BREAKING INSIGHTS

5129 Highlights from Recent Cancer Literature

REVIEWS

5131 Roles and Regulation of Long Noncoding RNAs in Hepatocellular Carcinoma
Lee Jin Lim, Samuel Y.S. Wong, Feiyang Huang, Sheng Lim, Samuel S. Chong, London Lucien Ooi, Oi Lian Kon, and Caroline G. Lee

5140 Value of Collaboration among Multi-Domain Experts in Analysis of High-Throughput Genomics Data
Daoud Meerzaman and Barbara K. Dunn

CANCER RESEARCH HIGHLIGHTS

5146 Targeting Semaphorin 4D in Cancer: A Look from Different Perspectives
Luca Tamagnone and Giulia Franzolin
See related article, p. 5328

5149 Stearoyl CoA Desaturase Regulates Ferroptosis in Ovarian Cancer Offering New Therapeutic Perspectives
Michele Carbone and Gerry Melino
See related article, p. 5355

PRIORITY REPORT

5151 miR-221 Targets QKI to Enhance the Tumorigenic Capacity of Human Colorectal Cancer Stem Cells
Junko Mukohyama, Taichi Isobe, Qingjiang Hu, Takanori Hayashi, Takashi Watanabe, Masao Maeda, Hisano Yanagi, Xin Qian, Kimihiro Yamashita, Hiromaru Minami, Koshi Mimori, Debashis Sahoo, Yoshihiro Kakeji, Akira Suzuki, Piero Dalerba, and Yohei Shimono
Significance: These findings uncover molecular mechanisms underlying the maintenance of cancer stem cell properties in colon cancer.

5159 ATMIN Is a Tumor Suppressor Gene in Lung Adenocarcinoma
Hanna Foster, E. Josue Ruiz, Christopher Moore, Gordon W.H. Stamp, Emma L. Nye, Ningning Li, Yihang Pan, Yulong He, Julian Downward, and Axel Behrens
Significance: These findings identify ATMIN as a tumor suppressor in LUAD; fragility at chr16q23 correlates with loss of ATMIN in human LUAD and deletion of Atmin increases tumor burden in a LUAD mouse model.

GENOME AND EPIGENOME

5167 Identification of Coding and Long Noncoding RNAs Differentially Expressed in Tumors and Preferentially Expressed in Healthy Tissues
Juan P. Unfried, Guillermo Serrano, Beatriz Suarez, Paloma Sangro, Valeria Ferretti, Celia Prior, Loreto Boix, Jordi Bruix, Bruno Sangro, Victor Segura, and Puri Fortes
Significance: Comprehensive analysis of coding and noncoding genes expressed in different tumors and normal tissues, which should be taken into account to predict side effects from potential coding and noncoding gene-targeting therapies.

5181 Banding Together: A Systematic Comparison of The Cancer Genome Atlas and the Mitelman Databases
Connor Denomy, Samuel Germain, Bjorn Haave, Frederick S. Vizeacoumar, Andrew Freywald, Beth A. Weaver, and Franco J. Vizeacoumar
Significance: A novel in silico approach compares cytogenetic data between the Mitelman database and TCGA, highlighting the advantages and limitations of both datasets.

METABOLISM AND CHEMICAL BIOLOGY

5191 Targeting Myeloperoxidase Disrupts Mitochondrial Redox Balance and Overcomes Cytarabine Resistance in Human Acute Myeloid Leukemia
Significance: These findings demonstrate the role of myeloperoxidase in the regulation of ROS levels and sensitivity of AML cells to cytarabine, an essential chemotherapeutic backbone in the therapy of AML.
MOLECULAR CELL BIOLOGY

5204 SF3B2-Mediated RNA Splicing Drives Human Prostate Cancer Progression
Norihiko Kawamura, Reisuke Nimura, Kotaro Saga, Aini Ishibashi, Koji Kitamura, Hiromichi Nagano, Yusuke Yoshikawa, Kyosho Ishida, Norio Nonomura, Mitsuhiro Arisawa, Jun Luo, and Yasufumi Kaneda

Significance: RNA splicing factor SF3B2 is essential for the generation of an androgen receptor (AR) variant that renders prostate cancer cells resistant to AR-targeting therapy.

5218 Mitochondrial NIX Promotes Tumor Survival in the Hypoxic Niche of Glioblastoma
Jinkyu Jung, Ying Zhang, Orieta Celiku, Wei Zhang, Hua Song, Brian J. Williams, Amber J. Giles, Jeremy N. Rich, Roger Abounader, Mark R. Gilbert, and Deric M. Park

Significance: NIX-mediated mitophagy regulates tumor survival in the hypoxic niche of glioblastoma microenvironment, providing a potential therapeutic target for glioblastoma.

