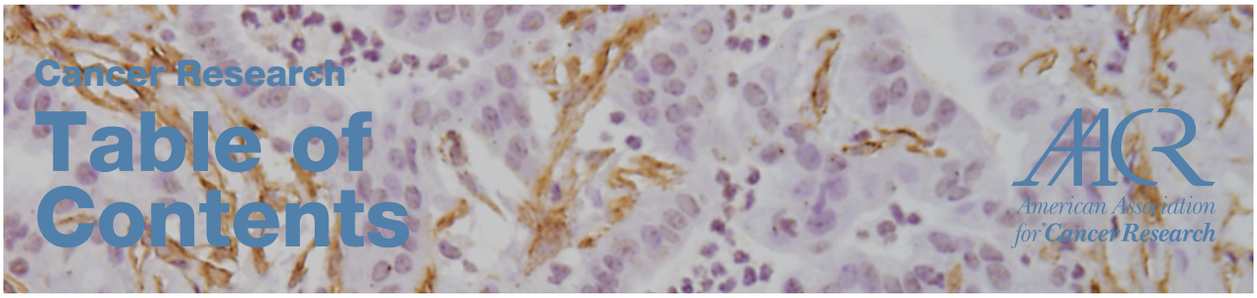

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BREAKING ADVANCES

3379 **Highlights from Recent Cancer Literature**

REVIEW

3381 **The Early Detection of Pancreatic Cancer: What Will It Take to Diagnose and Treat Curable Pancreatic Neoplasia?**
Anne Marie Lennon, Christopher L. Wolfgang, Marcia Irene Canto, Alison P. Klein, Joseph M. Herman, Michael Goggins, Elliot K. Fishman, Ihab Kamel, Matthew J. Weiss, Luis A. Diaz, Nickolas Papadopoulos, Kenneth W. Kinzler, Bert Vogelstein, and Ralph H. Hruban

PERSPECTIVE

3390 **Enhancement of the T-cell Armamentarium as a Cell-Based Therapy for Prostate Cancer**
W. Nathaniel Brennen, Charles G. Drake, and John T. Isaacs

MEETING REPORT

3396 **Oncolytic Viruses Targeting Tumor Stem Cells**
E. Antonio Chiocca, Donald Blair, and R. Allan Mufson

CLINICAL STUDIES

3399 **Favorable Prognostic Impact in Loss of *TP53* and *PIK3CA* Mutations after Neoadjuvant Chemotherapy in Breast Cancer**
Yi-Zhou Jiang, Ke-Da Yu, Jing Bao, Wen-Ting Peng, and Zhi-Ming Shao

Précis: *These findings of immediate translational impact may help optimize the choice of sequential neoadjuvant therapies used with increasing frequency in breast cancer patients to improve overall survival.*

MICROENVIRONMENT AND IMMUNOLOGY

3408 **Local and Systemic Protumorigenic Effects of Cancer-Associated Fibroblast-Derived GDF15**
Francesca Bruzzese, Christina Hägglöf, Alessandra Leone, Elin Sjöberg, Maria Serena Roca, Sara Kiflemariam, Tobias Sjöblom, Peter Hammarsten, Lars Egevad, Anders Bergh, Arne Östman, Alfredo Budillon, and Martin Augsten

Précis: *This study demonstrates for the first time that cancer-associated fibroblasts can exert systemic effects on malignant cell growth beyond the local tumor microenvironment, with potential implications for controlling metastatic progression.*

3418 **LSECtin Expressed on Melanoma Cells Promotes Tumor Progression by Inhibiting Antitumor T-cell Responses**
Feng Xu, Jing Liu, Di Liu, Biao Liu, Min Wang, Zhiyuan Hu, Xuemei Du, Li Tang, and Fuchu He

Précis: *A T-cell–suppressive molecule studied solely in antigen-presenting cells to date is found to be expressed frequently in melanoma cells, engendering a novel mechanism of immune escape with implications for novel therapeutic strategies.*

3429 **Metalloprotease-Mediated Tumor Cell Shedding of B7-H6, the Ligand of the Natural Killer Cell–Activating Receptor NKp30**
Eva Schlecker, Nathalie Fiegler, Annette Arnold, Peter Altevogt, Stefan Rose-John, Gerhard Moldenhauer, Antje Sucker, Annette Paschen, Elke Pogge von Strandmann, Sonja Textor, and Adelheid Cerwenka

