# Table of Contents

## BREAKING ADVANCES

- **6851** STK33 Promotes Growth and Progression of Pancreatic Cancer as a Critical Downstream Mediator of HIF1α
  Fanyang Kong, Xiangyu Kong, Yiqi Du, Ying Chen, Xuan Deng, Jianwei Zhu, Jiawei Du, Lei Li, Zhiliang Jia, Dacheng Xie, Zhaoshen Li, and Keping Xie
  Précis: These findings offer a preclinical proof of concept for targeting the serine/threonine kinase STK33 as a therapeutic approach to improve PDAC management.

## REVIEWS

- **6793** Highlights from Recent Cancer Literature

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

- **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 Meessen, Petar Kalev, Enrico Radaelli, Xavier Sagart, Eline Miermans, Dorien Haesen, Caroline Lambrecht, Mieke Dewerchin, Peter Carmeliet, Jukka Westermarck, Anna Sabrina, and Veerle Janssens
  Précis: This seminal study defines a haploinsufficient tumor suppressor gene that provides a high-penetration 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
  Xiaoliang L. Xu, Zhengke Li, Aihong Liu, Xianqun Fan, Dan-ning Hu, Dong-Lai Qi, David W. Chitty, Renbing Jia, Jianping Qui, Justin Q. Wang, Jake Sharaf, Jun Zou, Rebecca Weiss, Hongyan Huang, Walter J. Joseph, Richard Ng, Paul L. Blumenfeld, and Takeshi Kurita
  Précis: These findings identify the cellular mechanisms of a major nonandrogenic pathway that could be targeted to complement existing therapies in advanced prostate cancers.

- **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 palmistropin 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. Slifker, Yan Zhou, Avital Lev, Margret E. Einanson, 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 Aricuch, 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 J. Krulhak, 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, Qianjin Li, Eslivoh Suljevich, Zhen Han, Aiping Bai, Thomas Albers, Zaneta Beharry, Y. George Zheng, James S. Norris, Zdzislaw M. Szulc, 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, Jiapeng Wu, Jianqin Wan, Liqian Zhou, Hui Li, Zhen Li, Donghai Jiang, Peihong 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.

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 J. Krulhak, 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.

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

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 Ishikawa, Sudeep Prajapati, Ming-Hong Hao, Suzanna Bailey, Jeremy Wu, Victoria Rimkunas, Craig Karr, Vanitha Subramanian, Pavan Kumar, Crystal MacKenzie, Raelene Hurley, Takashi Satoh, Kun Yu, Enric Park, Nathalie Rious, Amy Kim, Weidong G. Lai, Li Hua 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.
Table of Contents

7049 A Synthetic CD8α:MyD88 Coreceptor Enhances CD8+ T-cell Responses to Weakly Immunogenic and Lowly Expressed Tumor Antigens
Sabina Kazanowska, Ann Mary Joseph, Jitao Guo, Alexander K Tsai, Jackline Joy Lasola, Kenisha Younger, Yujui Zhang, Cruz Velasco Gonzales, and Eduardo Davila
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.

7059 Restoration of Natural Killer Cell Antimetastatic Activity by IL.12 and Checkpoint Blockade
Isabel Ohs, Laura Ducimetiere, Joana Marinho, Paulina Kulig, Burkhard Becher, and Sonia Tugues
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.

7072 Paxillin Binding to the Cytoplasmic Domain of CD103 Promotes Cell Adhesion and Effector Functions for CD8+ Resident Memory T Cells in Tumors
Ludiane Gauthier, Stéphanie Corgnac, Marie Boutet, Gwendoline Gros, Pierre Validire, Georges Bismuth, and Fathia Mami-Chouaib
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.

7083 Emergence of High-Avidity Melan-A–Specific Clonotypes as a Reflection of Anti–PD-1 Clinical Efficacy
Sylvain Simon, Virginie Vignard, Emilie Varey, Tiphanie Parrot, Anne-Chantal Knol, Amir Khammari, Nadine Gervois, Francois Lang, Brigitte Dreno, and Nathalie Labarriere
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.

7094 TLR4-Mediated Inflammation Promotes KSHV-Induced Cellular Transformation and Tumorigenesis by Activating the STAT3 Pathway
Marion Gruffaz, Karthik Vasan, Brandon Tan, Suzane Ramos da Silva, and Shou-fang Gao
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.

MICROENVIRONMENT AND IMMUNOLOGY

7049 A Synthetic CD8α:MyD88 Coreceptor Enhances CD8+ T-cell Responses to Weakly Immunogenic and Lowly Expressed Tumor Antigens
Sabina Kazanowska, Ann Mary Joseph, Jitao Guo, Alexander K Tsai, Jackline Joy Lasola, Kenisha Younger, Yujui Zhang, Cruz Velasco Gonzales, and Eduardo Davila
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.

INTEGRATED SYSTEMS AND TECHNOLOGIES

7109 Distinct Angiogenic Changes during Carcinogenesis Defined by Novel Label-Free Dark-Field Imaging in a Hamster Cheek Pouch Model
Fangyao Hu, Hannah Martin, Amy Martinez, Jeffrey Everitt, Alaattin Eksanli, Walter T. Lee, Mark Dewhurst, and Nimmi Ramamujam
Précis: A novel method to image neovascularization allows for extraction and analysis of specific vascular features for the purposes of cancer screening and prevention.
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, Sang Ju Lee, Seung Jun 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

7133 A Systems Approach to Prostate Cancer Classification—Response
Sungyong You and Michael R. Freeman

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.
Cancer Res 2017;77:6793-7146.

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