BREAKING ADVANCES

2025  Highlights from Recent Cancer Literature

FROM THE EDITOR’S CHAIR

2027  Perspectives on Emerging Trends in Cancer Research
George C. Prendergast

REVIEWS

2029  Calcineurin Signaling as a Negative Determinant of Keratinocyte Cancer Stem Cell Potential and Carcinogenesis
G. Paolo Dotto

2034  MYC and Metastasis
Anita Wolfer and Sridhar Ramaswamy

PRIORITY REPORT

2038  Spontaneous Cytotoxic T-Cell Reactivity against Indoleamine 2,3-Dioxygenase-2
Rikke Bark Sørensen, Tania Køllgaard, Rikke Sick Andersen, Joost Huibert van den Berg, Inge Marie Svane, Per thor Straten, and Mads Hald Andersen

Précis: IDO2-specific T cells are present among peripheral blood lymphocytes in cancer patients and are able to recognize and kill cancer cells.

INTEGRATED SYSTEMS AND TECHNOLOGIES

2045  Genome-Wide Analysis of Alternative Splicing in Medulloblastoma Identifies Splicing Patterns Characteristic of Normal Cerebellar Development
Francesca Menghi, Thomas S. Jacques, Martino Barenco, Ed C. Schwalbe, Steven C. Cliftord, Mike Hubank, and Jonathan Ham

Précis: Increasing evidence points to a critical role for dysregulated patterns of alternate splicing in driving tumorigenesis, here illustrated by implications of a failure of differentiation pathways in a little understood but deadly childhood tumor.

MICROENVIRONMENT AND IMMUNOLOGY

2056  CCL11–CCR3 Interactions Promote Survival of Anaplastic Large Cell Lymphoma Cells via ERK1/2 Activation
Tomomitsu Miyagaki, Makoto Suaya, Takashi Murakami, Yoshihide Asano, Yayoi Tada, Takafumi Kadono, Hitoshi Okochi, Kunihiko Tamaki, and Shinichi Sato

Précis: Findings prompt a novel therapeutic approach to treat relapses of an aggressive form of lymphoma based on the discovery that a cell surface marker of disease junctions as a critical autocrine growth receptor.

2066  Cancer Immunotherapy Using a Bispecific NK Receptor Fusion Protein that Engages both T Cells and Tumor Cells
Tong Zhang and Charles L. Sentman

Précis: This study offers preclinical proof-of-concept for an interesting new biologic agent that stimulates effective host antitumor immunity, in support of clinical evaluation.

2077  Anti-IL-23 Monoclonal Antibody Synergizes in Combination with Targeted Therapies or IL-2 to Suppress Tumor Growth and Metastases
Michele W.L. Teng, Bianca von Scheidt, Helene Duret, Jennifer E. Towne, and Mark J. Smyth

Précis: This study offers the first description of therapeutic activity for anti-IL-23 antibody in preclinical mouse models of cancer.

MOLECULAR AND CELLULAR PATHOBIOLOGY

2087  Protein Kinase C ð Is a Downstream Effector of Oncogenic K-ras in Lung Tumors
Jennifer M. Symonds, Angela M. Ohm, Cristan J. Carter, Lynn E. Heasley, Theresa A. Boyle, Wilbur A. Franklin, and Mary E. Reynald

