

## CANCER RESEARCH

## TABLE OF CONTENTS

## BREAKING INSIGHTS

**5585** Highlights from Recent Cancer Literature

## OBITUARY

**5587** **Joseph R. Bertino: In Memoriam (1930–2021)**  
William N. Hait

## REVIEWS

**5589** **Epigenetic Alterations and Mechanisms That Drive Resistance to Targeted Cancer Therapies**  
Narendra Wajapeyee and Romi Gupta

**5596** **The Role of mRNA Translational Control in Tumor Immune Escape and Immunotherapy Resistance**  
Michaël Cerezo, Caroline Robert, Lunxu Liu, and Shensi Shen

## CANCER RESEARCH LANDMARKS

**5605** **PARP Inhibitors – Trapped in a Toxic Love Affair**  
Dragomir B. Krastev, Andrew J. Wicks, and Christopher J. Lord  
See related article by Murai and colleagues, *Cancer Res* 2012;72:5588–99

## CANCER RESEARCH HIGHLIGHTS

**5608** **mTOR-Dependent ARID1A Degradation: A New Twist in the Genetic–Epigenetic Interplay Driving Hepatocellular Carcinoma**  
David R. Pease and Martin E. Fernandez-Zapico  
See related article, p. 5652

**5611** **Collagen Linearization within Tumors**  
Craig E. Barcus and Gregory D. Longmore  
See related article, p. 5666

## GENOME AND EPIGENOME

**5613** **Therapeutic Potential of Chemically Modified, Synthetic, Triplex Peptide Nucleic Acid–Based Oncomir Inhibitors for Cancer Therapy**  
Karishma Dhuri, Ravinder Reddy Gaddam, Ajit Vikram, Frank J. Slack, and Raman Bahal  
This study demonstrates the utility of novel oncomir inhibitors as cancer therapeutics, providing a new approach for targeting miRNAs and other noncoding RNAs.

**5625** **Diverse Oncogenic Fusions and Distinct Gene Expression Patterns Define the Genomic Landscape of Pediatric Papillary Thyroid Carcinoma**  
Ana Stosic, Fabio Fuligni, Nathaniel D. Anderson, Scott Davidson, Richard de Borja, Meryl Acker, Vito Forte, Paolo Campisi, Evan J. Propst, Nikolaus E. Wolter, Rose Chami, Ozgur Mete, David Malkin, Adam Shlien, and Jonathan D. Wasserman  
This study highlights important distinctions between the genomes and transcriptomes of pediatric and adult papillary thyroid carcinoma, with implications for understanding the biology, diagnosis, and treatment of advanced disease in children.

## MOLECULAR CELL BIOLOGY

**5638** **CstF64-Induced Shortening of the *BID* 3'UTR Promotes Esophageal Squamous Cell Carcinoma Progression by Disrupting ceRNA Cross-talk with *ZFP36L2***  
Ai Lin, Ping Ji, Xiangjie Niu, Xuan Zhao, Yamei Chen, Weiling Liu, Yachen Liu, Wenyi Fan, Yanxia Sun, Chuanwang Miao, Shaosen Zhang, Wen Tan, Dongxin Lin, Eric J. Wagner, and Chen Wu  
High-throughput analysis of alternative polyadenylation in esophageal squamous cell carcinoma identifies recurrent shortening of the *BID* 3'UTR as a driver of disease progression.

**5652** **mTORC1 Promotes ARID1A Degradation and Oncogenic Chromatin Remodeling in Hepatocellular Carcinoma**  
Shanshan Zhang, Yu-Feng Zhou, Jian Cao, Stephen K. Burley, Hui-Yun Wang, and X.F. Steven Zheng  
mTOR promotes oncogenic chromatin remodeling by controlling ARID1A degradation, which is important for liver tumorigenesis and response to mTOR- and YAP-targeted therapies in hepatocellular carcinoma.  
See related commentary, p. 5608

# TABLE OF CONTENTS

## 5666 **Matricellular Protein WISP2 Is an Endogenous Inhibitor of Collagen Linearization and Cancer Metastasis**

Jagadeesh Janjanam, Glendin Pano, Ruishan Wang, Benjamin A. Minden-Birkenmaier, Hannah Breeze-Jones, Eleanor Baker, Cecile Garcin, Georgia Clayton, Abbas Shirinifard, Ana Maria Zaske, David Finkelstein, and Myriam Labelle

Two secreted factors, WISP1 and WISP2, antagonistically regulate collagen linearization, and therapeutically increasing the WISP2:WISP1 ratio in tumors limits collagen linearization and inhibits metastasis.

