

BREAKING ADVANCES

- 905** Highlights from Recent Cancer Literature

REVIEWS

- 907** Heat Shock Factor 1 in Protein Homeostasis and Oncogenic Signal Integration
Trisha Home, Roy A. Jensen, and Rekha Rao
- 913** "(Not) All (Dead) Things Share the Same Breath": Identification of Cell Death Mechanisms in Anticancer Therapy
Santiago Rello-Varona, David Herrero-Martín, Roser López-Alemany, Cristina Muñoz-Pinedo, and Oscar M. Tirado


PERSPECTIVE

- 918** Toward a Science of Tumor Forecasting for Clinical Oncology
Thomas E. Yankeelov, Vito Quaranta, Katherine J. Evans, and Erin C. Rericha

MEETING REPORT

- 924** Cancer Stem Cells: Targeting the Roots of Cancer, Seeds of Metastasis, and Sources of Therapy Resistance
Valery Adorno-Cruz, Golam Kibria, Xia Liu, Mary Doherty, Damian J. Junk, Dongyin Guan, Chris Hubert, Monica Venere, Erin Mulkearns-Hubert, Maksim Sinyuk, Alvaro Alvarado, Arnold I. Caplan, Jeremy Rich, Stanton L. Gerson, Justin Lathia, and Huiping Liu

INTEGRATED SYSTEMS AND TECHNOLOGIES

- 930** Emergence of Drug Tolerance in Cancer Cell Populations: An Evolutionary Outcome of Selection, Nongenetic Instability, and Stress-Induced Adaptation
Rebecca H. Chisholm, Tommaso Lorenzi, Alexander Lorz, Annette K. Larsen, Luís Neves de Almeida, Alexandre Escargueil, and Jean Clairambault
Précis: This study provides a new perspective on the inherent risks of interventional chemotherapy in cancer patients by showing how the adaptation of unstable cell populations exposed to antiproliferative drugs can be acted upon by selective forces that drive the outgrowth of rapidly proliferative drug-resistant cell populations.
- 940** Cell Division Patterns in Acute Myeloid Leukemia Stem-like Cells Determine Clinical Course: A Model to Predict Patient Survival
 Thomas Stiehl, Natalia Baran, Anthony D. Ho, and Anna Marciniak-Czochra
Précis: The dynamic behavior of stem-like cells in leukemia has a greater impact on clinical course than the behavior of non-stem-like cells, permitting the design of a mathematical model to stratify risks contributing to survival outcomes.

MICROENVIRONMENT AND IMMUNOLOGY

- 950** CSF1 Receptor Targeting in Prostate Cancer Reverses Macrophage-Mediated Resistance to Androgen Blockade Therapy
Jemima Escamilla, Shiruyeh Schokrpur, Connie Liu, Saul J. Priceman, Diana Moughon, Ziyue Jiang, Frederic Pouliot, Clara Magyar, James L. Sung, Jingying Xu, Gang Deng, Brian L. West, Gideon Bollag, Yves Fradet, Louis Lacombe, Michael E. Jung, Jiaoti Huang, and Lily Wu
Précis: Modulating the function of tumor-associated macrophages can leverage androgen blockade therapy in prostate cancer and may improve long-term treatment outcomes in patients.

