BREAKING INSIGHTS

5461  Highlights from Recent Cancer Literature

REVIEWS

5463  Use of Natural Language Processing to Extract Clinical Cancer Phenotypes from Electronic Medical Records
Guergana K. Savova, Ioana Danciu, Folami Alamudun, Timothy Miller, Chen Lin, Danielle S. Bitterman, Georgia Tourassi, and Jeremy L. Warner

5471  Targeting Cancer Cell Metastasis by Converting Cancer Cells into Fat
Dana Ishay-Ronen and Gerhard Christofori

CANCER RESEARCH HIGHLIGHTS

5476  Genetics Helps to Find Synergy for Immune Checkpoint and Targeted Combination Therapies
Ludmila Prokunina-Olsson
See related article, p. 5482

5479  α-Particle–Emitter Radiopharmaceutical Therapy: Resistance Is Futile
George Sgouros
See related article, p. 5640

PRIORITY REPORT

5482  HDAC6 Inhibition Synergizes with Anti-PD-L1 Therapy in ARID1A-Inactivated Ovarian Cancer
Takeshi Fukumoto, Nail Fatkhutdinov, Joseph A. Zundell, Evgenii N. Teyganov, Timothy Nacarelli, Sergey Karakanhev, Shuai Wu, Qin Liu, Dmitry I. Gabrilovich, and Rugang Zhang
Significance: These findings offer a mechanistic rationale for combining epigenetic modulators and existing immunotherapeutic interventions against a disease that has been so far resistant to checkpoint blockade as a monotherapy.
See related commentary, p. 5476

GENOME AND EPIGENOME

5490  Genetic Variants Implicate Dual Oxidase-2 in Familial and Sporadic Nonmedullary Thyroid Cancer
Darrin V. Bann, Qunyan Jin, Kathryn E. Sheldon, Kenneth R. Houser, Lan Nguyen, Joshua I. Warrick, Maria J. Baker, James R. Broach, Glenn S. Gerhard, and David Goldenberg
Significance: This study provides novel insights into the genetic and molecular mechanisms underlying familial and sporadic thyroid cancers.

5500  Dynamics of Genomic, Epigenomic, and Transcriptomic Aberrations during Stepwise Hepatocarcinogenesis
Byul A. Jee, Ji-Hye Choi, Hyungjin Rhee, Sarah Yoon, So Mee Kwon, Ji Hae Nahm, Jeong Eun Yoo, Youngsic Jeon, Gi Hong Choi, Hyun Goo Woo, and Young Nyun Park
Significance: Multitomics profiling and integrative analyses of stepwise hepatocarcinogenesis reveal novel mechanistic and clinical insights into hepatocarcinogenesis.

MOLECULAR CELL BIOLOGY

5513  Macrophage ABHD5 Suppresses NFκB-Dependent Matrix Metalloproteinase Expression and Cancer Metastasis
Shenglan Shang, Xinnan Ji, Lili Zhang, Jun Chen, Chuan Li, Rongchen Shi, Wei Xiang, Xia Kang, Dapeng Zhang, Fan Yang, Ronggang Dai, Peng Chen, Shan Chen, Yonghuan Chen, Yongsheng Li, and Hongming Miao
Significance: These findings highlight the mechanism by which reduced expression of the metabolic enzyme ABHD5 in macrophages promotes cancer metastasis.

5527  A Biophysical Model Uncovers the Size Distribution of Migrating Cell Clusters across Cancer Types
Federico Bocci, Mohit Kumar Jolly, and José Nelson Onuchic
Significance: A biophysical model of cancer cell invasion integrates phenotypic heterogeneity and cell migration to interpret experimental observations of circulating tumor cell clusters and provides new predictions.
Chromosomal Instability and mTORC1 Activation through PTEN Loss Contribute to Proteotoxic Stress in Ovarian Carcinoma

M. Herman Chui, Sasha A. Doodnauth, Natalie Erdmann, Rodger E. Tiedemann, Fabrice Sircoulomb, Ronny Drapkin, Patricia Shaw, and Robert Rottapel

Significance: Chromosome instability and protein synthesis are important factors that determine the efficacy of proteotoxic stress-inducing agents, such as proteasome inhibitors, in the treatment of ovarian cancer.

Activation of Aryl Hydrocarbon Receptor by Kynurenine Impairs Progression and Metastasis of Neuroblastoma


Significance: These findings show that AHR may function as a tumor suppressor in childhood neuroblastoma, potentially influencing the aetiologic and therapeutic targeting of the disease.

SNAI1 Promotes the Cholangiocellular Phenotype, but not Epithelial–Mesenchymal Transition, in a Murine Hepatocellular Carcinoma Model

Meng Xu, Jingxiao Wang, Zhong Xu, Rong Li, Pan Wang, Runze Shang, Antonio Cigliano, Silvia Ribback, Antonio Solinas, Giovanni Mario Pes, Katja Evert, Haichuan Wang, Xinhua Song, Shu Zhang, Li Che, Rosa Maria Pascale, Diego Francesco Calvisi, Quingguang Liu, and Xin Chen

Significance: These findings report a new function of SNAI1 to promote cholangiocellular transdifferentiation instead of epithelial–mesenchymal transition in hepatocellular carcinoma.

Kras/ADAM17-Dependent Jag1-ICD Reverse Signaling Sustains Colorectal Cancer Progression and Chemoresistance

Maria Pelullo, Francesca Nardozza, Sabrina Zerna, Roberta Quaranta, Carmine Nicoletti, Zein Mersini Besharat, Maria Pia Felli, Brunar Cercelli, Giulia d’Amati, Rocco Palermo, Carlo Capalbo, Claudio Talora, Lucia Di Marcello, Giuseppe Giannini, Saula Checquollo, Isabella Sperandio, and Dina Bellavia

Significance: These findings present a novel role of the transcriptionally active Jag1-ICD fragment to confer and mediate some of the activity of oncogenic KRAS.

