BREAKING ADVANCES

6375 Highlights from Recent Cancer Literature

REVIEWS

6377 A Genome-wide View of Microsatellite Instability: Old Stories of Cancer Mutations Revisited with New Sequencing Technologies
Tae-Min Kim and Peter J. Park

6383 Chimeric Antigen Receptor T-cell Therapy to Target Hematologic Malignancies
Saad Sirop Kenderian, Marco Ruella, Saar Gill, and Michael Kalos

PRIORITY REPORT

6390 Discrepancies in Cancer Genomic Sequencing Highlight Opportunities for Driver Mutation Discovery
Andrew M. Hudson, Tim Yates, Yaoyong Li, Eleanor W. Trotter, Shameem Fawdar, Phil Chapman, Paul Lorigan, Andrew Blankin, Crispin J. Miller, and John Brognaard
Précis: These findings highlight major discrepancies in mutational profiles of identical cancer cell lines sequenced by two different institutes, with implications for identifying previously undiscovered driver mutations.

INTEGRATED SYSTEMS AND TECHNOLOGIES

6397 Mathematical Modeling of Tumor Growth and Metastatic Spreading: Validation in Tumor-Bearing Mice
Niklas Hartung, Séverine Mollard, Dominique Barbolosi, Assia Benabdallah, Guillemette Chapuisat, Gerard Henry, Sarah Giacone, Athanasios Iliais, Joseph Ciccolini, Christian Faivre, and Florence Hubert
Précis: This work advances efforts to predict metastatic spreading during the earliest stages of cancer, at points that could help clinicians make the best decisions on treatment strategies.

6408 Direct Chemosensitivity Monitoring Ex Vivo on Undissociated Melanoma Tumor Tissue by Impedance Spectroscopy
Heinz-Georg Jahnke, Sarah Poenick, Jan Maschke, Michael Kendler, Jan C. Simon, and Andrea A. Robitsek
Précis: This study presents a novel and more accurate tissue-based method to determine chemotherapeutic drug sensitivity using small fragments of tumor tissue, addressing a need to personalize therapy for patients to improve treatment outcomes.

MICROENVIRONMENT AND IMMUNOLOGY

6419 CXM: A New Tool for Mapping Breast Cancer Risk in the Tumor Microenvironment
Michael J. Flister, Bradley T. Endres, Nathan Rudemiller, Allison B. Sarkis, Stephanie Santarriaga, Ishan Roy, Angela Lemke, Aron M. Geurs, Carol Moreno, Sophia Ran, Shing-Wern Tsaih, Jeffery De Pons, Daniel F. Carlson, Wenhong Tan, Scott C. Fahrenkrug, Zelmira Lazarova, Jozef Lazar, Paula E. North, Peter S. LaViolette, Michael B. Devlinell, James D. Shull, and Howard J. Jacob
Précis: These results establish the utility of a novel model of breast cancer that can localize genetic variants that affect breast cancer risk through actions on the tumor microenvironment, rather than the tumor cell itself.

6430 Ag-Presenting CpG-Activated pDCs Prime Th17 Cells That Induce Tumor Regression
Leslie Guéry, Juan Dubrot, Carla Lippens, Dale Brighouse, Pauline Malinge, Magali Irla, Caroline Pot, Walter Reith, Jean-Marc Waldburger, and Stéphanie Hugues
Précis: This study identifies a new antigen-presenting strategy that may improve cancer immunotherapy involving Th17 cells.

6441 SA-4-1BBL and Monophosphoryl Lipid A Constitute an Efficacious Combination Adjuvant for Cancer Vaccines
Abhishek K. Srivastava, Gunes Dinc, Rajesh K. Sharma, Esma S. Yolcu, Hong Zhao, and Haval Shirwan
Précis: These results offer preclinical proof of concept for the use of a powerful new adjuvant system for tumor antigen-based cancer vaccines, with immediate implications for its clinical evaluation in the oncology clinic.
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<td>6452</td>
<td>Host Deficiency in Caveolin-2 Inhibits Lung Carcinoma Tumor Growth by Impairing Tumor Angiogenesis</td>
<td>Yajun Liu, Sungchan Jang, Leike Xie, and Grzegorz Sowa</td>
<td>Precis: Loss of a protein that helps organize lipid rafts on the plasma membrane reduces cancerous cell growth, with possible implications for a generalized approach to cancer targeting.</td>
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<td>6509</td>
<td>The Notch Pathway Inhibits TGFβ Signaling in Breast Cancer through HEYI-Mediated Crosstalk</td>
<td>Liangfeng Han, Adam Diehl, Nguyen K. Nguyen, Preethi Korangath, Weiwen Teo, Soo nweng Cho, Scott Kominsky, David L. Huso, Lionel Feigenbaum, Alan Rein, Pedram Argani, Goran Landberg, Manfred Gessler, and Saraswati Sukumar</td>
<td>Precis: These findings identify a particular mechanism of TGFβ signaling as a key element in the development of drug resistance in breast cancer.</td>
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MPHOSPH1: A Potential Therapeutic Target for Hepatocellular Carcinoma
Xinran Liu, Yafan Zhou, Xinyuan Liu, Anlin Peng, Hao Gong, Lizi Huang, Kaige Ji, Robert B. Petersen, Ling Zheng, and Kun Huang

Précis: These results highlight a critical role for a mitotic kinesin as a critical oncogenic driver and candidate therapeutic target in liver cancer.