Précis: A protein kinase C isoform implicated in apoptosis has a differential effect on cancer cell growth depending on the involvement of oncogenic KRAS in proliferation and survival, with potential implications on how to improve therapeutic targeting of mutant KRAS-driven tumors.
<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
<th>Précis</th>
</tr>
</thead>
<tbody>
<tr>
<td>2098</td>
<td><strong>Shmt1</strong> Heterozygosity Impairs Folate-Dependent Thymidylate Synthesis Capacity and Modifies Risk of Apc&lt;sup&gt;min&lt;/sup&gt;-Mediated Intestinal Cancer Risk</td>
<td>Amanda J. MacFarlane, Cheryll A. Perry, Michael F. McEntee, David M. Lin, and Patrick J. Stover</td>
<td><strong>Précis:</strong> Folate-dependent thymidylate synthesis capacity modifies susceptibility to intestinal cancer, independent of cellular methylation potential.</td>
</tr>
<tr>
<td>2108</td>
<td>Intragenic Rearrangement and Altered RNA Splicing of the Androgen Receptor in a Cell-Based Model of Prostate Cancer Progression</td>
<td>Yingming Li, Majid Alsagabi, Danhua Fan, G. Steven Bova, Ahmed H. Tewfik, and Scott M. Delum</td>
<td><strong>Précis:</strong> This study describes a novel genomic aberration in prostate cancer cells that is associated with aberrant RNA splicing of the androgen receptor, leading to synthesis of truncated receptors that drive resistance to androgen depletion therapy.</td>
</tr>
<tr>
<td>2118</td>
<td>CARM1 Is an Important Determinant of ERα-Dependent Breast Cancer Cell Differentiation and Proliferation in Breast Cancer Cells</td>
<td>Mariam Al-Dhaheri, Jiacai Wu, Georgios P. Skiris, Jun Li, Ken Higashimato, Yidan Wang, Kevin P. White, Paul Lambert, Yuerong Zhu, Leigh Murphy, and Wei Xu</td>
<td><strong>Précis:</strong> Results define a histone arginine methyltransferase as a candidate therapeutic target in ER-positive breast cancers, with implications to improve the diagnosis of well-differentiated tumors and potentially to improve the chance for cures.</td>
</tr>
<tr>
<td>2129</td>
<td>Cep63 Recruits Cdk1 to the Centrosome: Implications for Regulation of Mitotic Entry, Centrosome Amplification, and Genome Maintenance</td>
<td>Harald Löffler, Anne Fechter, Marc Matuszewska, Rainer Saffrich, Martin Mistrik, Joachim Marhold, Christin Hornung, Frank Westermann, Jiri Bartek, and Alwin Kramer</td>
<td><strong>Précis:</strong> The discovery how Cdk1 kinase is recruited to centrosomes advances understanding of how mitosis is controlled and why centrosome amplification and chromosomal breakage occur so commonly in cancer cells.</td>
</tr>
<tr>
<td>2140</td>
<td>Oncogenic Synergism between ErbB1, Nucleolin, and Mutant Ras</td>
<td>Keren Farin, Sari Schokoroy, Roni Haklai, Ifat Cohen-Or, Gaït Elad-Sfadia, Merit E. Reyes-Reyes, Paula J. Bates, Adrienne D. Cox, Yoel Kloog, and Ronit Pinkas-Kramarski</td>
<td><strong>Précis:</strong> This study describes a fascinating protein complex that might be targeted as a general approach to attack the many human cancers driven by EGF family receptors and Ras small GTPases.</td>
</tr>
<tr>
<td>2152</td>
<td>HSulf-1 Modulates FGFR2- and Hypoxia-Mediated Migration and Invasion of Breast Cancer Cells</td>
<td>Ashwani Khurana, Peng Liu, Pasquale Mellone, Laura Lorenzon, Bruno Vincenzi, Kaustubh Datta, Bo Yang, Robert J. Linhardt, Wilma Lingle, Jeremy Chien, Alfonso Baldi, and Vij Shridhar</td>
