BREAKING INSIGHTS

5479 Highlights from Recent Cancer Literature

REVIEWS

5481 Low-Molecular-Weight Cyclin E in Human Cancer: Cellular Consequences and Opportunities for Targeted Therapies
Joseph A. Caruso, Mylinh T. Duong, Jason P. W. Carey, Kelly K. Hunt, and Khandan Keyomarsi

5492 Diverse Functions of Macrophages in Different Tumor Microenvironments
Ming Yang, Daniel McKay, Jeffrey W. Pollard, and Claire E. Lewis

CANCER RESEARCH HIGHLIGHTS

5504 Sexual Inequality in the Cancer Cell
Arthur P. Arnold and Christine M. Diesteche
See related articles by Li et al., p. 5527, and Lopes-Ramos et al., p. 5538

PERSPECTIVE

5506 Specific Targeting of Oncogenes Using CRISPR Technology
Felix Oppel, Matthias Schurmann, Peter Goon, Andreas E. Albers, and Holger Sudhoff

PRIORITY REPORTS

5513 Loss of MST/Hippo Signaling in a Genetically Engineered Mouse Model of Fusion-Positive Rhabdomyosarcoma Accelerates Tumorigenesis
Kristianne M. Ornstein, Lisa E.S. Crose, Nina Kuprasertkul, Rex C. Bentley, Yi-Tzu Lin, Nerissa Williams, David G. Kirsch, and Corinne M. Linardic
Significance: A novel mouse model sheds light on the critical role of Hippo/MST downregulation in PAX3-FOXO1–positive rhabdomyosarcoma tumorigenesis.

5521 Glutamate-Weighted Chemical Exchange Saturation Transfer Magnetic Resonance Imaging Detects Glutaminase Inhibition in a Mouse Model of Triple-Negative Breast Cancer
Rong Zhou, Puneet Bagga, Kavindra Nath, Hari Hariharan, David A. Mankoff, and Ravinder Reddy
Significance: A sensitive method enables noninvasive detection of tumor response to inhibitors of glutamine metabolism.

5527 Sex Differences in Cancer Driver Genes and Biomarkers
Constance H. Li, Syed Haider, Yu-Jia Shia, Kevin Thai, and Paul C. Boutros
Significance: This study provides a comprehensive catalog of sex differences in somatic alterations, including in cancer driver genes, which influence prognostic biomarkers that predict patient outcome after definitive local therapy.

5529 Gene Regulatory Network Analysis Identifies Sex-Linked Differences in Colon Cancer Drug Metabolism
Camila M. Lopes-Ramos, Marieke L. Kuijjer, Shuji Ogino, Charles S. Fuchs, Dawn L. DeMeeo, Kimberly Glass, and John Quackenbush
Significance: A network-based approach reveals that sex-specific patterns of gene targeting by transcriptional regulators are associated with survival outcome in colon cancer. This approach can be used to understand how sex influences progression and response to therapies in other cancers.

5548 Canonical Wnt Signaling Remodels Lipid Metabolism in Zebrafish Hepatocytes following Ras Oncogenic Insult
Yuxiao Yao, Shaoyang Sun, Jingjing Wang, Wei Fei, Zhaoru Dong, Al-Wu Ke, Ruoyu He, Lei Wang, Lili Zhang, Min-Biao Li, Qiang Li, Min Yu, Guo-Ming Shi, Jia Fan, Zhiyuan Gong, and Xu Wang
Significance: These findings identify FA desaturation as a significant downstream therapeutic target for antagonizing the combinatorial effects of Wnt and Ras signaling pathways in hepatocellular carcinoma.
Replication Protein A Availability during DNA Replication Stress Is a Major Determinant of Cisplatin Resistance in Ovarian Cancer Cells

Francois Belanger, Emile Fortier, Maxime Dubé, Jean-François Lemay, Rémi Buisson, Jean-Yves Masson, Abdelhamid Esherbiny, Santiago Costantino, Euridice Carmona, Anne-Marie Mes-Masson, Hugo Wurtele, and Elliot Drobetsky

**Significance:** The influence of replication protein A exhaustion on cisplatin sensitivity harbors important implications toward improving therapy of various cancers that initially respond to platinum-based agents but later relapse due to intrinsic or acquired drug resistance.

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Computational Characterization of Suppressive Immune Microenvironments in Glioblastoma

Suvi Luoto, Ismaïl Hermelo, Elisa M. Vuorinen, Paavo Hannus, Juha Kesseli, Matti Nylter, and Kirsi J. Granberg

**Significance:** This study utilizes a computational approach to characterize the immune environments in glioblastoma and shows that glioblastoma immune microenvironments can be classified into three major subgroups, which are linked to typical glioblastoma alterations such as IDH mutation, NF1 inactivation, and CDK4-MARCH9 locus amplification.