See related commentary, p. 5611

## 5678 **LncRNA HIF1A-AS1 Promotes Gemcitabine Resistance of Pancreatic Cancer by Enhancing Glycolysis through Modulating the AKT/YB1/HIF1 $\alpha$ Pathway**

Fengyu Xu, Mengqi Huang, Qingyong Chen, Yi Niu, Yuhang Hu, Ping Hu, Ding Chen, Chi He, Kang Huang, Zhu Zeng, Jiang Tang, Fan Wang, Yong Zhao, Chunyou Wang, and Gang Zhao

These findings show that a reciprocal feedback of HIF1A-AS1 and HIF1 $\alpha$  promotes gemcitabine resistance of pancreatic cancer, which provides an applicable therapeutic target.

## TUMOR BIOLOGY AND IMMUNOLOGY

### 5692 **FSTL1 Secreted by Activated Fibroblasts Promotes Hepatocellular Carcinoma Metastasis and Stemness**

Jia-Jian Loh, Tsz-Wai Li, Lei Zhou, Tin-Lok Wong, Xue Liu, Victor W.S. Ma, Chung-Mau Lo, Kwan Man, Terence K. Lee, Wen Ning, Man Tong, and Stephanie Ma

This study shows that FSTL1 secreted by activated fibroblasts in the liver microenvironment augments hepatocellular carcinoma malignancy, providing a potential new strategy to improve treatment of this aggressive disease.

### 5706 **TGFBI Production by Macrophages Contributes to an Immunosuppressive Microenvironment in Ovarian Cancer**

Laura S.M. Lecker, Chiara Berlato, Eleni Maniati, Robin Delaine-Smith, Oliver M.T. Pearce, Owen Heath, Samuel J. Nichols, Caterina Trevisan, Marian Novak, Jacqueline McDermott, James D. Brenton, Pedro R. Cutillas, Vinodhini Rajeeve, Ana Hennino, Ronny Drapkin, Daniela Loessner, and Frances R. Balkwill

Analysis of ECM changes during neoplastic transformation reveals a role for TGFBI secreted by macrophages in immunosuppression in early ovarian cancer.

### 5720 **Oxidized Low-Density Lipoprotein Links Hypercholesterolemia and Bladder Cancer Aggressiveness by Promoting Cancer Stemness**

Lin Yang, Jingya Sun, Meiqian Li, Yiming Long, Dianzheng Zhang, Hongqian Guo, Ruimin Huang, and Jun Yan

This study demonstrates how hypercholesterolemia-induced oxidized LDL promotes urinary bladder cancer stemness via a CD36/STAT3 signaling axis, highlighting these factors as biomarkers and potential therapeutic targets of aggressive disease.

## TRANSLATIONAL SCIENCE

### 5733 **MTH1 Inhibitor TH1579 Induces Oxidative DNA Damage and Mitotic Arrest in Acute Myeloid Leukemia**

Kumar Sanjiv, José Manuel Calderón-Montaño, Therese M. Pham, Tom Erkers, Viktoriia Tsuber, Ingrid Almlöf, Andreas Höglund, Yaser Heshmati, Brinton Seashore-Ludlow, Akhilesh Nagesh Danda, Helge Gad, Elisee Wiita, Camilla Göktürk, Azita Rasti, Stefanie Friedrich, Anders Centio, Montserrat Estruch, Thea Kristin Våtsveen, Nona Struyf, Torkild Visnes, Martin Scobie, Tobias Koolmeister, Martin Henriksson, Olov Wallner, Teresa Sandvall, Sören Lehmann, Kim Theilgaard-Mönch, Mathew J. Garnett, Päivi Östling, Julian Walfridsson, Thomas Helleday, and Ulrika Warpman Berglund

The MTH1 inhibitor TH1579 is a potential novel AML treatment, targeting both blasts and the pivotal leukemic stem cells while sparing normal bone marrow cells.