Précis: *Blocking the ability of tumor cells to proteolytically shed a cell surface ligand recognized by natural killer immune cells can enhance the recognition and destruction of tumor cells, with implications for how to promote or sustain NK cell–based immunotherapies for cancer.*

3441 **Immunosuppressive Myeloid Cells Induced by Chemotherapy Attenuate Antitumor CD4$^+$ T-Cell Responses through the PD-1–PD-L1 Axis**
Zhi-Chun Ding, Xiaoyun Lu, Miao Yu, Henrique Lemos, Lei Huang, Phillip Chandler, Kebin Liu, Matthew Walters, Antoni Krasinski, Matthias Mack, Bruce R. Blazar, Andrew L. Mellor, David H. Munn, and Gang Zhou

Précis: *Chemotherapy may restrain its own efficacy by eliciting myeloid cells that have immunosuppressive activities, with implications for creating regimens of immunochemotherapy that tilt toward more effective, durable responses.*

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3454 **Complement C5a Receptor Facilitates Cancer Metastasis by Altering T-Cell Responses in the Metastatic Niche**
Surya Kumari Vadrevu, Navin K. Chintala, Sharad K. Sharma, Priya Sharma, Clayton Cleveland, Linley Riediger, Sasikanth Manne, David P. Fairlie, Wojciech Gorczyca, Othon Almanza, Magdalena Karbowniczek, and Maciej M. Markiewski

Précis: *These findings offer a preclinical rationale to translate complement-based immunotherapies to the clinic as a strategy to prevent or reduce metastatic progression.*

3466 **Autologous T-cell Therapy for Cytomegalovirus as a Consolidative Treatment for Recurrent Glioblastoma**
Andrea Schuessler, Corey Smith, Leone Beagley, Glen M. Boyle, Sweera Rehan, Katherine Matthews, Linda Jones, Tania Crough, Vijayendra Dasari, Kerenaftali Klein, Amy Smalley, Hamish Alexander, David G. Walker, and Rajiv Khanna

Précis: *Early clinical findings for a CMV-based immunotherapy tested in aggressive brain tumors encourage further evaluation of the therapeutic efficacy of this platform technology.*

MOLECULAR AND CELLULAR PATHOBIOLOGY

3477 **NCOA1 Directly Targets *M-CSF1* Expression to Promote Breast Cancer Metastasis**
Li Qin, Ye-Lin Wu, Michael J. Toneff, Dabing Li, Lan Liao, Xiuhua Gao, Fiona T. Bane, Jean C.-Y. Tien, Yixiang Xu, Zhen Feng, Zhihui Yang, Yan Xu, Sarah M. Theissen, Yi Li, Leonie Young, and Jianming Xu

Précis: *These results define a regulatory axis controlled by a nuclear coactivator implicated in breast cancer relapse, which acts to promote metastasis by recruiting macrophages that drive this process.*

3489 **G Protein–Coupled Receptor Kinase GRK5 Phosphorylates Moesin and Regulates Metastasis in Prostate Cancer**
Prabir Kumar Chakraborty, Yushan Zhang, Alexandra S. Coomes, Wan-Ju Kim, Rachel Stupay, Lauren D. Lynch, Tamieka Atkinson, Jae I. Kim, Zhongzhen Nie, and Yehia Daaka

Précis: *G protein–coupled receptors are readily druggable targets for which significant opportunities may exist in cancer therapy, as suggested by this study of the prometastatic contributions of GRK5 to prostate cancer.*

3501 **NADPH Oxidase NOX4 Supports Renal Tumorigenesis by Promoting the Expression and Nuclear Accumulation of HIF2α**
Jennifer L. Gregg, Robert M. Turner II, Guimin Chang, Disha Joshi, Ye Zhan, Li Chen, and Jodi K. Maranchie

Précis: *These findings offer direct evidence that NOX4 is critical for renal tumorigenesis and offer a preclinical rationale to target NOX4 for therapeutic management of renal cancer.*

3512 **Galectin-1 Drives Pancreatic Carcinogenesis through Stroma Remodeling and Hedgehog Signaling Activation**
Neus Martínez-Bosch, Maite G. Fernández-Barrena, Mireia Moreno, Elena Ortiz-Zapater, Jessica Munné-Collado, Mar Iglesias, Sabine André, Hans-Joachim Gabius, Rosa F. Hwang, Françoise Poirier, Carolina Navas, Carmen Guerra, Martin E. Fernández-Zapico, and Pilar Navarro

