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<td>Highlights from Recent Cancer Literature</td>
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<td>Micronuclei Frequency in Tumors Is a Predictive Biomarker for Genetic Instability and Sensitivity to the DNA Repair Inhibitor AsiDNA</td>
<td>Wael Iidey, Sylvain Thierry, Tatiana Popova, Marc-Henri Stern, and Marie Dutreix</td>
<td>These findings identify RGS12 as a novel tumor suppressor gene in prostate cancer in African Americans, which may serve as an important prognostic marker and therapeutic target.</td>
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<td>Smurf2-Mediated Stabilization of DNA Topoisomerase II Controls Genomic Integrity</td>
<td>Andrea Emanuelli, Aurora P. Borroni, Liat Apel-Sand, Pooja A. Shah, Dhanoop Manikoth Ayyathan, Praveen Koganti, Gal Levy-Cohen, and Michael Blank</td>
<td>These findings illuminate how the stability of DNA topoisomerase II is controlled in cells, with implications for understanding this enzyme in chromosome inheritance and as a target of several important anticancer drugs.</td>
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<td>Acetylation of Mastermind-like 1 by p300 Drives the Recruitment of NACK to Initiate Notch-Dependent Transcription</td>
<td>Ke Jin, Wen Zhou, Xiaqing Han, Zhiqiang Wang, Bin Li, Shawn Jeffries, Wensi Tao, David J. Robbins, and Anthony J. Capobianco</td>
<td>These findings provide new insight for Notch signaling and a potential therapeutic strategy for Notch-dependent cancer.</td>
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<td>Utility of Genomic Analysis In Circulating Tumor DNA from Patients with Carcinoma of Unknown Primary</td>
<td>Shumei Kato, Nithya Krishnamurthy, Kimberly C. Banks, Pradip De, Kirstin Williams, Casey Williams, Brian Leyland-Jones, Scott M. Lippman, Richard B. Lanman, and Razelle Kurzrock</td>
<td>These findings represent a new treatment target for patients with NRAS-mutated cancer.</td>
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<td>RGS12 Is a Novel Tumor-Suppressor Gene in African American Prostate Cancer That Represses AKT and MNX1 Expression</td>
<td>Yongquan Wang, Jiahua Wang, Li Zhang, Omer Faruk Karatas, Longjiang Shao, Yiqun Zhang, Patricia Castro, Chad J. Creighton, and Michael Ittmann</td>
<td>These findings identify RGS12 as a novel tumor suppressor gene in prostate cancer in African Americans, which may serve as an important prognostic marker and therapeutic target.</td>
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<td>Unpaired Extracellular Cysteine Mutations of CSF3R Mediate Gain or Loss of Function</td>
<td>Haijiao Zhang, Sophie Means, Anna Reister Schultz, Kevin Watanabe-Smith, Bruno C. Medeiros, Daniel Bottomly, Beth Wilmot, Shannon K. McWeeny, Tim Kükenköhler, Oliver Hantschel, and Jeffrey W. Tyner</td>
<td>These findings demonstrate the structural and functional importance of conserved extracellular cysteine pairs in CSF3R, a gene possibly mutated frequently in leukemias, and suggesting the possibility of cysteine-mediated gain- and loss-of-function mutations in other oncogenic receptors.</td>
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<td>4268</td>
<td>EIF1AX and NRAS Mutations Co-occur and Cooperate in Low-Grade Serous Ovarian Carcinomas</td>
<td>Dariush Etemadmoghadam, Walid J. Azar, Ying Lei, Tania Moujaber, Dale W. Garsed, Catherine J. Kennedy, Sian Fereday, Chris Mitchell, Yoke-Eng Chiew, Joy Hendley, Raghwia Sharma, Paul R. Harnett, Jason Li, Elizabeth L. Christie, Ann-Marie Patch, Joshy George, George Au-Yeung, Gisela Mir Amnu, Timothy P. Holloway, Timothy Semple, John V. Pearson, Nicola Waddell, Sean M. Grimmond, Martin Köbel, Helen Rizos, Ivan B. Lomakin, David D. L. Bowtell, and Anna deFazio for The Australian Ovarian Cancer Study Group</td>
<td>These findings represent a new treatment target for patients with NRAS-mutated cancer.</td>
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Phosphoproteomic Profiling Reveals ALK and MET as Novel Actionable Targets across Synovial Sarcoma Subtypes

