

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, Wortia 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 IFN γ Signaling
Marco Donia, Katja Harbst, Marit van Buuren, Pia Kvistborg, Mattias F. Lindberg, Rikke Andersen, Manja Idorn, Shamaaila 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, Ton 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 IFN γ 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 Büttner, Jörg Lambert, Karolina Edlund, Iris Glaeser, Meinolf Blaszkewicz, Gregor Leonhardt, Lisa Marienhoff, Dariusz Kaszta, Moritz Anft, Carsten Watzl, Katrin Madjar, Marianna Grinberg, Eugen Rempel, Roland Hergenroder, Silvia Selinski, Jörg Rahnenführer, 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-Hei Chan, Stella Chai, Man Tong, Xin-Yuan Guan, Nikki 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.

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- 4613** 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, Aviad Tsherniak, Andrew O. Giacomelli, Jennifer A. Perry, Jennifer Trowbridge, Yuko Fujiwara, Glenn S. Cowley, Huaifeng Xie, Woojin 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.

THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

- 4626** Targeting Histone Demethylases in MYC-Driven Neuroblastomas with Ciclopirox
Jun Yang, Sandra Milasta, Dongli Hu, Alaa M. Altahan, Rodrigo B. Interiano, Junfang Zhou, Jesse Davidson, Jonathan Low, Wenwei Lin, Ju Bao, Pollyanna Goh, Amit C. Nathwani, Ruoning Wang, Yingdi Wang, Su Sien Ong, Vincent A. Boyd, Brandon Young, Sourav Das, Anang Shelat, Yinan Wu, Zhenmei Li, Jie J. Zheng, Ashutosh Mishra, Yong Cheng, Chunxu Qu, Junmin Peng, Douglas R. Green, Stephen White, R. Kiplin Guy, Taosheng Chen, and Andrew M. Davidoff
Précis: These findings provide new insights into epigenetic regulation of MYC function and suggest a novel pharmacologic basis to target histone demethylases as an indirect MYC-targeting approach for cancer therapy.
- 4639** Resistance to the Antibody–Drug Conjugate T-DM1 Is Based in a Reduction in Lysosomal Proteolytic Activity
Carla Ríos-Luci, Sara García-Alonso, Elena Díaz-Rodríguez, Mercedes Nadal-Serrano, Joaquín Arribas, Alberto Ocaña, and Atanasio Pandiella
Précis: Drug resistance that arises invariably to cancer cell–targeted therapy also poses a challenge to antibody–drug conjugates, in this case through a novel mechanism involving alterations in the lysosome-based proteolytic activity.
- 4652** LSD1 Inhibitor T-3775440 Inhibits SCLC Cell Proliferation by Disrupting LSD1 Interactions with SNAG Domain Proteins INSM1 and GF11B
Shinji Takagi, Yoshinori Ishikawa, Akio Mizutani, Shinji Iwasaki, Satoru Matsumoto, Yusuke Kamada, Toshiyuki Nomura, and Kazuhide Nakamura
Précis: These findings provide insights into how the interaction between LSD1 and SNAG domain proteins regulates transcription in neuroendocrine tumors and also offer a preclinical proof of concept for the therapeutic efficacy of targeting LSD1 in this setting.

- 4663** WEE1 Kinase Inhibitor AZD1775 Has Preclinical Efficacy in LKB1-Deficient Non–Small Cell Lung Cancer
Amanda L. Richer, Jacqueline M. Cala, Kelley O’Brien, Vashti M. Carson, Landon J. Inge, and Timothy G. 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.

MICROENVIRONMENT AND IMMUNOLOGY

- 4673** Identification of Interacting Stromal Axes in Triple-Negative Breast Cancer
Sadiq M.I. Saleh, Nicholas Bertos, Tina Gruosso, Mathieu Gigoux, Margarita Souleimanova, Hong Zhao, Atila Omeroglu, Michael T. Hallett, and Morag Park
Précis: This study shows how a signature of immune and desmoplastic stromal markers in an aggressive form of breast cancer can produce a simple ontology for gauging tumor heterogeneity and informing prognosis.
- 4684** Targeting Adenosine in BRAF-Mutant Melanoma Reduces Tumor Growth and Metastasis
Arabella Young, Shin Foong Ngiow, 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.
- 4697** MAPK Signaling and Inflammation Link Melanoma Phenotype Switching to Induction of CD73 during Immunotherapy
Julia Reinhardt, Jennifer Landsberg, Jonathan L. Schmid-Burgk, Bartomeu Bibiloni Ramis, Tobias Bald, Nicole Glodde, Dorys Lopez-Ramos, Arabella Young, Shin Foong Ngiow, Daniel Nettersheim, Hubert Schorle, Thomas Quast, Waldemar Kolanus, Dirk Schadendorf, Georgina V. Long, Jason Madore, Richard A. Scolyer, Antoni Ribas, Mark J. Smyth, Paul C. Tumei, Thomas Tüting, and Michael Hölzel
Précis: These findings indicate development of resistance to immunotherapy in melanoma and caution against CD73 expression as a pretreatment biomarker.



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- 4710** 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, Sangmyung Rhee, and Woo Keun Song

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

INTEGRATED SYSTEMS AND TECHNOLOGIES

- 4723** 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.

LETTERS TO THE EDITOR

- 4734** Transglutaminase 2 Is a Direct Target Gene of YAP/TAZ—Letter
Chen-Ying Liu, Ajaybabu V. Pobbati, Zhenyu Huang, Long Cui, and Wanjin Hong

- 4736** Transglutaminase 2 Is a Direct Target Gene of YAP/TAZ—Response
Matthew L. Fisher, Gautam Adhikary, Candace Kerr, Daniel Grun, and Richard L. Eckert

RETRACTION

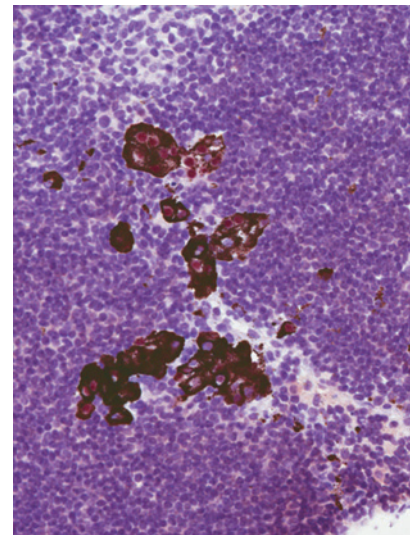
- 4737** Retraction: Abstract 408: ACP-196, An Orally Bioavailable Covalent Selective Inhibitor of Btk, Modulates the Innate Tumor Microenvironment, Exhibits Antitumor Efficacy and Enhances Gemcitabine Activity in Pancreatic Cancer

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ABOUT THE COVER

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 antimetastatic 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.



Cancer Research

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