<td><strong>Précis:</strong> This study describes regulation of heparan sulfatase-1 by hypoxia leading to increased cell migration and invasion in breast cancer cells.</td>
</tr>
<tr>
<td>2162</td>
<td>Identification of a Tumor Suppressor Relay between the FOXP3 and the Hippo Pathways in Breast and Prostate Cancers</td>
<td>Weiquan Li, Lizhong Wang, Hiroto Katoh, Runhua Liu, Pan Zheng, and Yang Liu</td>
<td><strong>Précis:</strong> Findings define a functional connection between two important tumor suppressor pathways in cancer, with potential theranostic implications.</td>
</tr>
<tr>
<td>2172</td>
<td>IMP-1 Displays Cross-Talk with K-Ras and Modulates Colon Cancer Cell Survival through the Novel Proapoptotic Protein CYFIP2</td>
<td>Perry S. Mongroo, Felicite K. Noubissi, Miriam Cuatrecasas, Jiri Kalabis, Catrina E. King, Cameron N. Johnstone, Mark J. Bowser, Antoni Castells, Vladimir S. Spiegelman, and Anil K. Rustgi</td>
<td><strong>Précis:</strong> Findings indicate that the Myc-interacting protein IMP-1 acts upstream of K-Ras to promote survival through a novel mechanism that may be important in colon cancer pathogenesis.</td>
</tr>
<tr>
<td>2183</td>
<td>CARMA3 is Crucial for EGFR-Induced Activation of NF-κB and Tumor Progression</td>
<td>Tang Jiang, Brian Grabiner, Yifan Zhu, Changqing Jiang, Hongxiu Li, Yun You, Jingyu Lang, Mien-Chie Hung, and Xin Lin</td>
<td><strong>Précis:</strong> Results elucidate how EGFR signaling leads to NF-κB activation and its role in tumor progression.</td>
</tr>
</tbody>
</table>
### THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
<th>Précis</th>
</tr>
</thead>
<tbody>
<tr>
<td>2230</td>
<td>Targeted Signal-Amplifying Enzymes Enhance MRI of EGFR Expression in an Orthotopic Model of Human Glioma</td>
<td>Mohammed S. Shazeeb, Christopher H. Sotak, Michael DeLeo III, and Alexei Bogdanov Jr.</td>
<td>Finds evidence of a signal amplification and contrast agent retention strategy for in vivo imaging of gliomas expressing EGFRvIII variants that are best suited to treatment with therapeutic EGFR antibodies.</td>
</tr>
<tr>
<td>2240</td>
<td>Heavy Chain Ferritin siRNA Delivered by Cationic Liposomes Increases Sensitivity of Cancer Cells to Chemotherapeutic Agents</td>
<td>Xiaoli Liu, A.B. Madhankumar, Becky Slagle-Webb, Jonas M. Sheehan, Nodar Surguladze, and James R. Connor</td>
<td>Provides preclinical demonstration of a siRNA-based targeting and delivery approach that can be used to sensitize brain tumor cells to chemotherapy.</td>
</tr>
<tr>
<td>2250</td>
<td>Influence of Affinity and Antigen Internalization on the Uptake and Penetration of Anti-HER2 Antibodies in Solid Tumors</td>
<td>Stephen I. Rudnick, Jianlong Lou, Calvin C. Shaller, Yong Tang, Andres J.P. Klein-Szanto, Louis M. Weiner, James D. Marks, and Gregory P. Adams</td>
<td>Determines the factors that influence how effectively a therapeutic antibody can penetrate tumors is important for optimizing efficacious effects in cancer treatment.</td>
</tr>
<tr>
<td>2260</td>
<td>NRF2 Blockade Suppresses Colon Tumor Angiogenesis by Inhibiting Hypoxia-Induced Activation of HIF-1α</td>
<td>Tae-Hyong Kim, Eu-gene Hur, Su-Jin Kang, Jung-Ae Kim, Dinesh Thapa, You Mie Lee, Sae Kwang Ku, Yunjin Jung, and Mi-Kyoung Kwak</td>
<td>Shows how blocking the NRF2 system, an important modifier of oxidative stress signaling in cells, could be an effective way to control tumor growth and angiogenesis.</td>
</tr>
</tbody>
</table>