Table of Contents

- 963** Tumor-Derived Osteopontin Reprograms Normal Mammary Fibroblasts to Promote Inflammation and Tumor Growth in Breast Cancer
Yoray Sharon, Yael Raz, Noam Cohen, Amir Ben-Shmuel, Hila Schwartz, Tamar Geiger, and Neta Erez
Précis: These findings deepen the causative influence of a proinflammatory protein secreted by breast carcinoma cells in programming a supportive role for fibroblasts in the tumor microenvironment, with implications for understanding the etiology of advanced cancer and its therapeutic management by renormalization of the tissue microenvironment.
- 974** RAGE Mediates S100A7-Induced Breast Cancer Growth and Metastasis by Modulating the Tumor Microenvironment
Mohd W. Nasser, Nissar Ahmad Wani, Dinesh K. Ahirwar, Catherine A. Powell, Janani Ravi, Mohamad Elbaz, Helong Zhao, Laura Padilla, Xiaoli Zhang, Konstantin Shilo, Michael Ostrowski, Charles Shapiro, William E. Carson III, and Ramesh K. Ganju
Précis: A signaling axis that conditions the inflammatory microenvironment in breast cancer helps drive the aggressive growth of these tumors, including deadly triple-negative tumors that occur more commonly in premenopausal women.
- 986** TLR2 Limits Development of Hepatocellular Carcinoma by Reducing IL18-Mediated Immunosuppression
Shinan Li, Rui Sun, Yongyan Chen, Haiming Wei, and Zhigang Tian
Précis: These findings illuminate a mechanism of immunosuppression in liver carcinogenesis that may assist the design of effective immunotherapies to treat hepatocellular carcinoma.
- 996** Carbonic Anhydrase IX Promotes Myeloid-Derived Suppressor Cell Mobilization and Establishment of a Metastatic Niche by Stimulating G-CSF Production
Shawn C. Chafe, Yuanmei Lou, Jaclyn Sceneay, Marylou Vallejo, Melisa J. Hamilton, Paul C. McDonald, Kevin L. Bennewith, Andreas Möller, and Shoukat Dedhar
Précis: Targeting the function of CAIX, an enzyme that is upregulated by hypoxia in the primary tumor, affects the mobilization of immunosuppressive myeloid cells that promote metastasis.

MOLECULAR AND CELLULAR PATHOBIOLOGY



- 1009** β -Arrestin-1 Mediates Nicotine-Induced Metastasis through E2F1 Target Genes That Modulate Epithelial–Mesenchymal Transition
Smitha Pillai, Jose Trevino, Bhupendra Rawal, Sandeep Singh, Michelle Kovacs, Xueli Li, Michael Schell, Eric Haura, Gerold Bepler, and Srikumar Chellappan
Précis: These important results show how nicotine promotes the metastatic progression of pulmonary lesions initiated by carcinogens found in cigarette smoke, deepening insights into how lung cancers are caused by smoking.
- 1021** Coordinate Loss of MAP3K7 and CHD1 Promotes Aggressive Prostate Cancer
Lindsey Ulkus Rodrigues, Leah Rider, Cera Nieto, Lina Romero, Anis Karimpour-Fard, Massimo Loda, M. Scott Lucia, Min Wu, Lihong Shi, Adela Cimic, S. Joseph Sirintrapun, Rosalie Nolley, Colton Pac, Haitao Chen, Donna M. Peehl, Jianfeng Xu, Wennuan Liu, James C. Costello, and Scott D. Cramer
Précis: This study addresses the major gap in information concerning molecular subtypes of aggressive prostate cancer, where insights might help direct the development of more effective prognostic and therapeutic tools.
- 1035** ERBB3-Independent Activation of the PI3K Pathway in EGFR-Mutant Lung Adenocarcinomas
 Xiaoling Song, Pang-Dian Fan, Amlak Bantikasegn, Udayan Guha, David W. Threadgill, Harold Varmus, and Katerina Politi
Précis: Activation of the PI3K pathway in EGFR mutant lung cancer cells is maintained even in the absence of the EGFR heterodimerization partner ERBB3, challenging the current thinking that ERBB3 is the main activator of PI3K in this disease setting.
- 1046** Interferon Regulatory Factor-1 Signaling Regulates the Switch between Autophagy and Apoptosis to Determine Breast Cancer Cell Fate
 Jessica L. Schwartz-Roberts, Katherine L. Cook, Chun Chen, Ayesha N. Shajahan-Haq, Margaret Axelrod, Anni Wärrä, Rebecca B. Riggins, Lu Jin, Bassem R. Haddad, Bhaskar V. Kallakury, William T. Baumann, and Robert Clarke
Précis: This study identifies a novel signaling axis that modulates responsiveness to antiestrogen drugs in human breast cancer, with implications for improving patient survival.



