BREAKING ADVANCES

1 Highlights from Recent Cancer Literature

CANCER RESEARCH 75TH ANNIVERSARY COMMENTARIES

3 Cancer Research: 75th Anniversary of the Field’s Most Highly Cited Basic Science Journal
George C. Prendergast

4 Tumor Heterogeneity—A ‘Contemporary Concept’ Founded on Historical Insights and Predictions
Danny R. Welch

7 Glutathione-Associated Enzymes In Anticancer Drug Resistance
Kenneth D. Tew

REVIEWS

10 It’s Totally Tubular…Riding The New Wave of Ovarian Cancer Research
Ruth Perets and Ronny Drapkin

18 A New View of Ras Isoforms in Cancers
Ruth Nussinov, Chung-Jung Tsai, Mayukh Chakrabarti, and Hyunbum Jang

PRIORITY REPORTS

24 A Sucrose-Enriched Diet Promotes Tumorigenesis in Mammary Gland in Part through the 12-Lipoxigenase Pathway
Yan Jiang, Yong Pan, Patrea R. Rhea, Lin Tan, Mihai Gagea, Lorenzo Cohen, Susan M. Fischer, and Peiyang Yang
Précis: Results offer preclinical evidence that fructose derived from dietary sugar increases risks of breast cancer development and metastasis via production of pro-inflammatory lipids.

30 Mitochondrial DNA Repair through OGG1 Activity Attenuates Breast Cancer Progression and Metastasis
Larysa V. Yuzefovich, Andrea G. Kahn, Michele A. Schuler, Lars Eide, Ritu Arora, Glenn L. Wilson, Ming Tan, and Lyudmila I. Rachek
Précis: These findings show that DNA damage in mitochondria promotes breast cancer progression and metastasis, offering a preclinical rationale to promote DNA repair in this organelle.

35 M-CSF and GM-CSF Receptor Signaling Differentially Regulate Monocyte Maturation and Macrophage Polarization in the Tumor Microenvironment
Eva Van Overmeire, Benoît Stijlemans, Felix Heymann, Jiri Keirse, Yannick Moris, Yvon Elkins, Lea Brey, Chloé Abele, Qods Lahmar, Can Ergen, Lars Vereecke, Frank Tacke, Patrick De Baetegier, Jo A. Van Ginderachter, and Damya Laoui
Précis: Myeloid colony-stimulating factors exert opposing effects in regulating the phenotype of tumor-associated macrophages, with potentially important implications for the development of cancer immunotherapies targeting innate immune cells.

43 Noninvasive Quantification of 2-Hydroxyglutarate in Human Gliomas with IDH1 and IDH2 Mutations
Uzay E. Emir, Sarah J. Larkin, Nick de Pennington, Natalie Voets, Punnet Plaha, Richard Stacey, Khalid Al-Qahtani, James McCullagh, Christopher J. Schofield, Stuart Clare, Peter Jezzard, Tom Cadoux-Hudson, and Olaf Ansorge
Précis: A rapid, noninvasive, and quantitative detection method for 2-hydroxyglutarate in human glioblastomas can distinguish IDH1 and IDH2 mutations in vivo, with implications for improving diagnosis and therapeutic monitoring of this disease.

MICROENVIRONMENT AND IMMUNOLOGY

50 Radiotherapy Combined with Novel STING-Targeting Oligonucleotides Results in Regression of Established Tumors
Jason R. Baird, David Friedman, Benjamin Cottam, Thomas W. Dubensky, Jr., David B. Kanne, Shelly Bambina, Keith Bahjat, Marka R. Crittenden, and Michael J. Gough
Précis: These exciting findings offer a preclinical rationale to immediately investigate in clinic the powerful properties of a novel ligand of STING—one of the most provocative immunotherapeutic targets at present—in enhancing the efficacy of neoadjuvant or adjuvant radiotherapy for human cancers.
Immunotargeting of Antigen xCT Attenuates Stem-like Cell Behavior and Metastatic Progression in Breast Cancer

Stefania Lanzardo, Laura Conti, Ronald Rooke, Roberto Ruiu, Nathalie Accart, Elisabetta Bolli, Maddalena Arigoni, Marco Macagno, Giuseppina Barrera, Stefania Pizzimenti, Luigi Aurisicchio, Raffaele Adolfo Calogero, and Federica Cavallo

Précis: Immunotargeting of breast cancer stem-like cells can sensitize them to chemotherapy, offering an effective strategy to overcome drug resistance and to limit metastatic progression.

An Effective Immuno-PET Imaging Method to Monitor CD8-Dependent Responses to Immunotherapy

Richard Taveau, Helena Escuin-Ordinas, Stephen Mok, Melissa N. McCracken, Kirstin A. Zettlitz, Felix B. Salazar, Owen N. Witte, Antoni Ribas, and Anna M. Wu

Précis: A sensitive noninvasive method to detect endogenous CD8⁺ cytotoxic T cells offers a tool to evaluate the response to many cancer immunotherapies.

