<table>
<thead>
<tr>
<th>PAGE</th>
<th>TITLE</th>
<th>VOLUME</th>
<th>NUMBER</th>
</tr>
</thead>
<tbody>
<tr>
<td>4963</td>
<td>Highlights from Recent Cancer Literature</td>
<td>73</td>
<td>16</td>
</tr>
<tr>
<td>4965</td>
<td>Targeting the Tumor Microenvironment: From Understanding Pathways to Effective Clinical Trials</td>
<td>73</td>
<td>16</td>
</tr>
<tr>
<td>4978</td>
<td>p63 Sharp1, and HIFs: Master Regulators of Metastasis in Triple-Negative Breast Cancer</td>
<td>73</td>
<td>16</td>
</tr>
<tr>
<td>4982</td>
<td>Early B-Cell Differentiation in Merkel Cell Carcinomas: Clues to Cellular Ancestry</td>
<td>73</td>
<td>16</td>
</tr>
<tr>
<td>4988</td>
<td>The 19th Annual Prostate Cancer Foundation Scientific Retreat: Meeting Report</td>
<td>73</td>
<td>16</td>
</tr>
<tr>
<td>4992</td>
<td>Metabolic Characterization of Hepatocellular Carcinoma Using Nontargeted Tissue Metabolomics</td>
<td>73</td>
<td>16</td>
</tr>
<tr>
<td>5003</td>
<td>Myeloid-Derived Suppressor Cells as a Vehicle for Tumor-Specific Oncolytic Viral Therapy</td>
<td>73</td>
<td>16</td>
</tr>
<tr>
<td>5016</td>
<td>TGF-β Modulates Ovarian Cancer Invasion by Upregulating CAF-Derived Microenvironment</td>
<td>73</td>
<td>16</td>
</tr>
<tr>
<td>5029</td>
<td>Gene Profiling of Canine B-Cell Lymphoma Reveals Germinal Center and Postgerminal Center Subtypes with Different Survival Times, Modeling Human DLBCL</td>
<td>73</td>
<td>16</td>
</tr>
</tbody>
</table>

**MICROENVIRONMENT AND IMMUNOLOGY**

**REVIEWS**

- **Targeting the Tumor Microenvironment: From Understanding Pathways to Effective Clinical Trials**
  - Hua Fang and Yves A. DeClerck

- **p63 Sharp1, and HIFs: Master Regulators of Metastasis in Triple-Negative Breast Cancer**
  - Stefano Piccolo, Elena Enzo, and Marco Montagner

**PERSPECTIVE**

- **Early B-Cell Differentiation in Merkel Cell Carcinomas: Clues to Cellular Ancestry**
  - Axel zur Hausen, Dorit Rennspiess, Veronique Winnepenninckx, Ernst-Jan Speel, and Anna Kordelia Kurz

**MEETING REPORT**

- **The 19th Annual Prostate Cancer Foundation Scientific Retreat: Meeting Report**
  - Guneet Walia, Kenneth J. Pienta, Jonathan W. Simons, and Howard R. Soule

**INTEGRATED SYSTEMS AND TECHNOLOGIES**

- **Metabolic Characterization of Hepatocellular Carcinoma Using Nontargeted Tissue Metabolomics**
  - Qiang Huang, Yexiong Tan, Peiyuan Yin, Guozhu Ye, Peng Gao, Xin Lu, Hongyang Wang, and Guowang Xu

**MOLECULAR AND CELLULAR PATHOBIOLOGY**

- **Myeloid-Derived Suppressor Cells as a Vehicle for Tumor-Specific Oncolytic Viral Therapy**
  - Samuel Eisenstein, Brian A. Cowley, Karen Briley-Sarbel, Ge Ma, Hui-ming Chen, Marcia Meseck, Stephen Ward, Celina Divino, Savio Woo, Shu-Hsia Chen, and Ping-Ying Pan

- **TGF-β Modulates Ovarian Cancer Invasion by Upregulating CAF-Derived Microenvironment**
  - Tsz-Lun Yeung, Cecilia S. Leung, Kwong-Woo Kong, Goli Samimi, Melissa S. Thompson, Jinsong Liu, Tarrick M. Zaid, Sue Ghosh, Michael J. Birrer, and Samuel C. Mok

- **Gene Profiling of Canine B-Cell Lymphoma Reveals Germinal Center and Postgerminal Center Subtypes with Different Survival Times, Modeling Human DLBCL**

**Précis**

- This preclinical study highlights the efficacy of a specific myeloid cell type to serve as a key delivery vehicle for oncolytic viruses that significantly improves tumor killing, prolonging survival and minimizing toxicity.

- These findings suggest a central mechanism through which TGF-β-targeted therapies may alter the invasive capacity of cancer cells by acting through their microenvironment.

