

CANCER RESEARCH

TABLE OF CONTENTS

BREAKING INSIGHTS

4887 Highlights from Recent Cancer Literature

REVIEW

4889 **Effects of Exercise on Cancer Treatment Efficacy: A Systematic Review of Preclinical and Clinical Studies**
Lin Yang, Andria R. Morielli, Emily Heer, Amy A. Kirkham, Winson Y. Cheung, Nawaid Usmani, Christine M. Friedenreich, and Kerry S. Courneya

CANCER RESEARCH LANDMARKS

4896 **Cancer Signaling Drives Cancer Metabolism: AKT and the Warburg Effect**
Aaron M. Hosios and Brendan D. Manning
See related article by Elstrom and colleagues, *Cancer Res* 2004;64:3892-9

CANCER RESEARCH HIGHLIGHTS

4899 **A Novel Long Noncoding RNA Finetunes the DNA Damage Response in Hepatocellular Carcinoma**
Marina Barcena-Varela and Amaia Lujambio
See related article, p. 4910

PRIORITY REPORT

4901 **Subclone Eradication Analysis Identifies Targets for Enhanced Cancer Therapy and Reveals L1 Retrotransposition as a Dynamic Source of Cancer Heterogeneity**
Kirsi Ketola, Heidi Kaljunen, Sinja Taavitsainen, Roosa Kaarijärvi, Emmi Järvelä, Bernardo Rodríguez-Martín, Kerstin Haase, Dan J. Woodcock, Jose Tubio, David C. Wedge, Matti Nykter, and G. Steven Bova
Differential analysis of eradicated and resistant subclones following cancer treatment identifies that L1 activity associated with resistance is induced by current therapies and blocked by the antiretroviral drug azidothymidine.

GENOME AND EPIGENOME

4910 **Long Noncoding RNA NIHCOLE Promotes Ligation Efficiency of DNA Double-Strand Breaks in Hepatocellular Carcinoma**
Juan P. Unfried, Mikel Marín-Baquero, Ángel Rivera-Calzada, Nerea Razquin, Eva M. Martín-Cuevas, Sara de Bragança, Clara Aicart-Ramos, Christopher McCoy, Laura Prats-Mari, Raquel Arribas-Bosacoma, Linda Lee, Stefano Caruso, Jessica Zucman-Rossi, Bruno Sangro, Gareth Williams, Fernando Moreno-Herrero, Oscar Llorca, Susan P. Lees-Miller, and Puri Fortes
This study characterizes the role of a lncRNA NIHCOLE in DNA repair and cellular fitness in HCC, thus implicating it as a therapeutic target.
See related commentary, p. 4899

4926 **The Evolving Genomic Landscape of Esophageal Squamous Cell Carcinoma Under Chemoradiotherapy**
Hidenari Hirata, Atsushi Niida, Nobuyuki Kakiuchi, Ryutaro Uchi, Keishi Sugimachi, Takaaki Masuda, Tomoko Saito, Shun-Ichiro Kageyama, Yushi Motomura, Shuhei Ito, Tadamasu Yoshitake, Daisuke Tsurumaru, Yusuke Nishimuta, Akira Yokoyama, Takanori Hasegawa, Kenichi Chiba, Yuichi Shiraishi, Junyan Du, Fumihito Miura, Masaru Morita, Yasushi Toh, Masakazu Hirakawa, Yoshiyuki Shioyama, Takashi Ito, Tetsuo Akimoto, Satoru Miyano, Tatsuhiko Shibata, Masaki Mori, Yutaka Suzuki, Seishi Ogawa, Kousei Ishigami, and Koshi Mimori
Whole-exome sequencing reveals the genetic evolution of ESCC during chemoradiotherapy, highlighting *MYC* gain in pretreatment tumors as a potential marker of therapy resistance.

4939 **Radiation-Induced Phosphorylation of a Prion-Like Domain Regulates Transformation by FUS-CHOP**
Mark Chen, Joseph P. Foster II, Ian C. Lock, Nathan H. Leisenring, Andrea R. Daniel, Warren Floyd, Eric Xu, Ian J. Davis, and David G. Kirscht
Prion-like domains, which are frequently translocated in cancers as oncogenic fusion proteins that drive global epigenetic changes, confer sensitivity to radiation via disruption of oncogenic interactions.