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A RIPK3-PGE2 Circuit Mediates Myeloid-Derived Suppressor Cell–Potentiated Colorectal Carcinogenesis

Guifang Yan, Huakan Zhao, Qi Zhang, Yu Zhou, Lei Wu, Juan Lei, Xiang Wang, Jiangang Zhang, Xiao Zhang, Lu Zheng, Guangsheng Du, Wei Dong Xiao, Lei Wu, Hongming Miao, and Yongsheng Li

**Significance:** A novel signaling circuit involving RIPK3 and PGE2 enhances accumulation and immunosuppressive activity of MDSC, implicating its potential as a therapeutic target in anticancer immunotherapy.

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Macrophage-Derived Neuropilin-2 Exhibits Novel Tumor-Promoting Functions


**Significance:** Neuropilin-2 in macrophages promotes tumor growth by regulating efferocytosis of apoptotic tumor cells and orchestrating immune suppression.

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Inhibition of the Stromal p38MAPK/MK2 Pathway Limits Breast Cancer Metastases and Chemotherapy-Induced Bone Loss

Bhavna Murrali, Qihao Ren, Xianmin Luo, Douglas V. Faget, Chun Wang, Radia Marie Johnson, Tina Gruosso, Kevin C. Flanagan, Yujie Fu, Kathleen Leahy, Elise Alspach, Xinning Su, Michael H. Ross, Barry Burnette, Katherine N. Weilbaecher, Morag Park, Gabriel Mbalaviele, Joseph B. Monahan, and Sheila A. Stewart

**Significance:** Pharmacologically targeting the stromal p38MAPK-MK2 pathway limits metastatic breast cancer growth, preserves bone quality, and extends survival.

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Inhibition of Casein Kinase 2 Disrupts Differentiation of Myeloid Cells in Cancer and Enhances the Efficacy of Immunotherapy in Mice

Ayumi Hashimoto, Chan Gao, Jerome Mastio, Andrew Kossenkov, Scott I. Abrams, Ashok V. Purandare, Heshani Desilva, Susan Wee, John Hunt, Maria Jure-Kunkel, and Dmitry I. Gabrilovich

**Significance:** These findings demonstrate the modulatory effects of casein kinase 2 inhibitors on myeloid cell differentiation in the tumor microenvironment, which subsequently synergize with the antitumor effects of checkpoint inhibitor CTLA4.

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Discovery and Characterization of Dual Inhibitors of MDM2 and NFAT1 for Pancreatic Cancer Therapy

Wei Wang, Jiang-Jiang Qin, Sukesh Voruganti, Bhaviraya Nijampatnam, Sadanandan E. Vehu, Ke-He Ruan, Ming Hu, Jianwei Zhou, and Ruiwen Zhang

**Significance:** These findings suggest that pharmacological inhibition of both MDM2 and NFAT1 is a promising strategy for the treatment of pancreatic cancer, even in tumors lacking functional p53.
CONVERGENCE AND TECHNOLOGIES

5706 IFNγ PET Imaging as a Predictive Tool for Monitoring Response to Tumor Immunotherapy
Heather M. Gibson, Brooke N. McKnight, Agnes Malysa, Greg Dyson, Wendy N. Wiesend, Claire E. McCarthy, Joyce Reyes, Wei-Zen Wei, and Nerissa T. Viola-Villegas
Significance: This study presents a novel approach to monitor therapeutic outcomes via IFNγ-targeted positron emission tomography.

CORRECTION

5718 Correction: Targeting Vascular Endothelial-Cadherin in Tumor-Associated Blood Vessels Promotes T-cell–Mediated Immunotherapy

RETRACTION

5719 Retraction: Dicer Elicits Paclitaxel Chemosensitization and Suppresses Cancer Stemness in Breast Cancer by Repressing AXL
ABOUT THE COVER

The components and transcriptional targets of the canonical Wnt signaling pathway are frequently altered and serve as major oncogenic drivers in hepatocellular carcinoma. Zebrafish larvae emerged as unique models for studying early stage tumorigenesis due to their small size and optical transparency. In a triple transgenic zebrafish larva, fabp10a:TetOn; TRE:GAL4-VP16 expresses the inducible transactivator TetOn via the hepatocyte-specific promoter; TRE:ABC-P2A-tcf7l2 expresses human CTNNB1 carrying four typical mutations and zebrafish tcf7l2 ectopically in the zebrafish liver; TCFSiam:mCherry, a transcriptional reporter for canonical Wnt activity, labels the Wnt-responsive cells. Meanwhile, TRE:eGFP-KrasV12 conditionally activates Ras signaling. Together, the zebrafish larva displays significant hepatomegaly and severe hyperplasia within three days in doxycycline induction, with double oncogenic pathway activated. For details, see article by Yao and colleagues on page 5548.