- This study reveals the remarkable molecular similarity between human and canine forms of a certain type of B-cell lymphoma, overcoming limitations in existing models that have impeded the advancement of etiologic and therapeutic insights.
DDB2: A Novel Regulator of NF-κB and Breast Tumor Invasion
Marie Ennen, Rémi Klotz, Nadège Touche, Sophie Pinel, Claire Barbieux, Vanessa Besancenot, Emilie Brunner, Denise Thiebaut, Alain C. Jung, Sonia Ledrappier, Lionel Domenjoud, Joseph Abecassis, François Plénat, Stéphanie Grandemange, and Philippe Becuwe

**Précis:** A DNA repair protein that also participates in the control of cell cycle and transcription is found to exert profound effects on the invasive behavior of breast cancer cells, defining a new function for this protein and suggesting further investigations into its potential as a prognostic factor and therapeutic target.

EGF Receptor Activates MET through MAPK to Enhance Non–Small Cell Lung Carcinoma Invasion and Brain Metastasis
Jerrica L. Breindel, Jonathan W. Haskins, Elizabeth P. Cowell, Minghui Zhao, Don X. Nguyen, and David F. Stern

**Précis:** These results show how EGFR-MET signaling is critical for aggressive behavior in lung adenocarcinomas and rationalize its continued investigation as a therapeutic target in NSCLC, whether tumors harbor wild-type or mutant EGFR at early stages of progression.

Regulation of the Transcriptional Coactivator FHL2 Licenses Activation of the Androgen Receptor in Castrate-Resistant Prostate Cancer
Meagan J. McGrath, Lauren C. Binge, Absorn Sriratana, Hong Wang, Paul A. Robinson, David Pook, Clare G. Fedele, Susan Brown, Jennifer M. Dyson, Denny L. Cottle, Belinda S. Cowling, Birunthi Niranjan, Gail R. Rishbridger, and Christina A. Mitchell

**Précis:** This potentially seminal paper not only provides insights into how the androgen receptor is activated in advanced prostate cancer but also offers broader import because the mechanism discovered may affect other oncogenic transcription factors that drive different human cancers.

Extracellular RNA Liberates Tumor Necrosis Factor-α to Promote Tumor Cell Trafficking and Progression
Silvia Fischer, Sabine Gesierich, Barbara Griermert, Anne Schänzer, Till Acker, Hellmut G. Augustin, Anna-Karin Olsson, and Klaus T. Preissner

**Précis:** These findings establish crucial functions for extracellular RNA released from tumor cells in driving invasion and progression, and suggest in vivo applications for RNase1 as a provocative therapeutic approach.
RHPN2 Drives Mesenchymal Transformation in Malignant Glioma by Triggering RhoA Activation
Carla Danussi, Uri David Akavia, Francesco Niola, Andreja Jovic, Anna Lasorella, Dana Pe’er, and Antonio Iavarone

 précis: These results identify a key genetic module promoting the most aggressive cancer phenotype in glioblastoma patients, leading to the worst outcomes.

PREVENTION AND EPIDEMIOLOGY

A Sequence Polymorphism in miR-608 Predicts Recurrence after Radiotherapy for Nasopharyngeal Carcinoma
Jian Zheng, Jieqiong Deng, Mang Xiao, Lei Yang, Liyuan Zhang, Yonghe You, Min Hu, Na Li, Hongchun Wu, Wei Li, Jiachun Lu, and Yifeng Zhou

 précis: A single-nucleotide polymorphism in a microRNA that affects chromatid break repair can predict clinical outcomes after radiotherapy in nasopharyngeal cancer, with potentially broader implications for other DNA damaging cancer therapies.

Gleason Grade Progression Is Uncommon

 précis: These findings suggest that prostate tumor grade may be established early in tumorigenesis, with one implication being that patients newly diagnosed with early-stage and lower-grade disease may feel more comfortable on an active surveillance protocol.

THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

A Novel Class of Anticancer Compounds Targets the Actin Cytoskeleton in Tumor Cells

 précis: This study offers a preclinical proof of concept for small molecules that target the actin cytoskeleton of cancer cells as an efficacious treatment strategy.

mTOR Signaling Feedback Modulates Mammary Epithelial Differentiation and Restrains Invasion Downstream of PTEN Loss
Susmita Ghosh, Lidenys Varela, Akshay Sood, Ben Ho Park, and Tamara L. Lotan

 précis: This report suggests additional new cautions regarding the use of mTOR inhibitors for cancer treatment, contributing to ongoing controversies about their potential utility.

RG7116, a Therapeutic Antibody That Binds the Inactive HER3 Receptor and Is Optimized for Immune Effector Activation
Christian Mirschberger, Christian B. Schiller, Michael Schraml, Nikolaos Dimoudis, Thomas Friess, Christian A. Gerdes, Ulrike Reiff, Valeria Lifke, Gabriele Hoelzlswimmer, Irene Kolm, Karl-Peter Hopfner, Gerhard Niederfellner, and Birgit Bossenmaier

 précis: As a central integrator of the EGF family receptor system in cancer, HER3 offers an appealing therapeutic target in many types of human cancer.