TABLE OF CONTENTS

METABOLISM AND CHEMICAL BIOLOGY

- 4949 Hypoxia Promotes Breast Cancer Cell Growth by Activating a Glycogen Metabolic Program**
Ke Tang, Liyan Zhu, Jie Chen, Dianheng Wang, Liping Zeng, Chen Chen, Liang Tang, Li Zhou, Keke Wei, Yabo Zhou, Jiadi Lv, Yuying Liu, Huafeng Zhang, Jingwei Ma, and Bo Huang

Hypoxic breast cancer cells trigger self-growth through PCK1-mediated glycogen metabolism reprogramming that leads to NADPH production to maintain a moderate ROS level.

- 4964 MTAP Deficiency-Induced Metabolic Reprogramming Creates a Vulnerability to Cotargeting *De Novo* Purine Synthesis and Glycolysis in Pancreatic Cancer**
Qiangsheng Hu, Yi Qin, Shunrong Ji, Xiuhui Shi, Weixing Dai, Guixiong Fan, Shuo Li, Wenyan Xu, Wensheng Liu, Mengqi Liu, Zheng Zhang, Zeng Ye, Zhijun Zhou, Jingxuan Yang, Qifeng Zhuo, Xianjun Yu, Min Li, and Xiaowu Xu

This study demonstrates that MTAP status impacts glucose and purine metabolism, thus identifying multiple novel treatment options against MTAP-deficient pancreatic cancer.

- 4981 Lipidomic Profiling of Clinical Prostate Cancer Reveals Targetable Alterations in Membrane Lipid Composition**
Lisa M. Butler, Chui Yan Mah, Jelle Machiels, Andrew D. Vincent, Swati Irani, Shadrack M. Mutuku, Xander Spotbeen, Muralidhararao Bagadi, David Waltregny, Max Moldovan, Jonas Dehairs, Frank Vanderhoydonc, Katarzyna Bloch, Rajdeep Das, Jurgen Stahl, James G. Kench, Thomas Gevaert, Rita Derua, Etienne Waelkens, Zeyad D. Nassar, Luke A. Selth, Paul J. Trim, Marten F. Snel, David J. Lynn, Wayne D. Tilley, Lisa G. Horvath, Margaret M. Centenera, and Johannes V. Swinnen

This study identifies malignancy and treatment-associated changes in lipid composition of clinical prostate cancer tissues, suggesting that mediators of these lipidomic changes could be targeted using existing metabolic agents.

MOLECULAR CELL BIOLOGY

- 4994 Unraveling Ewing Sarcoma Tumorigenesis Originating from Patient-Derived Mesenchymal Stem Cells**
Anna Sole, Sandrine Grossetête, Maxime Heintzé, Loelia Babin, Sakina Zaïdi, Patrick Revy, Benjamin Renouf, Anne De Cian, Carine Giovannangeli, Cécile Pierre-Eugène, Isabelle Janoueix-Lerosey, Lucile Couronné, Sophie Kaltenbach, Mark Tomishima, Maria Jasin, Thomas G.P. Grünwald, Olivier Delattre, Didier Surdez, and Erika Brunet

These findings demonstrate that Ewing sarcoma can originate from human bone-marrow-derived mesenchymal stem cells and that recurrent mutations support EWSR1-FLI1 translocation-mediated transformation.

- 5007 AMBRA1 Promotes TGF β Signaling via Nonproteolytic Polyubiquitylation of Smad4**

Jinquan Liu, Bo Yuan, Jin Cao, Hongjie Luo, Shuchen Gu, Mengdi Zhang, Ran Ding, Long Zhang, Fangfang Zhou, Mien-Chie Hung, Pinglong Xu, Xia Lin, Jianping Jin, and Xin-Hua Feng

This study identifies AMBRA1 as a novel regulator of TGF β signaling and breast cancer metastasis, supporting further exploration of AMBRA1 as a target for cancer therapy.

