BREAKING ADVANCES

4999 Highlights from Recent Cancer Literature

REVIEWS

5001 p53: Protection against Tumor Growth beyond Effects on Cell Cycle and Apoptosis
Xuyi Wang, Evan R. Simpson, and Kristy A. Brown

5008 Antibody-Dependent Phagocytosis of Tumor Cells by Macrophages: A Potent Effector Mechanism of Monoclonal Antibody Therapy of Cancer
Nuray Gül and Marjolein van Egmond

5014 Mechanisms of Cancer Cell Dormancy—Another Hallmark of Cancer?
Albert C. Yeh and Sriraj G. Ramaswamy

PRIORITY REPORT

5023 Fluorophore-NanoLuc BRET Reporters Enable Sensitive In Vivo Optical Imaging and Flow Cytometry for Monitoring Tumorigenesis
Franz X. Schaub, Md. Shamim Reza, Colin A. Flaveny, Weimin Li, Adele M. Muscianti, Sany Hooda, Min Guo, John L. Cleveland, and Antonio L. Amelio
Précis: This study describes an extremely bright luciferase reporter that can enable highly sensitive, yet inexpensive methods for in vivo monitoring of small numbers of tumor cells, such as found at early metastatic sites, with greatly reduced image acquisition times.

MICROENVIRONMENT AND IMMUNOLOGY

5034 Chemotherapy Induces Programmed Cell Death-Ligand 1 Overexpression via the Nuclear Factor-κB to Foster an Immunosuppressive Tumor Microenvironment in Ovarian Cancer
Jin Peng, Junzo Hamanishi, Noriomi Matsumura, Kaoru Abiko, Kumuruz Murat, Tsukasa Baba, Ken Yamaguchi, Naoki Horikawa, Yuko Hosoe, Susan K. Murphy, Ikuo Konishi, and Masaki Mandai
Précis: These findings highlight the potential mechanisms by which obesity contributes to ovarian cancer metastatic success, with important implications for patient outcomes.

5056 Obesity Contributes to Ovarian Cancer Metastatic Success through Increased Lipogenesis, Enhanced Vascularity, and Decreased Infiltration of M1 Macrophages
Précis: These findings highlight the potential mechanisms by which obesity contributes to ovarian cancer metastatic success, with important implications for patient outcomes.

5068 Fibulin-5 Blocks Microenvironmental ROS in Pancreatic Cancer
Miao Wang, Mary Topalowski, Jason E. Toombs, Christopher M. Wright, Zachary R. Moore, David A. Boothman, Hiromi Yanagisawa, Huanmin Wang, Agnieszka Witkiewicz, Diego H. Castrillon, and Rolf A. Brekken
Précis: These findings reveal an integrin-based mechanism that attenuates ROS production and promotes cancer progression, with implications for a novel general strategy to reprogram the tumor microenvironment to improve therapeutic response.

5082 The CUL4B/AKT/β-Catenin Axis Restricts the Accumulation of Myeloid-Derived Suppressor Cells to Prohibit the Establishment of a Tumor-Permissive Microenvironment
Yanyan Qian, Jupeng Yuan, Huili Hu, QiFeng Yang, Jisheng Li, Shuqian Zhang, Baichun Jiang, Changshun Shao, and YaQin Gong
Précis: These surprising findings describe a previously uncharacterized antitumorigenic role for CUL4B in the hematopoietic system, where it restricts the accumulation and activity of myeloid-derived suppressor cells to prevent the establishment of a tumor permissive microenvironment, underscoring mechanisms by which immunosurveillance may be compromised by certain therapeutic strategies.
Serum Immunoregulatory Proteins as Predictors of Overall Survival of Metastatic Melanoma Patients Treated with Ipilimumab


Précis: These findings define the immunomodulatory factors CXCL11 and sMICA as predictive markers in melanoma patients least likely to benefit from treatment with the checkpoint inhibitor ipilimumab.

MOLECULAR AND CELLULAR PATHOBIOLOGY

Checkpoint Kinase 2 Negatively Regulates Androgen Sensitivity and Prostate Cancer Cell Growth

Huy Q. Ta, Melissa L. Ivey, Henry F. Frierson Jr, Mark R. Conaway, Jaroslaw Dziegielewski, James M. Larner, and Daniel Gioeli

Précis: This study illuminates a DNA damage response pathway that intersects with the G2–M cell-cycle checkpoint to influence the development of castration-resistance prostate cancer, with potential implications for its treatment.

THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

Generation of a Selective Small Molecule Inhibitor of the CBF/p300 Bromodomain for Leukemia Therapy

Sarah Picaut, Oleg Fedorov, Angeliki Thanassopoulou, Katharina Leonards, Katherine Jones, Julia Meier, Heidi Olzscha, Octavio Monteiro, Sarah Martin, Martin Philpott, Anthony Tumber, Panagis Filippakopoulos, Clarence Yapp, Christopher Wells, Ka Hing Che, Andrew Bannister, Samuel Robson, Umesh Kumar, Nigel Parr, Kevin Lee, Dave Iugo, Philip Jeffrey, Simon Taylor, Matteo L. Yecellio, Chas Bountra, Paul E. Brennan, Alison O’Mahony, Sharlene Velichko, Susanne Müller, Duncan Hay, Danette L. Daniels, Marjeta Urh, Nicholas B. La Thangue, Tony Kouzarides, Rab Prinjha, Jürg Schwaller, and Stefan Knapp

Précis: These findings highlight a mechanistically potent strategy to inhibit a histone acetyltransferase that impairs self-renewal of leukemic cells, with implications to improve current treatment approaches for aggressive leukemias.

Hyperthermia Selectively Targets Human Papillomavirus in Cervical Tumors via p53-Dependent Apoptosis

Arlene L. Oei, Caspar M. van Leeuwen, Rosemarie ten Cate, Hans M. Rodermond, Marijke R. Buist, Lukas J. A. Stalpen, Johannes Crezee, H. Petra Kok, Jan Paul Medema, and Nicolaas A.P. Franken

Précis: These findings reveal mechanistic insights underlying the response of HPV-positive cervical cancers to hyperthermia therapy, with immediate implications for patient outcomes.

Naturally Occurring Isothiocyanates Exert Anticancer Effects by Inhibiting Deubiquitinating Enzymes

Ann P. Lawson, Marcus J.C. Long, Rory T. Coffey, Yu Qian, Eranthie Weerapan, Fadil El Oualid, and Lizbeth Hedstrom

Précis: This study offers a novel unifying mechanism to understand the cancer-fighting properties of a class of natural compounds found in broccoli and other cruciferous vegetables that might help fight a variety of diseases characterized by inflammatory pathology.

WDR5 Supports an N-Myc Transcriptional Complex That Drives a Protumorigenic Gene Expression Signature in Neuroblastoma

Yuting Sun, Jessica L. Bell, Daniel Carter, Samuele Gherardi, Rebecca C. Poulos, Giorgio Milazzo, Jason W.H. Wong, Rima Al-Awar, Andrew E. Tee, Pei Y. Liu, Bing Liu, Bernard Atmadibrata, Matthew Wong, Toby Trahair, Quan Zhao, Jason M. Shohet, Ygal Haupt, Johannes H. Schulte, Peter J. Brown, Cheryl H. Arrowsmith, Masoud Vedadi, Karen L. MacKenzie, Stefano Hettlmaier, Giovanni Petini, Glenn M Marshall, Antony Brailthwaite, and Tao Liu

Précis: These results identify the histone methylation regulator WDR5 as a key cofactor for N-Myc-driven transcriptional activation and tumorigenesis, offering evidence of its candidacy as a novel therapeutic target for MYCN-amplified neuroblastomas.
ATDC/TRIM29 Drives Invasive Bladder Cancer Formation through miRNA-Mediated and Epigenetic Mechanisms
Phillip L. Palmbos, Lidong Wang, Huibin Yang, Yin Wang, Jacob Leflein, McKenzie L. Ahmet, John E. Wilkinson, Chandan Kumar-Sinha, Gina M. Ney, Scott A. Tomlins, Stephanie Daignault, Lakshmi P. Kunju, Xue-Ru Wu, Yair Lotan, Monica Liebert, Mats E. Ljungman, and Diane M. Simeone

Précis: Identification of a novel oncogenic driver of bladder carcinogenesis introduces a candidate biomarker and therapeutic target in a setting that has not kept pace with progress made in other cancers.

Correction: CD38 in Hairy Cell Leukemia Is a Marker of Poor Prognosis and a New Target for Therapy

About the Cover
CBP/p300 is functionally implicated in the progression of multiple hematological malignancies. Picaud and colleagues developed a new selective and highly potent chemical probe I-CBP112 targeting the bromodomains of CBP/p300. Treatment of human acute myeloid leukemia (AML) cells growing in methylcellulose with 1, 3, and 5 µmol/L of the compound reduced the clonogenic growth of the cells in a dose-dependent manner. Cytospin preparations of I-CBP112-treated primary AML blasts showed morphologic signs of differentiation. For details, see article by Picaud and colleagues on page 5106.