5223 Phosphorylation of HSF1 by PIM2 Induces PD-L1 Expression and Promotes Tumor Growth in Breast Cancer
Tingting Yang, Chune Ren, Chao Lu, Pengyun Qiao, Xue Han, Li Wang, Dan Wang, Shijun Lv, Yonghong Sun, and Zhenhai Yu

Significance: These findings identify heat shock transcription factor 1 as a new substrate for PIM2 kinase and establish its role in breast tumor progression.

5245 CDK4 Regulates Lyosomal Function and mTORC1 Activation to Promote Cancer Cell Survival
Laia Martínez-Carreras, Julien Puyal, Lucia C. Leal-Esteban, Meritxell Orpinell, Judit Castilho-Armengol, Albert Giralt, Oleksandr Dergai, Catherine Moret, Valentin Barquissau, Anita Nasrallah, Angélique Pabois, Lianjun Zhang, Pedro Romero, Isabel C. Lopez-Mejia, and Iuïs Fajas

Significance: These findings uncover a novel function of CDK4 in lyosomal biology, which promotes cancer progression by activating mTORC1; targeting this function offers a new therapeutic strategy for cancer treatment.

5260 ZBTB7A Mediates the Transcriptional Repression Activity of the Androgen Receptor in Prostate Cancer
Dong Han, Sujun Chen, Wanting Han, Shuai Gao, Jude N. Owiredu, Muqing Li, Steven P. Balk, Housheng Hansen He, and Changmeng Cai

Significance: ZBTB7A is recruited to the EZF-Rb binding sites by AR and negatively regulates the transcriptional activity of E2F1 on DNA replication genes.

TUMOR BIOLOGY AND IMMUNOLOGY

5272 Serine-Phosphorylated STAT3 Promotes Tumorigenesis via Modulation of RNA Polymerase Transcriptional Activity
Jesse J. Balic, Daniel J. Garama, Mohamed I. Saad, Liang Yu, Alison C. West, Alice J. West, Thaleia Livis, Priithi S. Bhathal, Daniel J. Gough, and Brendon J. Jenkins

Significance: These findings reveal a new transcriptional role and mandatory requirement for constitutive STAT3 serine phosphorylation in gastric cancer.

5288 SRSF3-Regulated RNA Alternative Splicing Promotes Glioblastoma Tumorigenicity by Affecting Multiple Cellular Processes
Xiao Song, Xuechao Wan, Tianzhi Huang, Chang Zeng, Namratha Sastry, Bingli Wu, C. David James, Craig Horbinski, Ichiro Nakano, Wei Zhang, Bo Hu, and Shi-Yuan Cheng

Significance: SRSF3 is a significant regulator of glioma-associated alternative splicing, implicating SRSF3 as an oncogenic factor that contributes to the tumor biology of GBM.

5302 The Goldilocks Window of Personalized Chemotherapy: Getting the Immune Response Just Right
Derek S. Park, Mark Robertson-Tessi, Kimberley A. Luddy, Philip K. Maini, Michael B. Bonsall, Robert A. Gatenby, and Alexander R.A. Anderson

Significance: To maximize the synergy between chemotherapy and antitumor immune response, lymphodepleting therapy must be balanced in a "Goldilocks Window" of optimal dosing.

5316 Prolactin Promotes Fibrosis and Pancreatic Cancer Progression
Maruj Tandon, Gina M. Coudriet, Angela Crisicimanna, Mairobybs Soccoro, Mounnahed Elliswi, Asutor D. Singh, Zobaida Cruz-Monseerrate, Peter Bailey, Michael T. Lotze, Herbert Zeh, Jing Hu, Vincent Goffin, George K. Gittes, Andrew V. Biankin, and Farzad Esni

Significance: Prolactin is a key factor in the cross-talk between the stroma and neoplastic epithelium, functioning to promote fibrosis and PDAC progression.

5328 Antitumor Effects of Anti-Semaphorin 4D Antibody Unravel a Novel Proinvasive Mechanism of Vascular-Targeting Agents
Iratxe Zuazo-Gaztelu, Marta Paez-Ribes, Patricia Carrasco, Laura Martín, Adriana Soler, Mar Martínez-Lozano, Roser Pons, Judith Llena, Luis Palomero, Mariona Graupera, and Oriol Casanovas

Significance: An anti-semaphorin-4D vascular targeting agent demonstrates antitumor and prosurvival effects but also unravels a novel promalignant effect involving macrophage-derived SDF1 that promotes tumor invasion and metastasis, both in animal models and patients. See related commentary, p. 5146
Meflin+/
Early-stage cancer
Meflinlow/-/
Meflin+ PSCs or CAFs suppress PDAC progression by inhibiting ECM remodeling; they however give rise to Meflin-Positive Cancer-Associated Fibroblasts...α
SMA+ CAFs, which promote PDAC progression.