## CONVERGENCE AND TECHNOLOGIES

### 5745 **Raman Spectroscopy and Machine Learning Reveals Early Tumor Microenvironmental Changes Induced by Immunotherapy**

Santosh Kumar Paidi, Joel Rodriguez Troncoso, Piyush Raj, Paola Monterroso Diaz, Jesse D. Ivers, David E. Lee, Nathan L. Avaritt, Allen J. Gies, Charles M. Quick, Stephanie D. Byrum, Alan J. Tackett, Narasimhan Rajaram, and Ishan Barman

This study provides first-in-class evidence that optical spectroscopy allows sensitive detection of early changes in the biomolecular composition of tumors that predict response to immunotherapy with immune checkpoint inhibitors.

### 5756 **Characterization of Peptides Targeting Metastatic Tumor Cells as Probes for Cancer Detection and Vehicles for Therapy Delivery**

Shraddha Subramanian, Alexes C. Daquinag, Solmaz AghaAmiri, Sukhen C. Ghosh, Ali Azhdarinia, and Mikhail G. Kolonin

This study identifies new molecules that bind metastatic cells and demonstrates their application as noninvasive imaging probes and vehicles for cytotoxic therapy delivery in preclinical cancer models.

# TABLE OF CONTENTS

**5765**    **Computational Analysis of Cholangiocarcinoma Phosphoproteomes Identifies Patient-Specific Drug Targets**

Shirin Elizabeth Khorsandi, Arran D. Dokal, Vinothini Rajeeve, David J. Britton, Megan S. Illingworth, Nigel Heaton, and Pedro R. Cutillas

Phosphoproteomic and computational analyses identify patient-specific drug targets in cholangiocarcinoma, supporting the potential of a machine learning method to predict personalized therapies.

## CORRECTION

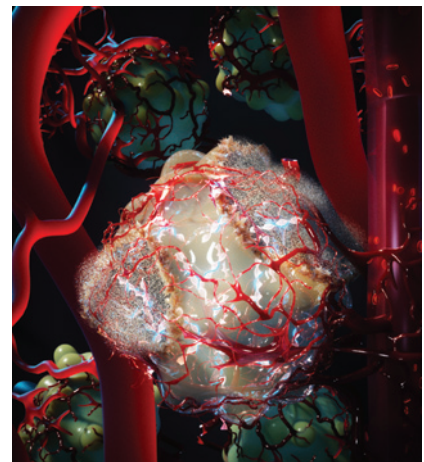
**5777**    **Correction: CXCL12 $\gamma$  Promotes Metastatic Castration-Resistant Prostate Cancer by Inducing Cancer Stem Cell and Neuroendocrine Phenotypes**

Younghun Jung, Frank C. Cackowski, Kenji Yumoto, Ann M. Decker, Jingcheng Wang, Jin Koo Kim, Eunsohl Lee, Yugang Wang, Jae-Seung Chung, Amy M. Gursky, Paul H. Krebsbach, Kenneth J. Pienta, Todd M. Morgan, and Russell S. Taichman

## ABOUT THE COVER

Various types of cancer overexpress oncogenic miRNAs, making them a potential therapeutic target. Next-generation chemically modified triplex peptide nucleic acid–based miR-155 inhibitors possess superior therapeutic efficacy compared with conventional full-length anti-miR-155. The cover depicts intratumoral treatment with the next-generation anti-miRNA-155 inhibitor. For details, see article by Dhuri and colleagues on page 5613.

doi: 10.1158/0008-5472.CAN-81-22-CVR



# Cancer Research

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

**81 (22)**

*Cancer Res* 2021;81:5585-5777.

**Updated version** Access the most recent version of this article at:  
<http://cancerres.aacrjournals.org/content/81/22>

**E-mail alerts** [Sign up to receive free email-alerts](#) related to this article or journal.

**Reprints and Subscriptions** To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at [pubs@aacr.org](mailto:pubs@aacr.org).

**Permissions** To request permission to re-use all or part of this article, use this link <http://cancerres.aacrjournals.org/content/81/22>.  
Click on "Request Permissions" which will take you to the Copyright Clearance Center's (CCC) Rightslink site.