Ubiquitin-Specific Protease 4-Mediated Deubiquitination and Stabilization of PRL-3 Is Required for Potentiating Colorectal Oncogenesis

Cheng Xing, Xing-Xing Lu, Peng-Da Guo, Tong Shen, Shen Zhang, Xiao-Shun He, Wen-Juan Gan, Xiu-Ming Li, Jing-Ru Wang, Yuan-Yuan Zhao, Hua Wu, and Jian-Ming Li

Précis: Proteolytic degradation pathways, which exert oncogenic effects in colorectal cancer, suggest a new class of therapeutic targets that are aberrantly expressed in that disease setting.

PLAC8 Localizes to the Inner Plasma Membrane of Pancreatic Cancer Cells and Regulates Cell Growth and Disease Progression through Critical Cell-Cycle Regulatory Pathways


Précis: A multifunctional protein absent from healthy or chronically inflamed pancreatic tissues, but widely expressed in most pancreatic cancers, is found to be a pivotal regulator of cell growth and progression in this disease.

Identification of Novel Fusion Genes in Testicular Germ Cell Tumors

Andreas M. Hoff, Sharmini Alagaratnam, Sen Zhao, Jarle Bruun, Peter W. Andrews, Raghlhild A. Lothe, and Rolf I. Skotheim

Précis: This study identifies genetic drivers of malignancy and biomarkers of disease progression in testicular tumors, specifically revealing fusion oncogenes that have not been described previously in this disease.

Multikinase Inhibitors Induce Cutaneous Toxicity through OAT6-Mediated Uptake and MAP3K7-Driven Cell Death


Précis: The mechanism underlying a side effect of multikinase inhibitors affecting the skin suggests a rational basis for therapeutic management of this condition.

Connexin 43 Inhibition Sensitizes Chemoresistant Glioblastoma Cells to Temozolomide

Susan F. Murphy, Robin T. Varghese, Samy Lamouille, Suzuan Guo, Kevin J. Pridham, Pratik Kanabar, Alyssa M. Osmani, Shaan Sharma, Jane Jourdan, Nathanael S. Gray, Brian J. Druker, and Jeffrey W. Tyner

Précis: A cell-cell communication channel may offer a theranostic biomarker to predict survival of certain glioblastoma patients who are resistant to temozolomide, a standard-of-care drug used widely for treatment.
Establishment and Characterization of an In Vitro Model of Ovarian Cancer Stem-like Cells with an Enhanced Proliferative Capacity


Précis: These findings highlight a new method to culture human ovarian stem-like cells, defining a reciprocal relationship between established regulators, which impact malignant progression in this disease setting.

H3K27 Demethylase JMJD3 Employs the NF-κB and BMP Signaling Pathways to Modulate the Tumor Microenvironment and Promote Melanoma Progression and Metastasis

Woo-Yong Park, Beom-Jin Hong, Jungsul Lee, Chulhee Choi, and Mi-Young Kim

Précis: This study focuses on a histone demethylase that appears to be critical for shaping a favorable tumor microenvironment for invasion and metastasis, with implications for broadly undercutting local tissue supports for malignant progression in a disease-selective manner.

Eva1 Maintains the Stem-like Character of Glioblastoma-Initiating Cells by Activating the Noncanonical NF-κB Signaling Pathway

Naoki Ohtsu, Yuka Nakatani, Daisuke Yamashita, Shiro Ohue, Takenori Ohnishi, and Toru Kondo

Précis: These findings define a new theranostic marker of glioblastoma-initiating cells and offer a preclinical rationale for its further exploration in targeted therapeutic strategies.

Correction: miR326 Maturation Is Crucial for VEGF-C–Driven Cortactin Expression and Esophageal Cancer Progression

ABOUT THE COVER

Cyclic dinucleotides injected into tumors result in rapid hemorrhagic necrosis by activating the sensor STING. To examine expression of STING in the tumor environment, Panc02 pancreatic adenocarcinoma tumors grown in immune competent mice were stained for the macrophage marker F4/80 (red), STING (green), and the DAPI nuclear counterstain (blue). Both the cancer cells and the tumor stroma, including F4/80+ tumor macrophages, expressed STING; however, in STING−/− mice, cyclic dinucleotides had no effect, indicating that it is the stromal rather than cancer expression of STING that mediates this effect. For details, see article by Baird and colleagues on page 50.
Cancer Research

76 (1)


Updated version
Access the most recent version of this article at:
http://cancerres.aacrjournals.org/content/76/1

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, contact the AACR Publications Department at permissions@aacr.org.