

Cancer Research

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BREAKING ADVANCES

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REVIEWS

- 1625 **Contributions of the Host Microenvironment to Cancer-Induced Bone Disease**
Sam W.Z. Olechnowicz and Claire M. Edwards
- 1632 **Optimization of Natural Killer T Cell-Mediated Immunotherapy in Cancer Using Cell-Based and Nanovector Vaccines**
C. Faveeuw and F. Trottein
- 1639 **Noncanonical Functions of Telomerase: Implications in Telomerase-Targeted Cancer Therapies**
Yinghui Li and Vinay Tergaonkar

PRIORITY REPORTS

- 1645 **Universal Marker and Detection Tool for Human Sarcoma Circulating Tumor Cells**
Arun Satelli, Abhisek Mitra, Jeffrey J. Cutrera, Marcos Devarie, Xueqing Xia, Davis R. Ingram, Denada Dibra, Neeta Somaiah, Keila E. Torres, Vinod Ravi, Joseph A. Ludwig, Eugenie S. Kleinerman, and Shulin Li
Précis: This study describes the first universal and specific marker to detect circulating sarcoma cells in the blood, with the capability to detect any type of sarcoma, offering a key prognostic tool to monitor cancer metastasis and relapse in sarcoma patients.
- 1651 **PCAT-1, a Long Noncoding RNA, Regulates BRCA2 and Controls Homologous Recombination in Cancer**
John R. Prensner, Wei Chen, Matthew K. Iyer, Qi Cao, Teng Ma, Sumin Han, Anirban Sahu, Rohit Malik, Kari Wilder-Romans, Nora Navone, Christopher J. Logothetis, John C. Araujo, Louis L. Pisters, Ashutosh K. Tewari, Christine E. Canman, Karen E. Knudsen, Naoki Kitabayashi, Mark A. Rubin, Francesca Demichelis, Theodore S. Lawrence, Arul M. Chinnaiyan, and Felix Y. Feng
Précis: A long noncoding RNA known to be oncogenic is found to promote cell death during genotoxic stress, suggesting a novel clinical correlation between this little-understood class of RNAs and genotoxic cancer therapies.

INTEGRATED SYSTEMS AND TECHNOLOGIES

- 1661 **Cancer-Associated Mutations in Healthy Individuals: Assessing the Risk of Carcinogenesis**
Ignacio A. Rodriguez-Brenes, Natalia L. Komarova, and Dominik Wodarz
Précis: Understanding how limits on cellular replication influence the fate of altered but nonneoplastic cells in healthy tissue may make it possible to estimate the risk posed by cancer-associated mutations found in healthy individuals.

MICROENVIRONMENT AND IMMUNOLOGY

- 1670 **Identification of Immune Factors Regulating Antitumor Immunity Using Polymeric Vaccines with Multiple Adjuvants**
Omar A. Ali, Catia Verbeke, Chris Johnson, R. Warren Sands, Sarah A. Lewin, Des White, Edward Doherty, Glenn Dranoff, and David J. Mooney
Précis: This paper utilizes a new method to identify immune components critical to the efficacy of antitumor immune responses to tumors.

MOLECULAR AND CELLULAR PATHOBIOLOGY

- 1682 **FoxO Transcription Factors Promote AKT Ser473 Phosphorylation and Renal Tumor Growth in Response to Pharmacologic Inhibition of the PI3K-AKT Pathway**
Aifu Lin, Hai-long Piao, Li Zhuang, Dos D. Sarbassov, Li Ma, and Boyi Gan
Précis: A transcription factor that functions in tumor suppression was unexpectedly found to instead promote renal tumor growth under conditions of PI3K-AKT inhibition, with implications on how to improve antitumor responses.
- 1694 **Immune Escape and Survival Mechanisms in Circulating Tumor Cells of Colorectal Cancer**
Gunnar Steinert, Sebastian Schölch, Thomas Niemiets, Naoki Iwata, Sebastián A. García, Bianca Behrens, Anita Voigt, Matthias Kloor, Axel Benner, Ulrich Bork, Nuh N. Rahbari, Markus W. Büchler, Nikolas H. Stoecklein, Jürgen Weitz, and Moritz Koch
Précis: These results show that circulating colon tumor cells are genetically different from the primary colon tumor, exhibiting an immunosuppressive phenotype that enables them to evade immune eradication.

