Highlights from Recent Cancer Literature

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

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

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

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

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

Spreadsers 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

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

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

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.
MOLECULAR AND CELLULAR
PATHOBIOLOGY

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 Graefen,
Thorsten Schlomm, Sarah Minner, Guido Sauter,
Huseyin 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.

Dynamics of Senescent Cell
Formation and Retention Revealed
by p14ARF Induction in the Epidermis
Ronit Tokarsky-Amiel, Narmen Azazmeh,
Aharon Helman, Yan Stein, Alia Hassan,
Alexander Maly, and Ittai Ben-Porath

Précis: Studies in a novel mouse model deepen
insights into the dynamics of cellular
senescence, a central mechanism of tumor
suppression.

TNRC9 Downregulates BRCA1
Expression and Promotes Breast
Cancer Aggressiveness
Jingxuan Shan, Shoba P. D Souza,
Sasha Bakhru, Eman K. Al-Azwani,
Maria L. Asciero, Kunduru S. Sastry,
Shahinaz Bedri, Dhanya Kizhakayil,
Idil I. Aigha, Joel Malek, Issam Al-Bozom,
Salah Gehani, Stacia Furtado,
Edith Mathiowitz, Ena Wang,
Francesco M. Marincola, and Lotfi Choucahne

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
Kevin J. Williams, Joseph P. Argus, Yue Zhu,
Moses Q. Wilks, Beth N. Marbois,
Autumn G. York, Yoko Kidani,
Alexandra L. Pourzia, David Ahkavan,
Dominique N. Lisiero,
Evangelia Komisopoulou, Amy H. Henkin,
Horacio Soto, Brian T. Chamberlain,
Laurent Vergnes, Michael E. Jung,
Jorge Z. Torres, Linda M. Liau,
Heather R. Christofk, Robert M. Prins,
Paul S. Mischel, Karen Reue,
Thomas G. Graeber, and Steven J. Bensinger

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.

PREVENTION AND EPIDEMIOLOGY

Genomic Aberrations Occurring in
Subsets of Serrated Colorectal Lesions
but not Conventional Adenomas
Andrea N. Burnett-Hartman, Polly A. Newcomb,
John D. Potter, Michael N. Passarelli,
Amanda L. Phipps, Michelle A. Wurscher,
William M. Grady, Lee-Ching Zhu,
Melissa P. Upton, and Karen W. Makar

Précis: Findings suggest that a newly
characterized type of colorectal poly, termed a
sessile-serrated poly, may be an important
precursor for a significant number of colorectal
cancers.
**THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY**

2873 | **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

*Précis:* 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.

2884 | **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

*Précis:* 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.

2897 | **Hepatocarcinogenesis Driven by GSNOR Deficiency Is Prevented by iNOS Inhibition**
Chi-Hui Tang, Wei Wei, Martha A. Hanes, and Limin Liu

*Précis:* 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.

**LETTER TO THE EDITOR**

2926 | **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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