

## BREAKING ADVANCES

- 591** Highlights from Recent Cancer Literature

## OBITUARY

- 593** Richmond T. Prehn: In Memoriam (1922–2016)  
Lawrence A. Loeb

## REVIEW

- 595** Out-RANKing BRCA1 in Mutation Carriers  
Emma Nolan, Geoffrey J. Lindeman, and  
Jane E. Visvader


## INTEGRATED SYSTEMS AND TECHNOLOGIES

- 601** The NCI-60 Methylome and Its Integration into CellMiner  
William C. Reinhold, Sudhir Varma, Margot Sunshine, Vinodh Rajapakse, Augustin Luna, Kurt W. Kohn, Holly Stevenson, Yonghong Wang, Holger Heyn, Vanesa Nogales, Sebastian Moran, David J. Goldstein, James H. Doroshow, Paul S. Meltzer, Manel Esteller, and Yves Pommier  
*Précis:* A mineable datasource places the DNA methylation levels for 17,559 genes into cell line signatures for easy comparison to molecular and pharmacological data.

- 613** Differential Regulation of the Melanoma Proteome by eIF4A1 and eIF4E  
Cailin E. Joyce, Adrienne G. Yanez, Akihiro Mori, Akinori Yoda, Johanna S. Carroll, and Carl D. Novina  
*Précis:* The first global proteomic analysis of eIF4F-dependent translation in cancer provides a new perspective on the role of eIF4F in cancer and the use of selective eIF4F inhibitors for treating cancer.

- 623** Threshold Analysis and Biodistribution of Fluorescently Labeled Bevacizumab in Human Breast Cancer  
Maximilian Koch, Johannes S. de Jong, Jürgen Glatz, Panagiotis Symvoulidis, Laetitia E. Lamberts, Arthur L.L. Adams, Mariëtte E.G. Kranendonk, Anton G.T. Terwisscha van Scheltinga, Michaela Aichler, Liesbeth Jansen, Jakob de Vries, Marjolijn N. Lub-de Hooge, Carolien P. Schröder, Annelies Jorritsma-Smit, Matthijs D. Linssen, Esther de Boer, Bert van der Vegt, Wouter B. Nagengast, Sjoerd G. Elias, Sabrina Oliveira, Arjen J. Witkamp, Willem P.T.M. Mali, Elske Van der Wall, P. Beatriz Garcia-Allende, Paul J. van Diest, Elisabeth G.E. de Vries, Axel Walch, Gooitzen M. van Dam, and Vasilis Ntziachristos  
*Précis:* A new fluorescent-labeling technique provides a quantitative, high-resolution map of tumor tissue in vivo.

## MICROENVIRONMENT AND IMMUNOLOGY

- 632** Transcriptional Induction of Periostin by a Sulfatase 2–TGF $\beta$ 1–SMAD Signaling Axis Mediates Tumor Angiogenesis in Hepatocellular Carcinoma  
 Gang Chen, Ikuo Nakamura, Renumathy Dhanasekaran, Eriko Iguchi, Ezequiel J. Tolosa, Paola A. Romecin, Renzo E. Vera, Luciana L. Almada, Alexander G. Miamen, Roongruedee Chaiteerakij, Mengtao Zhou, Michael K. Asiedu, Catherine D. Moser, Shaoshan Han, Chunling Hu, Bubu A. Banini, Abdul M. Oseini, Yichun Chen, Yong Fang, Dongye Yang, Hassan M. Shaleh, Shaoqing Wang, Dehai Wu, Tao Song, Ju-Seog Lee, Snorri S. Thorgeirsson, Eric Chevet, Vijay H. Shah, Martin E. Fernandez-Zapico, and Lewis R. Roberts  
*Précis:* These findings define an important axis controlling angiogenesis in metastatic liver cancers and a mechanistic foundation for rational drug development.
- 646** Selective Reversible Inhibition of Autophagy in Hypoxic Breast Cancer Cells Promotes Pulmonary Metastasis  
Christopher M. Dower, Neema Bhat, Edward W. Wang, and Hong-Gang Wang  
*Précis:* This seminal study suggests cautions in the development of autophagy-based strategies for cancer treatment, based on findings that blocking hypoxia-regulated autophagy can actually drive metastasis.