### PREVENTION AND EPIDEMIOLOGY

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
<th>Précis</th>
</tr>
</thead>
<tbody>
<tr>
<td>2222</td>
<td>Contribution of Inherited Mutations in the BRCA2-Interacting Protein PALB2 to Familial Breast Cancer</td>
<td>Silvia Casadei, Barbara M. Norquist, Tom Walsh, Sunday Stray, Jessica B. Mandell, Ming-K. Lee, John A. Stamatoyannopoulos, and Mary-Claire King</td>
<td>This study characterizes the mutational spectrum of the tumor suppressor gene PALB2, which is mutated in a fraction of familial breast cancer patients and is particularly strongly associated with male breast cancer and pancreatic cancer.</td>
</tr>
</tbody>
</table>
MYC Phosphorylation, Activation, and Tumorigenic Potential in Hepatocellular Carcinoma Are Regulated by HMG-CoA Reductase
Zhongwei Cao, Hua Fan-Minogue, David I. Bellovin, Aleksey Vetodiyenko, Julia Arzeno, Qiwei Yang, Sanjiv Sam Gambhir, and Dean W. Feldser

Précis: The ability of statins to suppress MYC oncogenic activity suggests their evaluation as novel adjuvant modalities in cancer therapy.

Human CD59 Inhibitor Sensitizes Rituximab-Resistant Lymphoma Cells to Complement-Mediated Cytolysis
Weiguo Hu, Xiaowen Ge, Tao You, Ting Xu, Jinyan Zhang, Gongxiong Wu, Zhilitai Peng, Michael Chorov, Bertal H. Aetua, Jose A. Halperin, Jennifer R. Brown, and Xuebin Qin

Précis: Findings rationalize a tractable method to reduce or abolish resistance to rituximab, a monoclonal antibody therapy used widely to treat certain common blood malignancies.

Overcoming Temozolomide Resistance in Glioblastoma via Dual Inhibition of NAD+ Biosynthesis and Base Excision Repair
Eva M. Goellner, Bradford Grimme, Ashley R. Brown, Ying-Chih Lin, Xiao-Hong Wang, Kelsey F. Sugrue, Leah Mitchell, Ram N. Trivedi, Jiang-bo Tang, and Robert W. Sobol

Précis: Temozolomide resistance in glioblastoma can be overcome by dual inhibition of NAD+ biosynthesis and base excision repair.

Genetic Ablation of PKC Epsilon Inhibits Prostate Cancer Development and Metastasis in Transgenic Mouse Model of Prostate Adenocarcinoma
Bilal Bin Hafeez, Weixiong Zhong, Jamey Weichert, Nancy E. Dreckschmidt, Mohammad Sarwar Jamal, and Ajit K. Verma

Précis: Findings provide first genetic evidence of the role of PKC epsilon in prostate cancer development and metastasis, suggesting novel preventive and therapeutic strategies.

DCAMKL-1 Regulates Epithelial–Mesenchymal Transition in Human Pancreatic Cells through a miR-200a–Dependent Mechanism

Précis: Findings indicate that a microtubule associated kinase previously identified as a pancreatic stem cell marker can serve as an effective therapeutic target in pancreatic cancer treatment.

Outgrowth of Drug-Resistant Carcinomas Expressing Markers of Tumor Aggression after Long-term TβRI/II Kinase Inhibition with LY2109761
Erin C. Connolly, Elise F. Saunier, David Quigley, Minh Thu Lau, Angela De Sapiol, Byron Hann, Jonathan M. Yingling, and Rosemary J. Akhurst

Précis: Long-term pharmacological TGF-β receptor inhibition potentiates chemically-induced skin cancer progression and promotes outgrowth of a tumor type with molecular features which contrasts with short-term effects of TGF-β inhibition.

Zyxin Is a Critical Regulator of the Apoptotic HIPK2-p53 Signaling Axis
Johanna Crone, Carolina Glas, Kathrin Schultheiss, Jutta Moehlenbrink, Eva Krieghoff-Henning, and Thomas G. Hofmann

Précis: Findings identify Zyxin as novel regulator of DNA damage-induced cell death through controlling the HIPK2-p53 signaling axis.