Targeting SRC Coactivators Blocks the Tumor-Initiating Capacity of Cancer Stem-like Cells
Aarti D. Rohira, Fei Yan, Lei Wang, Jin Wang, Suoling Zhou, Andrew Lu, Yang Yu, Jianming Xu, David M. Lonard, and Bert W. O'Malley

Hypoxia-Induced Downregulation of DUSP-2 Phosphatase Drives Colon Cancer Stemness
Pei-Chi Hou, Yo-Hua Li, Shih-Chieh Lin, Shau-Chieh Lin, Jenq-Chang Lee, Bo-Wen Lin, Jing-Ping Liou, Jang-Yang Chang, Ching-Chuan Kuo, Yi-Min Liu, H. Sunny Sun, and Shaw-Jenq Tsai

Loss of FAM46C Promotes Cell Survival in Myeloma

Fructose-1,6-bisphosphatase Inhibits ERK Activation and Bypasses Gemcitabine Resistance in Pancreatic Cancer by Blocking IQGAP1–MAPK Interaction
Xin Jin, Yunqian Pan, Liguo Wang, Tao Ma, Lizi Zhang, Amy H. Tang, Daniel D. Billadeau, Heshui Wu, and Haojie Huang

Inhibiting p53 Acetylation Reduces Cancer Chemotoxicity
Shunsheng Zheng, Xin Yu Koh, Hui Chin Goh, Siti Aishah B. Rahmat, Le Ann Hwang, and David P. Lane

Glucose Catabolism in Liver Tumors Induced by c-MYC Can Be Sustained by Various PKM1/PKM2 Ratios and Pyruvate Kinase Activities
Andrés Méndez-Lucas, Xiaolei Li, Junjie Hu, Li Che, Xinhua Song, Jiao Yuan Jia, Jingxiao Wang, Chencheng Xie, Paul C. Driscoll, Darjus F. Tschaharganeh, Diego F. Calvisi, Maria Yuneva, and Xin Chen

Infection Exposure Promotes ETV6-RUNX1 Precursor B-cell Leukemia via Impaired H3K4 Demethylases

Impaired epigenetic regulation and high RAG expression provides a genetic basis for why only a small fraction of patients with multiple oncogenic mutations in pre-leukemic clones develop precursor B cell acute lymphocytic leukemia.
Amlexanox Downregulates S100A6 to Sensitize KMT2A/AF11-Positive Acute Lymphoblastic Leukemia to TNFα Treatment
Hayato Tamai, Hiroki Yamaguchi, Koichi Miyake, Miyuki Takatori, Tomoaki Kitano, Satoshi Yamanaka, Syunsuke Yui, Keiko Fukunaga, Kazutaka Nakayama, and Koiti Inokuchi

Précis: This study shows how repositioning an approved allergy drug can undercut immune escape and enhance graft-versus-leukemia effects of stem cell transplants in preclinical models of an acute form of pediatric leukemia, providing a mechanistic rationale for immediate clinical testing in this setting.

Targeting Vascular Endothelial-Cadherin in Tumor-Associated Blood Vessels Promotes T-cell–Mediated Immunotherapy
Yang Zhao, Ka Ka Ting, Jia Li, Victoria C. Cogger, Jinbiao Chen, Anna Johansson-Percival, Shin Foong Ngioi, Jef Holst, Georges Grau, Shom Goel, Thorlef Muller, Elisabetta Dejana, Geoff McCaughan, Mark J. Smyth, Ruth Ganss, Mathew A. Vadas, and Jennifer R. Gamble

Précis: These findings identify the miR-27/VE-cadherin interaction as a verified target to improve immunotherapy via stabilization of VE-cadherin levels in solid tumor vasculature.

GLI1 Blockade Potentiates the Antitumor Activity of PI3K Antagonists in Lung Squamous Cell Carcinoma
Sadba Kasiri, Chunli Shao, Baozhi Chen, Alexandra N. Wilson, Paul Yenerall, Brenda C. Timmons, Luc Girard, Hui Tian, Carmen Behrens, Ignacio I. Wistuba, Adi F. Gazdar, and James Kim

Précis: Combined targeting of the PI3K-mTOR pathway and the transcription factor GLI1 may improve outcomes in PI3K pathway-driven lung cancers, providing an opportunity to address the failure of PI3K antagonists as effective monotherapies.

