REVIEWS

2709  Stalling the Engine of Resistance: Targeting Cancer Metabolism to Overcome Therapeutic Resistance
Ethan B. Butler, Yuhua Zhao, Cristina Muñoz-Pinedo, Jianrong Lu, and Ming Tan

2718  Animal Models of Human Prostate Cancer: The Consensus Report of the New York Meeting of the Mouse Models of Human Cancers Consortium Prostate Pathology Committee

PERSPECTIVE

2737  The Emerging "Hallmarks" of Metabolic Reprogramming and Immune Evasion: Distinct or Linked?
Irina Kareva and Philip Hahnfeldt

PRIORITY REPORT

2743  A Model of Postsurgical Advanced Metastatic Breast Cancer More Accurately Replicates the Clinical Efficacy of Antiangiogenic Drugs
Eric Guerin, Shan Man, Ping Xu, and Robert S. Kerbel

Precis: This important study provides the first glimpse of a paradigm shift in preclinical mouse models that can more reliably predict the clinical efficacy of new drugs, based on evaluation of new drugs in mice with macroscopic metastases seeded by a primary tumor that had been surgically resected.

CLINICAL STUDIES

2749  Drug–Gene Modeling in Pediatric T-Cell Acute Lymphoblastic Leukemia Highlights Importance of 6-Mercaptopurine for Outcome
Alex H. Beesley, Martin J. Firth, Denise Anderson, Amy L. Samuels, Jette Ford, and Ursula R. Kees

Precis: Methodologies developed in this study might be applied to other cancers to achieve patient stratification at the time of diagnosis.

INTEGRATED SYSTEMS AND TECHNOLOGIES

2760  Spreaders and Sponges Define Metastasis in Lung Cancer: A Markov Chain Monte Carlo Mathematical Model
Paul K. Newton, Jeremy Mason, Kelly Bethel, Lyudmila Bazhenova, Jorge Nieva, Larry Norton, and Peter Kuhn

Precis: Multidirectional cancer progression in patients is a systemic process whose pathways are largely determined by the stochastic nature of the first metastatic site to which it spreads.

MICROENVIRONMENT AND IMMUNOLOGY

2770  Fibroblast-Specific Protein 1/S100A4–Positive Cells Prevent Carcinoma through Collagen Production and Encapsulation of Carcinogens
Jinhua Zhang, Lin Chen, Xiaoman Liu, Thomas Kammertoens, Thomas Blankenstein, and Zhihai Qin

Precis: This interesting study shows how fibroblasts can act to prevent epithelial tumor development triggered by carcinogen exposure.

2782  CSF1R Signaling Blockade Stanches Tumor-Infiltrating Myeloid Cells and Improves the Efficacy of Radiotherapy in Prostate Cancer
Jingying Xu, Jemima Escamilla, Stephen Mok, John David, Saul Priceman, Brian West, Gideon Bollag, William McBride, and Lily Wu

Precis: Findings suggest that CSF1 inhibitors being evaluated in clinical trials should be tested in combination with radiotherapy based on their ability to thwart the function of tumor-infiltrating myeloid cells that are increased by radiotherapy and limit its efficacy.
CHD1 Is a 5q21 Tumor Suppressor Required for ERG Rearrangement in Prostate Cancer
Lia Burkhardt, Sarah Fuchs, Antje Krohn, Sawinee Masser, Malte Mader, Martina Kluth, Frederik Bachmann, Hartwig Huland, Thomas Steuber, Markus Graeven, Thorsten Schlomm, Sarah Minner, Guido Sauter, Husayn Sirma, and Ronald Simon

Précis: Seminal findings identify a key epigenetic driver in advanced prostate cancers that by recruiting mutated forms of the androgen receptor drives ERG fusion-independent forms in this deadly disease.

Deficiency of Phospholipase A2 Group 7 Decreases Intestinal Polyposis and Colon Tumorigenesis in ApcMin/+ Mice
Changxin Xu, Ethan C. Reichert, Tomoyuki Nakano, Mariah Lohse, Alison A. Gardner, Mónica P. Revelo, Matthew K. Topham, and Diana M. Stafforini

Précis: Deficiency in a phospholipase A2 that participates in inflammatory responses inhibits colon tumorigenesis and may be a novel target for reprogramming inflammation as a strategy for therapeutic intervention.