Stearoyl-CoA Desaturase 1 Protects Ovarian
In Vivo
SMA+ CAFs, which promote PDAC progression. α
Meflin
Meflinlow/-/
α
SMA+ CAFs

Advanced-stage cancer

Chemorefractory Disease and Metastasis
Neuroblastoma Provides New Insights into Antitumoral effects.
a subset of cancer-associated fibroblasts that exert antitumoral effects.

Meflin marks and functionally contributes to a subset of cancer-associated fibroblasts that exert antitumoral effects.

NR
H2O2 -
reactive group
+ −
H2O2

An activatable and cancer-targeted hydrogen peroxide probe enables photoacoustic molecular imaging, paving the way for visualization of hydrogen peroxide at high spatiotemporal resolution in living subjects.

This work presents an approach to sensitively, specifically, and quantitatively detect and localize native mRNA and protein interactions for analysis of abnormal post-transcriptional regulation in patient-derived archival tumor samples.

MALAT1 rs664589 Polymorphism Inhibits Binding to miR-194-5p, Contributing to Colorectal Cancer Risk, Growth, and Metastasis
Shenshen Wu, Hao Sun, Yajie Wang, Xi Yang, Qingtao Meng, Hongbao Yang, Haitao Zhu, Weiyan Tang, Shenshen Wu, Hao Sun, Yajie Wang, Xi Yang, Qingtao Meng, Hongbao Yang, Haitao Zhu, Weiyan Tang, Xiaobo Li, Michael Aschner, and Rui Chen

Significance: These findings highlight the functional role of MALAT1 polymorphism in colorectal cancer metastasis and survival as well as the underlying mechanism.

Systemic administration of an immuno-nanoparticle in a murine breast tumor model drives a robust tumor site-specific APC response by delivering two synergistic immune-potentiating molecules, highlighting the potential of nanoparticles for immunotherapy.

The combination of SCD1 inhibitors and ferroptosis inducers may provide a new therapeutic strategy for the treatment of ovarian cancer patients.

These findings highlight the functional role of MALAT1 polymorphism in colorectal cancer metastasis and survival as well as the underlying mechanism.

In Vivo Modeling of Chemoresistant Neuroblastoma Provides New Insights into Chemorefractory Disease and Metastasis

Significance: An in vivo mouse model of high-risk treatment-resistant neuroblastoma exhibits changes in the tumor microenvironment, widespread metastases, and sensitivity to JAK1/2 inhibition.
High Levels of C-Reactive Protein Are Associated with an Increased Risk of Ovarian Cancer: Results from the Ovarian Cancer Cohort Consortium


Significance: C-reactive protein is involved in ovarian carcinogenesis, and chronic inflammation may be particularly implicated in the etiology of mucinous and endometrioid carcinomas.

Curatopes Melanoma: A Database of Predicted T-cell Epitopes from Overly Expressed Proteins in Metastatic Cutaneous Melanoma

Christopher Lischer, Martin Eberhardt, Tanushree Jaitly, Cornelia Schinzel, Niels Schaft, Jan Dörrie, Gerold Schuler, and Julio Vera

Significance: A database is presented that predicts and scores antitumor T-cell epitopes, with a focus on tolerability and avoidance of severe autoimmunity, offering a supplementary epitope set for further investigation in immunotherapy.

Editor's Note: Estrogen Receptor α Promotes Breast Cancer by Reprogramming Choline Metabolism

Min Jia, Trygve Andreassen, Lasse Jensen, Tone Frost Bathen, Indranil Sinha, Hui Gao, Chunyan Zhao, Lars-Arne Haldosen, Yihai Cao, Leonard Gimita, Siver Andreas Moestue, and Karin Dahlman-Wright

Retraction: The Raf Inhibitor BAY 43-9006 (Sorafenib) Induces Caspase-Independent Apoptosis in Melanoma Cells

David J. Panka, Wei Wang, Michael B. Atkins, and James W. Mier
ABOUT THE COVER

Chemotherapeutic elimination (green) of the tumor is a complex challenge. Mathematical modeling of tumor-immune interactions reveals that optimal therapy, which may initially seem black and white, requires delicate navigation through a complex multidimensional landscape personalized to each patient. Cytotoxic efficacy (purple) must be balanced with supporting patient antitumor immune responses stimulated by lymphodepletion (blue). Optimal therapy treads an intermediate path (gold) that maintains dosing within a maximally effective window. The authors acknowledge the help of Dr. Chandler D. Gatenbee who provided coding expertise on the coloring for the image. For details, see article by Park and colleagues on page 5302.