TUMOR BIOLOGY AND IMMUNOLOGY

- 5021 The CD200-CD200R Axis Promotes Squamous Cell Carcinoma Metastasis via Regulation of Cathepsin K**
Iasha Z. Khan, Christina A. Del Guzzo, Anqi Shao, Jiyeon Cho, Rong Du, Adrienne O. Cohen, and David M. Owens

These findings highlight the relationship between CD200-CD200R and cathepsin K in cutaneous squamous cell carcinoma metastasis and suggest that either of these components may serve as a viable therapeutic target in this disease.

- 5033 Mutant *Idh2* Cooperates with a *NUP98-HOXD13* Fusion to Induce Early Immature Thymocyte Precursor ALL**
Liat Goldberg, Vijay Negi, Yang Jo Chung, Masahiro Onozawa, Yuelin J. Zhu, Robert L. Walker, Rachel Pierce, Daxesh P. Patel, Kristopher W. Krausz, Frank J. Gonzalez, Margaret A. Goodell, Benjamin A.T. Rodriguez, Paul S. Meltzer, and Peter D. Aplan

T-cell leukemia induced in *Idh2^{RI40Q}/NUP98-HOXD13* mice is immunophenotypically, transcriptionally, and genetically similar to human EITP ALL, providing a model for studying disease development and treatment.

- 5047 Neuroblastoma Formation Requires Unconventional CD4 T Cells and Arginase-1-Dependent Myeloid Cells**
Lee-Ann Van de Velde, E. Kaitlynn Allen, Jeremy Chase Crawford, Taylor L. Wilson, Clifford S. Guy, Marion Russier, Leonie Zeitler, Armita Bahrami, David Finkelstein, Stephane Pelletier, Stacey Schultz-Cherry, Paul G. Thomas, and Peter J. Murray

A new model of human neuroblastoma provides ways to track tumor formation and expansion in living animals, allowing identification of CD4⁺ T-cell and macrophage functions required for oncogenesis.

- 5060 Endothelial Reprogramming Stimulated by Oncostatin M Promotes Inflammation and Tumorigenesis in *VHL*-Deficient Kidney Tissue**

Hieu-Huy Nguyen-Tran, Thi-Ngoc Nguyen, Chen-Yun Chen, and Tien Hsu

A novel mechanism of cross-talk between ECs and *VHL*-deficient kidney tubules that stimulates inflammation and tumorigenesis is discovered, suggesting OSM could be a potential target for ccRCC intervention.

TABLE OF CONTENTS

5074 Epstein-Barr Virus-Encoded Circular RNA CircBART2.2 Promotes Immune Escape of Nasopharyngeal Carcinoma by Regulating PD-L1

Junshang Ge, Jie Wang, Fang Xiong, Xianjie Jiang, Kunjie Zhu, Yian Wang, Yongzhen Mo, Zhaojian Gong, Shanshan Zhang, Yi He, Xiayu Li, Lei Shi, Can Guo, Fuyan Wang, Ming Zhou, Bo Xiang, Yong Li, Guiyuan Li, Wei Xiong, and Zhaoyang Zeng

This work demonstrates that *circBART2.2* binding to RIG-I is essential for the regulation of PD-L1 and subsequent immune escape in nasopharyngeal carcinoma.

5102 Targeting Notch Inhibitors to the Myeloma Bone Marrow Niche Decreases Tumor Growth and Bone Destruction without Gut Toxicity

Hayley M. Sabol, Adam J. Ferrari, Manish Adhikari, Tania Amorim, Kevin McAndrews, Judith Anderson, Michele Vigolo, Rajwinder Lehal, Meloney Cregor, Sharmin Khan, Pedro L. Cuevas, Jill A. Helms, Noriyoshi Kurihara, Venkat Srinivasan, Frank H. Ebetino, Robert K. Boeckman Jr, G. David Roodman, Teresita Bellido, and Jesus Delgado-Calle

Development of a bone-targeted Notch inhibitor reduces multiple myeloma growth and mitigates cancer-induced bone destruction without inducing the gastrointestinal toxicity typically associated with inhibition of Notch.