Précis: *These findings identify a lectin-like molecule in the tumor microenvironment in pancreatic cancer as a tractable target for therapy, with potential impact at several levels in both malignant and stromal cells.*

PREVENTION AND EPIDEMIOLOGY

3525 **No Causal Association Identified for Human Papillomavirus Infections in Lung Cancer**
Devasena Anantharaman, Tarik Gheit, Tim Waterboer, Gordana Halec, Christine Carreira, Behnoush Abedi-Ardekani, Sandrine McKay-Chopin, David Zaridze, Anush Mukeria, Neonila Szeszenia-Dabrowska, Jolanta Lissowska, Dana Mates, Vladimir Janout, Lenka Foretova, Vladimir Bencko, Peter Rudnai, Eleonora Fabianova, Anne Tjønneland, Ruth C. Travis, Heiner Boeing, J. Ramón Quirós, Mikael Johansson, Vittorio Krogh, H. Bas Bueno-de-Mesquita, Anastasia Kotanidou, Françoise Clavel-Chapelon, Elisabete Weiderpass, Mattias Johansson, Michael Pawlita, Ghislaine Scelo, Massimo Tommasino, and Paul Brennan

Précis: *Although HPV DNA has been detected in some lung cancers, hinting at a causal connection like that in cervical cancer, the deeper analysis performed in this study does not encourage this hypothesis.*

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THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

3535 **Targeting Mitochondrial Oxidative Metabolism in Melanoma Causes Metabolic Compensation through Glucose and Glutamine Utilization**
Ji-Hong Lim, Chi Luo, Francisca Vazquez, and Pere Puigserver

Précis: *Because cancer cells are as metabolically flexible as they are genetically malleable, therapeutic strategies to attack cancer cell metabolism need to address multiple pathways at once.*

3546 **The RAD51-Stimulatory Compound RS-1 Can Exploit the RAD51 Overexpression That Exists in Cancer Cells and Tumors**
Jennifer M. Mason, Hillary L. Logan, Brian Budke, Megan Wu, Michal Pawlowski, Ralph R. Weichselbaum, Alan P. Kozikowski, Douglas K. Bishop, and Philip P. Connell

Précis: *This study describes a novel therapeutic strategy to turn the heightened DNA repair capabilities of cancer cells against themselves, offering a preclinical proof of concept for a generalized approach to treat many kinds of human cancer.*

3556 **API5 Confers Tumoral Immune Escape through FGF2-Dependent Cell Survival Pathway**
Kyung Hee Noh, Seok-Ho Kim, Jin Hee Kim, Kwon-Ho Song, Young-Ho Lee, Tae Heung Kang, Hee Dong Han, Anil K. Sood, Joanne Ng, Kwanghee Kim, Chung Hee Sonn, Vinay Kumar, Cassian Yee, Kyung-Mi Lee, and Tae Woo Kim

Précis: *These findings identify a novel pathway of immune escape in tumors that could be targeted to potentiate the efficacy of cancer vaccines or T-cell immunotherapies in the clinic, with immediate implications for the design of immunochemotherapy combinations that could heighten antitumor efficacy.*

3567 **Re-engineering Vesicular Stomatitis Virus to Abrogate Neurotoxicity, Circumvent Humoral Immunity, and Enhance Oncolytic Potency**
Alexander Muik, Lawton J. Stubbert, Roza Z. Jahedi, Yvonne Geiβ, Janine Kimpel, Catherine Dold, Reinhard Tober, Andreas Volk, Sabine Klein, Ursula Dietrich, Beta Yadollahi, Theresa Falls, Hrvoje Miletic, David Stojdl, John C. Bell, and Dorothee von Laer

Précis: *As cancer treatment tools, oncolytic viruses have mostly fallen short of expectations, with only sparse evidence for clinical efficacy so far, but the engineered viral platform described here lacks several of the major drawbacks that have hampered clinical development.*

3579 **The Cancer Stem Cell Marker Aldehyde Dehydrogenase Is Required to Maintain a Drug-Tolerant Tumor Cell Subpopulation**
Debasish Raha, Timothy R. Wilson, Jing Peng, David Peterson, Peng Yue, Marie Evangelista, Catherine Wilson, Mark Merchant, and Jeff Settleman

