BREAKING ADVANCES

Highlights from Recent Cancer Literature

REVIEWS

Long Intergenic Noncoding RNAs: New Links in Cancer Progression
Miao-Chih Tsai, Robert C. Spitale, and Howard Y. Chang

Fetal Cell Microchimerism and Cancer: A Nexus of Reproduction, Immunology, and Tumor Biology
Lisa R. Kallenbach, Kirby L. Johnson, and Diana W. Bianchi

PRIORITY REPORT

Lactate Dehydrogenase B Is Critical for Hyperactive mTOR-Mediated Tumorigenesis
Xiaojun Zha, Fang Wang, Ying Wang, Shaozong He, Yanling Jing, Xuexian Wu, and Hongbing Zhang

Précis: Findings offer preclinical proof-of-concept for targeting a key glycolytic enzyme as a therapeutic strategy to attack cancers driven by mTOR signaling.

CLINICAL STUDIES

Glioblastoma Recurrence after Cediranib Therapy in Patients: Lack of "Rebound" Revascularization as Mode of Escape
Emmanuelle di Tomaso, Matija Snuderl, Walid S. Kamoun, Dan G. Duda, Pavan K. Auluck, Ladan Fazlollahi, Ovidiu C. Andronesi, Matthew P. Frosch, Patrick Y. Wen, Scott R. Plotkin, E. Tessa Hedley-Whyte, A. Gregory Sorensen, Tracy T. Batchelor, and Bakesh K. Jain

Précis: Glioblastomas switch their growth pattern after anti-VEGF therapy in the absence of a second wave of angiogenesis.

INTEGRATED SYSTEMS AND TECHNOLOGIES

Genetic and Structural Variation in the Gastric Cancer Kinome Revealed through Targeted Deep Sequencing
Zhi Jiang Zang, Choong Kiat Ong, Ioana Cutcutache, Willie Yu, Shen Li Zhang, Dachuan Huang, Lian Dee Ler, Karl Dykema, Anna Gan, Jiong Tao, Siyu Lim, Yujing Liu, P. Andrew Futreal, Heike Grabsch, Kyle A. Furge, Liang Kee Goh, Steve Rozen, Bin Tean Teh, and Patrick Tan

Précis: Deep sequencing of the gastric cancer cell genome identifies hundreds of new kinase variants, revealing new extremes of genetic complexity in cancer development and progression.

MICROENVIRONMENT AND IMMUNOLOGY

Endothelial Cell-Specific Deletion of Transcription Factor FoxM1 Increases Urethane-Induced Lung Carcinogenesis
David Balli, Yufang Zhang, Jonathan Snyder, Vladimir V. Kalinichenko, and Tanya V. Kalin

Précis: A known oncogene in lung tumorigenesis functions in an opposing manner as a tumor suppressor in endothelial cells, acting to restrict pulmonary inflammation and canonical Wnt signaling.

Tamoxifen, Flaxseed, and the Lignan Enterolactone Increase Stroma- and Cancer Cell-Derived IL-1Ra and Decrease Tumor Angiogenesis in Estrogen-Dependent Breast Cancer
Gabriel Lindahl, Niina Saarinen, Annelie Abrahamsson, and Charlotta Dabrosin

Précis: Antiestrogen therapies may act in part by depriving an inflammatory signal that supports angiogenesis, through a mechanism that might also be targeted by the IL-1 receptor antagonist anakinra, a clinically approved agent.

In vivo Antitumor Activity of a Recombinant IL-7/HGFβ Hybrid Cytokine in Mice
Laijun Lai, Jingjun Jin, and Irving Goldschneider

Précis: Findings offer preclinical proof-of-concept for use of a naturally occurring cytokine heterodimer as a potentially universal biological therapy in cancer treatment.
### MOLECULAR AND CELLULAR PATHOBIOLOGY

#### page 68
**BRCA2 and Nucleophosmin Coregulate Centrosome Amplification and Form a Complex with the Rho Effector Kinase ROCK2**

Hui-Feng Wang, Katsuya Takenaka, Akira Nakanishi, and Yoshio Miki

**Précis:** Findings suggest that interactions between BRCA2 and NPM mediate suppression of hereditary breast and ovarian cancer.

