

CANCER RESEARCH

# TABLE OF CONTENTS

**BREAKING INSIGHTS**

**1903** Highlights from Recent Cancer Literature

**REVIEW**

**1905** Targeting the SAGA and ATAC Transcriptional Coactivator Complexes in MYC-Driven Cancers  
Lisa Maria Mustachio, Jason Roszik, Aimee Farria, and Sharon Y.R. Dent

**CANCER RESEARCH HIGHLIGHTS**

**1912** Artificial Intelligence Will Not Replace Health Professionals, but the Proper Use of Artificial Intelligence Will Make Health Professionals Better  
Carlos Rodriguez-Antolin  
See related article, p. 2056

**MOLECULAR CELL BIOLOGY**

**1914** Endonuclease FEN1 Coregulates ER $\alpha$  Activity and Provides a Novel Drug Interface in Tamoxifen-Resistant Breast Cancer  
Koen D. Flach, Manikandan Periyasamy, Ajit Jadhav, Dorjbal Dorjsuren, Joseph C. Siefert, Theresa E. Hickey, Mark Opdam, Hetal Patel, Sander Canisius, David M. Wilson III, Maria Donaldson Collier, Stefan Prekovic, Marja Nieuwland, Roelof J.C. Kluin, Alexey V. Zakharov, Jelle Wesseling, Lodewyk F.A. Wessels, Sabine C. Linn, Wayne D. Tilley, Anton Simeonov, Simak Ali, and Wilbert Zwart  
These findings show that pharmacologic inhibition of FEN1, which is predictive of outcome in tamoxifen-treated patients, effectively blocks ER $\alpha$  function and inhibits proliferation of tamoxifen-resistant tumor cells.

**TUMOR BIOLOGY AND IMMUNOLOGY**

**1927** A Feed-Forward Mechanosignaling Loop Confers Resistance to Therapies Targeting the MAPK Pathway in BRAF-Mutant Melanoma  
**AC** Christophe A. Girard, Margaux Lecacheur, Rania Ben Jouira, Ilona Berestjuk, Serena Diazzi, Virginie Prod'homme, Aude Mallavialle, Frédéric Larbret, Maéva Gesson, Sébastien Schaub, Sabrina Pisano, Stéphane Audebert, Bernard Mari, Cédric Gaggioli, Eleonora Leucci, Jean-Christophe Marine, Marcel Deckert, and Sophie Tartare-Deckert  
These findings reveal a biomechanical adaptation of melanoma cells to oncogenic BRAF pathway inhibition, which fuels a YAP/MRTF-dependent feed-forward loop associated with tumor stiffening, mechanosensing, and therapy resistance.

**1942** Melanoma-Secreted Lysosomes Trigger Monocyte-Derived Dendritic Cell Apoptosis and Limit Cancer Immunotherapy  
Nadine Santana-Magal, Leen Farhat-Younis, Amit Gutwillig, Annette Gleiberman, Diana Rasoulouniriana, Lior Tal, Dvir Netanel, Ron Shamir, Rachel Blau, Meora Feinmesser, Oran Zlotnik, Haim Gutman, Ian L. Linde, Nathan E. Reticker-Flynn, Peleg Rider, and Yaron Carmi  
This work redefines the role of monocyte-derived dendritic cells in melanoma and provides a novel strategy to increase the efficacy of T-cell-based immunotherapies in nonresponding individuals.

**1957** Epstein-Barr Virus miRNA BART2-5p Promotes Metastasis of Nasopharyngeal Carcinoma by Suppressing RND3  
Chen Jiang, Lei Li, Yan-Qun Xiang, Maria Li Lung, Tingting Zeng, Jiabin Lu, Sai Wah Tsao, Mu-Sheng Zeng, Jing-Ping Yun, Dora L.W. Kwong, and Xin-Yuan Guan  
This study shows that EBV-encoded BART2-5p miRNA suppresses expression of the RND3 Rho family GTPase, consequently promoting ROCK signaling, cell motility, and metastatic behavior of NPC cells.