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1705 UTX and MLL4 Coordinately Regulate Transcriptional Programs for Cell Proliferation and Invasiveness in Breast Cancer Cells

Jae-Hwan Kim, Amrish Sharma, Shilpa S. Dhar, Sung-Hun Lee, Bingnan Gu, Chia-Hsin Chan, Hui-Kuan Lin, and Min Gyu Lee

Précis: *These findings show how coordinated regulation of gene expression programs by two distinct epigenetic modifiers drives malignant properties in breast cancer cells.*

1718 Neuroplastic Changes Occur Early in the Development of Pancreatic Ductal Adenocarcinoma

Rachelle E. Stopczynski, Daniel P. Normolle, Douglas J. Hartman, Haoqiang Ying, Jennifer J. DeBerry, Klaus Bielefeldt, Andrew D. Rhim, Ronald A. DePinho, Kathryn M. Albers, and Brian M. Davis

Précis: *These studies show that changes in the peripheral nervous system occur early during tumor development and may play an important role in disease progression.*

1728 HDAC2 Provides a Critical Support to Malignant Progression of Hepatocellular Carcinoma through Feedback Control of mTORC1 and AKT

Ji Heon Noh, Hyun Jin Bae, Jung Woo Eun, Qingyu Shen, Se Jin Park, Hyung Seok Kim, Boas Nam, Woo Chan Shin, Eun Kyung Lee, Kyungbun Lee, Ja-Jun Jang, Won Sang Park, Jung Young Lee, and Suk Woo Nam

Précis: *This study of a histone deacetylase that is essential for mitogenic signaling in liver cancers may offer a new interventional target for more effective therapy.*

1739 p16INK4A Impairs Homologous Recombination–Mediated DNA Repair in Human Papillomavirus–Positive Head and Neck Tumors

Rüveyda Dok, Peter Kaley, Evert Jan Van Limbergen, Layka Abbasi Asbagh, Iria Vázquez, Esther Hauben, Anna Sablina, and Sandra Nuyts

Précis: *These findings reveal an unexpected function of the tumor suppressor p16INK4A in promoting the homologous recombination pathway of DNA repair, suggesting that p16INK4A status in head and neck cancer patients may offer an independent marker to predict their response to radiotherapy.*

THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

1752 Genetic Validation of the Protein Arginine Methyltransferase PRMT5 as a Candidate Therapeutic Target in Glioblastoma

Fengting Yan, Lapo Alinari, Mark E. Lustberg, Ludmila Katherine Martin, Hector M. Cordero-Nieves, Yeshavanth Banasavadi-Siddegowda, Selene Virk, Jill Barnholtz-Sloan, Erica Hlavin Bell, Jeffrey Wojton, Naduparambil K. Jacob, Arnab Chakravarti, Michal O. Nowicki, Xin Wu, Rosa Lapalombella, Jharna Datta, Bo Yu, Kate Gordon, Amy Haseley, John T. Patton, Porsha L. Smith, John Ryu, Xiaoli Zhang, Xiaokui Mo, Guido Marcucci, Gerard Nuovo, Chang-Hyuk Kwon, John C. Byrd, E. Antonio Chiocca, Chenglong Li, Said Sif, Samson Jacob, Sean Lawler, Balveen Kaur, and Robert A. Baiocchi

Précis: *This study presents a novel candidate prognostic and therapeutic target in aggressive brain cancers, with implications for understanding the basis for poor patient survival.*

1766 Activated ERBB2/HER2 Licenses Sensitivity to Apoptosis upon Endoplasmic Reticulum Stress through a PERK-Dependent Pathway

