


BREAKING ADVANCES

- 1 Highlights from Recent Cancer Literature

INTEGRATED SYSTEMS AND TECHNOLOGIES

- 3  Enhanced Detection of Cancer Biomarkers in Blood-Borne Extracellular Vesicles Using Nanodroplets and Focused Ultrasound

Robert J. Paproski, Juan Jovel, Gane Ka-Shu Wong, John D. Lewis, and Roger J. Zemp

Précis: Ultrasound and nanodroplets stimulate release of extracellular vesicles from solid tumors, which enter the blood, suggesting that biomarkers from localized solid tumors can be analyzed from blood samples.

MICROENVIRONMENT AND IMMUNOLOGY

- 14 The Beta Subunit of Hemoglobin (HBB2/HBB) Suppresses Neuroblastoma Growth and Metastasis


Shelly Maman, Orit Sagi-Assif, Weirong Yuan, Ravit Ginat, Tsipi Meshel, Inna Zubrilov, Yona Keisari, Weiyue Lu, Wuyuan Lu, and Isaac P. Witz

Précis: This study reveals a moonlighting function for the beta subunit of hemoglobin in blocking tumor growth and metastatic progression, possibly offering a biologic agent to prevent and treat cancer metastases.

- 27 Dietary Emulsifier-Induced Low-Grade Inflammation Promotes Colon Carcinogenesis

Emilie Viennois, Didier Merlin, Andrew T. Gewirtz, and Benoit Chassaing

Précis: Dietary emulsifier consumption perturbs host-microbiota interactions, leading to low-grade inflammation that favors colon carcinogenesis.

- 41  Heterogeneous Stromal Signaling within the Tumor Microenvironment Controls the Metastasis of Pancreatic Cancer

Agnieszka A. Rucki, Kelly Foley, Pingbo Zhang, Qian Xiao, Jennifer Kleponis, Annie A. Wu, Rajni Sharma, Guanglan Mo, Angen Liu, Jennifer Van Eyk, Elizabeth M. Jaffee, and Lei Zheng

Précis: Newfound interactions between tumors and supporting stroma provide a rationale for simultaneous inhibition of multiple stromal signaling pathways in PDAC therapy.

- 53 Kv1.3 Channels Mark Functionally Competent CD8⁺ Tumor-Infiltrating Lymphocytes in Head and Neck Cancer

Ameet A. Chimote, Peter Hajdu, Alexandros M. Sfyris, Brittany N. Gleich, Trisha Wise-Draper, Keith A. Casper, and Laura Conforti


Précis: Ca²⁺ signaling is suppressed in tumor-infiltrating lymphocytes in head and neck cancer patients and is associated with loss of effector functions in CD8⁺ T cells.

MOLECULAR AND CELLULAR PATHOBIOLOGY

- 62 Loss of the Methyl-CpG-Binding Protein ZBTB4 Alters Mitotic Checkpoint, Increases Aneuploidy, and Promotes Tumorigenesis

Audrey Roussel-Gervais, Ikrame Naciri, Olivier Kirsh, Laetitia Kasprzyk, Guillaume Velasco, Giacomo Grillo, Pierre Dubus, and Pierre-Antoine Defossez

Précis: A new molecular actor links DNA methylation as an epigenetic mark to the maintenance of genomic stability and cancer prevention.

- 74  HER2 and EGFR Overexpression Support Metastatic Progression of Prostate Cancer to Bone

Kathleen C. Day, Guadalupe Lorenzatti Hiles, Molly Kozminsky, Scott J. Dawsey, Alyssa Paul, Luke J. Brodes, Rajal Shah, Lakshmi P. Kunja, Christopher Hall, Nallasivam Palanisamy, Stephanie Daignault-Newton, Layla El-Sawy, Steven James Wilson, Andrew Chou, Kathleen Woods Ignatoski, Evan Keller, Dafydd Thomas, Sunitha Nagrath, Todd Morgan, and Mark L. Day

Précis: Simultaneous inhibition of HER2 and EGFR exploits their distinct roles supporting metastatic progression in human prostate cancer, given preclinical evidence of the efficacy of combination treatment.

