



## BREAKING ADVANCES

- 2555** Highlights from Recent Cancer Literature

## REVIEWS

- 2557**  **Models in Translational Oncology: A Public Resource Database for Preclinical Cancer Research**  
 Claudia Galuschka, Rumyana Proynova, Benjamin Roth, Hellmut G. Augustin, and Karin Müller-Decker
- 2564** **Tumor Dormancy and Relapse: From a Natural Byproduct of Evolution to a Disease State**  
 Masoud H. Manjili

## INTEGRATED SYSTEMS AND TECHNOLOGIES


- 2570** **A Model-Based Personalized Cancer Screening Strategy for Detecting Early-Stage Tumors Using Blood-Borne Biomarkers**  
 Sharon Seiko Hori, Amelie M. Lutz, Ramasamy Paulmurugan, and Sanjiv Sam Gambhir  
*Précis: The cancer screening strategy presented here is applicable to any solid cancer and the biomarkers they shed, enabling one to distinguish between aggressive and nonaggressive tumors based on blood biomarker sampling data alone.*
- 2585**  **Morphoproteomic Characterization of Lung Squamous Cell Carcinoma Fragmentation, a Histological Marker of Increased Tumor Invasiveness**  
 Ruben Casanova, Daniel Xia, Undine Rulle, Paolo Nanni, Jonas Grossmann, Bart Vrugt, Reto Wettstein, Rafael Ballester-Ripoll, Alberto Astolfo, Walter Weder, Holger Moch, Marco Stampanoni, Andrew H. Beck, and Alex Soltermann  
*Précis: A new histologic factor is proposed as an independent unfavorable prognostic marker for lung squamous carcinomas, possibly representing a new grading parameter in this setting.*

## MICROENVIRONMENT AND IMMUNOLOGY

- 2594** **HDAC Inhibitor Panobinostat Engages Host Innate Immune Defenses to Promote the Tumoricidal Effects of Trastuzumab in HER2<sup>+</sup> Tumors**  
 Mikolaj Medon, Eva Vidacs, Stephin J Vervoort, Jason Li, Misty R. Jenkins, Kelly M. Ramsbottom, Joseph A. Trapani, Mark J. Smyth, Phillip K. Darcy, Peter W. Atadja, Michael A. Henderson, Ricky W. Johnstone, and Nicole M. Haynes  
*Précis: These findings illustrate the immune-enhancing effects of the HDAC inhibitor panobinostat for recruiting NK cell-mediated responses, which as illustrated can allow trastuzumab to eradicate otherwise trastuzumab-resistant HER2<sup>+</sup> tumors.*
- 2607** **Anti-PD-L1 Efficacy Can Be Enhanced by Inhibition of Myeloid-Derived Suppressor Cells with a Selective Inhibitor of PI3K $\delta/\gamma$**   
 Ruth J. Davis, Ellen C. Moore, Paul E. Clavijo, Jay Friedman, Harrison Cash, Zhong Chen, Chris Silvin, Carter Van Waes, and Clint Allen  
*Précis: These findings highlight the therapeutic balance required between blocking immunosuppressive myeloid cells and blocking effector immune cells in response to isoform-specific PI3K $\delta/\gamma$  inhibitors.*
- 2620** **Locoregional Effects of Microbiota in a Preclinical Model of Colon Carcinogenesis**  
 Sarah Tomkovich, Ye Yang, Kathryn Winglee, Josee Gauthier, Marcus Mühlbauer, Xiaolun Sun, Mansour Mohamadzadeh, Xiuli Liu, Patricia Martin, Gary P. Wang, Eric Oswald, Anthony A. Fodor, and Christian Jobin  
*Précis: Age-related factors drive tumor development in the small intestine, whereas in the large intestine, inflammation and specific bacterial strains are the primary drivers.*

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## MOLECULAR AND CELLULAR PATHOBIOLOGY

