V. Long, Glen M. Boyle, Michael Hölzel, Richard A. Scolyer, and Mark J. Smyth

Précis: In melanoma, combining an antagonist of the immunosuppressive adenosine receptor A2A with BRAF and MEK inhibitors augments antitumor immunity to limit metastatic progression.

MAPK Signaling and Inflammation Link Melanoma Phenotype Switching to Induction of CD73 during Immunotherapy

Précis: These findings indicate development of resistance to immunotherapy in melanoma and caution against CD73 expression as a pretreatment biomarker.
SPIN90 Depletion and Microtubule Acetylation Mediate Stromal Fibroblast Activation in Breast Cancer Progression
Eunae You, Yun Hyun Huh, Ahreum Kwon, So Hee Kim, In Hee Chae, Ok-Jun Lee, Je-Hwang Ryu, Min Ho Park, Ga-Eon Kim, Ji Shin Lee, Kun Ho Lee, Yong Seok Lee, Jung Woong Kim, Sangmung Rhee, and Woo Keun Song

Précis: Disrupting expression of a determinant of microtubule acetylation may pose an effective therapeutic strategy to treat breast cancers.

Pharmacokinetics and Pharmacodynamics-Based Mathematical Modeling Identifies an Optimal Protocol for Metronomic Chemotherapy
Joseph Ciccolini, Dominique Barbolosi, Christophe Meille, Aurélie Lombard, Cindy Serdjebi, Sarah Giacometti, Laetitia Padovani, Eddy Pasquier, and Nicolas André

Précis: Studies in a mouse model of chemoresistant neuroblastoma highlight the utility of mathematical modeling to optimize metronomic chemotherapy.

Transglutaminase 2 Is a Direct Target Gene of YAP-TAZ—Letter
Chen-Ying Liu, Ajaybabu V. Pobbati, Zhenyu Huang, Long Cui, and Wanjin Hong

Transglutaminase 2 Is a Direct Target Gene of YAP-TAZ—Response
Matthew L. Fisher, Gautam Adhikary, Candace Kerr, Daniel Gurn, and Richard L. Eckert


Adenosine is an immunosuppressive metabolite that prevents antitumor immunity and promotes metastatic dissemination. In BRAF-mutant melanoma, adenosine signaling by the A2A adenosine receptor impedes the activity of clinically approved BRAF/MEK-targeted therapies. Using preclinical melanoma models, it was found that targeting adenosine signaling in combination with BRAF/MEK inhibition provided improved tumor control and antitumor activity. In addition, combination BRAF/MEK treatment in melanoma patients regulates the expression of CD73, the enzyme that generates adenosine. For details, see article by Young and colleagues on page 4684.