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**Microenvironment and Immunology**

2743 | 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.
CHD1 Is a 5q21 Tumor Suppressor Required for ERG Rearrangement in Prostate Cancer
Lia Burkhardt, Sarah Fuchs, Antje Krohn, Sawinee Masser, Malte Mader, Martina Kloth, Frederik Bachmann, Hartwig Huland, Thomas Steuber, Markus Graefen, Thorsten SchloMann, Sarah Minner, Guido Sauter, Huseyin Sirma, and Ronald Simon

Precis: 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

Precis: 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

Precis: 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 pathobiology.

TNRC9 Downregulates BRCA1 Expression and Promotes Breast Cancer Aggressiveness

Precis: 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

Precis: 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

Precis: 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

**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.

### TUMOR AND STEM CELL BIOLOGY

**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 Iván, 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.

### LETTER TO THE EDITOR

**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

**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 Ghoubnem, Mohamed Abdelkarim, Benjamin Pierre Bouchet, Anny-Claude Luissant, Imène Bouhélé, Marina Morel, Eléne Sapharikas, Anne Di Tommaso, Stéphane Honoré, Diane Bragaer, Nadège Gruel, Anne Vincent-Salomon, Olivier Delattre, Brigitte Sigal-Zafrani, Fabrice André, Benoît Terris, Anna Akhmanova, Mélanie Di Benedetto, Clara Nahmis, and Sylvie Rodrigues-Ferreira

**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.

### 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.