BREAKING ADVANCES

2585  Highlights from Recent Cancer Literature

REVIEWS

2587  Evaluating Robustness and Sensitivity of the NanoString Technologies nCounter Platform to Enable Multiplexed Gene Expression Analysis of Clinical Samples

2594  Network-Based Approaches to Understand the Roles of miR-200 and Other microRNAs in Cancer
Cameron P. Bracken, Yeesim Khew-Goodall, and Gregory J. Goodall

PRIORITY REPORT

2600  High-Frequency Targetable EGFR Mutations in Sinonasal Squamous Cell Carcinomas Arising from Inverted Sinonasal Papilloma
Aaron M. Udager, Delphine C.M. Rolland, Jonathan B. McHugh, Bryan L. Betz, Carlos Munga-Zamalloa, Thomas E. Carey, Lawrence J. Marentette, Mario A. Hermsen, Kathleen E. DuRoss, Megan S. Lim, Kojo S.J. Elenitoba-Johnson, and Noah A. Brown
Précis: These results identify a role for activating EGFR mutations in sinonasal squamous cell carcinomas arising from inverted papillomas, providing the first genetic evidence of a biologic link between these tumors and demonstrating the opportunity for targeted therapy with irreversible EGFR inhibitors.

INTEGRATED SYSTEMS AND TECHNOLOGIES

2607  Quantifying the Landscape for Development and Cancer from a Core Cancer Stem Cell Circuit
Chunhe Li and Jin Wang
Précis: A pictorial “cancer landscape” theory described in this study offers quantitative insights into underlying mechanisms of cancer stem-like cell formation and the interplay with normal development, with possible applications to a variety of disease-related regulatory networks.

MICROENVIRONMENT AND IMMUNOLOGY

2619  Blocking Tumor Necrosis Factor α Enhances CD8 T-cell–Dependent Immunity in Experimental Melanoma
Florie Bertrand, Julia Rochotte, Céline Colacios, Anne Montfort, Anne-Françoise Tilkin-Mariamé, Christian Touriol, Philippe Rochaix, Isabelle Lajoie-Mazenc, Nathalie Andrieu-Abadie, Thierry Levade, Hervé Benoist, and Bruno Séguin
Précis: This study challenges the view that TNF in the inflammatory microenvironment of melanoma is protumorigenic, with immediate implications for possible clinical evaluation of the effects of anti-TNF antibodies in melanoma treatment.

2629  Chemotherapy-Derived Inflammatory Responses Accelerate the Formation of Immunosuppressive Myeloid Cells in the Tissue Microenvironment of Human Pancreatic Cancer
Shintaro Takeuchi, Muhammad Baghdadi, Takahiroyo Tsuchikawa, Haruka Wada, Toru Nakamura, Hirotake Abe, Sayaka Nakanishi, Yuu Usui, Kohtaro Higuchi, Mizuna Takahashi, Kazuhiko Inoko, Sosuke Sato, Hirohito Takano, Toshiaki Shichinohe, Ken-ichiro Seino, and Satoshi Hirano
Précis: These findings challenge the use of therapeutic regimens employing GM-CSF as part of a cancer vaccine by providing preclinical evidence that GM-CSF ablation may benefit patients with pancreatic cancer, who generally respond poorly to chemotherapy, through helping defeat a powerful immune escape mechanism.
### Molecular and Cellular Pathobiology

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### Therapeutics, Targets, and Chemical Biology

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<td>2716</td>
<td>A Novel Cinnamon-Related Natural Product with Pim-1 Inhibitory Activity Inhibits Leukemia and Skin Cancer</td>
<td>Jong-Eun Kim, Joe Eun Son, Hyein Jeong, Dong Joon Kim, Sang Gwon Seo, Eunjun Lee, Tae Gyu Lim, Jong Rhan Kim, Yengo Raymond Kimbung, Han Yong Chen, Ann M. Bode, Ki Won Lee, and Zigang Dong</td>
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Hepatocellular Shuttling and Recirculation of Sorafenib-Glucuronide Is Dependent on Abcc2, Abcc3, and Oatp1a/1b
Aksana Vasilyeva, Selvi Durmus, Lie Li, Els Wagenaar, Shuiying Hu, Alice A. Gibson, John C. Panetta, Sridhar Mani, Alex Sparreboom, Sharyn D. Baker, and Alfred H. Schinkel

Précis: These results suggest broad relevance of a hepatocyte shuttling process known as “hepatocyte hopping”—a novel concept in clinical pharmacology—for detoxification of targeted cancer drugs that undergo hepatic glucuronidation, such as sorafenib.

Paracrine Effect of NRG1 and HGF Drives Resistance to MEK Inhibitors in Metastatic Uveal Melanoma
Hanyin Cheng, Mizue Terai, Ken Kageyama, Shinji Ozaki, Peter A. McCue, Takami Sato, and Andrew E. Aplin

Précis: These findings offer a preclinical proof of concept for the combination of MEK inhibitor plus a growth factor receptor targeting antibody in the treatment of highly aggressive uveal melanomas.

Tracking and Functional Characterization of Epithelial–Mesenchymal Transition and Mesenchymal Tumor Cells during Prostate Cancer Metastasis
Marcus Ruscetti, Bill Quach, Eman L. Dadashian, David J. Mulholland, and Hong Wu

Précis: EMT prostate tumor cells, which transition readily between epithelial and mesenchymal states, can recapitulate each stage of the metastatic cascade, supporting the use of therapeutic agents that target tumor cell plasticity for the treatment of lethal metastatic prostate cancer.

Paracrine Effect of NRG1 and HGF Drives Resistance to MEK Inhibitors in Metastatic Uveal Melanoma
Hanyin Cheng, Mizue Terai, Ken Kageyama, Shinji Ozaki, Peter A. McCue, Takami Sato, and Andrew E. Aplin

Précis: These findings offer a preclinical proof of concept for the combination of MEK inhibitor plus a growth factor receptor targeting antibody in the treatment of highly aggressive uveal melanomas.

Retraction: Concurrent Suppression of Integrin α5, Radixin, and RhoA Phenocopies the Effects of miR-31 on Metastasis

Correction: miR145 Targets the SOX9/ADAM17 Axis to Inhibit Tumor-Initiating Cells and IL6-Mediated Paracrine Effects in Head and Neck Cancer

ABOUT THE COVER
TNFα plays a central, but still enigmatic, role in melanoma. Using immunofluorescence, it was found that TNF deficiency or blockade enhanced intratumor content of high endothelial venules surrounded by high CD8⁺ T lymphocyte density. Consequently, the tumor growth of melanoma cell lines expressing MHC-I molecules at high levels was dramatically impaired. Counteracting TNF signaling may potentiate the immune response in melanoma. For details, see article by Betrand and colleagues on page 2619.