#### page 78
**Identification of New MicroRNAs in Paired Normal and Tumor Breast Tissue Suggests a Dual Role for the ERBB2/Her2 Gene**

Helena Persson, Anders Kvist, Natalia Rego, Johan Staaf, Johan Vallon-Christersson, Lena Luts, Niklas Loman, Goran Jonsson, Hugo Naya, Mattias Hoglund, Ake Borg, and Carlos Rovira

**Précis:** Characterization of known and new microRNAs leads to the discovery of a new gene within the human ERBB2 oncogene.

#### page 87
**Molecular Pathobiology of Human Cervical High-Grade Lesions: Paracrine STAT3 Activation in Tumor-Instructed Myeloid Cells Drives Local MMP-9 Expression**

Nadine Schröer, Jennifer Pahne, Barbara Walch, Claudia Wickenhauser, and Sigrun Smola

**Précis:** Findings define a molecular cascade that mechanistically rationalizes the design of new adjuvant therapies to treat cervical precancerous lesions and prevent their malignant progression.

#### page 98
**Appearance of the Novel Activating F1174S ALK Mutation in Neuroblastoma Correlates with Aggressive Tumor Progression and Unresponsiveness to Therapy**

Tommy Martinsson, Therese Eriksson, Jonas Abrahamsson, Helena Caren, Magnus Hansson, Per Kogner, Sattu Kamaraj, Christina Schönherr, Joel Weinmar, Kristina Rauth, Ruth H. Palmer, and Bengt Hallberg

**Précis:** Mutation of a critical kinase in neuroblastoma progression may be missed in the initial tumor biopsy, requiring testing later at progression.

### PREVENTION AND EPIDEMIOLOGY

#### page 116
**Risk of Infection-Related Cancers after the Loss of a Child: A Follow-up Study in Sweden**

Fang Fang, Katja Fall, Pär Sparén, Hans-Olov Adami, Heiddis B. Valdimarsdóttir, Mats Lambe, and Unnur Valdimarsdóttir

**Précis:** Loss of a child associates with a higher risk of several cancers, chiefly ones that are associated with HPV infections.

### THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

#### page 134
**Carminomycin I Is an Apoptosis Inducer That Targets the Golgi Complex in Clear Cell Renal Carcinoma Cells**

Girma M. Woldemichael, Thomas J. Turbyville, W. Marston Linehan, and James B. McMahon

**Précis:** Use of a natural products-based small molecule screening approach reveals a novel targeting strategy to attack clear cell renal cell carcinoma.
<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>143</td>
<td>VEGF-PET Imaging Is a Noninvasive Biomarker Showing Differential Changes in the Tumor during Sunitinib Treatment</td>
<td>Wouter B. Nagengast, Marjolijn N. Lub-de Hooge, Sjoukje F. Oosting, Wilfred F.A. den Dunnen, Frank-Jan Warnders, Adrienne H. Brouwers, Johan R. de Jong, Patricia M. Price, Harry Hollema, Geke A.P. Hospers, Philip H. Elsinga, Jan Willem Hesselink, Jouk A. Gietema, and Elisabeth G.E. de Vries</td>
</tr>
<tr>
<td>154</td>
<td>A Dual PI3K/mTOR Inhibitor, PI-103, Cooperates with Stem Cell–Delivered TRAIL in Experimental Glioma Models</td>
<td>Tugba Bagci-Onder, Hiroaki Wakimoto, Maarten Anderegg, Cody Cameron, and Khalid Shah</td>
</tr>
<tr>
<td>164</td>
<td>PDGFR Signaling Blockade in Marrow Stroma Impairs Lung Cancer Bone Metastasis</td>
<td>Raúl Catena, Diego Luis-Ravelo, Iker Antón, Carolina Zandueta, Pablo Salazar-Colocho, Leyre Larzábal, Alfonso Calvo, and Fernando Lecanda</td>
</tr>
<tr>
<td>175</td>
<td>TGF-β/RI Kinase Inhibitor SD-208 Reduces the Development and Progression of Melanoma Bone Metastases</td>
<td>Khalid S. Mohammad, Delphine Javelaud, Pierrick G. J. Fournier, Maria Niewolna, C. Ryan McKenna, Xiang H. Peng, Vu Duong, Lauren K. Dunn, Alain Mauriel, and Theresa A. Guise</td>
</tr>
<tr>
<td>197</td>
<td>Novel Synthetic Antagonists of Canonical Wnt Signaling Inhibit Colorectal Cancer Cell Growth</td>
<td>Jo Waaler, Ondrej Machon, Jens Peter von Kries, Steven Ray Wilson, Elsa Lundenes, Doris Wedlich, Dietmar Gradi, Jan Erik Paulsen, Olga Machonova, Jennifer L. Dombinski, Huyen Dinh, and Stefan Krauss</td>
</tr>
<tr>
<td>206</td>
<td>Activation and Involvement of Ral GTPases in Colorectal Cancer</td>
<td>Timothy D. Martin, Jonathan C. Samuel, Elizabeth D. Routh, Channing J. Der, and Jen Jen Yeh</td>
</tr>
<tr>
<td>216</td>
<td>Biological Activity of 4-Substituted Methoxybenzoyl-Aryl-Thiazole: An Active Microtubule Inhibitor</td>
<td>Chien-Ming Li, Zhao Wang, Yan Lu, Sunjoo Ahn, Ramesh Narayanan, Jeffrey D. Kearsby, Deanna N. Parke, Wei Li, Duane D. Miller, and James T. Dalton</td>
</tr>
<tr>
<td>225</td>
<td>MiR-26a Inhibits Cell Growth and Tumorigenesis of Nasopharyngeal Carcinoma through Repression of EZH2</td>
<td>Juan Lu, Ming-Liang He, Lu Wang, Ying Chen, Xiong Liu, Qi Dong, Yang-Chao Chen, Ying Peng, Kai-Tai Yao, Hsiang-Fu Kung, and Xiang-Ping Li</td>
</tr>
</tbody>
</table>

