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## 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, Huilui 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 RBPI Inhibits IDH1R132H-Mediated Tumorigenesis

**Rahi S. Deshmukh, Shalakha Sharma, and Sanjeev Das**

**Significance:** These findings reveal mechanistic insights into the key role of the cyclin F-RBPI 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, Zhaoyao 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.
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, Hiro-yuki 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.

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, Shobita 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.

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

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.

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.

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

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

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.
LETTERS TO THE EDITOR

6523  Tau Mutations as a Novel Risk Factor for Cancer—Letter
Angela B. Deutschländer, 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

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.