- 86 Targeting of PYK2 Synergizes with EGFR Antagonists in Basal-like TNBC and Circumvents HER3-Associated Resistance via the NEDD4-NDRG1 Axis

Nandini Verma, Anna-Katharina Müller, Charu Kothari, Effrosini Panayotopoulou, Amir Kedan, Michael Selitrennik, Gordon B. Mills, Lan K. Nguyen, Sungyoung Shin, Thomas Karn, Uwe Holtrich, and Sima Lev

Précis: These findings offer preclinical proof of concept for a strategy of dual targeting of the EGFR and PYK2/FAK kinases to treat triple-negative breast cancers with high EGFR levels, with near term clinical implications.

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- 100** KRAS/NF- κ B/YY1/miR-489 Signaling Axis Controls Pancreatic Cancer Metastasis
Peng Yuan, Xiao-Hong He, Ye-Fei Rong, Jing Cao, Yong Li, Yun-Ping Hu, Yingbin Liu, Dangsheng Li, Wenhui Lou, and Mo-Fang Liu

Précis: These results establish a pivotal mechanism of metastasis in KRAS-driven pancreatic cancers and suggest miR-489 as a candidate therapeutic target to address this disease.

- 112** CRLX101, a Nanoparticle–Drug Conjugate Containing Camptothecin, Improves Rectal Cancer Chemoradiotherapy by Inhibiting DNA Repair and HIF1 α

Xi Tian, Minh Nguyen, Henry P. Foote, Joseph M. Caster, Kyle C. Roche, Christian G. Peters, Pauline Wu, Lata Jayaraman, Edward G. Garmey, Joel E. Tepper, Scott Eliasof, and Andrew Z. Wang

Précis: These findings offer preclinical proof of concept for a cytotoxic nanotherapy to improve outcomes in rectal cancer patients receiving neoadjuvant chemoradiotherapy, in support of ongoing clinical evaluation of this nanotherapy.

- 123** PTEN Signaling in the Postnatal Perivascular Progenitor Niche Drives Medulloblastoma Formation

Guo Zhu, Sherri L. Rankin, Jon D. Larson, Xiaoyan Zhu, Lionel M.L. Chow, Chunxu Qu, Jinghui Zhang, David W. Ellison, and Suzanne J. Baker

Précis: Unexpected effects of deregulated PI3K signaling on neural progenitor cells identify alternative cells of origin for medulloblastoma, possibly underlying the heterogeneity found within the sonic hedgehog subgroup of this brain tumor.

PREVENTION AND EPIDEMIOLOGY

- 134** Human Chorionic Gonadotropin Does Not Correlate with Risk for Maternal Breast Cancer: Results from the Finnish Maternity Cohort

Renée T. Fortner, Helena Schock, Rudolf Kaaks, Matti Lehtinen, Eero Pukkala, Hans-Åke Lakso, Minna Tanner, Raija Kallio, Heikki Joensuu, Jaana Korpela, Adetunji T. Toriola, Göran Hallmans, Kjell Grankvist, Anne Zeleniuch-Jacquotte, Paolo Toniolo, Eva Lundin, and Heljä-Marja Surcel

Précis: Despite provocative earlier findings, this study finds no evidence that circulating hCG concentrations in early pregnancy act as a risk factor in mothers for later breast cancer risk.

THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

- 142** Phospholipase D1 Acts through Akt/TopBP1 and RB1 to Regulate the E2F1-Dependent Apoptotic Program in Cancer Cells

Dong Woo Kang, Shin Wha Lee, Won Chan Hwang, Bo Hui Lee, Yong-Seok Choi, Young-Ah Suh, Kang-Yell Choi, and Do Sik Min

Précis: A phospholipase that functions as a nodal modifier of colon cancer susceptibility mediates the cross-talk between two major tumor suppressor and oncogenic pathways, with implications for disease-selective therapeutic targeting.

- 153** A Transcriptional Signature Identifies LKB1 Functional Status as a Novel Determinant of MEK Sensitivity in Lung Adenocarcinoma

Jacob M. Kaufman, Tadaaki Yamada, Kyungho Park, Cynthia D. Timmers, Joseph M. Amann, and David P. Carbone

Précis: In silico analysis of a transcriptional fingerprint assay reveals LKB1 loss to accurately predict sensitivity of tumors to MEK inhibitors.

- 164** Alox5 Blockade Eradicates JAK2V617F-Induced Polycythemia Vera in Mice

Yaoyu Chen, Yi Shan, Min Lu, Ngoc DeSouza, Zhiru Guo, Ronald Hoffman, Aibin Liang, and Shaoguang Li

Précis: This study defines a lipid metabolic enzyme as a critical driver of JAK2-mutant forms of an untreatable myeloproliferative disease, with implications to improve its therapeutic management.

