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

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 Meensen, Petar Kalev, Enrico Radaelli, Xavier Sagarte, Eline Miernmans, Dorein 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.

6841 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.

6863 PACE4 Undergoes an Oncogenic Alternative Splicing Switch in Cancer
Frédéric Couture, Robert Sabbagh, Anna Kwiatkowska, Roxane Desjardins, Simon-Pierre Guay, Luigi Bouchard, and Robert Day
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 F. 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. Slifker, Yan Zhou, Avital Lev, Margret B. Einaron, 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.
6914 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 Arctich, 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.

TUMOR AND STEM CELL BIOLOGY

6927 NFkB 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. Kruhlak, Eric Batchelor, Fathi Elloumi, Margaret C. Cam, and Christina M. Annunziata

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

6941 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.

THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

6963 New Generation Nanomedicines Constructed from Self-Assembling Small-Molecule Prodrugs Alleviate Cancer Drug Toxicity
Hangxiang Wang, Zhongjie Lu, Lijiang Wang, Tingting Guo, Jiaping Wu, Jianqin Wan, Liqian Zhou, Hui Li, Zhen Li, Donghai Jiang, Penghong Song, Haiyang Xie, Lin Zhou, Xiao Xu, and Shuwen Zheng

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

6975 SOCS1 Gene Therapy Improves Radiosensitivity and Enhances Irradiation-Induced DNA Damage in Esophageal Squamous Cell Carcinoma
Takahito Sugase, Tsuyoshi Takahashi, Satoshi Serada, Minoru Fujimoto, Kosuke Hiramatsu, Tomoharu Ohkawara, Koji Tanaka, Yasuhiro Miyazaki, Tomoki Makino, Yukinori Kurokawa, Makoto Yamashita, Kiyokazu Nakajima, Tadamitsu Kishimoto, Masaki Morii, Yuichiro Doki, and Tetsuji Naka

Précis: This paper presents a mechanistic rationale for a strategy to improve the response of esophageal cancers to radiotherapy, which tends to be resistant to this modality.

6987 Genomic Activation of PPARG Reveals a Candidate Therapeutic Axis in Bladder Cancer
Jonathan T. Goldstein, Ashton C. Berger, Juliann Shiff, Fujiko F. Duke, Laura Furst, David J. Kwiatkowski, Andrew D. Cherniack, Matthew Meyerson, and Craig A. Strathdee

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

6999 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 Prajapati, Ming-Hong Hao, Suzanna Bailey, Jeremy Wu, Victoria Rimkunas, Craig Karr, Vanitha Subramanian, Pavan Kumar, Crystal MacKenzie, Raelene Hurley, Takashi Sato, Kun Yu, Enrice Park, Nathalie Rious, 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.
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, Ji Tao Guo, Alexander K Tsai, Jackline Joy Lasola, Kenisha Younger, Yuji 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 IL12 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, Tiphaine Parrot, Anne-Chantal Knol, Amir Khammari, Nadine Gervois, François Lang, Brigitte Dreno, and Nathalie Labriare

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-Jiang 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, Ji Tao Guo, Alexander K Tsai, Jackline Joy Lasola, Kenisha Younger, Yuji 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

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-Jiang 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.
[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

A Systems Approach to Prostate Cancer Classification—Letter

Elin Thysell, Erik Bovinder Ylitalo, Emma Jernberg, Anders Bergh, and Pernilla Wikström

CORRECTION

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

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.

Updated version  Access the most recent version of this article at: http://cancerres.aacrjournals.org/content/77/24

E-mail alerts  Sign up to receive free email-alerts related to this article or journal.

Reprints and Subscriptions  To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at pubs@aacr.org.

Permissions  To request permission to re-use all or part of this article, use this link http://cancerres.aacrjournals.org/content/77/24. Click on "Request Permissions" which will take you to the Copyright Clearance Center's (CCC) Rightslink site.