BREAKING ADVANCES
2961 Highlights from Recent Cancer Literature

REVIEWS
2963 Maintaining Tumor Heterogeneity in Patient-Derived Tumor Xenografts
John W. Cassidy, Carlos Caldas, and Alejandra Bruna

2969 Plasminogen Activator Inhibitor-1 in Cancer: Rationale and Insight for Future Therapeutic Testing
Veronica R. Placencio and Yves A. DeClerck

INTEGRATED SYSTEMS AND TECHNOLOGIES
2975 Neuroendocrine Transdifferentiation in Human Prostate Cancer Cells: An Integrated Approach
Marianna Cerasuolo, Debora Paris, Fabio A. Iannotti, Dominique Melck, Roberta Verde, Enrico Mazzarella, Andrea Motta, and Alessia Ligresti

Precis: These provocative findings show how depriving androgen-dependent prostate cancer cells of androgen not only compromises cell survival, but also helps create a nonmalignant neuroendocrine phenotype in surviving cells that can ultimately support the outgrowth of androgen-independent tumors.

2987 Identification of Prognostic Groups in High-Grade Serous Ovarian Cancer Treated with Platinum–Taxane Chemotherapy
Ping Chen, Kaisa Huhtinen, Katja Kaipio, Piia Milkonen, Viljami Attonmäki, Rony Lindell, Johanna Hyninnen, Annika Auranen, Seija Grénman, Rainer Lehtonen, Olli Carpén, and Sampsa Hautaniemi

Precis: This study introduces a novel computational method that may accurately predict whether a patient with high-grade ovarian cancer will benefit from first-line chemotherapy.

2999 IDH1 Mutation Induces Reprogramming of Pyruvate Metabolism

Precis: Beyond their other effects, IDH1 mutations in brain tumors confer an imageable reduction in pyruvate dehydrogenase activity that is essential for proliferation of malignant cells, a finding with therapeutic implications.

3010 A Systematic Approach to Defining the microRNA Landscape in Metastasis

Precis: This article offers a systematic definition of the entire metastasis-associated miRNA landscape using an unbiased profiling approach of metastasis tissues from patients.

MIRCOENVIRONMENT AND IMMUNOLOGY
3020 Novel Cell-Penetrating Peptide-Based Vaccine Induces Robust CD4+ and CD8+ T Cell-Mediated Antitumor Immunity
Madiha Derouazi, Wilma Di Berardino-Besson, Elodie Belnoue, Sabine Hoepner, Romy Walther, Mahdia Benkhoucha, Patrick Teta, Yannick Dufour, Céline Yacoub Maroun, Andres M. Salazar, Denis Martinvalet, Pierre-Yves Dietrich, and Paul R. Walker

Precis: These results offer preclinical proof of concept for the use of a cell-penetrating peptide vaccine with robust antitumor activity in multiple aggressive tumor models.

3032 Oncogenic Transformation Can Orchestrate Immune Evasion and Inflammation in Human Mesenchymal Stem Cells Independently of Extrinsic Immune-Selective Pressure
Alex Miranda, Juan M. Funes, Nilda Sánchez, Celia M. Linia, Mónica Mesa, Sergio A. Quezada, Rolando Pérez, and Joel de León

Precis: This conceptually powerful study illuminates how the effects of oncogene activation extend beyond well-studied cell autonomous roles in proliferation, apoptosis, and invasion to suppressive effects on the local immune microenvironment, which are essential to license immune escape as the critical step in tumorigenesis.

3043 Neuroblastoma Arginase Activity Creates an Immunosuppressive Microenvironment That Impairs Autologous and Engineered Immunity
Francis Musssal, Sharon Egan, Stuart Hunter, Hannah Webber, Jonathan Fisher, Rachel Wheat, Carmel McConville, Yordan Shirkov, Kate Wheeler, Gavin Bendle, Kevin Petrie, John Anderson, Louis Chesler, and Carmela De Santo

