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**1902** Noninvasive Quantification of Solid Tumor Microstructure Using VERDICT MRI
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**1913** Apoptosis Imaging for Monitoring DR5 Antibody Accumulation and Pharmacodynamics in Brain Tumors Noninvasively

### MICROENVIRONMENT AND IMMUNOLOGY

**1924** VISTA Is an Immune Checkpoint Molecule for Human T Cells
J. Louise Lines, Erirni Pantazi, Justin Mak, Lorenzo F. Sempere, Li Wang, Samuel O’Connell, Sabrina Ceeraz, Ariel F. Suriavinata, Shaoleng Yan, Marc S. Ernstoff, and Randolph Noelle

**1933** VISTA Regulates the Development of Protective Antitumor Immunity
Isabelle Le Mercier, Wenna Chen, Janet L. Lines, Maria Day, Jiannan Li, Petra Sergent, Randolph J. Noelle, and Li Wang

**1945** Vaccine-Mediated Immunotherapy Directed against a Transcription Factor Driving the Metastatic Process
Andressa Ardián, Sofia R. Gameiro, Claudia Palena, Duane H. Hamilton, Anna Kwilas, Thomas H. King, Jeffrey Schlam, and James W. Hodge

**1958** T Lymphocytes Restrain Spontaneous Metastases in Permanent Dormancy
Irene Romero, Cristina Garrido, Ignacio Algarra, Antonia Collado, Federico Garrido, and Angel M. García-Lora

**1969** IL-17A Produced by γδ T Cells Promotes Tumor Growth in Hepatocellular Carcinoma
Shoubao Ma, Qiao Cheng, Yifeng Cai, Huanle Gong, Yan Wu, Xiao Yu, Liyun Shi, Depei Wu, Chen Dong, and Haiyan Liu

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<td>1983</td>
<td>β-Catenin Inhibitor ICAT Modulates the Invasive Motility of Melanoma Cells</td>
<td>Mélanie J. Domingues, Florian Rambow, Bastien Job, Laura Papon, Wanguo Liu, Lionel Larue, and Jacky Bonaventure</td>
<td>ICAT inhibition reduces the mesenchymal-amoeboid transition involved in invasive cancer cell motility, limiting metastasis formation.</td>
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<td>1996</td>
<td>Src Kinase Is a Novel Therapeutic Target in Lymphangioleiomyomatosis</td>
<td>Alexey Tyryshkin, Abhisek Bhattacharya, and N. Tony Eissa</td>
<td>This study provides a mechanistic rationale to immediately reposition the use of Src inhibitors currently in clinical trials for the treatment of malignancies associated with mutation of the tumor suppressor gene TSC2.</td>
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<td>2006</td>
<td>PP2A-B55β Antagonizes Cyclin E1 Proteolysis and Promotes Its Dysregulation in Cancer</td>
<td>YingMeei Tan, Dahui Sun, Weijian Jiang, Kathleen Klotz-Noack, Ajay A. Vashishth, James Wohlschlegel, Martin Widschwendter, and Charles Spruck</td>
<td>As a candidate therapeutic target, overexpressed cyclin E1 is a driving force of hormone-independent growth, genetic instability, and progression of &quot;triple-negative&quot; breast cancers and other aggressive cancers.</td>
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<td>2015</td>
<td>LRH-1 Governs Vital Transcriptional Programs in Endocrine-Sensitive and -Resistant Breast Cancer Cells</td>
<td>Stéphanie Blanco, Mylène Brunelle, Maïka Jangal, Luca Magnani, and Nicolas Gévy</td>
<td>This study shows how the nuclear receptor LRH-1 modulates the sensitivity of breast cancer cells to antiestrogen therapy, suggesting new insights into how resistance may emerge to limit treatment effectiveness.</td>
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<td>2026</td>
<td>Latency-Associated Nuclear Antigen of Kaposi Sarcoma–Associated Herpesvirus Promotes Angiogenesis through Targeting Notch Signaling Effector Hey1</td>
<td>Xing Wang, Zhisheng He, Tian Xia, Xiaofan Li, Deguang Liang, Xianzhi Lin, Hao Wen, and Ke Lan</td>
<td>These findings identify a therapeutic target for treatment of Kaposi sarcoma, a cancer best known for its association with AIDS patients at highest risk of this herpesvirus-driven disease.</td>
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**THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY**

