### BREAKING ADVANCES

#### 1907
**Highlights from Recent Cancer Literature**

### REVIEWS

#### 1909
**Anti-VEGF/VEGFR Therapy for Cancer: Reassessing the Target**
Basel Sitohy, Janice A. Nagy, and Harold F. Dvorak

#### 1915
**Nodal Expression and Detection in Cancer: Experience and Challenges**
Luigi Strizzi, Katharine M. Hardy, Dawn A. Kirschmann, Lars Ahrlund-Richter, and Mary J.C. Hendrix

### PRIORITY REPORTS

#### 1921
**Detection of Redundant Fusion Transcripts as Biomarkers or Disease-Specific Therapeutic Targets in Breast Cancer**
Yan W. Asmann, Brian M. Necela, Krishna B. Kalari, Asif Hossain, Tiffany R. Baker, Jennifer M. Carr, Caroline Davis, Julie E. Getz, Galen Hostetter, Xing Li, Sarah A. McLaughlin, Derek C. Radisky, Gary P. Schrotth, Heather E. Cunliffe, Edith A. Perez, and E. Aubrey Thompson

**Précis:** Fusion transcripts generating cancer-specific chimeric molecules have been widely used in hematopoietic cancers for diagnosis, prognosis, and treatment, but these genomic features have not been exploited in solid tumors due to the lack of a technology that could readily define targets to exploit, as this important study now addresses.

#### 1929
**The Mixed Lineage Leukemia (MLL) Fusion–Associated Gene API Promotes CD133 Transcription**
Anthony B. Mak, Allison M.L. Nixon, and Jason Moffat

**Précis:** Findings illuminate the regulation of a stem cell marker that functions in a variety of cancers, including the class of pediatric leukemias studied here.

### INTEGRATED SYSTEMS AND TECHNOLOGIES

#### 1935
**Concordant Release of Glycolysis Proteins into the Plasma Preceding a Diagnosis of ER+ Breast Cancer**
Lynn M. Amon, Sharon J. Pitteri, Christopher I. Li, Martin McIntosh, Jon J. Ladil, Mary Disis, Peggy Porter, Chee Hong Wong, Qing Zhang, Paul Lampe, Ross L. Prentice, and Samir M. Hanash

**Précis:** Through a combination of mass spectrometry and gene set analysis, glycolysis pathway proteins are identified in the blood of breast cancer patients prior to diagnosis, suggesting that these proteins may serve as circulating biomarkers and potentially complement mammography in breast cancer screening.

### MICROENVIRONMENT AND IMMUNOLOGY

#### 1943
**Dermatan Sulfate Is Involved in the Tumorigenic Properties of Esophageal Squamous Cell Carcinoma**
Martin A. Thelin, Katrin J. Svensson, Xiaofeng Shi, Mariam Bagher, Jakob Axelsson, Anna Isinger-Ekstrand, Toin H. van Kuppevelt, Jan Johansson, Mef Nilbert, Joseph Zaia, Mattias Beltling, Marco Maccarana, and Anders Malmström

**Précis:** Expression and structure of an extracellular proteoglycan that is altered widely in esophageal cancer is responsible for driving invasive cell migration, suggesting a novel targeting approach to attack this deadly cancer.

#### 1953
**Genetic Deficiency in Plasma Protein HRG Enhances Tumor Growth and Metastasis by Exacerbating Immune Escape and Vessel Abnormalization**
Sónia Tugues, Satoshi Honjo, Christian König, Oriol Noguer, Marie Hedlund, Johan Bolling, Sofie Descheemaeker, Mathias Wenes, Charlotte Rolny, Wilhelm Jahnus-Dechent, Massimiliano Mazzone, and Lena Claesson-Welsh

**Précis:** Findings establish an important link between deficiency of a highly expressed plasma protein and tumor progression via activation of protumoral macrophages and immune suppression.
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<td>2017</td>
<td>FGFR2 Isoforms Support Epithelial–Stromal Interactions in Thyroid Cancer Progression</td>
<td>Miao Gao, Wei Liu, Stefano Serra, Sylvia L. Asa, and Shereen Ezzat</td>
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<td>2017</td>
<td>PREVENTION AND EPIDEMIOLOGY</td>
<td></td>
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<td>2028</td>
<td>Effect of Depo-Medroxyprogesterone Acetate on Breast Cancer Risk among Women 20 to 44 Years of Age</td>
<td>Christopher I. Li, Elisabeth F. Beaber, Mei Tzu Chen Tang, Peggy L. Porter, Janet R. Daling, and Kathleen E. Malone</td>
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**MOLECULAR AND CELLULAR PATHOBIOLOGY**

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AZD4547: An Orally Bioavailable, Potent, and Selective Inhibitor of the Fibroblast Growth Factor Receptor Tyrosine Kinase Family


Précis: A potent and highly selective small-molecule inhibitor may offer a broad-based approach for treatment of many kinds of tumors that involve activation of the fibroblast growth factor receptor.