Rosa Martín-Pérez, Carmen Palacios, Rosario Yerbés, Ana Cano-González, Daniel Iglesias-Serret, Joan Gil, Mauricio J. Reginato, and Abelardo López-Rivas

Précis: *These findings offer a rationale for the therapeutic exploration of treatments inducing ER stress against mutant ERBB2-expressing breast tumor cells.*


1778 ATDC/TRIM29 Phosphorylation by ATM/ MAPKAP Kinase 2 Mediates Radioresistance in Pancreatic Cancer Cells



Lidong Wang, Huibin Yang, Phillip L. Palmbo, Gina Ney, Taylor Ann Detzler, Dawn Coleman, Jacob Leflein, Mary Davis, Min Zhang, Wenhua Tang, J. Kevin Hicks, Corey M. Helchowski, Jayendra Prasad, Theodore S. Lawrence, Liang Xu, Xiaochun Yu, Christine E. Canman, Mats Ljungman, and Diane M. Simeone

Précis: *These findings link a TRIM family protein that binds DNA and p53 to radioresistance in pancreatic cancer, suggesting its candidacy as a therapeutic target to improve the efficacy of DNA-damaging treatments used to treat this disease.*

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1789  **Alarmin IL-33 Acts as an Adjuvant to Enhance Antigen-Specific Tumor Immunity**

Daniel O. Villarreal, Megan C. Wise, Jewell N. Walters, Emma L. Reuschel, Min Joung Choi, Nyamekye Obeng-Adjei, Jian Yan, Matthew P. Morrow, and David B. Weiner


Précis: These findings offer a preclinical proof of concept that IL-33 improves the immune potency of tumor vaccines, promoting tumor cell clearance and regressions to fully empower cancer immunotherapy.

1801 **miR-30-5p Functions as a Tumor Suppressor and Novel Therapeutic Tool by Targeting the Oncogenic Wnt/ β -Catenin/BCL9 Pathway**

Jian-Jun Zhao, Jianhong Lin, Di Zhu, Xujun Wang, Daniel Brooks, Ming Chen, Zhang-Bo Chu, Kohichi Takada, Bryan Ciccarelli, Samir Admin, Jianguo Tao, Yu-Tzu Tai, Steven Treon, Geraldine Pinkus, Winston Patrick Kuo, Teru Hideshima, Mary Boussein, Nikhil Munshi, Kenneth Anderson, and Ruben Carrasco

Précis: These findings offer a preclinical rationale to explore delivery of a tumor-suppressive microRNA as an effective therapeutic strategy to eradicate multiple myeloma cells.

TUMOR AND STEM CELL BIOLOGY

1814  **Chromosome 10, Frequently Lost in Human Melanoma, Encodes Multiple Tumor-Suppressive Functions**

Lawrence N. Kwong and Lynda Chin

Précis: These results show how regional aberrations in chromosome copy number can lead to loss of multiple important tumor-suppressor functions in cancer.

1822 **Id2 Mediates Oligodendrocyte Precursor Cell Maturation Arrest and Is Tumorigenic in a PDGF-Rich Microenvironment**


Matthew C. Havrda, Brenton R. Paoletta, Cong Ran, Karola S. Jering, Christina M. Wray, Jaclyn M. Sullivan, Audrey Nailor, Yasuyuki Hitoshi, and Mark A. Israel

Précis: This study of distinct subsets of adult tissue progenitors points to a maturation arrest of oligodendroglial precursor cells in the pathogenesis of PDGF-dependent brain tumors.

1833 **Sox2 Is Required to Maintain Cancer Stem Cells in a Mouse Model of High-Grade Oligodendroglioma**

Rebecca Favaro, Irene Appolloni, Serena Pellegatta, Alexandra Badiola Sanga, Pierfrancesco Pagella, Eleonora Gambini, Federica Pisati, Sergio Ottolenghi, Maria Foti, Gaetano Finocchiaro, Paolo Malatesta, and Silvia K. Nicolis

Précis: These findings define an immunotherapeutic target for treatment of a form of brain malignancy, which acts by depleting cancer stem-like cells required to sustain the malignancy in a mouse model system.

