BREAKING ADVANCES

6793 Highlights from Recent Cancer Literature

REVIEWS

6795 Discovery of IDO1 Inhibitors: From Bench to Bedside
George C. Prendergast, William P. Malachowski, James B. DuHadaway, and Alexander J. Muller

6812 Emerging Role of CRISPR/Cas9 Technology for MicroRNAs Editing in Cancer Research
Guillermo Aquino-Jarquin

PRIORITY REPORT

6818 RUNX1 Upregulation by Cytotoxic Drugs Promotes Apoptosis
Daniel Speidel, Jasmin Wellbrock, and Melissa Abas
Précis: These findings reveal a proapoptotic function for a gene primarily known as a differentiation factor, offering a possible explanation for its association with drug resistance in leukemia.

MOLECULAR AND CELLULAR PATHOBIOLOGY

6825 PP2A Inactivation Mediated by PPP2R4 Haploinsufficiency Promotes Cancer Development
Ward Sents, Bob Meesen, Petar Kalez, Enrico Radaelli, Xavier Sagartz, Eline Mierrmans, Dorien Haesen, Caroline Lambrecht, Mieke Dewerchin, Peter Carmeliet, Jukka Westermarck, Anna Sablina, and Veerle Janssens
Précis: This seminal study defines a haploinsufficient tumor suppressor gene that provides a high-penetrance mechanism for inhibition of the antioncogenic phosphatase PP2A in human cancer.

6838 SKP2 Activation by Thyroid Hormone Receptor β2 Bypasses Rb-Dependent Proliferation in Rb-Deficient Cells
Précis: Sensitivity to germline RB1 mutations can be conferred by a cell type–restricted thyroid hormone receptor isoform that fulfills otherwise Rb-dependent cell-cycle and survival function.

6880 Protein Acyltransferase DHHC3 Regulates Breast Tumor Growth, Oxidative Stress, and Senescence
Chandan Sharma, Hong-Xing Wang, Qinglin Li, Konstantin Knoblich, Emily S. Reisenbichler, Andrea L. Richardson, and Martin E. Hemler
Précis: Through its palmitoylation activity, the protein acyltransferase DHHC3 negatively regulates oxidative stress, senescence, and immune surveillance in breast cancer.

6891 Subtype-Specific Tumor-Associated Fibroblasts Contribute to the Pathogenesis of Uterine Leiomyoma
Xin Wu, Vanida A. Serna, Justin Thomas, Wenan Qiang, Michael L. Blumenfeld, and Takeshi Kurita
Précis: Tumor-associated fibroblasts regulate smooth muscle cells containing MED12 mutations to drive development of uterine leiomyoma.

6902 miR-6883 Family miRNAs Target CDK4/6 to Induce G1 Phase Cell-Cycle Arrest in Colon Cancer Cells
Amriti R. Lulla, Michael J. Sliker, Yan Zhou, Avital Lev, Margret B. Einarsdottir, David T. Dicker, and Wafik S. El-Deiry
Précis: These findings provide a rationale for use of miRNA mimics as adjuvant therapy for colorectal cancer.
SGK1 Is a Critical Component of an AKT-Independent Pathway Essential for PI3K-Mediated Tumor Development and Maintenance
Arturo Orlacchio, Michela Ranieri, Martina Brave, Valeria Antico Arciuch, Toni Forde, Daniela De Martino, Karen E. Anderson, Phillip Hawkins, and Antonio Di Cristofano

Précis: Targeting the AGC kinase SGK1 along with AKT inhibits proliferation of neoplastically transformed cells more efficiently than blocking both PI3K and AKT, a finding with potential implications for treating tumors with increased PI3K signaling.

NFκB Promotes Ovarian Tumorigenesis via Classical Pathways That Support Proliferative Cancer Cells and Alternative Pathways That Support ALDH+ Cancer Stem–like Cells
Carrie D. House, Elizabeth Jordan, Lidia Hernandez, Michelle Ozaki, Jana M. James, Marianne Kim, Michael I. Kruhlik, Eric Batchelor, Fathi Elloumi, Margaret C. Cam, and Christina M. Annunziata

Précis: Classical and alternate NFκB signaling pathways sustain tumor-initiating cells in advanced ovarian cancer, with implications for improved understanding of disease recurrence.

