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Samuel Eisenstein, Brian A. Coakley, Karen Briley-Saebo, Ge Ma, Hui-ming Chen, Marcia Meseck, Stephen Ward, Celia Divino, Savio Woo, Shu-Hsia Chen, and Ping-Ying Pan

PRÉCIS: This preclinical study highlights the efficacy of a specific myeloid cell type to serve as a key delivery vehicle for oncolytic viruses that significantly improves tumor killing, prolonging survival and minimizing toxicity.

5016  TGF-β Modulates Ovarian Cancer Invasion by Upregulating CAF-Derived Versican in the Tumor Microenvironment
Tsz-Lun Yeung, Cecilia S. Leung, Kwong-Kwok Wong, Goli Samimi, Melissa S. Thompson, Jinsong Liu, Tarrik M. Zaid, Sue Ghosh, Michael J. Birrer, and Samuel C. Mok

PRÉCIS: These findings suggest a central mechanism through which TGF-β-targeted therapies may alter the invasive capacity of cancer cells by acting through their microenvironment.

MOLECULAR AND CELLULAR PATHOBIOLOGY
5029  Gene Profiling of Canine B-Cell Lymphoma Reveals Germinal Center and Postgerminal Center Subtypes with Different Survival Times, Modeling Human DLBCL
Kristy L. Richards, Alison A. Motsinger-Reif, Hsiao-Wei Chen, Yuri Fedoriw, Cheng Fan, Dahlia M. Nielsen, George W. Small, Rachael Thomas, Chris Smith, Sandeep S. Dave, Charles M. Perou, Matthew Breen, Luke B. Borst, and Steven E. Suter

PRÉCIS: This study reveals the remarkable molecular similarity between human and canine forms of a certain type of B-cell lymphoma, overcoming limitations in existing models that have impeded the advancement of etiologic and therapeutic insights.
DDB2: A Novel Regulator of NF-κB and Breast Tumor Invasion
Marie Emen, Rémi Klotz, Nadège Touche, Sophie Pinel, Claire Barbieux, Vanessa Besancenot, Emilie Brunner, Denise Thiebaut, Alain C. Jung, Sonia Ledrappier, Lionel Domenjoud, Joseph Abecassis, François Plénat, Stéphanie Grandemange, and Philippe Becuwe

Precisé: A DNA repair protein that also participates in the control of cell cycle and transcription is found to exert profound effects on the invasive behavior of breast cancer cells, defining a new function for this protein and suggesting further investigations into its potential as a prognostic factor and therapeutic target.

EGF Receptor Activates MET through MAPK to Enhance Non–Small Cell Lung Carcinoma Invasion and Brain Metastasis
Jessica L. Breindel, Jonathan W. Haskins, Elizabeth P. Cowell, Minghui Zhao, Don X. Nguyen, and David F. Stern

Precisé: These results show how EGFR–MET signaling is critical for aggressive behavior in lung adenocarcinomas and rationalize its continued investigation as a therapeutic target in NSCLC, whether tumors harbor wild-type or mutant EGFR at early stages of progression.

Regulation of the Transcriptional Coactivator FHL2 Licenses Activation of the Androgen Receptor in Castrate-Resistant Prostate Cancer
Meagan J. McGrath, Lauren C. Binge, Absorn Sriratana, Hong Wang, Paul A. Robinson, David Pook, Clare G. Fedele, Susan Brown, Jennifer M. Dyson, Denny L. Cottle, Belinda S. Cowling, Birunthi Niranjan, Gail P. Risbridger, and Christina A. Mitchell

Precisé: This potentially seminal paper not only provides insights into how the androgen receptor is activated in advanced prostate cancer but also offers broader import because the mechanism discovered may affect other oncogenic transcription factors that drive different human cancers.

Extracellular RNA Liberates Tumor Necrosis Factor-α to Promote Tumor Cell Trafficking and Progression
Silvia Fischer, Sabine Gesierich, Barbara Griersheimer, Anne Schänzer, Till Acker, Hellmut G. Augustin, Anna-Karin Olsson, and Klaus T. Preisner

Precisé: These findings establish crucial functions for extracellular RNA released from tumor cells in driving invasion and progression, and suggest in vivo applications for RNase1 as a provocative therapeutic approach.

Critical Tumor Suppressor Function Mediated by Epithelial Mig-6 in Endometrial Cancer
Tae Hoon Kim, Dong-Kee Lee, Sung-Nam Cho, Grant D. Orvis, Richard R. Behringer, John P. Lydon, Bon Jeong Ku, Adrienne S. McCampbell, Russell R. Broaddus, and Jae-Wook Jeong

Precisé: This study provides insights into how progesterone prevents endometrial cancer, a long-standing question for which mechanistic knowledge might advance thinking about how to use this hormone in treatment.

Acquired Expression of NFATc1 Downregulates E-Cadherin and Promotes Cancer Cell Invasion
Tsukasa Oikawa, Atsuko Nakamura, Nobuyuki Onishi, Taketo Yamada, Koichi Matsuo, and Hideyuki Saya

Precisé: Carcinoma cells that switch on expression of an important hematopoietic transcription factor acquire new capacities for invasive movement and growth.

14-3-3 Proteins Modulate the ETS Transcription Factor ETV1 in Prostate Cancer
Sangphil Oh, Sook Shin, Stan A. Lightfoot, and Ralf Janknecht

Precisé: This article provides mechanistic insight into the pathophysiology of multiple tumors, including prostate cancer and melanomas.