- 2633** **Differential Expression of VEGFA Isoforms Regulates Metastasis and Response to Anti-VEGFA Therapy in Sarcoma**  
 William R. English, Sarah Jane Lunt, Matthew Fisher, Diane V. Lefley, Mohit Dhingra, Yu-Chin Lee, Karina Bingham, Jack E. Hurrell, Scott K. Lyons, Chryso Kanthou, and Gillian M. Tozer  
*Précis: Evidence for a candidate tumor cell biomarker predicting therapeutic response to bevacizumab should prompt prospective testing in the clinic.*
- 2647** **Lipocalin-2 Promotes Pancreatic Ductal Adenocarcinoma by Regulating Inflammation in the Tumor Microenvironment**  
Sobeyda B. Gomez-Chou, Agnieszka Katarzyna Swidnicka-Siergiejko, Niharika Badi, Myrriah Chavez-Tomar, Gregory B. Lesinski, Tanios Bekaii-Saab, Matthew R. Farren, Thomas A. Mace, Carl Schmidt, Yan Liu, Defeng Deng, Rosa F. Hwang, Liran Zhou, Todd Moore, Deyali Chatterjee, Huamin Wang, Xiaohong Leng, Ralph B. Arlinghaus, Craig D. Logsdon, and Zobeida Cruz-Monserrate  
*Précis: Lipocalin-2 acts through its receptor SLC22A17 to modulate secretion of proinflammatory cytokines in human pancreatic cancer stellate cells.*
- 2661** **Pancreatic Cancer Progression Relies upon Mutant p53-Induced Oncogenic Signaling Mediated by NOP14**  
 Yongxing Du, Ziwen Liu, Lei You, Pengjiao Hou, Xiaoxia Ren, Tao Jiao, Wenjing Zhao, Zongze Li, Hong Shu, Changzheng Liu, and Yupei Zhao  
*Précis: NOP14, a stress response factor needed for 40S ribosome production, is critical in pancreatic cancer cells for stabilizing mutant p53 mRNA and thereby the prometastatic effects of mutant p53 in this setting.*
- 2674** **SSRP1 Cooperates with PARP and XRCC1 to Facilitate Single-Strand DNA Break Repair by Chromatin Priming**  
Ying Gao, Changling Li, Leizhen Wei, Yaqu Teng, Satoshi Nakajima, Xiukai Chen, Jianquan Xu, Brittany Legar, Hongqiang Ma, Stephen T. Spagnol, Yong Wan, Kris Noel Dahl, Yang Liu, Arthur S. Levine, and Li Lan  
*Précis: By establishing how the histone H2A/H2B chaperone SSRP1 helps facilitate DNA single strand break repair, this study offers a mechanistic rationale to target SSRP1 as a general way to attack tumors.*

## THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

- 2686** **Antibody–Drug Conjugates Bearing Pyrrolobenzodiazepine or Tubulysin Payloads Are Immunomodulatory and Synergize with Multiple Immunotherapies**  
Jonathan Rios-Doria, Jay Harper, Raymond Rothstein, Leslie Wetzel, Jon Chesebrough, Allison Marrero, Cui Chen, Patrick Strout, Kathy Mulgrew, Kelly McGlinchey, Ryan Fleming, Binyam Bezabeh, John Meekin, David Stewart, Maureen Kennedy, Philip Martin, Andrew Buchanan, Nazzareno Dimasi, Emil Michelotti, and Robert Hollingsworth  
*Précis: These preclinical findings suggest that antitumor response rates to cancer immunotherapy can be increased significantly by combinations with antibody-drug conjugates, which are found to exert immunomodulatory activities beyond their targeted cytotoxic effects on cancer cells.*
- 2699** **Development of a T-cell Receptor Mimic Antibody against Wild-Type p53 for Cancer Immunotherapy**  
Demin Li, Carol Bentley, Amanda Anderson, Sarah Wiblin, Kirstie L.S. Cleary, Sofia Koustoulidou, Tasneem Hassanali, Jenna Yates, Jenny Greig, Marloes Olde Nordkamp, Iva Trenevskaa, Nicola Temette, Benedikt M. Kessler, Bart Cornelissen, Mark S. Cragg, and Alison H. Banham  
*Précis: An antibody recognizes a T-cell epitope derived from p53 and presented on the surface of cancer cells, representing a new agent in cancer immunotherapy.*
- 2712** **Response Heterogeneity of EGFR and HER2 Exon 20 Insertions to Covalent EGFR and HER2 Inhibitors**  
Takayuki Kosaka, Junko Tanizaki, Raymond M. Paranal, Hideki Endoh, Christine Lydon, Marzia Capelletti, Claire E. Repellin, Jihyun Choi, Atsuko Ogino, Antonio Calles, Dalia Ercan, Amanda J. Redig, Magda Bahcall, Geoffrey R. Oxnard, Michael J. Eck, and Pasi A. Jänne  
*Précis: These findings identify a common marker illuminating sensitivity of lung cancers to covalent EGFR/HER2 inhibitors for cancers that harbor EGFR/HER2 exon 20 insertions.*