Mitochondrial Haplotype Alters Mammary Cancer Tumorigenicity and Metastasis in an Oncogenic Driver–Dependent Manner
Amanda E. Brinker, Carolyn J. Vivian, Devin C. Koestler, Trevor T. Tsue, Roy A. Jensen, and Danny R. Welch

Précis: These seminal findings show that the influence of mitochondrial genetics on cancer metastasis occurs in conjunction with oncogenic drivers.

Blocking Myristoylation of Src Inhibits Its Kinase Activity and Suppresses Prostate Cancer Progression
Sungjin Kim, Omar Awad Alsaidan, Octavia Goodwin, Qianjun Li, Ensilvo Suljevani, Zhen Han, Aiping Bai, Thomas Albers, Zanina Beharry, Y. George Zheng, James S. Norris, Zdzislaw M. Szule, Alicja Bielawska, Iryna Lebedyeva, Scott D. Pegan, and Houjian Cai

Précis: These results offer preclinical proof of concept for the development of N-myristoyltransferase inhibitors as a therapeutic modality to improve the management of prostate cancer.

New Generation Nanomedicines Constructed from Self-Assembling Small-Molecule Prodrugs Alleviate Cancer Drug Toxicity
Hangxiang Wang, Zhongjie Lu, Lijiang Wang, Tingting Guo, Jiaoping Wu, Jianqin Wan, Liqian Zhou, Hui Li, Zhen Li, Donghai Jiang, Perghong Song, Haiyang Xie, Lin Zhou, Xiao Xu, and Shunen Zheng

Précis: This report offers an innovative scalable strategy for generating stable and better tolerated cytotoxic nanomedicines.

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Précis: This report offers an innovative scalable strategy for generating stable and better tolerated cytotoxic nanomedicines.

Genomic Activation of PPARG Reveals a Candidate Therapeutic Axis in Bladder Cancer
Jonathan T. Goldstein, Ashton C. Berger, Juliann Shih, Fujiko F. Duke, Laura Forst, David J. Kwiatkowski, Andrew D. Cherniack, Matthew Meyerson, and Craig A. Strathean

Précis: These results offer a preclinical proof of concept for a nuclear receptor PPARG as a candidate therapeutic target in bladder cancer.

H3B-6527 Is a Potent and Selective Inhibitor of FGFR4 in FGF19-Driven Hepatocellular Carcinoma
Jaya Julie Joshi, Heather Coffey, Erik Corcoran, Jennifer Tsai, Chia-Ling Huang, Kana Ichikawa, Sudeep Pratapati, Ming-Hong Hao, Suzanna Bailey, Jeremy Wu, Victoria Rinkunas, Craig Karr, Vanitha Subramanian, Pavan Kumar, Crystal MacKenzie, Raelene Hurley, Takashi Seatoh, Kun Yu, Eunice Park, Nathalie Riaux, Amy Kim, Weidong G. Lai, Lihua Yu, Ping Zhu, Silvia Buonamici, Nicholas Larsen, Peter Fekkes, John Wang, Markus Warmuth, Dominic J. Reynolds, Peter G. Smith, and Anand Selvaraj