Précis: *These findings identify a potential therapeutic strategy for overcoming the resistance to cancer drugs that is invariably observed in cancer patients, even following an initial response to drug treatment.*

TUMOR AND STEM CELL BIOLOGY

3591 **Oncogenic Protein MTBP Interacts with MYC to Promote Tumorigenesis**
Brian C. Grieb, Mark W. Gramling, Maria Pia Arrate, Xi Chen, Stephen L. Beauparlant, Dale S. Haines, Hua Xiao, and Christine M. Eischen

Précis: *Although it was one of the first human oncogenes to be discovered over three decades ago, MYC continues to resist all efforts to develop tractable therapeutic approaches or to fully understand the basis for its powerful cancer-promoting effects.*

3603 **Prolyl Isomerase Pin1 Acts Downstream of miR200c to Promote Cancer Stem–like Cell Traits in Breast Cancer**
Man-Li Luo, Chang Gong, Chun-Hau Chen, Daniel Y. Lee, Hai Hu, Pengyu Huang, Yandan Yao, Wenjun Guo, Ferenc Reinhardt, Gerburg Wulf, Judy Lieberman, Xiao Zhen Zhou, Erwei Song, and Kun Ping Lu

Précis: *These findings identify a targetable enzyme as a pivotal regulator of breast cancer stem-like cell development, highlighting a new therapeutic target that may be useful to eradicate advanced drug-resistant breast cancers.*

3617 **Loss of the Polycomb Mark from Bivalent Promoters Leads to Activation of Cancer-Promoting Genes in Colorectal Tumors**
Maria A. Hahn, Arthur X. Li, Xiwei Wu, Richard Yang, David A. Drew, Daniel W. Rosenberg, and Gerd P. Pfeifer

Précis: *Tumor-promoting genes with bivalent promoters in normal tissue can lose the Polycomb mark H3K27me3 and become activated in tumors, thus providing a new epigenetic mechanism for tumorigenesis.*

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3630 **Oxidative Stress Activates SIRT2 to Deacetylate and Stimulate Phosphoglycerate Mutase**
Yanping Xu, Fulong Li, Lei Lv, Tingting Li, Xin Zhou, Chu-Xia Deng, Kun-Liang Guan, Qun-Ying Lei, and Yue Xiong

Précis: *These results reveal a mechanism that maintains NADPH homeostasis in response to oxidative stress, not only easing cell proliferation in tumors but also licensing conditions for metabolic adaptation to otherwise growth-inhibitory conditions.*

CORRECTIONS

3643 **Correction: Curative Properties of Noninternalizing Antibody–Drug Conjugates Based on Maytansinoids**

3644 **Correction: Emergence, Involution, and Progression to Carcinoma of Mutant Clones in Normal Endometrial Tissues**

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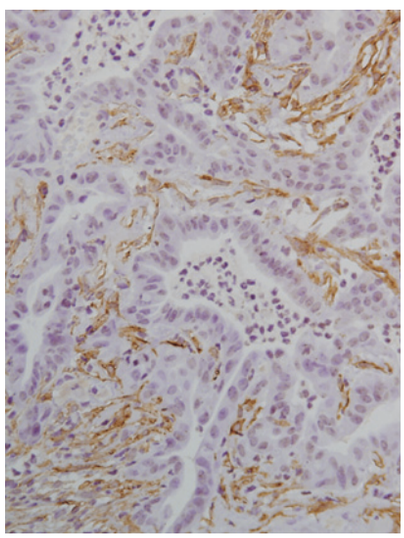
ABOUT THE COVER

Pancreatic cancer is the most aggressive tumor, showing almost identical incidence and mortality values. Emerging data have highlighted the paramount contribution of tumor epithelium-stroma cross-talk in tumor progression. Galectin-1, a glycan-binding protein, is highly expressed in the stroma of pancreatic ductal tumors from *Ela-myc* mice, suggesting a role in cancer progression. Interestingly, genetic depletion of Galectin-1 in this model decreases tumor proliferation, angiogenesis, stroma formation and acinar to ductal metaplasia, and restores the immune surveillance, leading to a significant increase in animal lifespan. These results show that Galectin-1 favors tumor progression by modulation of the tumor microenvironment, suggesting that this lectin is a potential target for therapy. For details, see article by Martínez-Bosch and colleagues on page 3512.



Cancer Research
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