Inhibitor-Sensitive FGFR2 and FGFR3 Mutations in Lung Squamous Cell Carcinoma

 précis: These findings provide a rationale to target certain lung or head and neck squamous cell carcinomas with FGFR inhibitors that are currently in clinical trials, possibly identifying patient populations that may benefit the most.

Cotargeting Androgen Receptor and Clusterin Delays Castrate-Resistant Prostate Cancer Progression by Inhibiting Adaptive Stress Response and AR Stability
Hiroaki Matsumoto, Yoshiaki Yamamoto, Masaki Shiota, Hidetoshi Kuruma, Eliana Beraldi, Hideyasu Matsuyama, Amina Zoubedi, and Martin Gleave

 précis: This study offers a mechanism-based strategy to leverage the therapeutic effects of androgen receptor antagonists in advanced prostate cancer, which remains a deadly scourge.

mTOR Signaling Feedback Modulates Mammary Epithelial Differentiation and Restrains Invasion Downstream of PTEN Loss
Susmita Ghosh, Lidenys Varela, Akshay Sood, Ben Ho Park, and Tamara L. Lotan

 précis: This report suggests additional new cautions regarding the use of mTOR inhibitors for cancer treatment, contributing to ongoing controversies about their potential utility.
Manganoporphyrins Increase Ascorbate-Induced Cytotoxicity by Enhancing H₂O₂ Generation
Malvika Rawal, Samuel R. Schroeder, Brett A. Wagner, Cameron M. Cushing, Jessemee L. Welsh, Anna M. Button, Juan Du, Zita A. Sibenaller, Garry R. Buettner, and Joseph J. Cullen

 précis: A class of porphyrins being developed as superoxide dismutase mimics have the potential to safely leverage the anticancer effects of pharmacologic ascorbate therapy.

Intratumoral Modeling of Gefitinib Pharmacokinetics and Pharmacodynamics in an Orthotopic Mouse Model of Glioblastoma
Jyoti Sharma, Hua Lv, and James M. Gallo

 précis: The major issue of heterogeneity in solid tumors, having been characterized yet again by deep sequencing studies, dramatically affects intratumoral drug activities, for which better models are needed to enhance our understanding.

Potassium Channel KCNA1 Modulates Oncogene-Induced Senescence and Transformation
Hélène Lallet-Daher, Clotilde Wiel, Delphine Gitenay, Naveenan Navaratnam, Arnaud Augert, Benjamin Le Calvé, Stéphanie Verbeke, David Carling, Sébastien Aubert, David Vindrieux, and David Bernard

 précis: This study identifies a novel tumor suppressor pathway that restricts oncogenesis by triggering premature senescence.

CTEN Prolongs Signaling by EGFR through Reducing Its Ligand-Induced Degradation
Shiao-Ya Hong, Yi-Ping Shih, Tianhong Li, Kermit L. Carraway III, and Su Hao Lo

 précis: The most effective therapeutic targeting of EGFR for cancer therapy will likely be based in part on an understanding of the epigenetic conditions that contribute to its effective stabilization.

O-GlcNAc Transferase Integrates Metabolic Pathways to Regulate the Stability of c-MYC in Human Prostate Cancer Cells
Harri M. Itkonen, Sarah Minner, Ingrid J. Guldvik, Mareike Julia Sandmann, Maria Christina Tsourlakis, Viktor Berge, Aud Svindland, Thorsten Schlomm, and Ian G. Mills

 précis: Targeting a protein glycosylation pathway that is dysregulated by metabolic flux in cancer cells blocks MYC and inhibits cancer cell proliferation, possibly offering a broad-based anticancer strategy.

JAK-STAT Blockade Inhibits Tumor Initiation and Clonogenic Recovery of Prostate Cancer Stem-like Cells
Paula Kroon, Paul A. Berry, Michael J. Stower, Greta Rodrigues, Vincent M. Mann, Matthew Simms, Deepak Bhasin, Somasundaram Chettiar, Chenglong Li, Pui-Kai Li, Norman J. Maitland, and Anne T. Collins

 précis: The most primitive cells in prostate cancer require STAT3 for survival, further rationalizing this molecule as a therapeutic target to treat advanced prostate cancer.

AC icon indicates Author Choice
For more information please visit www.aacrjournals.org
ABOUT THE COVER

The actin cytoskeleton, due to its role in many processes involved in cellular transformation, has long been a sought after anticancer target, yet attempts to develop such compounds have been hampered by unacceptable toxicity. By targeting the other core polymer system of the microfilaments, tropomyosin, it is possible to discriminate between actin filaments required for sarcomeric function and those required for tumor growth. In silico modeling shows the predicted association of the first in class anti-tropomyosin compound, TR100, with the C-terminus of a cancer-associated tropomyosin, Tm5NM1. The interaction between Tm5NM1 and TR100 results in disruption of actin filament organization and death of tumor cells, both in vitro and in vivo. For details, see article by Stehn and colleagues on page 5169.