# Table of Contents

## BREAKING ADVANCES

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>6793</td>
<td>Highlights from Recent Cancer Literature</td>
<td></td>
</tr>
</tbody>
</table>

## REVIEWS

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>6795</td>
<td>Discovery of IDO1 Inhibitors: From Bench to Bedside</td>
<td>George C. Prendergast, William P. Malachowski, James B. DuHadaway, Alexander J. Müller</td>
</tr>
<tr>
<td>6812</td>
<td>Emerging Role of CRISPR/Cas9 Technology for MicroRNAs Editing in Cancer Research</td>
<td>Guillermo Aquino-Jarquin</td>
</tr>
</tbody>
</table>

## PRIORITY REPORT

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>6818</td>
<td>RUNX1 Upregulation by Cytotoxic Drugs Promotes Apoptosis</td>
<td>Daniel Speidel, Jasmin Wellbrock, and Melissa Abas</td>
</tr>
</tbody>
</table>

## MOLECULAR AND CELLULAR PATHOBIOLOGY

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>6825</td>
<td>PP2A Inactivation Mediated by PPP2R4 Haploinsufficiency Promotes Cancer Development</td>
<td>Ward Sents, Bob Meussen, Petar Kalev, Enrico Radaelli, Xaver Sagner, Eline Miermans, Dorien Haesen, Caroline Lambrecht, Mieke Dewerchin, Peter Carmeliet, Jukka Westermarck, Anna Sablina, and Veerle Janssens</td>
</tr>
<tr>
<td>6838</td>
<td>SKP2 Activation by Thyroid Hormone Receptor β2 Bypasses Rb-Dependent Proliferation in Rb-Deficient Cells</td>
<td>Xiaoliang L. Xu, Zhengke Li, Aihong Liu, Xianqun Fan, Dan-ning Hu, Dong-Lai Qi, David W. Chitty, Renbing Jia, Jianping Qui, Justin Q. Wang, Jie Chao, Jun Zou, Rebecca Weiss, Hongyan Huang, Walter J. Joseph, Lily Ng, Richard Rosen, Binghui Shen, Mark W. Reid, Douglas Forrest, David H. Abramson, Samuel Singer, David Coblentz, and Suresh C. Jhanwar</td>
</tr>
</tbody>
</table>

## MOLECULAR AND CELLULAR PATHOBIOLOGY

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>6851</td>
<td>STK33 Promotes Growth and Progression of Pancreatic Cancer as a Critical Downstream Mediator of HIF1α</td>
<td>Fanyang Kong, Xiangyu Kong, Yiqi Du, Ying Chen, Xuan Deng, Jianwei Zhu, Jiawei Du, Lei Li, Zhiliang Jia, Dacheng Xie, Zhaoshen Li, and Keping Xie</td>
</tr>
<tr>
<td>6863</td>
<td>PAGE4 Undergoes an Oncogenic Alternative Splicing Switch in Cancer</td>
<td>Frédéric Couture, Robert Sabbagh, Anna Kwiatkowska, Roxane Desjardins, Simon-Pierre Guay, Luigi Bouchard, and Robert Day</td>
</tr>
<tr>
<td>6880</td>
<td>Protein Acyltransferase DHHC3 Regulates Breast Tumor Growth, Oxidative Stress, and Senescence</td>
<td>Chandan Sharma, Hong-Xing Wang, Qinglin Li, Konstantin Knoblich, Emily S. Reisenbichler, Andrea L. Richardson, and Martin E. Hemler</td>
</tr>
</tbody>
</table>

## MOLECULAR AND CELLULAR PATHOBIOLOGY

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>6891</td>
<td>Subtype-Specific Tumor-Associated Fibroblasts Contribute to the Pathogenesis of Uterine Leiomyoma</td>
<td>Xin Wu, Vanida A. Sema, Justin Thomas, Wenan Jiang, Michael L. Blumenfeld, and Takeshi Kurita</td>
</tr>
<tr>
<td>6902</td>
<td>miR-6883 Family miRNAs Target CDK4/6 to Induce G1 Phase Cell-Cycle Arrest in Colon Cancer Cells</td>
<td>Amriti R. Lulla, Michael J. Sliker, Yan Zhou, Avivai Le, Margret B. Einarson, David T. Dicker, and Wafik S. El-Deiry</td>
</tr>
</tbody>
</table>

