# Contents

## Breaking Advances

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>5847</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>5849</td>
<td>Why Your Preferred Targeted Drugs May Become Unaffordable</td>
<td>Martine J. Piccart</td>
</tr>
<tr>
<td>5852</td>
<td>The Emerging Role of Immunosurveillance in Dictating Metastatic Spread in Breast Cancer</td>
<td>Clare Y. Slaney, Jai Rautela, and Belinda S. Parker</td>
</tr>
</tbody>
</table>

## Perspective

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
</table>

## Microenvironment and Immunology

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>5869</td>
<td>Cetuximab Attenuates Its Cytotoxic and Radiosensitizing Potential by Inducing Fibronectin Biosynthesis</td>
<td>Iris Eke, Katja Storch, Mechthild Krause, and Nils Cordes</td>
</tr>
<tr>
<td>5880</td>
<td>Complementary Populations of Human Adipose CD34+ Progenitor Cells Promote Growth, Angiogenesis, and Metastasis of Breast Cancer</td>
<td>Stefania Orecchioni, Giuliana Gregato, Ines Martin-Padura, Francesca Reggiani, Paola Braidotti, Patrizia Mancuso, Angelica Calleri, Jessica Quarna, Paola Marighetti, Chiara Aldeni, Giancarlo Pruner, Stefano Martella, Andrea Manconi, Jean-Yves Petit, Mario Rietjens, and Francesco Bertoloni</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>5914</td>
<td>Constitutive β-Catenin Activation Induces Male-Specific Tumorigenesis in the Bladder Urothelium</td>
<td>Congxing Lin, Yan Yin, Kristina Stemler, Peter Humphrey, Adam S. Kibel, Indira U. Myorekar, and Liang Ma</td>
</tr>
<tr>
<td>5926</td>
<td>FGFR4 Promotes Stroma-Induced Epithelial-to-Mesenchymal Transition in Colorectal Cancer</td>
<td>Rui Liu, Jingyi Li, Ke Xie, Tao Zhang, Yunlong Lei, Yi Chen, Lu Zhang, Kai Huang, Kui Wang, Hong Wu, Min Wu, Edouard C. Nice, Canhua Huang, and Yuquan Wei</td>
</tr>
</tbody>
</table>

---

**Dysregulated Hematopoiesis Caused by Mammary Cancer Is Associated with Epigenetic Changes and Hox Gene Expression in Hematopoietic Cells**

Alexander Sio, Manreet K. Chehal, Kevin Tsai, Xueling Fan, Morgan E. Roberts, Brad H. Nelson, Jolanta Grembecka, Tomasz Cierpicki, Danielle L. Krebs, and Kenneth W. Harder

**Précis:** These findings provide insight into how tumor-secreted factors profoundly disturb hematopoiesis, for example by causing myeloproliferative-like disease (leukemoid reaction), anemia, and disrupted bone marrow stem compartments.

**Adenomatous Polyps Are Driven by Microbe-Instigated Focal Inflammation and Are Controlled by IL-10–Producing T Cells**

Kristen L. Dennis, Yunwei Wang, Nichole R. Blatner, Shuya Wang, Abdulrahman Saadalla, Ervin Trudeau, Axel Roers, Casey T. Weaver, James J. Lee, Jack A. Gilbert, Eugene B. Chang, and Khashayarsha Khazaie

**Précis:** IL-10 provided by T cells in the colon is critical to control bacterial-driven inflammation and polyp growth, providing a rationale for this cytokine as a candidate target for immunotherapy in colon cancer.

---

**Constitutive β-Catenin Activation Induces Male-Specific Tumorigenesis in the Bladder Urothelium**

Congxing Lin, Yan Yin, Kristina Stemler, Peter Humphrey, Adam S. Kibel, Indira U. Mysorekar, and Liang Ma

**Précis:** Investigations in a preclinical model of bladder cancer suggest that males have a predilection for this disease due to a synergy between the β-catenin and androgen receptor signaling pathways.