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<td>2038</td>
<td>Tumor-Infiltrating Myeloid Cells Activate DLL4/Notch/TGF-β Signaling to Drive Malignant Progression</td>
<td>Hidetaka Ohtuku, Kan Jiang, Dunrui Wang, Ombretta Salvucci, Hyeongil Kwak, David Sánchez-Martín, Dragan Maric, and Giovanna Tosato</td>
<td>This study describes a myeloid cell–cancer cell signaling network that links the tumor microenvironment in new ways with tumor growth, highlighting opportunities to target tumors where this network is active.</td>
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<td>2050</td>
<td>CRP Loss Cooperates with PTEN Haploinsufficiency to Drive Prostate Cancer: Implications for Epigenetic Therapy</td>
<td>Liya Ding, Shuai Chen, Ping Liu, Yunqian Pan, Jian Zhong, Kevin M. Regan, Liguo Wang, Chunrong Yu, Anthony Rizzardi, Liang Cheng, Jun Zhang, Stephen C. Schmechel, John C. Cheville, Jan Van Deursen, Donald J. Tindall, and Haojie Huang</td>
<td>These findings suggest new insights into prostate cancer etiology, establishing a central role for histone modification and providing a rationale for clinical evaluation of epigenetic-targeted therapy in prostate cancer patients.</td>
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<td>2062</td>
<td>Novel Mechanistic Insights into Ectodomain Shedding of EGFR Ligands Amphiregulin and TGF-α: Impact on Gastrointestinal Cancers Driven by Secondary Bile Acids</td>
<td>Nagaraja S. Nagathihalli, Yugandhar Beesetty, Wooin Lee, M. Kay Washington, Xi Chen, A. Craig Lockhart, and Nipun B. Merchant</td>
<td>These findings define an EGF-related signaling pathway that mediates the oncogenic effects of secondary bile acids in gastrointestinal cancers, the targeting of which may enhance therapeutic responses.</td>
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<td>2073</td>
<td>Bioluminescent Imaging of HPV-Positive Oral Tumor Growth and Its Response to Image-Guided Radiotherapy</td>
<td>Rong Zhong, Matt Pytynia, Charles Pelizzari, and Michael Spiotto</td>
<td>More rapid visualization of HPV-positive oral tumor growth will assist the development of chemotherapeutic and radiotherapeutic strategies to stem this rapidly growing disease.</td>
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Small GTPase RhoE/Rnd3 Is a Critical Regulator of Notch1 Signaling

Précis: These findings describe an important regulatory feedback on a key tumor suppressor pathway that may have a pivotal role in epithelial tumors.

Attenuation of microRNA-126 Expression That Drives CD34^+38^- Stem/Progenitor Cells in Acute Myeloid Leukemia Leads to Tumor Eradication

Précis: These findings define miR-126 as a therapeutic focus to specifically eradicate stem-like cells in acute myeloid leukemias that tend to relapse in patients despite early positive responses to chemotherapy.

NOTCH3 Signaling Regulates MUSASHI-1 Expression in Metastatic Colorectal Cancer Cells
Anna Pastò, Valentina Serafin, Giorgia Pilotto, Claudia Lago, Chiara Bellio, Livio Trusolino, Andrea Bertotti, Timothy Hoey, Michella Plateroti, Giovanni Esposito, Marica Pinazza, Marco Agostini, Donato Nitti, Alberto Amadori, and Stefano Indraccolo

Précis: These findings point to a specific inhibition of NOTCH2/3, rather than NOTCH1, as a strategy for attacking cancer stem-like cells in metastatic colon cancer.

shRNA Kinome Screen Identifies TBK1 as a Therapeutic Target for HER2^+ Breast Cancer

Précis: These results identify a novel target to improve treatment of HER2-positive breast cancer through leveraging existing anti-HER2 therapy.

Correction: Epithelial Junction Opener J0-1 Improves Monoclonal Antibody Therapy of Cancer

ABOUT THE COVER
Numerous reports have now demonstrated that the epithelial-to-mesenchymal transition (EMT) process is involved in solid tumor progression, metastases, and drug resistance. Several transcription factors have been implicated as drivers of EMT and metastatic progression, including Twist, which has been shown to be associated with poor prognosis and drug resistance for many carcinomas and other tumor types. The role of a Twist vaccine in experimental cancer metastases has been principally studied in the 4T1 mammary tumor model, where there is a greater than 3-fold increase in Twist expression in lung metastases (shown) vs. the primary tumor. Vaccination of mice reduced the size of primary transplanted 4T1 tumors and had an even greater antitumor effect on lung metastases of the same mice, which was dependent on Twist-specific T cells. These studies provide the rationale for vaccine-induced T-cell-mediated therapy of transcription factors involved in driving the metastatic process. For details, see article by Ardiani and colleagues on page 1945.