December 15, 2017 • Volume 77 • Number 24
## Tumor and Stem Cell Biology

**6927**  
NFκB Promotes Ovarian Tumorigenesis via Classical Pathways That Support Proliferative Cancer Cells and Alternative Pathways That Support ALDH+ Cancer Stem–like Cells  
Carrie D. House, Elizabeth Jordan, Lidia Hernandez, Michelle Ozaki, Jana M. James, Marianne Kim, Michael J. Kruhlak, Eric Batchelor, Fathi Elloumi, Margaret C. Cam, and Christina M. Annunziata  
**Précis:** Classical and alternate NFκB signaling pathways sustain tumor-initiating cells in advanced ovarian cancer, with implications for improved understanding of disease recurrence.

**6941**  
Mitochondrial Haplotype Alters Mammary Cancer Tumorigenicity and Metastasis in an Oncogenic Driver–Dependent Manner  
Amanda E. Brinker, Carolyn J. Vivian, Devin C. Koestler, Trevor T. Tsue, Roy A. Jensen, and Danny R. Welch  
**Précis:** These seminal findings show that the influence of mitochondrial genetics on cancer metastasis occurs in conjunction with oncogenic drivers.

## Therapeutics, Targets, and Chemical Biology

**6950**  
Blocking Myristoylation of Src Inhibits Its Kinase Activity and Suppresses Prostate Cancer Progression  
Sungjin Kim, Omar Awad Alsaidan, Octavia Goodwin, Qianjin Li, Eslshal Suljevic, Zhen Han, Aiping Bai, Thomas Albers, Zaneta Beharry, Y. George Zheng, James N. Norris, Zdzislaw M. Szule, Alicja Bielawska, Iryna Lebedyeva, Scott D. Pegan, and Houjian Cai  
**Précis:** These results offer preclinical proof of concept for the development of N-myristoyltransferase inhibitors as a therapeutic modality to improve the management of prostate cancer.
### Table of Contents

#### 7014 ATR Is a Therapeutic Target in Synovial Sarcoma

**Précis:** Reliance of synovial sarcomas on the DNA damage signaling factor ATR underscores the mechanistic relevance of ATR inhibitors to treat this cancer, either as single-agent therapy or in combination with cisplatin or PARP inhibitors.

#### 7027 Cathepsin B Is Dispensable for Cellular Processing of Cathepsin B-Cleavable Antibody–Drug Conjugates
Niita G. Caculitan, Josefa dela Cruz Chuh, Yong Ma, Donglu Zhang, Katherine R. Kozak, Yichin Liu, Thomas H. Pillow, Jack Sadowsky, Tommy K. Cheung, Qui Phung, Benjamin Haley, Byoung-Chul Lee, Robert W. Akita, Mark X. Sliwkowski, and Andrew G. Polson

**Précis:** The findings of this study challenge the assumed mechanism of action by which an antibody-drug conjugate releases its drug to achieve targeted cancer cell killing.

#### 7038 MALTI Inhibition Is Efficacious in Both Naïve and Ibrutinib-Resistant Chronic Lymphocytic Leukemia

**Précis:** This important study shows how a small-molecule inhibitor of the paracaspase MALTI1 could offer an effective strategy to treat chronic lymphocytic leukemias that become resistant to ibrutinib.

#### 7059 Restoration of Natural Killer Cell Antimetastatic Activity by IL12 and Checkpoint Blockade
Isabel Ohs, Laura Ducimetriere, Joana Marinho, Paulina Kulig, Burkhard Becher, and Sonia Tugues

**Précis:** These findings extend understanding of the mechanism of action of immune checkpoint therapy by broadening its targets beyond T cells to include natural killer cells, an innate arm of antitumor immunity.

#### 7072 Paxillin Binding to the Cytoplasmic Domain of CD103 Promotes Cell Adhesion and Effector Functions for CD8⁺ Resident Memory T Cells in Tumors
Luciane Gauthier, Stéphanie Corgnac, Marie Boutet, Gwendoline Gros, Pierre Validire, Georges Bismuth, and Fathia Mami-Chouaib

**Précis:** These findings identify a signaling event required for functional activities of an intratumoral class of memory T cells, with implications for the success of T-cell-based immunotherapies for cancer.

