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

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. Laid, Mary Disis, Peggy Porter, Chue 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, Meif Nilbert, Joseph Zaia, Mattias Belting, 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

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.
**MOLECULAR AND CELLULAR PATHOBIOLOGY**

1964  
**Densely Granulated Murine NK Cells Eradicate Large Solid Tumors**  
Rebecca B. Liu, Boris Engels, Ainhoa Arina, Karin Schreiber, Elizabeth Hyjek, Andrea Schietinger, David C. Binder, Eric Butz, Thomas Krausz, Donald A. Rowley, Bana Jabri, and Hans Schreiber  
**Précis:** If present, high levels of a cytokine implicated in immune memory in the tumor microenvironment will promote the accumulation of densely granulated natural killer cells that are capable of eradicating large solid tumors.

1975  
**Increased CD8<sup>+</sup> T-cell Function following Castration and Immunization Is Countered by Parallel Expansion of Regulatory T Cells**  
Shuai Tang, Miranda L. Moore, Jason M. Grayson, and Purnima Dubey  
**Précis:** Findings show that androgen ablation expands both the effector and inhibitory arms of the immune response to tumors, resulting in only a transient enhancement of immune function.

1986  
**A Potent Vaccination Strategy That Circumvents Lymphodepletion for Effective Antitumor Adoptive T-cell Therapy**  
Hyun-Il Cho, Eduardo Reyes-Vargas, Julio C. Delgado, and Esteban Celis  
**Précis:** Findings suggest a simple, effective strategy to improve adoptive T-cell therapy for melanoma treatment that avoids complications associated with lymphodepletion and high-dose interleukin-2 treatment.

**PREVENTION AND EPIDEMIOLOGY**

2017  
**FGFR2 Isoforms Support Epithelial–Stromal Interactions in Thyroid Cancer Progression**  
Miao Guo, Wei Liu, Stefano Serra, Sylvia L. Asa, and Shereen Ezzat  
**Précis:** This study highlights the importance of the context in the tumor of the regulatory properties of different growth factor receptor isoforms by illustrating how alternative splicing can confer different functions depending on whether the receptor is expressed in tumor versus tumor stromal cells.

2028  
**Effect of Depo-Medroxyprogesterone Acetate on Breast Cancer Risk among Women 20 to 44 Years of Age**  
Christopher I. Li, Elisabeth F. Beaber, Mei Tzu Chen Tang, Peggy L. Porter, Janet R. Daling, and Kathleen E. Malone  
**Précis:** The most common injectable contraceptive may increase breast cancer risk among young women who use it.

2036  
**Characterization of Gene–Environment Interactions for Colorectal Cancer Susceptibility Loci**  
**Précis:** This study reveals a colon cancer risk locus variant that appears to be modified by vegetable consumption, motivating further work to elucidate environmental influences on cancer susceptibility genes.
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<tr>
<td>2057</td>
<td>Intratracheal Administration of a Nanoparticle-Based Therapy with the Angiotensin II Type 2 Receptor Gene Attenuates Lung Cancer Growth</td>
<td>Atsushi Kawabata, Abdulgader Baoum, Naomi Obta, Stephanie Jacquez, Cory Berkland, and Masaaki Tamura</td>
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<td>2089</td>
<td>&quot;OA02&quot; Peptide Facilitates the Precise Targeting of Paclitaxel-Loaded Micellar Nanoparticles to Ovarian Cancer In Vivo</td>
<td>Kai Xiao, Yuanpei Li, Joyce S. Lee, Abby M. Genik, Tiffany Dong, Gabriel Fung, Eduardo Sanchez, Li Xing, Holland R. Cheng, Juntao Luo, and Kit S. Lam</td>
</tr>
<tr>
<td>2111</td>
<td>Type I and II IFNs Inhibit Merkel Cell Carcinoma via Modulation of the Merkel Cell Polyomavirus T Antigens</td>
<td>Christoph Willmes, Christian Adam, Miriam Alh, Lena Völkert, Roland Houben, Jürgen C. Becker, and David Schrama</td>
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A Journal of the American Association for Cancer Research www.aacrjournals.org

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

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

Deficiency in Mammalian Histone H2B Ubiquitin Ligase Br61 (Rnf20/Rnf40) Leads to Replication Stress and Chromosomal Instability

Type I and II IFNs Inhibit Merkel Cell Carcinoma via Modulation of the Merkel Cell Polyomavirus T Antigens
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<td>2129</td>
<td>CDK8 Maintains Tumor Dedifferentiation and Embryonic Stem Cell Pluripotency</td>
<td>Adam S. Adler, Mark L. McCleland, Tom Truong, Shari Lau, Zora Modrusan, Tim M. Soukup, Merone Roose-Girma, Elizabeth M. Blackwood, and Ron Firestein</td>
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<td>2140</td>
<td>Expression of a Truncated Active Form of VDAC1 in Lung Cancer Associates with Hypoxic Cell Survival and Correlates with Progression to Chemotherapy Resistance</td>
<td>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</td>
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**Précis:** Therapeutic targeting of the cyclin-dependent kinase CDK8 may specifically blunt stem-like properties in cancer cells.

**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.

**Correction:** Preclinical Profile of a Potent γ-Secretase Inhibitor Targeting Notch Signaling with *In vivo* Efficacy and Pharmacodynamic Properties

**Correction:** p53 Pre- and Postbinding Event Theories Revisited: Stresses Reveal Specific and Dynamic p53-Binding Patterns on the p21 Gene Promoter

**Correction:** Potentiation of the Novel Topoisomerase I Inhibitor Indenoisoquinoline LMP-400 by the Cell Checkpoint and Chk1-Chk2 Inhibitor, AZD7762

**OBITUARY**

Ricardo Renzo Brentani: In Memoriam (1937–2011)
Luisa L. Villa and Eduardo L. Franco

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**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.