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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, Helmut 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 Vrugi, Reto Wettstein, Rafael Ballester-Ripoll, Alberto Astolfi, 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\(^+\) Tumors
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\(^+\) 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 Wingler, Josee Gauthier, Marcu Mühlbauer, Xiaojun 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.
MOLECULAR AND CELLULAR PATHOBIOLOGY

2633 Differential Expression of VEGFA Isoforms Regulates Metastasis and Response to Anti-VEGFA Therapy in Sarcoma

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, Zixen Liu, Lei You, Pengjiao Hou, Xiaoxia Ren, Tao Hao, Wenhong Zhao, Zongze Li, Hong Shu, Changzheng Liu, and Yuepei 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, Yaqun Teng, Satoshi Nakajima, Xiukai Chen, Jiangquan Xu, Brittany Legar, Hongjiang 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

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 Bendley, Amanda Anderson, Sarah Wiblin, Kirstie L.S. Cearly, Sofia Koustoulioudou, Taneeza Hassanali, Jenna Yates, Jenny Greig, Marloes Olde Nordkamp, Iva Treneska, Nicola Ternette, Benedikt M. Kessler, Bart Cornelissen, Mark S. Czagg, 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 Balbazzol, 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.
TUMOR AND STEM CELL BIOLOGY

2722 Cell-Cycle Regulation Accounts for Variability in Ki-67 Expression Levels
Michal Sobecki, Karim Mrouj, Jacques Coliné, 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.

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

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.
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