Plk1 Inhibition Enhances the Efficacy of Androgen Signaling Blockade in Castration-Resistant Prostate Cancer
Zhe Zhang, Xianzeng Hou, Chen Shao, Junjie Li, Ji-Xin Cheng, Shihuan Kuang, Nihal Ahmad, Timothy Ratliff, and Xiaoqi Liu

Précis: These results offer a mechanistic rationale for evaluating Plk1 inhibitors in clinical development to enhance the efficacy of androgen signaling inhibitors in patients with castration-resistant prostate cancer.

MicroRNA100 Inhibits Self-Renewal of Breast Cancer Stem–like Cells and Breast Tumor Development
Lu Deng, Li Shang, Shoumin Bai, Ji Chen, Xueyan He, Rachel Martin-Trevino, Shanshan Chen, Xiao-yan Li, Xiaojie Meng, Bin Yu, Xiaolin Wang, Yajing Liu, Sean P. McDermott, Alexa E. Ariazi, Christophe Cinestier, Ingrid Ibarra, Jia Ke, Tahra Luther, Shawn G. Clouthier, Liang Xu, George Shan, Herui Yao, Gregory J. Hannon, Stephen J. Weiss, and Suling Liu

Précis: These studies provide insight into the mechanisms by which microRNA gene regulates the self-renewal and tumor-forming potential of cancer stem-like cells, suggesting theranostic applications for this microRNA in identifying and targeting these cells for cancer treatment.

RABL6A Promotes G1–S Phase Progression and Pancreatic Neuroendocrine Tumor Cell Proliferation in an Rb1-Dependent Manner

Précis: These findings provide insights into Rb1 regulation and cell proliferation in pancreatic neuroendocrine tumors, potentially offering new targets for diagnosis and therapy of this disease.

A Hypusine–eIF5A–PEAK1 Switch Regulates the Pathogenesis of Pancreatic Cancer
Ken Fujimura, Tracy Wright, Jan Strnadl, Sharmeela Kaushal, Cristina Metirdi, Andrew M. Lowy, Michael Bouvet, Jonathan A. Kelber, and Richard L. Klemke

Précis: A selective posttranslational modification important for the development of pancreatic cancers may offer a new therapeutic strategy to treat this disease.

CD66+ Cells in Cervical Precancers Are Partially Differentiated Progenitors with Neoplastic Traits

Précis: Neoplastic cell subsets in cervical cancer emerge early in the disease and are linked to the life cycle of HPV virus, which drives this disease.

TRAP1 Is Involved in BRAF Regulation and Downstream Attenuation of ERK Phosphorylation and Cell-Cycle Progression: A Novel Target for BRAF-Mutated Colorectal Tumors
Valentina Condelli, Annamaria Piscazzi, Lorenza Sisini, Danilo Swann Matassa, Francesca Maddalena, Giacomo Lettini, Vittorio Simeon, Giuseppe Palladino, Maria Rosaria Amoroso, Stefania Trino, Frana Esposito, and Matteo Landriscina

Précis: This study illuminates the regulation of the BRAF oncoprotein at the level of its posttranslational ubiquitination.

Tumor-Derived Osteopontin Suppresses Antitumor Immunity by Promoting Extramedullary Myelopoiesis
Eun-Kyung Kim, Insu Jeon, Hyungseok Seo, Young-Jun Park, Boyeong Song, Kyoo-A Lee, Yongwoo Jang, Yeonseok Chung, and Chang-Yuil Kang

Précis: These findings unveil a novel immunosuppressive role for a factor widely associated with the inflammatory tumor microenvironment, with implications for a general therapeutic strategy in cancer treatment.
GPx2 Suppression of H2O2 Stress Links the Formation of Differentiated Tumor Mass to Metastatic Capacity in Colorectal Cancer
Benjamin L. Emmink, Jamila Laoukili, Anna P. Kipp, Jan Koster, Klaas M. Govaert, Szabolcs Fatrai, Andre Verheem, Ernst J.A. Steller, Regina Brigelius-Flohé, Connie R. Jimenez, Inne H.M. Borel Rinkes, and Onno Kranenburg

Précis: Results reveal an unexpected redox-controlled link between formation of a tumor mass and its capacity for metastasis.

RETRACTION

Retraction: Novel HSP90 Inhibitor NVP-HSP990 Targets Cell-Cycle Regulators to Ablate Olig 2-Positive Glioma Tumor–Initiating Cells

ABOUT THE COVER

CD8⁺ T cells are critical for elimination of cancer. A major limitation of therapeutic cancer vaccines is their inability to activate and mobilize CD8⁺ T cells for infiltration into tumor. A vaccine formulation containing SA-4-1BBL and MPL, as a novel adjuvant system shows robust efficacy in activating and recruiting CD8⁺ T cells into the tumor, with subsequent effective tumor destruction in preclinical models. For details, see article by Srivastava and colleagues on page 6441.
Cancer Research

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