


BREAKING INSIGHTS

- 6347** Highlights from Recent Cancer Literature

REVIEW

- 6349**  Posttranslational Modifications of PD-L1 and Their Applications in Cancer Therapy
Jung-Mao Hsu, Chia-Wei Li, Yun-Ju Lai, and Mien-Chie Hung

PRIORITY REPORTS

- 6354** Downregulation of *Dipeptidyl Peptidase 4* Accelerates Progression to Castration-Resistant Prostate Cancer
Joshua W. Russo, Ce Gao, Swati S. Bhasin, Olga S. Voznesensky, Carla Calagua, Seiji Arai, Peter S. Nelson, Bruce Montgomery, Elahe A. Mostaghel, Eva Corey, Mary-Ellen Taplin, Huihui Ye, Manoj Bhasin, and Steven P. Balk
Significance: These findings identify DPP4 as an AR-stimulated tumor suppressor gene that is downregulated during progression to castration-resistant prostate cancer, warning that treatment with DPP4 inhibitors, commonly used to treat type 2 diabetes, may accelerate prostate cancer progression following androgen deprivation therapy.
- 6363** Synthetic DNA-Encoded Monoclonal Antibody Delivery of Anti-CTLA-4 Antibodies Induces Tumor Shrinkage *In Vivo*
Elizabeth K. Duperret, Aspen Trautz, Regina Stoltz, Ami Patel, Megan C. Wise, Alfredo Perales-Puchalt, Trevor Smith, Kate E. Broderick, Emma Masteller, J. Joseph Kim, Laurent Humeau, Kar Muthumani, and David B. Weiner
Significance: DNA-encoded monoclonal antibodies represent a novel technology for delivery and expression of immune checkpoint blockade antibodies, thus expanding patient access to, and possible clinical applications of, these therapies.

MOLECULAR CELL BIOLOGY

- 6371**  HERC2 Facilitates BLM and WRN Helicase Complex Interaction with RPA to Suppress G-Quadruplex DNA


Wenwen Wu, Nana Rokutanda, Jun Takeuchi, Yongqiang Lai, Reo Maruyama, Yukiko Togashi, Hiroyuki Nishikawa, Naoko Arai, Yasuo Miyoshi, Nao Suzuki, Yasushi Saeki, Keiji Tanaka, and Tomohiko Ohta

Significance: HERC2 is revealed as a master regulator of G-quadruplex, a DNA secondary structure that triggers genomic instability and may serve as a potential molecular target in cancer therapy.

- 6386** Cyclin F-Dependent Degradation of RBPJ Inhibits IDH1^{R132H}-Mediated Tumorigenesis

Ruhi S. Deshmukh, Shalakra Sharma, and Sanjeev Das

Significance: These findings reveal mechanistic insights into the key role of the cyclin F-RBPJ axis in response to metabolic stress in cancer cells.

- 6399**  An ATM/TRIM37/NEMO Axis Counteracts Genotoxicity by Activating Nuclear-to-Cytoplasmic NF-κB Signaling

Geyan Wu, Libing Song, Jinrong Zhu, Yameng Hu, Lixue Cao, Zhanyao Tan, Shuxia Zhang, Ziwen Li, and Jun Li

Significance: In response to genotoxic stress, TRIM37 activates NF-κB signaling via monoubiquitination of NEMO, which subsequently promotes cisplatin chemoresistance and tumor relapse in cancer.

TUMOR BIOLOGY AND IMMUNOLOGY

- 6413**  Genomic Characterization of Six Virus-Associated Cancers Identifies Changes in the Tumor Immune Microenvironment and Altered Genetic Programs

Frederick S. Varn, Evelien Schaafsma, Yue Wang, and Chao Cheng

Significance: This study uses TCGA and other genomic datasets to further our understanding of how viruses affect the tumor immune response in different cancer types.

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6424 Glycoprotein nmb Is Exposed on the Surface of Dormant Breast Cancer Cells and Induces Stem Cell-like Properties

Chen Chen, Yukari Okita, Yukihide Watanabe, Fumie Abe, Muhammad Ali Fikry, Yumu Ichikawa, Hiroyuki Suzuki, Akira Shibuya, and Mitsuyasu Kato

Significance: These findings suggest that cell surface expression of GPNMB could serve as a marker and promising therapeutic target of breast cancer cells with stem cell-like properties.

6436 Astrocyte Elevated Gene-1 Regulates Macrophage Activation in Hepatocellular Carcinogenesis

Chadia L. Robertson, Rachel G. Mendoza, Nidhi Jariwala, Mikhail Dozmorov, Nitai D. Mukhopadhyay, Mark A. Subler, Jolene J. Windle, Zhao Lai, Paul B. Fisher, Shobha Ghosh, and Devanand Sarkar

Significance: These findings distinguish a novel role of macrophage-derived oncogene AEG-1 from hepatocellular AEG-1 in promoting inflammation and driving tumorigenesis.

