## BREAKING ADVANCES

### Highlights from Recent Cancer Literature

## REVIEWS

### Why Your Preferred Targeted Drugs May Become Unaffordable
Martine J. Piccart

### The Emerging Role of Immunosurveillance in Dictating Metastatic Spread in Breast Cancer
Clare Y. Slaney, Jai Rautela, and Belinda S. Parker

## PERSPECTIVE

### The CpG Island Methylator Phenotype: What’s in a Name?
Laura A.E. Hughes, Veerle Melotte, Joachim de Schrijver, Michiel de Maat, Vincent T.H.R.M. Smit, Judith V.A.M.G. Bovée, Pim J. French, Piet A. van den Brandt, Leo J. Schouten, Tim de Meyer, Wim van Criekinge, Nita Ahuja, James G. Herman, Matty P. Weijenberg, and Manon van Engeland

## MICROENVIRONMENT AND IMMUNOLOGY

### Cetuximab Attenuates Its Cytotoxic and Radiosensitizing Potential by Inducing Fibronectin Biosynthesis
Iris Eke, Katja Storch, Mechthild Krause, and Nils Cordes

### Complementary Populations of Human Adipose CD34<sup>+</sup> Progenitor Cells Promote Growth, Angiogenesis, and Metastasis of Breast Cancer
Stefania Orecchioni, Giuliana Gregato, Ines Martin-Padura, Francesca Reggiani, Paola Braidotti, Patrizia Mancuso, Angelica Calleri, Jessica Quarna, Paola Marighetti, Chiara Aldeni, Giancarlo Pruneri, Stefano Martella, Andrea Manconi, Jean-Yves Petit, Mario Rietjens, and Francesco Bertolini

## MOLECULAR AND CELLULAR PATHOBIOLOGY

### 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, Erkin Tradue, 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 predisposition 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.
Downregulation of microRNA-515-5p by the Estrogen Receptor Modulates Sphingosine Kinase 1 and Breast Cancer Cell Proliferation

Precis: This study links the estrogen receptor and a microRNA implicated in breast cancer risk to a key lipid kinase that is essential for maintaining continuous cell proliferation in breast cancer.

Nm23-H1 Binds to Gelsolin and Inactivates Its Actin-Severing Capacity to Promote Tumor Cell Motility and Metastasis
Natascia Marino, Jean-Claude Marshall, Joshua W. Collins, Ming Zhou, Yongzhen Qian, Timothy Veenstra, and Patricia S. Steeg

Precis: A protein with protean and somewhat confusing functions in cancer is found to limit the metastasis in breast cancer by blocking the action of an actin-severing protein in breast cancer cells.

Cyclin D1-Dependent Induction of Luminal Inflammatory Breast Tumors by Activated Notch3
Hua Ling, Jean-Rene Sylvestre, and Paul Jolicoeur

Precis: Activated forms of Notch3 may preferentially induce expansion of luminal progenitor cells in the mammary gland that can contribute to inflammatory breast cancer, a particularly aggressive and poorly managed disease.

Notch1 Is Required for Kras-Induced Lung Adenocarcinoma and Controls Tumor Cell Survival via p53
Silvia Licciulli, Jacquline L. Avila, Linda Hanlon, Scott Troutman, Matteo Cesarini, Smitha Kota, Brian Keith, M. Celeste Simon, Ellen Puré, Fred Radtke, Anthony J. Capobianco, and Joseph L. Kissil

Precis: These findings define a novel role for the Notch1 receptor in lung cancer, offering a molecular basis for observations related to patient prognosis and reinforcing the notion that Notch1 is a worthy therapeutic target in this setting.

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

Precis: 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.

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

Precis: 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.
### TUMOR AND STEM CELL BIOLOGY

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<td>MicroRNA-218 Inhibits Glioma Invasion, Migration, Proliferation, and</td>
<td>Yanyang Tu, Xingchun Gao, Gang Li, Hualin Fu, Daxiang Cui, Hui Liu, Weilin Jin, and Yongsheng Zhang</td>
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<td>Cancer Stem-like Cell Self-Renewal by Targeting the Polycomb Group</td>
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<td><em>Precis</em>: A tumor-suppressive microRNA acts by regulating a central</td>
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<td>transcriptional corepressor molecule implicated in glioblastoma, from</td>
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<td>Mesenchymal Transition in Prostate Cancer</td>
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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.