An Allosteric PRC2 Inhibitor Targeting EED Suppresses Tumor Progression by Modulating the Immune Response

Hongping Dong, Shaojun Liu, Xuejie Zhang, Sheng Chen, Lijing Kang, Yanni Chen, Shichao Ma, Xianlei Fu, Yanchao Liu, Hai-long Zhang, and Bin Zou

Significance: BR-001, a potent inhibitor of the EED subunit of the PRC2 complex, suppresses tumor progression by modulating the tumor microenvironment.

Drug Sensitivity Prediction Models Reveal a Link between DNA Repair Defects and Poor Prognosis in HNSCC

Paul B.M. Essers, Martijn van der Heijden, Caroline V.M. Verhagen, Emily M. Flegg, Reinout H. de Roest, C. René van der Aa, Ruud H. Brakenhoff, Michiel W.M. van den Brekel, Harry Bartelink, Marcel Verheij, and Conchita Vens

Significance: This study uses innovative machine learning-based approaches to derive models that predict the effect of DNA repair defects on treatment outcome in HNSCC.

Predictive Signatures Inform the Effective Repurposing of Decitabine to Treat KRAS–Dependent Pancreatic Ductal Adenocarcinoma

Carla Mottini, Hideo Tomihara, Diego Carrella, Alessia Lamolinara, Manuela Iezzi, Justin K. Huang, Carla A. Amoreo, Simonetta Buglioni, Isabella Manni, Frederic S. Robinson, Rosalba Minelli, Yan’an Kang, Jason B. Fleming, Michael P. Kim, Christopher A. Bristow, Daniella Trisciuoglio, Antonina Iuliano, Donatella Del Bufalo, Diego Di Bernardo, Davide Melisi, Giulio F. Draetta, Gennaro Caliberto, Alessandro Carugo, and Luca Cardone

Significance: Decitabine is a promising drug for cancer cells dependent on RAS signaling.

Neutrophil Extracellular Traps Drive Mitochondrial Homeostasis in Tumors to Augment Growth


Significance: Neutrophils through the release of NETs facilitate the growth of stressed cancer cells by altering their bioenergetics, the inhibition of which induces cell death.
Cellular and Genetic Determinants of the Sensitivity of Cancer to α-Particle Irradiation
Brian D. Yard, Priyanka Gopal, Kristina Dannik, Gerhard Siemeister, Urs B. Hagemann, and Mohamed E. Abazeed

Significance: These findings address limitations in the preclinical guidance and prediction of radionuclide tumor sensitivity by identifying intrinsic cellular and genetic determinants of cancer cell survival following exposure to α-particle irradiation.

See related commentary, p. 5479

Drugging MYCN Oncogenic Signaling through the MYCN-PA2G4 Binding Interface
Jessica Koach, Jessica K. Holien, Hassina Massudi, Daniel R. Carter, Olivia C. Giampa, Mika Herath, Taylor Lim, Janith A. Seneviratne, Giorgio Milazzo, Jayne E. Murray, Joshua A. McCarroll, Bing Liu, Chelsea Mayoh, Bryce Keenan, Brendan W. Stevenson, Michael A. Gorman, Jessica L. Bell, Larissa Doughty, Stefan Hüttelmaier, Andre Oberthuer, Matthias Fischer, Andrew J. Gifford, Tao Liu, Xiaohua Wan, Qi Wen Fan, Guido Reifenberger, and William A. Weiss

Significance: Competitive chemical inhibition of the PA2G4–MYCN protein interface provides a basis for drug design of small molecules targeting MYC and MYCN-binding partners in malignancies driven by MYC family oncoproteins.

PEG10 Promoter–Driven Expression of Reporter Genes Enables Molecular Imaging of Lethal Prostate Cancer
Mariya Shapovalova, John K. Lee, Yingming Li, Donald J. Vander Griend, Ilja M. Coleman, Peter S. Nelson, Scott M. Dehm, and Aaron M. LeBeau

Significance: PEG10 is expressed by prostate cancer with constitutively active AR-splice variants that can be exploited for noninvasive molecular imaging of this aggressive prostate cancer subtype.

Correction: EGFR Cooperates with EGFRvIII to Recruit Macrophages in Glioblastoma
Zhenyi An, Christiane B. Knobbe-Thomsen, Xiaohua Wan, Qi Wen Fan, Guido Reifenberger, and William A. Weiss

Correction: Upregulation of PD-L1 via HMGB1-Activated IRF3 and NF-κB Contributes to UV Radiation–Induced Immune Suppression
Wei Wang, Nicole M. Chapman, Bo Zhang, Mingqi Li, Mehrun Fan, R. Nicholas Laribee, M. Raza Zaidi, Lawrence M. Pfeffer, Hongbo Chi, and Zhao-Hui Wu

The fallopian tube precursor lesion for high-grade serous ovarian cancer is characterized by chromosomal instability and a high level of aneuploidy. Treatment of fallopian tube epithelial cells with inhibitors to Mps1 and CENP-E induces chromosomal instability and formation of "atypical mitoses," characterized by multipolar spindles, polar chromosomes, and lagging chromosomes during anaphase. The aneuploid post-mitotic cells incur proteotoxic stress and acquire sensitivity to proteasome inhibition. For details, see the article by Chui and colleagues on page 5536.