# TABLE OF CONTENTS

## 1970 **Blocking SHH/Patched Interaction Triggers Tumor Growth Inhibition through Patched-Induced Apoptosis**

Pierre-Antoine Bissey, Pauline Mathot, Catherine Guix, Mélissa Jasmin, Isabelle Goddard, Clélia Costechareyre, Nicolas Gadot, Jean-Guy Delcros, Sachitanand M. Mali, Rudi Fasan, André-Patrick Arrigo, Robert Dante, Gabriel Ichim, Patrick Mehlen, and Joanna Fombonne

Sonic Hedgehog-overexpressing tumors express PTCH-induced cell death effectors, suggesting that this death signaling could be activated as an antitumor strategy.

## 1981 **IL33 Is a Key Driver of Treatment Resistance of Cancer**

Chie Kudo-Saito, Takahiro Miyamoto, Hiroshi Imazeki, Hirokazu Shoji, Kazunori Aoki, and Narikazu Boku

These findings indicate that the functional role of IL33 in cancer polyploidy contributes to intrinsic and extrinsic mechanisms underlying treatment failure.

## 1991 **Perineural Invasion Reprograms the Immune Microenvironment through Cholinergic Signaling in Pancreatic Ductal Adenocarcinoma**

Min-Wei Yang, Ling-Ye Tao, Yong-Sheng Jiang, Jian-Yu Yang, Yan-Miao Huo, De-Jun Liu, Jiao Li, Xue-Liang Fu, Ruizhe He, Chaoyi Lin, Wei Liu, Jun-Feng Zhang, Rong Hua, Qing Li, Shu-Heng Jiang, Li-Peng Hu, Guang-Ang Tian, Xiao-Xin Zhang, Ningning Niu, Ping Lu, Juanjuan Shi, Gary G. Xiao, Li-Wei Wang, Jing Xue, Zhi-Gang Zhang, and Yong-Wei Sun

These findings provide a promising therapeutic strategy to modulate the immunosuppressive microenvironment of pancreatic ductal adenocarcinoma with severe perineural invasion.

## 2004 **Blockade of $\beta$ -Catenin-Induced CCL28 Suppresses Gastric Cancer Progression via Inhibition of Treg Cell Infiltration**

Lu Ji, Wei Qian, Liming Gui, Zhongzhong Ji, Pan Yin, Guan Ning Lin, You Wang, Bin Ma, and Wei-Qiang Gao

These findings demonstrate an immunosuppressive role of tumor-intrinsic  $\beta$ -catenin signaling and the therapeutic potential of CCL28 blockade in gastric cancer.

## TRANSLATIONAL SCIENCE

### 2017 **Drug Sensitivity and Allele Specificity of First-Line Osimertinib Resistance *EGFR* Mutations**

Jacqueline H. Starrett, Alexis A. Guernet, Maria Emanuela Cuomo, Kamrine E. Poels, Iris K. van Alderwerelt van Rosenburgh, Amy Nagelberg, Dylan Farnsworth, Kristin S. Price, Hina Khan, Kumar Dilip Ashtekar, Mmaserame Gaefele, Deborah Ayeni, Tyler F. Stewart, Alexandra Kuhlmann, Susan M. Kaech, Arun M. Unni, Robert Homer, William W. Lockwood, Franziska Michor, Sarah B. Goldberg, Mark A. Lemmon, Paul D. Smith, Darren A.E. Cross, and Katerina Politi

This study provides insight into the biological and molecular properties of osimertinib resistance *EGFR* mutations and evaluates therapeutic strategies to overcome resistance.

**AC** icon indicates Author Choice

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## 2031 **Targeting of CD38 by the Tumor Suppressor miR-26a Serves as a Novel Potential Therapeutic Agent in Multiple Myeloma**

Yi Hu, Huimin Liu, Chuanfeng Fang, Chen Li, Fjorela Xhyliu, Hayley Dysert, Juraj Bodo, Gabriel Habermehl, Benjamin E. Russell, Wenjun Li, Marcia Chappell, Xiaofeng Jiang, Sarah L. Ondrejka, Eric D. Hsi, Jaroslaw P. Maciejewski, Qing Yi, Kenneth C. Anderson, Nikhil C. Munshi, Geyou Ao, Jason N. Valent, Jianhong Lin, and Jianjun Zhao

These results highlight the tumor suppressor function of miR-26a via its targeting of CD38 and suggest the therapeutic potential of miR-26a in patients with multiple myeloma.