Histone Methyltransferase EZH2 Induces Akt-Dependent Genomic Instability and BRCA1 Inhibition in Breast Cancer
Maria E. Gonzalez, Matthew L. DuPrie, Heather Krueger, Sofia D. Merajver, Alejandra C. Ventura, Kathy A. Toy, and Celina G. Kleer

Précis: Findings offer mechanistic insight into how elevated activity of an important chromatin modifier drives breast cancer progression.
Activation of the Aryl Hydrocarbon Receptor AhR Promotes Retinoic Acid–Induced Differentiation of Myeloblastic Leukemia Cells by Restricting Expression of the Stem Cell Transcription Factor Oct4
Rodica P. Bunaciu and Andrew Yen

Précis: Findings suggest a mechanism-based rationale to enhance the therapeutic effects of retinoic acid, which is used to treat certain cancers, through co-treatment with activators of AhR signaling.

miR-218 Suppresses Nasopharyngeal Cancer Progression through Downregulation of Survivin and the SLIT2-ROBO1 Pathway
Nehad M. Alajez, Michelle Lenarduzzi, Emma Ito, Angela B.Y. Hui, Wei Shi, Jeff Bruce, Shijun Yue, Shao H. Huang, Wei Xu, John Waldron, Brian O’Sullivan, and Fei-Fei Liu

Précis: Findings suggest a tumor suppressor function for the microRNA mi-218 that integrates control of two important cell survival and migratory mechanisms.

MAP Kinase-Interacting Kinase 1 Regulates SMAD2-Dependent TGF-β Signaling Pathway in Human Glioblastoma
Michal Grzmil, Pier Jr Morin, Maria Maddalena Lino, Adrian Merlo, Stephan Frank, Yuhua Wang, Gerald Moncayo, and Brian A. Hemmings

Précis: Findings identify a pathway that controls translation of key cancer-related RNAs including SMAD2, a key component of the TGF-β-signaling pathway, with implications for targeting deadly brain tumors more effectively.

LETTER TO THE EDITOR

Essential Requirement for PP2A Inhibition by the Oncogenic Receptor c-KIT Suggests PP2A Reactivation as a Strategy to Treat c-KIT+ Cancers — Letter
Amaury G. Dumont, David G. Reynoso, and Jonathan C. Trent

Essential Requirement for PP2A Inhibition by the Oncogenic Receptor c-KIT Suggests PP2A Reactivation as a Strategy to Treat c-KIT+ Cancers — Response
Kathryn G. Roberts, Fiona McDougall, and Nicole M. Verrills

CORRECTIONS

Correction: Glioblastoma Recurrence after Cediranib Therapy in Patients: Lack of "Rebound" Revascularization as Mode of Escape

Correction: Phospholipase D Meets Wnt Signaling: A New Target for Cancer Therapy

Correction: Breast Cancer Stem Cells Are Regulated by Mesenchymal Stem Cells through Cytokine Networks

Correction: Online Publication Dates for Cancer Research January 15, 2011 Articles
ABOUT THE COVER

Diminished angiogenesis in NRF2 knockdown colon cancer cells. Matrigel-loaded colon cancer cells (HCT116 and HT29) with stable expression of interfering RNA of NRF2 (NRF2i) were inoculated on the CAM of 10-day-old chicken embryos and the branch points of formed blood vessels were counted as a marker of angiogenesis. NRF2 knockdown cancer cells developed fewer blood vessels; the numbers of vessel branch points in HCT-NRF2i and HT-NRF2i cells reduced to 73% and 58% of those in the control cells (SCi). The data represent means ± SD of at least 8 embryos. For details, see the article by Kim and colleagues on page 2260 of this issue.
71 (6)


Updated version
Access the most recent version of this article at:
http://cancerres.aacrjournals.org/content/71/6

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