The Major Reverse Transcriptase–Incompetent Splice Variant of the Human Telomerase Protein Inhibits Telomerase Activity but Protects from Apoptosis
Imke Listerman, Jie Sun, Francesca S. Gazzaniga, Jason L. Lukas, and Elizabeth H. Blackburn

Précis: Results reveal that a major hTERT splice variant can confer a growth advantage to cancer cells independent of telomere maintenance, suggesting hTERT makes multiple contributions to cancer pathophysiology.

TNRC9 Downregulates BRCA1 Expression and Promotes Breast Cancer Aggressiveness

Précis: This potentially seminal study unveils a new paradigm in regulation of BRCA1 that may advance evidence that its epigenetic regulation contributes widely to the development of sporadic breast cancers where BRCA genes are unmutated.

An Essential Requirement for the SCAP/SREBP Signaling Axis to Protect Cancer Cells from Lipotoxicity

Précis: Findings suggest that the differential between a tumor’s ability to synthesize and desaturate fatty acids might stratify cancer patient populations that could respond strongly to inhibitors of fatty acid metabolism.

Genomic Aberrations Occurring in Subsets of Serrated Colorectal Lesions but not Conventional Adenomas

Précis: Findings suggest that a newly characterized type of colorectal polyp, termed a sessile-serrated polypl, may be an important precursor for a significant number of colorectal cancers.
High-Throughput Tyrosine Kinase Activity Profiling Identifies FAK as a Candidate Therapeutic Target in Ewing Sarcoma

Brian D. Crompton, Anne L. Carlton, Aaron R. Thorner, Amanda L. Christie, Jinyan Du, Monica L. Calicchio, Miguel N. Rivera, Mark D. Fleming, Nancy E. Kohl, Andrew L. Kung, and Kimberly Stegmaier

Precise: By leveraging a kinase profiling approach to identify new targets, this study identified and validated a druggable target in a well-studied disease where clinical management remains problematic.

Prooncogenic Factors miR-23b and miR-27b Are Regulated by Her2/Neu, EGF, and TNF-α in Breast Cancer

Lianjin Jin, Oliver Wessely, Eric G. Marcusson, Cristina Ivan, George A. Calin, and Suresh K. Alahari

Precise: Her2/Neu oncogene is highly expressed in 30% of breast cancers, and this study reveals how Her2 regulates the tumor suppressor Nischarin in breast cancer via miRNA expression.

Hepatocarcinogenesis Driven by GSNOR Deficiency Is Prevented by iNOS Inhibition

Chi-Hui Tang, Wei Wei, Martha A. Hanes, and Limin Liu

Precise: This important study offers preclinical proof that iNOS inhibitors can be used to attack liver cancers driven by uncontrolled nitrosative stress, possibly offering an effective therapeutic approach for some liver cancer patients.

ATIP3, a Novel Prognostic Marker of Breast Cancer Patient Survival, Limits Cancer Cell Migration and Slows Metastatic Progression by Regulating Microtubule Dynamics


Precise: As a clinically validated target for cancer drug development, microtubules offer a focus to expand the armamentarium of possible approaches to attack malignant disease.

Activation of HIF2α in Kidney Proximal Tubule Cells Causes Abnormal Glycogen Deposition but not Tumorigenesis

Leiping Fu, Gang Wang, Maria M. Shevchuk, David M. Nanus, and Lorraine J. Gudas

Precise: One of two factors thought to be causative in driving formation of clear cell renal cancers does not appear to be relevant when examined in a tissue-relevant mouse model, challenging an existing orthodoxy.

Interactions of Abiraterone, Eplerenone, and Prednisolone with Wild-Type and Mutant Androgen Receptor: A Rationale for Increasing Abiraterone Exposure or Combining with MDV3100—Letter

David End, Arturo Molina, Mary Todd, and Michael L. Meyers

ABOUT THE COVER

Fluorescence in-situ hybridization (FISH) analysis using an ERG break-apart probe in LNCaP prostate cancer cells with three copies of chromosome 21. The intact ERG loci at 21q22.3 is shown by three pairs of adjacent red and green FISH signals, corresponding to the 5’ and 3’ ends of the ERG gene, per blue cell nucleus. ERG rearrangement, as indicated by separate red and green FISH signals, resulting from intragenic breakage and translocation of part of the ERG gene in the cell nucleus at the bottom of the picture, was induced by treating the cells with doxorubicin and dihydrotestosterone. Inactivation of chromodomain helicase DNA-binding protein 1 (CHD1) by genomic deletion of its gene locus at chromosome 5q21 attenuates androgen receptor (AR) signaling and impairs formation of AR-dependent ERG rearrangements in prostate cancer. For details, see article by Burkhardt and colleagues on page 2795.
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