Précis: This study contributes significant new information concerning the molecular pathogenesis of nasopharyngeal carcinoma, a major cancer in China where it is associated with Epstein-Barr virus infection.
Phosphatase PRL-3 Is a Direct Regulatory Target of TGFb in Colon Cancer Metastasis
Yanjun Jiang, Xiao-Qiong Liu, Ashwani Rajput, Liying Geng, Melanie Ongchin, Qi Zeng, Gregory S. Taylor, and Jing Wang

Précis: Findings link TGFβ signaling in cancer progression to upregulation of a survival pathway that could be a determinant of metastasis, with implications for its therapeutic attack.

Snail2 is an Essential Mediator of Twist1-Induced Epithelial Mesenchymal Transition and Metastasis
Esmeralda Casas, Jihoon Kim, Andrés Bendesky, Lucila Ohno-Machado, Cecily J. Wolfe, and Jing Yang

Précis: Findings identify an essential regulatory relationship between two key factors that control the EMT program to promote metastasis.

Higher miRNA Tolerance in Immortal Li-Fraumeni Fibroblasts with Abrogated Interferon Signaling Pathway
Qunfang Li and Michael A. Tainsky

Précis: Results reveal the first solid evidence that disruption of IFN signaling is a checkpoint tolerizing cells to deregulation of miRNA expression, providing new insight into how certain transcription factors in innate immunity can promote cellular immortalization.

hTERT Overexpression Alleviates Intracellular ROS Production, Improves Mitochondrial Function, and Inhibits ROS-Mediated Apoptosis in Cancer Cells
Inthirani R. Indran, Manoor P. Hande, and Shazib Pervaiz

Précis: Findings define a novel function for TERT in alleviating cellular ROS levels, endowing cancer cells with an additional mechanism to evade cell death stimuli.

Plasminogen Activator uPA is a Direct Transcriptional Target of the JAG1-Notch Receptor Signaling Pathway in Breast Cancer
Mamiko Shimizu, Brenda Cohen, Pavel Goldvasser, Hal Berman, Carl Virtanen, and Michael Reedijk

Précis: Important new mechanistic findings link two pathways of poor prognosis in breast cancer.

Fish Oil Exacerbates Colitis in SMAD3 Mice
Lesley M. Butler and Mimi C. Yu

Correction: F3-Targeted Cisplatin-Hydrogel Nanoparticles as an Effective Therapeutic that Targets Both Murine and Human Ovarian Tumor Endothelial Cells In vivo

Correction: Induction of Human Epithelial Stem/Progenitor Expansion by FOXM1

Double immunofluorescence for nestin (pink) and the endothelial marker CD34 (green) with EGFR fluorescence in situ hybridization (red) confirms expression of nestin in endothelial cells and in GBM cells of patients treated with cediranib. For details, see the article by di Tomaso et al. on page 19 of this issue.
Cancer Research


71 (1)


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<thead>
<tr>
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