Table of Contents

- 1056** Starvation Promotes REV1 SUMOylation and p53-Dependent Sensitization of Melanoma and Breast Cancer Cells
Hong Seok Shim, Min Wei, Sebastian Brandhorst, and Valter D. Longo

Précis: These findings suggest how dietary fasting may offer a nontoxic strategy to increase the efficacy of cytotoxic therapies that act in part by activating p53.

- 1068** Tumorigenic Activity of Merkel Cell Polyomavirus T Antigens Expressed in the Stratified Epithelium of Mice
Megan E. Spurgeon, Jingwei Cheng, Roderick T. Bronson, Paul F. Lambert, and James A. DeCaprio

Précis: Use of a new mouse model of Merkel cell polyomavirus-associated tumorigenesis provides deeper insights into how viral tumor antigens alter the cellular microenvironment in vivo, with potential relevance to various human cancers that involve virus infection.

THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

- 1080** Targeting LUNX Inhibits Non–Small Cell Lung Cancer Growth and Metastasis
Xiaohu Zheng, Min Cheng, Binqing Fu, Xiaolei Fan, Qing Wang, Xiaoqing Yu, Rui Sun, Zhigang Tian, and Haiming Wei

Précis: These results offer preclinical proof of concept for a candidate immunotherapy target in non–small cell lung cancers.

- 1091** Genetic Events That Limit the Efficacy of MEK and RTK Inhibitor Therapies in a Mouse Model of KRAS-Driven Pancreatic Cancer



Piergiorgio Pettazzoni, Andrea Viale, Parantu Shah, Alessandro Carugo, Haoqiang Ying, Huamin Wang, Giannicola Genovese, Sahil Seth, Rosalba Minelli, Tessa Green, Emmet Huang-Hobbs, Denise Corti, Nora Sanchez, Luigi Nezi, Matteo Marchesini, Avnish Kapoor, Wantong Yao, Maria E. Di Francesco, Alessia Petrocchi, Angela K. Deem, Kenneth Scott, Simona Colla, Gordon B. Mills, Jason B. Fleming, Timothy P. Heffernan, Philip Jones, Carlo Toniatti, Ronald A. DePinho, and Giulio F. Draetta

Précis: Understanding the activation status of various oncogenic drivers as they exist in specific treatment contexts in vivo may be important to achieve beneficial outcomes, increasing the complexity in how to use targeted drugs that were designed only with cancer cells in mind.

- 1102** Genetic and Pharmacologic Inhibition of eIF4E Reduces Breast Cancer Cell Migration, Invasion, and Metastasis

Filippa Pettersson, Sonia V. del Rincon, Audrey Emond, Bonnie Huor, Elaine Ngan, Jonathan Ng, Monica C. Dobocan, Peter M. Siegel, and Wilson H. Miller Jr

Précis: These findings offer a powerful rationale to broaden the clinical evaluation of ribavirin, a small molecule inhibitor of the translation initiation factor eIF4E currently being tested in leukemia patients, as a strategy to treat advanced solid tumors such as metastatic breast cancer in which eIF4E is commonly overexpressed.

TUMOR AND STEM CELL BIOLOGY

- 1113** Constitutive Activation of Myosin-Dependent Contractility Sensitizes Glioma Tumor-Initiating Cells to Mechanical Inputs and Reduces Tissue Invasion

Sophie Y. Wong, Theresa A. Ulrich, Loic P. Deleyrolle, Joanna L. MacKay, Jung-Ming G. Lin, Regina T. Martuscello, Musa A. Jundi, Brent A. Reynolds, and Sanjay Kumar

Précis: Because recurrences of brain cancer are tied to local invasion of tumor cells, strategies to restrict the motility of stem-like cells by increasing their cellular contractility may help limit relapses and prolong survival.

