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Cancer Research

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Eric Guerin, Shan Man, Ping Xu, and Robert S. Kerbel
Précis: 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

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Alex H. Beesley, Martin J. Firth, Denise Anderson, Amy L. Samuels, Jette Ford, and Ursula R. Kees
Précis: 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
Précis: 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
Précis: 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
Précis: 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.

2795 | **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, Hüseyin 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.

2806 | **Deficiency of Phospholipase A₂ Group 7 Decreases Intestinal Polyposis and Colon Tumorigenesis in *Apc^{Min/+}* 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.

2817 | **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.

2829 | **Dynamics of Senescent Cell Formation and Retention Revealed by p14^{ARF} 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.

2840 | **TNRC9 Downregulates BRCA1 Expression and Promotes Breast Cancer Aggressiveness**

Jingxuan Shan, Shoba P. DSouza, Sasha Bakhru, Eman K. Al-Azwani, Maria L. Ascierto, Konduru 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 Chouchane

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.

2850 | **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 Akhavan, 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

2863 | **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 I. 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 polyp, termed a sessile-serrated polyp, 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.

TUMOR AND STEM CELL BIOLOGY

2905 **ATIP3, a Novel Prognostic Marker of Breast Cancer Patient Survival, Limits Cancer Cell Migration and Slows Metastatic Progression by Regulating Microtubule Dynamics**

Angie Molina, Lauriane Velot, Lydia Ghouinem, Mohamed Abdelkarim, Benjamin Pierre Bouchet, Anny-Claude Luissint, Imène Bouhlel, Marina Morel, Elène Sapharikas, Anne Di Tommaso, Stéphane Honoré, Diane Braguer, Nadège Gruel, Anne Vincent-Salomon, Olivier Delattre, Brigitte Sigal-Zafrani, Fabrice André, Benoit Terris, Anna Akhmanova, Mélanie Di Benedetto, Clara Nahmias, and Sylvie Rodrigues-Ferreira

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

2916 **Activation of HIF2 α 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

Précis: 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.

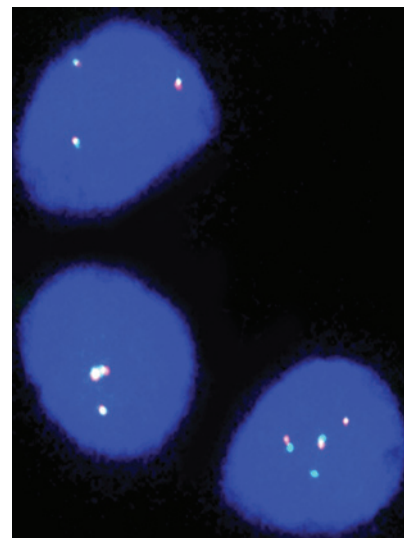
LETTER TO THE EDITOR

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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