- 175** Targeting BRK-Positive Breast Cancers with Small-Molecule Kinase Inhibitors

Jie Jiang, Fu Gui, Zhixiang He, Li Li, Yunzhan Li, Shunying Li, Xinrui Wu, Zhou Deng, Xihuan Sun, Xiaoxing Huang, Wei Huang, Shang Han, Ting Zhang, Zheng Wang, Bo Jiao, Siyang Song, Hongrui Wang, Lanfen Chen, Dawang Zhou, Qiang Liu, Ruibao Ren, Jianming Zhang, and Xianming Deng

Précis: These findings offer preclinical proof of concept for therapeutic use of a small-molecule inhibitor of the oncogenic kinase BRK in breast cancer.

- 187** PROTOCADHERIN 7 Acts through SET and PP2A to Potentiate MAPK Signaling by EGFR and KRAS during Lung Tumorigenesis

Xiaorong Zhou, Barrett L. Updegraff, Yabin Guo, Michael Peyton, Luc Girard, Jill E. Larsen, Xian-Jin Xie, Yunyun Zhou, Tae Hyun Hwang, Yang Xie, Jaime Rodriguez-Canales, Pamela Villalobos, Carmen Behrens, Ignacio I. Wistuba, John D. Minna, and Kathryn A. O'Donnell

Précis: Results suggest a therapeutic target and a cell surface biomarker to select lung adenocarcinoma patients who might benefit from treatment with a clinically approved SET inhibitor.



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TUMOR AND STEM CELL BIOLOGY

198 DNA Repair Capacity in Multiple Pathways Predicts Chemoresistance in Glioblastoma Multiforme

Zachary D. Nagel, Gaspar J. Kitange, Shiv K. Gupta, Brian A. Joughin, Isaac A. Chaim, Patrizia Mazzucato, Douglas A. Lauffenburger, Jann N. Sarkaria, and Leona D. Samson

Précis: Recently developed multiplex DNA repair assays combine with mathematical modeling to provide a strategy for predicting the effectiveness of cancer therapy in individual patients.

207 Mutational Landscape and Gene Expression Patterns in Adult Acute Myeloid Leukemias with Monosomy 7 as a Sole Abnormality

Ann-Kathrin Eisfeld, Jessica Kohlschmidt, Krzysztof Mrózek, Stefano Volinia, James S. Blachly, Deedra Nicolet, Christopher Oakes, Karl Kroll, Shelley Orwick, Andrew J. Carroll, Richard M. Stone, John C. Byrd, Albert de la Chapelle, and Clara D. Bloomfield

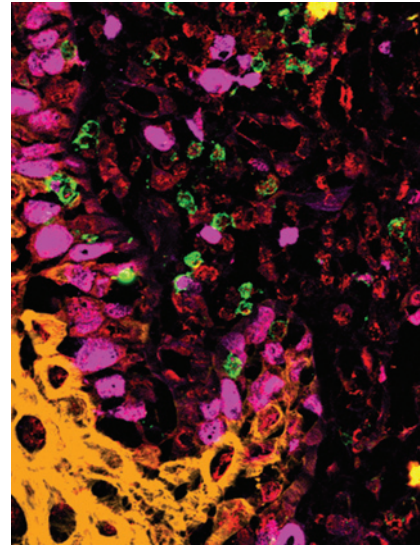
Précis: This study illuminates the molecular pathobiology underlying extremely aggressive cases of adult acute myeloid leukemia, which associated with monosomy of chromosome 7, with possible implications to improve its treatment.

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ABOUT THE COVER

Infiltration of functionally competent cytotoxic (CD8⁺) T lymphocytes is necessary for effective immune surveillance in cancer. Kv1.3 potassium channels regulate the activation and function of T cells. This image depicts a section from a head and neck cancer stained for cytokeratin (tumor cell marker, yellow), CD8 (green), Ki-67 (cell proliferation marker, magenta), and Kv1.3 channels (red). The CD8⁺ lymphocytes that showed low Kv1.3 expression also showed decreased cell proliferation, indicating that Kv1.3 channels could be potential markers of the function of tumor-infiltrating T cells in head and neck cancer. For details, see article by Chimote and colleagues on page 53.



Cancer Research

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

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