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**658** T Cells Redirected to a Minor Histocompatibility Antigen Instruct Intratumoral TNF $\alpha$  Expression and Empower Adoptive Cell Therapy for Solid Tumors

Teresa Manzo, Tabea Sturmheit, Veronica Basso, Elisabetta Petrozziello, Rodrigo Hess Michelini, Michela Riba, Massimo Freschi, Angela R. Elia, Matteo Grioni, Flavio Curnis, Maria Pia Protti, Ton N. Schumacher, Reno Debets, Melody A. Swartz, Angelo Corti, Matteo Bellone, and Anna Mondino

*Précis:* These results validate the importance of targeting both the tumor and its associated stroma in establishing the potency of a new combination therapy that can trigger efficacious allogeneic graft versus tumor effects.

**672** Human Pancreatic Cancer Cells Induce a MyD88-Dependent Stromal Response to Promote a Tumor-Tolerant Immune Microenvironment



Daniel Delitto, Andrea E. Delitto, Bayli B. DiVita, Kien Pham, Song Han, Emily R. Hartlage, Brittney N. Newby, Michael H. Gerber, Kevin E. Behrns, Lyle L. Moldawer, Ryan M. Thomas, Thomas J. George Jr, Todd M. Brusko, Clayton E. Mathews, Chen Liu, Jose G. Trevino, Steven J. Hughes, and Shannon M. Walle

*Précis:* Stromal cells respond to danger-associated factors secreted by pancreatic cancer cells, ultimately leading to profound stromal-mediated suppression of antitumor immunity.

## MOLECULAR AND CELLULAR PATHOBIOLOGY

**684** Mesothelial Cells Create a Novel Tissue Niche That Facilitates Gastric Cancer Invasion

Masamitsu Tanaka, Sei Kuriyama, Go Itoh, Daichi Maeda, Akiteru Goto, Yutaro Tamiya, Kazuyoshi Yanagihara, Masakazu Yashiro, and Namiko Aiba

*Précis:* Peritoneal mesothelial cells generate a tissue microenvironment favorable to cancer cell infiltration, with possible therapeutic implications for blocking progression.

**696** A Metastatic Mouse Model Identifies Genes That Regulate Neuroblastoma Metastasis

Bo Kyung A. Seong, Kelly E. Fathers, Robin Hallett, Christina K. Yung, Lincoln D. Stein, Samar Mouaaz, Lynn Kee, Cynthia E. Hawkins, Meredith S. Irwin, and David R. Kaplan

*Précis:* A new mouse model of human metastatic neuroblastoma was exploited to identify novel genes, signaling pathways, candidate therapeutics, and a prognostic gene expression that could improve the treatment of this deadly pediatric disease.

**707** H-Ras and K-Ras Oncoproteins Induce Different Tumor Spectra When Driven by the Same Regulatory Sequences

Matthias Drosten, Lucía Simón-Carrasco, Isabel Hernández-Porras, Carmen G. Lechuga, María T. Blasco, Harrys K.C. Jacob, Salvatore Fabbiano, Nicoletta Potenza, Xosé R. Bustelo, Carmen Guerra, and Mariano Barbacid

*Précis:* This study addresses the long-standing question about why H-Ras and K-Ras oncogenes are associated with induction of different tumor types, which results here suggest that subtle differences in MAP kinase signaling in tumor cells may offer one explanation for functional nonequivalence.

## THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

**719** Targeting Tumor-Associated Fibroblasts for Therapeutic Delivery in Desmoplastic Tumors

Lei Miao, Qi Liu, C. Michael Lin, Cong Luo, Yuhua Wang, Lina Liu, Weiyang Yin, Shihao Hu, William Y. Kim, and Leaf Huang

*Précis:* These results offer a preclinical proof of concept for the use of nanoparticles to modify cancer-associated fibroblasts as a strategy to treat desmoplastic cancers.

**732** PAX3-FOXO1A Expression in Rhabdomyosarcoma Is Driven by the Targetable Nuclear Receptor NR4A1

Alexandra Lacey, Aline Rodrigues-Hoffman, and Stephen Safe

*Précis:* These results provide a preclinical rationale to use a class of specific nuclear receptor antagonists to treat a particularly aggressive type of pediatric soft tissue tumors driven by the fusion gene PAX3-FOXO1A.

**742** Pifithrin- $\mu$  Prevents Cisplatin-Induced Chemobrain by Preserving Neuronal Mitochondrial Function



Gabriel S. Chiu, Magdalena A. Maj, Sahar Rizvi, Robert Dantzer, Elisabeth G. Vichaya, Geoffroy Laumet, Annemieke Kavelaars, and Cobi J. Heijnen

*Précis:* Chemotherapy-induced cognitive impairment—often informally referred to as "chemobrain"—is a widespread side-effect in cancer survivors who receive classical cytotoxic chemotherapy as part of their treatment.