1845  **Expression of Variant Isoforms of the Tyrosine Kinase SYK Determines the Prognosis of Hepatocellular Carcinoma**

Jian Hong, Yunfei Yuan, Jianping Wang, Yadi Liao, Ruhai Zou, Chuanlong Zhu, Binkui Li, Yi Liang, Pinzhu Huang, Zongwei Wang, Wenyu Lin, Yixin Zeng, Jia Le Dai, and Raymond T. Chung

Précis: These findings define opposing functions of the two isoforms of the SYK kinase in liver cancer, with the larger isoform enhancing invasion and the smaller isoform enhancing metastasis, patterns that in patient specimens offer strong predictors of overall survival.

1857 **MET Signaling in Colon Cancer Stem-like Cells Blunts the Therapeutic Response to EGFR Inhibitors**

Paolo Luraghi, Gigliola Reato, Elia Cipriano, Francesco Sassi, Francesca Orzan, Viola Bigatto, Francesca De Bacco, Elena Menietti, May Han, William M. Rideout III, Timothy Perera, Andrea Bertotti, Livio Trusolino, Paolo M. Comoglio, and Carla Boccaccio

Précis: Using cancer stem-like cells isolated directly from metastatic colorectal patients, this study reveals the importance of both EGFR and MET signaling and offers a strong preclinical proof of concept for concurrent targeting of both of these receptors in the clinical setting.

1870 **p300 Acetyltransferase Regulates Androgen Receptor Degradation and PTEN-Deficient Prostate Tumorigenesis**

Jian Zhong, Liya Ding, Laura R. Bohrer, Yunqian Pan, Ping Liu, Jun Zhang, Thomas J. Sebo, R. Jeffrey Karnes, Donald J. Tindall, Jan van Deursen, and Haojie Huang

Précis: This article identifies a key determinant in degradation of the androgen receptor, highlighting its importance as a candidate therapeutic target in managing prostate cancers marked by loss of the tumor suppressor PTEN.

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CORRECTION

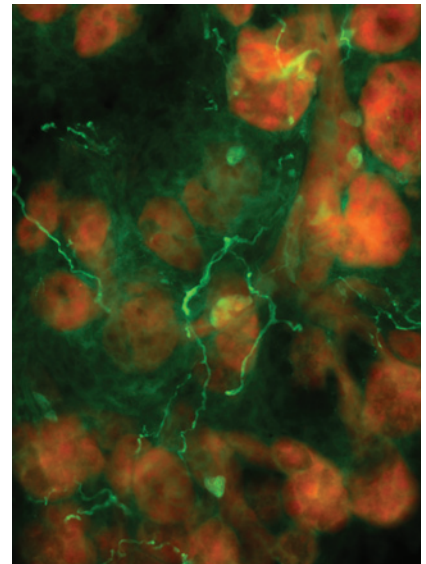
- 1881 **Correction: EPR Oxygen Images Predict Tumor Control by a 50% Tumor Control Radiation Dose**

 AC icon indicates Author Choice

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ABOUT THE COVER

Pancreas from a 12-week-old KPCT (p48-Cre; LSL-Kras^{G12D}; p53^{Lox/7+}; Rosa26-LSL-tdTomato) mouse with precancerous PanIN lesions but no tumor. dtTomato-label (red) marks pancreas epithelial-derived cells, in this case normal-appearing acinar cells. PGP 9.5 antibody (green) was used to stain nerve fibers that exhibit hypertrophy and sprouting within pancreatic tissue, beginning at histologic precancer stages and increasing as the disease progresses. For details, see article by Stopczynski and colleagues on page 1718.



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The Journal of Cancer Research (1916–1930) | The American Journal of Cancer (1931–1940)

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