#### 7083 Emergence of High-Avidity Melan-A–Specific Clonotypes as a Reflection of Anti–PD-1 Clinical Efficacy
Sylvain Simon, Virginie Vignard, Emilie Varey, Tiphaine Parrot, Anne-Chantal Knol, Amir Khammari, Nadine Gervois, Francois Lang, Brigitte Dreno, and Nathalie Labarriere

**Précis:** These results suggest a candidate surrogate marker that may predict positive antitumor responses to anti-PD-1 therapy, addressing a question of great clinical interest.

#### 7094 TLR4-Mediated Inflammation Promotes KSHV-Induced Cellular Transformation and Tumorigenesis by Activating the STAT3 Pathway
Marion Gruffaz, Karthik Vasan, Brandon Tan, Suzane Ramos da Silva, and Shou-Jiang Gao

**Précis:** These findings suggest a complex relationship between infections, metabolic syndromes, and innate immune responses in patients who have AIDS-related Kaposi sarcoma, with implications for understanding how the immune system attacks cancers or fails to do so.

---

**Microenvironment and Immunology**

#### 7049 A Synthetic CD8α:MyD88 Coreceptor Enhances CD8⁺ T-cell Responses to Weakly Immunogenic and Lowly Expressed Tumor Antigens
Sabina Kaczanowska, Ann Mary Joseph, Jitao Guo, Alexander K Tsai, Jackline Joy Lasola, Reneisha Younger, Yuij Zhang, Cruz Velasco Gonzales, and Eduardo Davila

**Précis:** These findings highlight a unique method to lower the T-cell receptor recognition threshold to any antigen and the ability to reshape the tumor environment to one that favors antitumor immunity independent of HLA type.

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**Integrated Systems and Technologies**

#### 7099 Distinct Angiogenic Changes during Carcinogenesis Defined by Novel Label-Free Dark-Field Imaging in a Hamster Cheek Pouch Model
 Fangyao Hu, Hannah Martin, Amy Martinez, Jeffrey Everett, Alaaatun Ekanli, Walter T. Lee, Mark Dewhurst, and Nimmi Ramamujam

**Précis:** A novel method to image neovascularization allows for extraction and analysis of specific vascular features for the purposes of cancer screening and prevention.
7120 \[\text{\[^{18}\text{F}]fluorothymidine PET Informs the Synergistic Efficacy of Capecitabine and Trifluridine/Tipiracil in Colon Cancer}

Seog-Young Kim, Jin Hwa Jung, Haeng Jung Lee, Hyunsu Soh, Sang Ju Lee, Seung Jun Oh, Sun Young Chae, Jai Hyuen Lee, Seung Jin Lee, Yong Sang Hong, Tae Won Kim, and Dae Hyuk Moon

Précis: These findings suggest that any inhibitor with a primary target mechanism of thymidylate synthase inhibition may be combined with trifluridine/tipiracil in colon cancer and possibly other cancer types.

7131 \[\text{A Systems Approach to Prostate Cancer Classification—Letter}

Elin Thysell, Erik Bovinder Ylitalo, Emma Jernberg, Anders Bergh, and Pernilla Wikström

7133 \[\text{A Systems Approach to Prostate Cancer Classification—Response}

Sungyong You and Michael R. Freeman

7136 \[\text{Correction: JARID1B Enables Transit between Distinct States of the Stem-like Cell Population in Oral Cancers}

7137 \[\text{Acknowledgment to Reviewers}

ABOUT THE COVER

Mitochondrial polymorphisms are associated with defining human clades (races) and with susceptibility to mammary tumor development and metastasis. Brinker and colleagues show that metastatic efficiency changes with different mitochondrial haplotypes in an oncogenic driver-dependent manner. Vimentin is a marker of an epithelial-mesenchymal transition, a process that is often associated with tumor invasion and metastasis. Unexpectedly, no effect on vimentin immunohistochemical staining was observed in HER2-driven mammary tumors despite changes in metastatic efficiency. For details, see article by Brinker and colleagues on page 6941.