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## TUMOR AND STEM CELL BIOLOGY

### 753 Castration Resistance in Prostate Cancer Is Mediated by the Kinase NEK6

Atish D. Choudhury, Anna C. Schinzel, Maura B. Cotter, Rosina T. Lis, Katherine Labella, Ying Jie Lock, Francesca Izzo, Isil Guney, Michaela Bowden, Yvonne Y. Li, Jinal Patel, Emily Hartman, Steven A. Carr, Monica Schenone, Jacob D. Jaffe, Philip W. Kantoff, Peter S. Hammerman, and William C. Hahn

*Précis:* These findings define a new kinase signaling pathway in mediating castration-resistant prostate cancer, the most aggressive form of the disease, with implications for the development of therapeutic agents needed for more effective control.

### 766 Transcriptional Regulator CNOT3 Defines an Aggressive Colorectal Cancer Subtype

Paloma Cejas, Alessia Cavazza, C.N. Yandava, Victor Moreno, David Horst, Juan Moreno-Rubio, Emilio Burgos, Marta Mendiola, Len Taing, Ajay Goel, Jaime Feliu, and Ramesh A. Shivdasani

*Précis:* Expression of a little studied chromatin modifier appears to mark a subset of colon cancer cells with self-renewal properties, suggesting its use as a biomarker of early-stage colorectal cancers likely to have a poor prognosis.

### 780 S100A4 Elevation Empowers Expression of Metastasis Effector Molecules in Human Breast Cancer

Thamir M. Ismail, Daimark Bennett, Angela M. Platt-Higgins, Morteta Al-Medhity, Roger Barraclough, and Philip S. Rudland

*Précis:* These results suggest the existence of evolutionarily conserved pathways used by S100A4 to promote metastatic dissemination in the nervous system, which is not well understood but preferentially exploited by certain glandular tumors.

### 790 Aspirin Suppresses Growth in PI3K-Mutant Breast Cancer by Activating AMPK and Inhibiting mTORC1 Signaling

Whitney S. Henry, Tyler Laszewski, Tiffany Tsang, Francisco Beca, Andrew H. Beck, Sandra S. McAllister, and Alex Tokor

*Précis:* These findings reposition aspirin as a tool to treat breast cancer cell growth, supporting a rationale for its combination with PI3K inhibitors in therapy.

### 802 Mouse Models of Pediatric Supratentorial High-grade Glioma Reveal How Cell-of-Origin Influences Tumor Development and Phenotype

Smitha Sreedharan, Naga Prathyusha Maturi, Yuan Xie, Anders Sundström, Malin Jarvius, Sylwia Libard, Irina Alafuzoff, Holger Weishaupt, Märten Fryknäs, Rolf Larsson, Fredrik J. Swartling, and Lene Uhrbom

*Précis:* These findings propose that the cell of origin may have an important role for clinicopathological features of HGG such as malignancy and drug sensitivity.

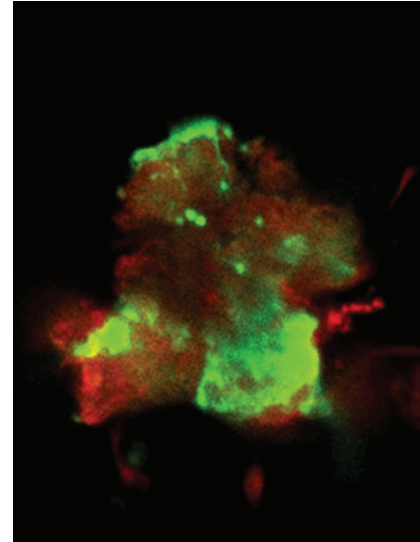
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## ABOUT THE COVER

When the metastasis-inducing protein S100A4 is overexpressed in human cancers, it is often associated with poor prognosis. In a *Drosophila* model where protein expression is directed exclusively to the optic lobes, oncogenic Ras<sup>Val12</sup> produces GFP-labeled tumors within these structures (green fluorescence), but when coexpressed with S100A4, these tumors disseminate to the ventral nerve chord and elsewhere in the fly. Genetic and chemical blockades establish a metastatic pathway leading from S100A4 to a matrix metalloproteinase, MMP (red fluorescence). In human breast cancer, certain MMPs are coexpressed with S100A4 and are also associated with premature demise of patients from metastatic cancer. For details, see article by Ismail and colleagues on page 780.



# Cancer Research

The Journal of Cancer Research (1916–1930) | The American Journal of Cancer (1931–1940)

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