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## TUMOR AND STEM CELL BIOLOGY

- 2722** Cell-Cycle Regulation Accounts for Variability in Ki-67 Expression Levels  
Michal Sobceki, Karim Mrouj, Jacques Colinge, François Gerbe, Philippe Jay, Liliana Krasinska, Vjekoslav Dulic, and Daniel Fisher

*Précis:* This study uncovers the reasons for variability in expression of Ki-67 and finds that it is a good biomarker for the effects of CDK4/CDK6 inhibitors such as palbociclib.

- 2735** IL33 Promotes Colon Cancer Cell Stemness via JNK Activation and Macrophage Recruitment

Min Fang, Yongkui Li, Kai Huang, Shanshan Qi, Jian Zhang, Witold Zgodzinski, Marek Majewski, Grzegorz Wallner, Stanislaw Gozdz, Pawel Macek, Artur Kowalik, Marcin Pasiarski, Ewelina Grywalska, Linda Vatan, Nisha Nagarsheth, Wei Li, Lili Zhao, Ilona Kryczek, Guobin Wang, Zheng Wang, Weiping Zou, and Lin Wang

*Précis:* IL33 promotes stemness in colon cancer cells by activating JNK signaling and macrophage recruitment.

- 2746** miR-34a and miR-34b/c Suppress Intestinal Tumorigenesis

Longchang Jiang and Heiko Hermeking

*Précis:* By defining novel tumor suppressor genes in an established mouse model of colon tumorigenesis, this study suggests novel candidate biomarkers and therapeutic targets in colorectal cancer.

- 2759** Individualized Breast Cancer Characterization through Single-Cell Analysis of Tumor and Adjacent Normal Cells

Manjushree Anjanappa, Angelo Cardoso, Lijun Cheng, Safa Mohamad, Andrea Gunawan, Susan Rice, Yan Dong, Lang Li, George E. Sandusky, Edward F. Srour, and Harikrishna Nakshatri

*Précis:* This study highlights the importance of using normal tissue from the same individual as a control to distinguish tumor-specific gene expression from genes whose differential expression reflects cellular precursors of tumors.

## CORRECTIONS

- 2770** Correction: Tumor-intrinsic PD-L1 Signals Regulate Cell Growth, Pathogenesis, and Autophagy in Ovarian Cancer and Melanoma

- 2771** Correction: Pulsed High-Intensity Focused Ultrasound Enhances Delivery of Doxorubicin in a Preclinical Model of Pancreatic Cancer

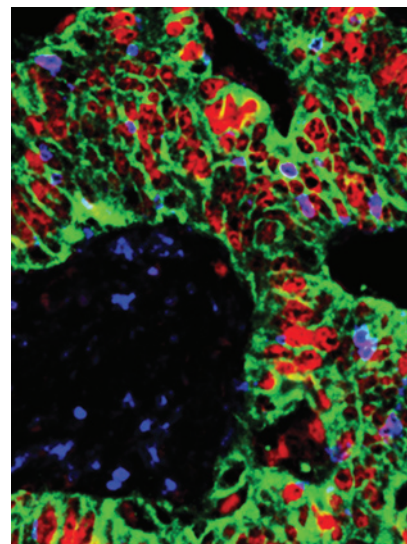
- 2772** Correction: Metastatic Progression of Prostate Cancer Is Mediated by Autonomous Binding of Galectin-4-O-Glycan to Cancer Cells

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## ABOUT THE COVER

IL33 is expressed by vascular endothelial cells and tumor cells in the human colon cancer microenvironment, suggesting their important role in colon cancer. Using multiplexed immunophenotyping microscopy, Fang and colleagues found that PAN-Keratin-positive (green) tumor cells and CD31-positive (blue) vascular endothelial cells expressed IL33 (red) in primary and metastatic colon cancer tissues. When colon cancer cells were IL33-positive, the adjacent colon epithelial cells were IL33 negative. For details, see article by Fang and colleagues on page 2735.



# Cancer Research

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

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