- 1123** miR340 Suppresses the Stem-like Cell Function of Glioma-Initiating Cells by Targeting Tissue Plasminogen Activator

Daisuke Yamashita, Toru Kondo, Shiro Ohue, Hisaaki Takahashi, Madoka Ishikawa, Ryo Matoba, Satoshi Suehiro, Shohei Kohno, Hironobu Harada, Junya Tanaka, and Takanori Ohnishi

Précis: A tumor suppressor gene that functions in glioma stem-like cells acts to inhibit their expression of tissue plasminogen activator, with the provocative implication that targeting this central coagulation factor may ablate cancer stem-like functions in the brain.

- 1134** Host Age Is a Systemic Regulator of Gene Expression Impacting Cancer Progression

Afshin Beheshti, Sébastien Benzekry, J. Tyson McDonald, Lili Ma, Michael Peluso, Philip Hahnfeldt, and Lynn Hlatky

Précis: This study offers direct support for age dependence in determining the host tumor control dynamic and provides initial mechanism-based insights into how aging modulates tumor progression in ways that may be actionable for therapy or prevention.

Table of Contents

1144 p21 Ablation in Liver Enhances DNA Damage, Cholestasis, and Carcinogenesis

Haksier Ehedego, Mark V. Boekschoten, Wei Hu, Carina Doler, Johannes Haybaeck, Nikolaus Gafner, Michael Müller, Christian Liedtke, and Christian Trautwein

Précis: These findings illuminate the ways in which loss of the NF- κ B pathway regulator NEMO (also known as IKK γ) promotes liver inflammation and carcinogenesis by elevating p21, which acts in this setting to protect against the generation of DNA damage that contributes to chronic hepatitis and hepatocarcinoma formation in patients.

LETTERS TO THE EDITOR

1156 Bufalin Is a Steroid Receptor Coactivator Inhibitor—Letter

José Manuel Calderón-Montaño, Estefanía Burgos-Morón, Manuel Luis Orta, Irene García-Domínguez, Dolores Maldonado-Navas, and Miguel López-Lázaro

1157 Bufalin Is a Steroid Receptor Coactivator Inhibitor—Response

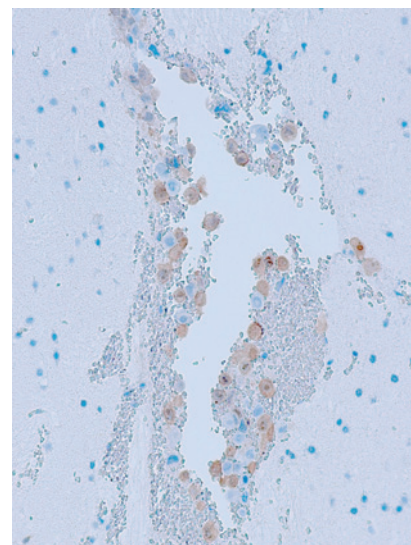
David M. Lonard, Jianming Xu, and Bert W. O'Malley

 AC icon indicates Author Choice

For more information please visit www.aacrjournals.org

ABOUT THE COVER

miR340 is a tumor suppressor whose overexpression in human glioma-initiating cells (GIC) inhibits their proliferation, invasive, and migratory properties. Transplantation of miR340-overexpressed GICs in NOD/SCID mouse brains completely suppressed the tumor formation of malignant gliomas. Among factors related to antitumorigenesis, the transplanted GICs with miR340 overexpression showed a positive immunostain for an active form of caspase-3 in the early stage of transplantation, suggesting that antitumorigenic activity of miR340 in GICs may be due to tumor cell apoptosis. For details, see the article by Yamashita and colleagues on page 1123.



Cancer Research

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

75 (6)

Cancer Res 2015;75:905-1157.

Updated version Access the most recent version of this article at:
<http://cancerres.aacrjournals.org/content/75/6>

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/75/6>. Click on "Request Permissions" which will take you to the Copyright Clearance Center's (CCC) Rightslink site.