---

**FGFR4 Promotes Stroma-Induced Epithelial-to-Mesenchymal Transition in Colorectal Cancer**

Rui Liu, Jingyi Li, Ke Xie, Tao Zhang, Yunlong Lei, Yi Chen, Lu Zhang, Kai Huang, Kui Wang, Hong Wu, Min Wu, Edouard C. Nice, Canhua Huang, and Yuquan Wei

**Précis:** An FGFR receptor is found to be pivotal for the process by which the tumor stromal microenvironment triggers conversion of epithelial cancer cells to mesenchymal phenotypes that are more invasive and metastatic.
**PREVENTION AND EPIDEMIOLOGY**

5985  **Chemoprevention of Prostate Cancer by D,L-Sulforaphane Is Augmented by Pharmacological Inhibition of Autophagy**
Avani R. Vyas, Eun-Ryeong Hahm, Julie A. Arlotti, Simon Watkins, Donna Beer Stolz, Dhimant Desai, Shantu Amin, and Shivendra V. Singh

**Précis:** Autophagic inhibitors may leverage the chemoprevention of prostate cancer, perhaps also delaying the progression of early, noninvasive lesions to more advanced cancers, addressing an important clinical challenge.

5996  **Telomere Length in Peripheral Blood Lymphocytes Contributes to the Development of HPV-Associated Oropharyngeal Carcinoma**
Yang Zhang, Erich M. Sturgis, Kristina R. Dahlstrom, Juyi Wen, Hongliang Liu, Qingyi Wei, Guojun Li, and Zhensheng Liu

**Précis:** Individuals with HPV16 exposure plus shorter telomere lengths in their blood lymphocytes may have a higher risk of developing oral cancers, compared with those with either HPV16 exposure or shorter telomere lengths alone.

**THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY**

6004  **Indirubin Derivative 6BIO Suppresses Metastasis**
Simone Braig, Christine A. Kressirer, Johanna Liebl, Fabian Bischoff, Stefan Zahler, Laurent Meijer, and Angelika M. Vollmar

**Précis:** These findings highlight the antimetastatic activity of a compound that blocks multiple kinase pathways involved in metastasis, supporting a concept termed “polypharmacology” in developing drugs to attack this most deadly aspect of cancer.

6013  **Combination of Antibody That Inhibits Ligand-Independent HER3 Dimerization and a p110δ Inhibitor Potently Blocks PI3K Signaling and Growth of HER2+ Breast Cancers**

**Précis:** These preclinical findings suggest a strategy to effectively manage HER2-overexpressing cancers that have progressed on the HER2-targeted drug trastuzumab, addressing a key clinical challenge.
An Antibody That Locks HER3 in the Inactive Conformation Inhibits Tumor Growth Driven by HER2 or Neuregulin

Precis: HER3 is a member of the EGFR family that mediates oncogenic functions of other family members, thereby offering a target that can more generally shut down signaling by this common cancer cell system.

TUMOR AND STEM CELL BIOLOGY

Double Minute Chromosomes in Glioblastoma Multiforme Are Revealed by Precise Reconstruction of Oncogenic Amplicons
J. Zachary Sanborn, Sofie R. Salama, Mia Griffof, Cameron W. Brennan, Tom Mikkelsen, Suresh Jhanwar, Sol Katzman, Lynda Chin, and David Haussler

Precis: Oncogenic amplicons, a feature of many glioblastomas, were precisely reconstructed by high-throughout sequencing data, a process that could be useful for diagnosis and monitoring of disease.

MicroRNA-218 Inhibits Glioma Invasion, Migration, Proliferation, and Cancer Stem-like Cell Self-Renewal by Targeting the Polycomb Group Gene Bmi1
Yanyang Tu, Xingchun Gao, Guang Li, Hualin Fu, Daxiang Cui, Hui Liu, Weilin Jin, and Yongsheng Zhang

Precis: A tumor-suppressive microRNA acts by regulating a central transcriptional corepressor molecule implicated in glioblastoma, from which insights into its downstream targets in stem cell populations have emerged recently.

CORRECTIONS

Correction: A Novel Class of Anticancer Compounds Targets the Actin Cytoskeleton in Tumor Cells

Correction: Constitutive HER2 Signaling Promotes Breast Cancer Metastasis through Cellular Senescence

Correction: PTK6 Activation at the Membrane Regulates Epithelial–Mesenchymal Transition in Prostate Cancer
ABOUT THE COVER

Tumor cells evolve by interacting with the local microenvironment. In this study, an FGF receptor (FGFR4) is found to be pivotal for the process by which the tumor stromal microenvironment triggers conversion of epithelial cancer cells to mesenchymal phenotypes that are more invasive and metastatic. Tumor-associated fibroblasts-mediated FGFR4 activation is strongly related to a high risk of tumor metastasis and poor patient outcome, suggesting novel therapeutic opportunities for the treatment of colorectal cancer. For details, see article by Liu and colleagues on page 5926.