Precis: These findings show how pediatric neuroblastomas inactivate antitumor immune responses, including in the setting of immunotherapy, correlating with a worse patient survival.
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<td>3054</td>
<td>Tristetraprolin Limits Inflammatory Cytokine Production in Tumor-Associated Macrophages in an mRNA Decay–Independent Manner</td>
<td>Franz Kratochvill, Nina Grat, Joseph E. Qualls, Lee-Ann Van De Velde, Hongbo Chi, Pavel Kovarik, and Peter J. Murray</td>
<td>Precis: Manipulation of a p38 kinase-related signaling axis in macrophages appears to strongly affect the growth of solid tumors, suggesting a new strategy to reprogram inflammation in tumor microenvironments.</td>
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<td>3098</td>
<td>Interleukin-6 Stimulates Defective Angiogenesis</td>
<td>Ganga Gopinathan, Carla Milagre, Oliver M.T. Pearce, Louise E. Reynolds, Kaijaan Hodivala-Dille, David A. Leinster, Haihong Zhong, Robert E. Hollingsworth, Richard Thompson, James R. Whiteford, and Frances Ballwill</td>
<td>Precis: These findings have important implications for understanding abnormal angiogenic processes in cancer, as well as their connection to immune escape and the use of VEGF or IL6 targeting therapies in cancer patients.</td>
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<td>3065</td>
<td>Cytomegalovirus Immediate-Early Proteins Promote Stemness Properties in Glioblastoma</td>
<td>Liliana Sorocceanu, Lisa Matlaf, Sabeena Khan, Armin Akhavan, Eric Singer, Vladimir Bezrookove, Stacy Decker, Saleena Ghanny, Piotr Hadaczek, Henrik Bengtsson, John Ohiost, Maria-Gloria Luciani-Torres, Lualhati Harkins, Arie Perry, Hong Guo, Patricia Soteropoulos, and Charles S. Cobbs</td>
<td>Precis: This study unveils a novel paradigm in viral oncogenesis, exposing the role of human cytomegalovirus in driving the growth of cancer stem cells in glioblastoma.</td>
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<td>3077</td>
<td>EGF Receptor Promotes Prostate Cancer Bone Metastasis by Downregulating miR-1 and Activating TWIST1</td>
<td>Yung-Sheng Chang, Wei-Yu Chen, Juan Juan Yin, Heather Sheppard-Tillman, Jiaotu Huang, and Yen-Nien Liu</td>
<td>Precis: The findings of this study raise the interesting idea that miRNA expression might be directly targeted by nuclear growth factor receptor isoforms, with relevance for the coordinated progression of malignancy.</td>
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<td>3087</td>
<td>KIAA1324 Suppresses Gastric Cancer Progression by Inhibiting the Oncoprotein GRP78</td>
<td>Jin Muk Kang, Sujin Park, Staci Iakjoyng Kim, Hyojuung Kim, Bona Lee, Junil Kim, Jinah Park, Shin Tae Kim, Han-Kwang Yang, Woo Ho Kim, and Seong-Jin Kim</td>
<td>Precis: These findings provide evidence of a novel mechanism of gastric carcinogenesis and also suggest a novel potential biomarker and therapeutic target for gastric cancer.</td>
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Minor Changes in Expression of the Mismatch Repair Protein MSH2 Exert a Major Impact on Glioblastoma Response to Temozolomide
José L. McFaline-Figueroa, Christian J. Braun, Monica Stanciu, Zachary D. Nagel, Patrizia Mazzucato, Dewakar Sangaraju, Edvinas Cerniauskas, Kelly Barford, Amanda Vargas, Yinlin Chen, Natalia Tret’yakova, Jacqueline A. Lees, Michael T. Hemann, Forest M. White, and Leona D. Samson

Précis: Modest decreases in DNA mismatch repair factor MSH2 can dramatically alter chemosensitivity to a drug used commonly to treat aggressive cancers, with little effect on the mismatch repair itself, suggesting that subtle mismatch repair changes mediating drug resistance may be more prevalent than appreciated.

Identification of Oncogenic and Drug-Sensitizing Mutations in the Extracellular Domain of FGFR2

Précis: Based on other advances in targeting FGF receptors in cancer, the novel mutations identified in this study in the extracellular domain of the FGF receptor FGFR2 could offer therapeutic targets in a variety of solid tumors.

Improving Drug Penetrability with iRGD Leverages the Therapeutic Response to Sorafenib and Doxorubicin in Hepatocellular Carcinoma

Précis: These findings establish a clinically tractable method to safely widen the therapeutic window for chemotherapy in patients with liver cancer, along with a noninvasive method to identify candidate subjects, offering immediate translational impact for evaluation in human trials.

CASC15-S Is a Tumor Suppressor IncRNA at the 6p22 Neuroblastoma Susceptibility Locus

Précis: This unbiased genetic association study identifies the involvement of a long noncoding RNA in initiating pediatric neuroblastoma, helping explain the low somatic mutation rates in protein coding genes observed in this lethal malignancy and suggesting new directions for therapeutic intervention.

Improving Drug Penetrability with iRGD Leverages the Therapeutic Response to Sorafenib and Doxorubicin in Hepatocellular Carcinoma
Tao Li, Junjie Xie, Chunsheng Dong, Chengyong Cheng, Yuan Shi, Zhichong Wu, Xiaoxing Deng, Hao Chen, Baiyong Shen, Chenghong Peng, Hongwei Li, Qian Zhan, and Zhecheng Zhu

Précis: These findings illuminate the oncogenic function of a noncoding RNA that acts by opposing tumor-suppressive effects of miR-150, suggesting utility as a prognostic biomarker or target for clinical management of HCC.
ABOUT THE COVER

The immunofluorescence image is of an aortic ring treated with IL6 stained for vessels (green), pericytes (red), and cell nuclei (blue). Here, it is shown that IL6 stimulates angiogenesis with defective pericyte coverage. Treatment of peritoneal xenografts of ovarian cancer with an anti-IL6 antibody restored pericyte coverage of the tumor blood vessels. The authors' findings have implications for the use of cancer therapies that target IL6 and for understanding abnormal angiogenesis in cancers, chronic inflammatory disease, and stroke. For details, see article by Gopinathan and colleagues on page 3098.
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