The DREAM Complex Mediates GIST Cell Quiescence and Is a Novel Therapeutic Target to Enhance Imatinib-Induced Apoptosis
Sergei Boichuk, Joshua A. Parry, Kathleen R. Makieški, Larisa Litovchick, Julianne L. Baron, James P. Zewe, Agnieszka Woźniak, Keith R. Mehall, Nina Korzeniewski, Danushka S. Seneviratne, Patrick Schoißfi, Maria Debier-Rychter, James A. DeCaprio, and Anette Duensing

Precisé: Dissecting the molecular pathways that lead to tumor cell quiescence after targeted therapies leads to novel treatment strategies that potentially can extend survival.

Reprogramming the Chromatin Landscape: Interplay of the Estrogen and Glucocorticoid Receptors at the Genomic Level
Tina B. Miranda, Ty C. Yoss, Myong-Hee Sung, Songjoon Baek, Sam John, Mary Hawkins, Lars Granstedt, R. Louis Schiltz, and Gordon L. Hager

Precisé: These results define an epigenetic mechanism that can explain how the estrogen and glucocorticoid receptors can dictate the binding patterns of other steroid receptors across the genome.
**RHPN2 Drives Mesenchymal Transformation in Malignant Glioma by Triggering RhoA Activation**  
Carla Danussi, Uri David Akavia, Francesco Niola, Andreja Jovic, Anna Lasorella, Dana Pe’er, and Antonio Iavarone

Précis: These results identify a key genetic module promoting the most aggressive cancer phenotype in glioblastoma patients, leading to the worst outcomes.

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**PREVENTION AND EPIDEMIOLOGY**

**A Sequence Polymorphism in miR-608 Predicts Recurrence after Radiotherapy for Nasopharyngeal Carcinoma**  
Jian Zheng, Jieqiong Deng, Mang Xiao, Lei Yang, Liyuan Zhang, Yonghe You, Min Hu, Na Li, Hongchun Wu, Wei Li, Jiachun Lu, and Yifeng Zhou

Précis: A single-nucleotide polymorphism in a microRNA that affects chromatid break repair can predict clinical outcomes after radiotherapy in nasopharyngeal cancer, with potentially broader implications for other DNA damaging cancer therapies.

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**Gleason Grade Progression Is Uncommon**  

Précis: These findings suggest that prostate tumor grade may be established early in tumorigenesis, with one implication being that patients newly diagnosed with early-stage and lower-grade disease may feel more comfortable on an active surveillance protocol.

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**THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY**

**A Novel Class of Anticancer Compounds Targets the Actin Cytoskeleton in Tumor Cells**  

Précis: This study offers a preclinical proof of concept for small molecules that target the actin cytoskeleton of cancer cells as an efficacious treatment strategy.

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**RG7116, a Therapeutic Antibody That Binds the Inactive HER3 Receptor and Is Optimized for Immune Effector Activation**  
Christian Mirschberger, Christian B. Schiller, Michael Schraml, Nikolaos Dimoudis, Thomas Friess, Christian A. Gerdes, Ulrike Reiff, Valeria Lifke, Gabriele Hoelzlswimmer, Irene Kolm, Karl-Peter Hopfner, Gerhard Niederfellner, and Birgit Bossenmaier

Précis: As a central integrator of the EGF family receptor system in cancer, HER3 offers an appealing therapeutic target in many types of human cancer.

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**Inhibitor-Sensitive FGFR2 and FGFR3 Mutations in Lung Squamous Cell Carcinoma**  

Précis: These findings provide a rationale to target certain lung or head and neck squamous cell carcinomas with FGFR inhibitors that are currently in clinical trials, possibly identifying patient populations that may benefit the most.

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**Cotargeting Androgen Receptor and Clusterin Delays Castrate-Resistant Prostate Cancer Progression by Inhibiting Adaptive Stress Response and AR Stability**  
Hiroaki Matsumoto, Yoshiaki Yamamoto, Masaki Shiota, Hidetoshi Kuruma, Eliana Beraldi, Hideyasu Matsuyama, Amina Zoubedi, and Martin Gleave

Précis: This study offers a mechanism-based strategy to leverage the therapeutic effects of androgen receptor antagonists in advanced prostate cancer, which remains a deadly scourge.

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**mTOR Signaling Feedback Modulates Mammary Epithelial Differentiation and Restrains Invasion Downstream of PTEN Loss**  
Susmita Ghosh, Lidenys Varela, Akshay Sood, Ben Ho Park, and Tamara L. Lotan

Précis: This report suggests additional new cautions regarding the use of mTOR inhibitors for cancer treatment, contributing to ongoing controversies about their potential utility.
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ABOUT THE COVER

The actin cytoskeleton, due to its role in many processes involved in cellular transformation, has long been a sought after anticancer target, yet attempts to develop such compounds have been hampered by unacceptable toxicity. By targeting the other core polymer system of the microfilaments, tropomyosin, it is possible to discriminate between actin filaments required for sarcomeric function and those required for tumor growth. In silico modeling shows the predicted association of the first in class anti-tropomyosin compound, TR100, with the C-terminus of a cancer-associated tropomyosin, Tm5NM1. The interaction between Tm5NM1 and TR100 results in disruption of actin filament organization and death of tumor cells, both in vitro and in vivo. For details, see article by Stehn and colleagues on page 5169.