Intratracheal Administration of a Nanoparticle-Based Therapy with the Angiotensin II Type 2 Receptor Gene Attenuates Lung Cancer Growth

Atsushi Kawabata, Abdulgader Baoum, Naomi Ohta, Stephanie Jacquez, Gwi-Moon Seo, Cory Berkland, and Masaaki Tamura

Précis: Findings offer a preclinical validation for a nontoxic cationic, peptide-based nanoparticle vector that can deliver genes via the trachea for effective treatment of lung cancers.

Common Variation at BARD1 Results in the Expression of an Oncogenic Isoform That Influences Neuroblastoma Susceptibility and Oncogenicity


Précis: Genetic predisposition studies not only can identify mechanisms of cancer susceptibility but also can reveal therapeutically relevant oncogenic vulnerabilities that may be exploitable clinically.

Tumor Vascular Microenvironment Determines Responsiveness to Photodynamic Therapy

Amanda L. Maas, Shirron L. Carter, E. Paul Wileyto, Joann Miller, Min Yuan, Guoqiang Yu, Amy C. Durham, and Theresa M. Busch

Précis: Collagen in the basement membrane of vascular cells is a site of drug localization and treatment effect in photodynamic therapy, with implications that may help to improve the effectiveness of these treatments for cancer.

Mitigating Age-Related Immune Dysfunction Heightens the Efficacy of Tumor Immunotherapy in Aged Mice


Précis: The ability of the immune system to control cancer is increasingly compromised with a patient's age, but emerging strategies to reprogram immunity in the elderly may heighten these patients' ability to respond efficiently to cancer immunotherapy.

"OA02" Peptide Facilitates the Precise Targeting of Paclitaxel-Loaded Micellar Nanoparticles to Ovarian Cancer In Vivo

Kai Xiao, Yuanpei Li, Joyce S. Lee, Abhy M. Genik, Tiffany Dong, Gabriel Fung, Eduardo Sanchez, Li Xing, Holland R. Cheng, Juntao Luo, and Kit S. Lam

Précis: Findings offer preclinical proof-of-concept for a peptidyl nanoformulation with significant potential to improve treatment of patients with ovarian cancer.

Deficiency in Mammalian Histone H2B Ubiquitin Ligase Bre1 (Rnf20/Rnf40) Leads to Replication Stress and Chromosomal Instability

Sophia B. Chernikova, Olga V. Razorenova, John P. Higgins, Brock J. Sih, Monica Nicolau, Jennifer A. Dorth, Diana A. Chernikova, Shirley Kwok, James D. Brooks, Susan M. Bailey, John C. Game, and Martin Brown

Précis: Genomic instability caused by deficiency in a histone ubiquitin ligase may be an important initial step in acquisition of an invasive phenotype by an early-stage noninvasive tumor.

Type I and II IFNs Inhibit Merkel Cell Carcinoma via Modulation of the Merkel Cell Polyomavirus T Antigens

Christoph Willmes, Christian Adam, Miriam Alh, Lena Völkert, Roland Houben, Jürgen C. Becker, and David Schrama

Précis: Merkel cell carcinoma, a rare but highly aggressive skin cancer driven by a polyomavirus tumor antigen, may be susceptible to IFN therapies found to modulate the antigen's expression.
CDK8 Maintains Tumor Dedifferentiation and Embryonic Stem Cell Pluripotency
Adam S. Adler, Mark L. McCleland, Tom Truong, Shari Lau, Zora Modrusan, Tim M. Soukup, Merone Roose-Girma, Elizabeth M. Blackwood, and Ron Firestein

Précis: Therapeutic targeting of the cyclin-dependent kinase CDK8 may specifically blunt stem-like properties in cancer cells.

Expression of a Truncated Active Form of VDAC1 in Lung Cancer Associates with Hypoxic Cell Survival and Correlates with Progression to Chemotherapy Resistance
M. Christiane Brahimi-Horn, Danya Ben-Hail, Marius Ilie, Pierre Gounon, Matthieu Rouleau, Véronique Hofman, Jérôme Doyen, Bernard Mari, Varda Shoshan-Barmatz, Paul Hofman, Jacques Pouysségur, and Nathalie M. Mazure

Précis: Blockade of a mitochondria anion channel may improve response to lung cancer therapy by restoring apoptotic sensitivity and circumventing chemoresistance in hypoxic tumor cells.

ABOUT THE COVER
The HIV-1 TAT peptide was dimerized and used to formulate a nanoparticle vector (dTAT NP) to leverage efficient tumor-targeted gene delivery following intratracheal administration. In vitro expression efficiency for dTAT NP–encapsulated luciferase or angiotensin II type 2 receptor (AT2R) plasmid DNA (pDNA) revealed effective pDNA transfection with negligible cytotoxicity. In orthotopic tumor grafts, immunohistochemical analysis confirmed that dTAT NP successfully delivered pDNA to the tumor, and gene expression in tumor tissues persisted at least 14 days after intratracheal administration. Bolus administration of dTAT NP–encapsulated AT2R or TRAIL pDNA, both endogenous apoptosis inducers, markedly attenuated tumor growth. For details, see article by Kawabata and colleagues on page 2057.