6447 Induction of Paracrine Signaling in Metastatic Melanoma Cells by PPAR γ Agonist Rosiglitazone Activates Stromal Cells and Enhances Tumor Growth

Christine Pich, Patrick Meylan, Beatris Mastelic-Gavillet, Thanh Nhan Nguyen, Romain Loyon, Bao Khanh Trang, Hélène Moser, Catherine Moret, Christine Goepfert, Jürg Hafner, Mitchell P. Levesque, Pedro Romero, Camilla Jandus, and Liliane Michalik

Significance: These findings uncover a novel mechanism by which the thiazolidinedione compound rosiglitazone contributes to tumorigenesis, thus highlighting a potential risk associated with its use in patients with established tumors.

6462 UBE2N Promotes Melanoma Growth via MEK/FRA1/SOX10 Signaling

Anushka Dikshit, Yingai J. Jin, Simone Degan, Jihwan Hwang, Matthew W. Foster, Chuan-Yuan Li, and Jennifer Y. Zhang

Significance: These findings identify ubiquitin conjugase UBE2N and its variant partners as novel regulators of MAPK signaling and potential therapeutic targets in melanoma.

6473 Semaphorin 7A Promotes Macrophage-Mediated Lymphatic Remodeling during Postpartum Mammary Gland Involution and in Breast Cancer

Alan M. Elder, Beth A.J. Tamburini, Lyndsey S. Crump, Sarah A. Black, Veronica M. Wessells, Pepper J. Schedin, Virginia F. Borges, and Traci R. Lyons

Significance: SEMA7A, which is expressed on mammary cells during glandular involution, alters macrophage biology and lymphangiogenesis to drive breast cancer metastasis.

6486 Comutations in DNA Damage Response Pathways Serve as Potential Biomarkers for Immune Checkpoint Blockade



Zhijie Wang, Jing Zhao, Guoqiang Wang, Fan Zhang, Zemin Zhang, Fan Zhang, Yuzi Zhang, Hua Dong, Xiaochen Zhao, Jianchun Duan, Hua Bai, Yanhua Tian, Rui Wan, Miao Han, Yan Cao, Lei Xiong, Li Liu, Shuhang Wang, Shangli Cai, Tony S.K. Mok, and Jie Wang

Significance: Identification of comutations in specific DDR pathways as predictors of superior survival outcomes in response to immune checkpoint blockade provide a clinically convenient approach for estimation of tumor mutational burden and delivery of ICB therapy.

TRANSLATIONAL SCIENCE

6497 CBP Modulates Sensitivity to Dasatinib in Pre-BCR⁺ Acute Lymphoblastic Leukemia



Jesús Duque-Afonso, Chiou-Hong Lin, Kyuho Han, David W. Morgens, Edwin E. Jeng, Ziming Weng, Johan Jeong, Stephen Hon Kit Wong, Li Zhu, Michael C. Wei, Hee-Don Chae, Martin Schrappe, Gunnar Cario, Justus Duyster, Xiangshu Xiao, Kathleen M. Sakamoto, Michael C. Bassik, and Michael L. Cleary

Significance: These findings reveal mechanisms that modulate sensitivity to dasatinib and suggest therapeutic strategies to improve the outcome of patients with acute lymphoblastic leukemia.

6509 A Novel Small-Molecule Inhibitor of MRCK Prevents Radiation-Driven Invasion in Glioblastoma

Joanna L. Birch, Karen Strathdee, Lesley Gilmour, Antoine Vallatos, Laura McDonald, Ariadni Kouzeli, Richa Vasani, Abdulrahman Hussain Qaisi, Daniel R. Croft, Diane Crighton, Kathryn Gill, Christopher H. Gray, Jennifer Konczal, Mokdad Mezna, Duncan McArthur, Alexander W. Schüttelkopf, Patricia McConnell, Mairi Sime, William M. Holmes, Justin Bower, Heather J. McKinnon, Martin Drysdale, Michael F. Olson, and Anthony J. Chalmers

Significance: An effective new strategy for the treatment of glioblastoma uses a novel, anti-invasive chemotherapeutic to prevent infiltration of the normal brain by glioblastoma cells.

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LETTERS TO THE EDITOR

6523 Tau Mutations as a Novel Risk Factor for Cancer—Letter

Angela B. Deuschländer, Bradley F. Boeve, Howard J. Rosen, Adam L. Boxer, and Zbigniew K. Wszolek, on behalf of the LEFFTDS Consortium

6525 Tau Mutations as a Novel Risk Factor for Cancer—Response

Giacomina Rossi, Veronica Redaelli, Paola Perego, Raffaele Ferrari, Giorgio Giaccone, and Fabrizio Tagliavini

RETRACTION

6526 Retraction: Disruption of the NAD(P)H:Quinone Oxidoreductase 1 (NQO1) Gene in Mice Causes Myelogenous Hyperplasia

Delwin J. Long II, Amos Gaikwad, Asha Multani, Sen Pathak, Charles A. Montgomery, Frank J. Gonzalez, and Anil K. Jaiswal

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ABOUT THE COVER

Lymphatic vessels may play a role in the removal of cellular debris and tissue remodeling during postpartum mammary gland involution. During involution, lymphatic vessel density and macrophage recruitment are greatly increased in the mammary gland. Using immunofluorescence and 3D reconstruction, it was observed that involution mammary macrophages (red) not only express lymphatic markers (green), but are associated with the lymphatic vasculature and form chimeric lymphatic-macrophage vessels. Photo courtesy of Gavin Ryan, Ph.D. For details, see article by Elder and colleagues on page 6473.