## 2045 **A Protease-Activated Fluorescent Probe Allows Rapid Visualization of Keratinocyte Carcinoma during Excision**

Ethan Walker, Yiqiao Liu, InYoung Kim, Mark Biro, Sukanya Raj Iyer, Harib Ezaldein, Jeffrey Scott, Miesha Merati, Rachel Mistur, Bo Zhou, Brian Straight, Joshua J. Yim, Matthew Bogoyo, Margaret Mann, David L. Wilson, James P. Basilion, and Daniel L. Popkin

A fluorescent-probe-tumor-visualization platform was developed and validated in human keratinocyte carcinoma excision specimens that may provide simple, rapid, and global assessment of margins during skin cancer excision, allowing same-day reexcision when needed.

## RESOURCE REPORTS

### 2056 **Computational Staining of Pathology Images to Study the Tumor Microenvironment in Lung Cancer**

Shidan Wang, Ruichen Rong, Donghan M. Yang, Junya Fujimoto, Shirley Yan, Ling Cai, Lin Yang, Danni Luo, Carmen Behrens, Edwin R. Parra, Bo Yao, Lin Xu, Tao Wang, Xiaowei Zhan, Ignacio I. Wistuba, John Minna, Yang Xie, and Guanghua Xiao

These findings present a deep learning-based analysis tool to study the TME in pathology images and demonstrate that the cell spatial organization is predictive of patient survival and is associated with gene expression.

See related commentary, p. 1912

### 2067 **LncSpA: LncRNA Spatial Atlas of Expression across Normal and Cancer Tissues**

Dezhong Lv, Kang Xu, Xiyun Jin, Junyi Li, Yuchen Shi, Mengying Zhang, Xiaoyan Jin, Yongsheng Li, Juan Xu, and Xia Li

LncSpA is a new interactive resource that provides the spatial expression pattern of lncRNA across thousands of normal and cancer samples representing major tissue types.

## CORRECTION

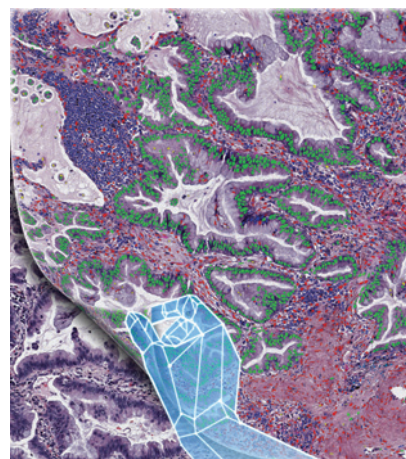
### 2072 **Correction: Activation of MAPK Signaling by CXCR7 Leads to Enzalutamide Resistance in Prostate Cancer**

Shangze Li, Ka-wing Fong, Galina Gritsina, Ali Zhang, Jonathan C. Zhao, Jung Kim, Adam Sharp, Wei Yuan, Caterina Aversa, Ximing J. Yang, Peter S. Nelson, Felix Y. Feng, Arul M. Chinnaiyan, Johann S. de Bono, Colm Morrissey, Matthew B. Rettig, and Jindan Yu

# TABLE OF CONTENTS

## ABOUT THE COVER

Pathology images of tumor tissues provide detailed information on the different types of cells that constitute the tumor microenvironment. Artificial intelligence can automatically and accurately identify and stain the nuclei of tumor cells, stromal cells, lymphocytes, macrophages, blood cells, and karyorrhexis from pathology images of lung adenocarcinoma. The computational power aids in clinical diagnosis and enables the quantification of tumor microenvironment-related features that correlate with patient survival and the gene expression of biological pathways. For details, see article by Wang and colleagues on page 2056.



# Cancer Research

The Journal of Cancer Research (1916–1930) | The American Journal of Cancer (1931–1940)

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