TRANSLATIONAL SCIENCE

5089 TET2 and DNMT3A Mutations Exert Divergent Effects on DNA Repair and Sensitivity of Leukemia Cells to PARP Inhibitors

Silvia Maifrede, Bac Viet Le, Margaret Nieborowska-Skorska, Konstantin Golovine, Katherine Sullivan-Reed, Wangisa M.B. Dunuwille, Joseph Nacson, Michael Hulse, Kelsey Keith, Jozef Madzo, Lisa Beatrice Caruso, Zachary Gazze, Zhaorui Lian, Antonella Padella, Kumaraswamy N. Chitrala, Boris A. Bartholdy, Ksenia Matlawska-Wasowska, Daniela Di Marcantonio, Giorgia Simonetti, Georg Greiner, Stephen M. Sykes, Peter Valent, Elisabeth M. Paietta, Martin S. Tallman, Hugo F. Fernandez, Mark R. Litzow, Mark D. Minden, Jian Huang, Giovanni Martinelli, George S. Vassiliou, Italo Tempera, Katarzyna Piwocka, Neil Johnson, Grant A. Challen, and Tomasz Skorski

TET2 and *DNMT3A* mutations affect distinct DNA repair mechanisms and govern the differential sensitivities of oncogenic tyrosine kinase-positive leukemia cells to PARP inhibitors.

CONVERGENCE AND TECHNOLOGIES

5115 Predicting Molecular Phenotypes from Histopathology Images: A Transcriptome-Wide Expression-Morphology Analysis in Breast Cancer

Yinxi Wang, Kimmo Kartasalo, Philippe Weitz, Balázs Ács, Masi Valkonen, Christer Larsson, Pekka Ruusuvauro, Johan Hartman, and Mattias Rantalainen

Transcriptome-wide expression morphology deep learning analysis enables prediction of mRNA expression and proliferation markers from routine histopathology whole slide images in breast cancer.

CORRECTION

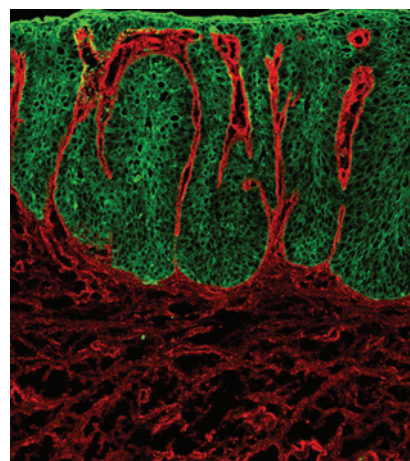
5127 Correction: YAP Suppresses Lung Squamous Cell Carcinoma Progression via Deregulation of the Dnp63-GPX2 Axis and ROS Accumulation

Hsinyi Huang, Wenjing Zhang, Yafang Pan, Yijun Gao, Lei Deng, Fuming Li, Fei Li, Xueyan Ma, Shenda Hou, Jing Xu, Peixue Li, Xiaoxun Li, Guohong Hu, Cheng Li, Haiquan Chen, Lei Zhang, and Hongbin Ji

ABOUT THE COVER

The CD200-CD200R signaling axis plays an etiological role in the survival and spread of numerous cancers. CD200 stimulates metastasis of cutaneous squamous cell carcinoma (cSCC) via inducing expression of cysteine protease cathepsin K (Ctsk) in CD200R⁺ tumor-infiltrating myeloid cells. Inhibition of Ctsk blocks cSCC cell migration through collagen and blocks cSCC metastasis. The cover image depicts pan-cytokeratin⁺ (green) human cutaneous squamous cell carcinoma invading through type I collagen⁺ (red) stroma. For details, see the article by Khan and colleagues on page 5021.

doi: 10.1158/0008-5472.CAN-81-19-CVR



Cancer Research

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

81 (19)

Cancer Res 2021;81:4887-5127.

Updated version Access the most recent version of this article at:
<http://cancerres.aacrjournals.org/content/81/19>

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.

Permissions To request permission to re-use all or part of this article, use this link <http://cancerres.aacrjournals.org/content/81/19>.
Click on "Request Permissions" which will take you to the Copyright Clearance Center's (CCC) Rightslink site.