Posttranscriptional Upregulation of IDH1 by HuR Establishes a Powerful Survival Phenotype in Pancreatic Cancer Cells

Précis: This important study highlights the HuR-IDH1 regulatory axis as a critical, actionable therapeutic target in pancreatic cancer.
MICROENVIRONMENT AND IMMUNOLOGY

4472 Heme-oxygenase-1 Production by Intestinal CX3CR1⁺ Macrophages Helps to Resolve Inflammation and Prevents Carcinogenesis
Giulia Marelli, Marco Erreni, Achille Anselmo, Valentina Taverniti, Simone Guglielmetti, Alberto Mantovani, and Paola Allavena
Précis: These findings demonstrate how colon-resident CX3CR1⁺ macrophages help prevent the establishment of chronic inflammation and cancer by producing HMOX-1.

4486 NF1⁻/⁻ Hematopoietic Cells Accelerate Malignant Peripheral Nerve Sheath Tumor Development without Altering Chemotherapy Response
Rebecca D. Dodd, Chang-Lung Lee, Tess Overton, Wesley Huang, William C. Eward, Lixia Luo, Yan Ma, Davis R. Ingram, Keila E. Torres, Diana M. Cardona, Alexander J. Lazar, and David G. Kirsch
Précis: Mouse models demonstrate how the genetics of myeloid cells in the tumor microenvironment influence the biology of a type of pediatric tumor of the connective tissues that surround nerves, with potential clinical implications.

INTEGRATED SYSTEMS AND TECHNOLOGIES

4498 MET Exon 14 Mutation Encodes an Actionable Therapeutic Target in Lung Adenocarcinoma
Xinyuan Lu, Nir Peled, John Greer, Wei Wu, Peter Choi, Alice H. Berger, Sergio Wong, Kuang-Yu Jen, Youngho Seo, Byron Hann, Angela Brooks, Matthew Meyerson, and Eric A. Collisson
Précis: MET exon 14-skipping mutations are relatively common in NSCLC, encoding an active and druggable target and genomically evolving to overcome therapeutic targeting.

4506 Raman-Encoded Molecular Imaging with Topically Applied SERS Nanoparticles for Intraoperative Guidance of Lumpectomy
Yu "Winston" Wang, Nicholas P. Reder, Soyoung Kang, Adam K. Glaser, Qian Yang, Matthew A. Wall, Sara H. Javid, Suzanne M. Dintzis, and Jonathan T.C. Liu
Précis: This study introduces a novel noninvasive imaging technique that can rapidly detect positive surgical margins with high sensitivity and specificity in breast carcinoma.

CLINICAL STUDIES

4517 Functionally Null RAD51D Missense Mutation Associates Strongly with Ovarian Carcinoma
Précis: Carriers of a pathogenic missense mutation in the gene encoding the DNA repair protein RAD51D are at higher risk for ovarian cancer that may respond favorably to PARP inhibitor therapy.

4530 Quantitative Whole Genome Sequencing of Circulating Tumor Cells Enables Personalized Combination Therapy of Metastatic Cancer
Natali Gulbahce, Mark Jesus M. Magbanua, Robert Chin, Misha R. Agarwal, Xuhao Luo, Jia Liu, Daniel M. Hayden, Qing Mao, Serban Ciotlos, Zhenyu Li, Yanxiang Chen, Xingpeng Chen, Yuxiang Li, Rebecca Yu Zhang, Katharine Lee, Rick Tearle, Emily Park, Snezana Drmanac, Hope S. Rugo, John W. Park, Radoje Drmanac, and Brock A. Peters
Précis: These findings demonstrate the feasibility of generating high quality whole genome data from a small number of circulating tumor cells and show that this information can be extremely informative for personalized therapy.

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ABOUT THE COVER

DNA topoisomerase IIa (Topo IIa) plays a pivotal role in chromatin organization and unaltered chromosome inheritance. Moreover, Topo IIa is a core target of several anticancer drugs. Smurf2, an E3 ubiquitin ligase and suggested tumor suppressor, acts as a key cellular factor that directly binds and stabilizes Topo IIa and prevents the formation of pathological chromatin bridges. The image shows molecular biodistribution of Smurf2 and Topo IIa in human interphase and mitotic cells. For details, see article by Emanuelli and colleagues on page 4217.