Précis: These results offer a preclinical proof of concept for a selective FGFR-4 inhibitor as a candidate therapeutic agent to treat liver cancers that exhibit increased expression of FGF19, including in effective combinations with the CDK4/6 inhibitor palbociclib.
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<td>7049</td>
<td>A Synthetic CD8α:MyD88 Coreceptor Enhances CD8+ T-cell Responses to Weakly Immunogenic and Lowly Expressed Tumor Antigens</td>
<td>Sabina Kaczanowska, Ann Mary Joseph, Jitao Guo, Alexander K Tsai, Jackline Joy Lasola, Keniisha Younger, Yuij Zhang, Cruz Velasco Gonzales, and Eduardo Davila</td>
<td>Précis: These findings highlight a unique method to lower the T-cell receptor recognition threshold to any antigen and the ability to reshape the tumor environment to one that favors antitumor immunity independent of HLA type.</td>
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<td>7059</td>
<td>Restoration of Natural Killer Cell Antimetastatic Activity by IL12 and Checkpoint Blockade</td>
<td>Isabel Ohs, Laura Ducimetiere, Joana Marinho, Paulina Kulig, Burkhard Becher, and Sonia Tugues</td>
<td>Précis: These findings extend understanding of the mechanism of action of immune checkpoint therapy by broadening its targets beyond T cells to include natural killer cells, an innate arm of antitumor immunity.</td>
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<td>7072</td>
<td>Paxillin Binding to the Cytoplasmic Domain of CD103 Promotes Cell Adhesion and Effector Functions for CD8+ Resident Memory T Cells in Tumors</td>
<td>Ludiane Gauthier, Stéphanie Cogna, Marie Boutet, Gwendoline Gros, Pierre Validire, Georges Bismuth, and Fathia Mami-Chouaib</td>
<td>Précis: These findings identify a signaling event required for functional activities of an intratumoral class of memory T cells, with implications for the success of T-cell-based immunotherapies for cancer.</td>
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<td>7083</td>
<td>Emergence of High-Avidity Melan-A–Specific Clonotypes as a Reflection of Anti–PD-1 Clinical Efficacy</td>
<td>Sylvain Simon, Virginie Vignard, Emilie Varey, Tiphaine Parrot, Anne-Chantal Knol, Amir Khammari, Nadine Gervois, Francois Lang, Brigitte Dreno, and Nathalie Labariere</td>
<td>Précis: These results suggest a candidate surrogate marker that may predict positive antitumor responses to anti-PD-1 therapy, addressing a question of great clinical interest.</td>
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<td>7094</td>
<td>TLR4-Mediated Inflammation Promotes KSHV-Induced Cellular Transformation and Tumorigenesis by Activating the STAT3 Pathway</td>
<td>Marion Griffaz, Karthik Vasan, Brandon Tan, Suzane Ramos da Silva, and Shou-jiang Gao</td>
<td>Précis: These findings suggest a complex relationship between infections, metabolic syndromes, and innate immune responses in patients who have AIDS-related Kaposi sarcoma, with implications for understanding how the immune system attacks cancers or fails to do so.</td>
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**MICROENVIRONMENT AND IMMUNOLOGY**

**INTEGRATED SYSTEMS AND TECHNOLOGIES**
7120  

[18F]fluorothymidine PET Informs the Synergistic Efficacy of Capecitabine and Trifluridine/Tipiracil in Colon Cancer
Seog-Young Kim, Jin Hwa Jung, Haeng Jung Lee, Hyunsu Soh, Seung Jin Oh, Sun Young Chae, Jai Hyuen Lee, Seung Jin Lee, Yong Sang Hong, Tae Won Kim, and Dae Hyuk Moon

Précis: These findings suggest that any inhibitor with a primary target mechanism of thymidylate synthase inhibition may be combined with trifluridine/tipiracil in colon cancer and possibly other cancer types.

LETTER TO THE EDITOR

7131  

A Systems Approach to Prostate Cancer Classification—Letter
Elin Thysell, Erik Bovinder Ylitalo, Emma Jernberg, Anders Bergh, and Pernilla Wikström

CORRECTION

7136  

Correction: JARID1B Enables Transit between Distinct States of the Stem-like Cell Population in Oral Cancers

7137  

Acknowledgment to Reviewers

ABOUT THE COVER

Mitochondrial polymorphisms are associated with defining human clades (races) and with susceptibility to mammary tumor development and metastasis. Brinker and colleagues show that metastatic efficiency changes with different mitochondrial haplotypes in an oncogenic driver-dependent manner. Vimentin is a marker of an epithelial-mesenchymal transition, a process that is often associated with tumor invasion and metastasis. Unexpectedly, no effect on vimentin immunohistochemical staining was observed in HER2-driven mammary tumors despite changes in metastatic efficiency. For details, see article by Brinker and colleagues on page 6941.