CLINICAL STUDIES

7017 MRE11 Expression Is Predictive of Cause-Specific Survival following Radical Radiotherapy for Muscle-Invasive Bladder Cancer
Ananya Choudhury, Louisa D. Nelson, Mark T.W. Teo, Sameer Chilka, Selina Bhattacharai, Colin F. Johnston, Faye Elliott, Johanna Lowery, Claire F. Taylor, Michael Churchman, Johanne Bentley, Margaret A. Knowles, Patricia Harnden, Robert G. Bristow, D. Timothy Bishop, and Anne E. Kiltie
Précis: Findings define a biopsy marker that may predict the type of therapy most likely to cure individual patients of invasive bladder cancer.

REVIEW

7027 The Promise of MicroRNA Replacement Therapy
Andreas G. Bader, David Brown, and Matthew Winkler

INTEGRATED SYSTEMS AND TECHNOLOGIES

7031 Visible Drug Delivery by Supramolecular Nanocarriers Directing to Single-Platformed Diagnosis and Therapy of Pancreatic Tumor Model
Sachiko Kaida, Horacio Cabral, Michiaki Kuma-gai, Akihiro Kishimura, Yasuko Terada, Masaki Sekino, Ichio Aoki, Nobuhiro Nishiyama, Toru Tani, and Kazunori Kataoka
Précis: Study illustrates how cytotoxic nanoparticle therapies can incorporate an approved MRI contrast agent for superior noninvasive imaging in vivo, easing analysis of preclinical and clinical pharmacology.
MOLECULAR AND CELLULAR PATHOBIOLOGY

7114

PTEN Loss Accelerates KrasG12D-Induced Pancreatic Cancer Development
Reginald Hill, Joseph Hargan Calvopina, Christine Kim, Ying Wang, David W. Dawson, Timothy R. Donahue, Sarah Dry, and Hong Wu

Précis: Cooperation between K-ras activation and PTEN loss during pancreatic carcinogenesis occurs at the early stage of acinar-to-ductal metaplasia.

7125

The Neutrophil Elastase Inhibitor Elafin Triggers Rb-Mediated Growth Arrest and Caspase-Dependent Apoptosis in Breast Cancer
Joseph A. Caruso, Kelly K. Hunt, and Khandan Keyomarsi

Précis: Findings suggest applications of a neutrophil protease inhibitor that can attack breast cancer cells without affecting normal proliferating cells.

7137

hnRNP A2/B1 Modulates Epithelial-Mesenchymal Transition in Lung Cancer Cell Lines
Jordi Tauler, Enrique Zudaire, Huaitian Liu, Joanna Shih, and James L. Mulshine

Précis: Findings contribute to growing evidence that modification of hnRNP A2/B1 expression exerts a major impact on the proliferation and invasive capacity of lung cancer cells.

7148

Spontaneous Tumorigenesis in Mice Overexpressing the p53-Negative Regulator Mdm4
Shunbin Xiong, Vinod Pant, Young-Ah Suh, Carolyn S. Van Pelt, Yongxing Wang, Yasmine A. Valentin-Vega, Sean M. Post, and Guillermima Lozano

Précis: Findings offer preclinical genetic proof that an Mdm2 relative is a critical regulator of p53 and thus a valid therapeutic target to activate p53 in tumors.

7073

Hyaluronan Deficiency in Tumor Stroma Impairs Macrophage Trafficking and Tumor Neovascularization
Nobutaka Kobayashi, Seiji Miyoshi, Takahide Mikami, Hiroshi Koyama, Masato Kitazawa, Michiko Takeoka, Kenji Sano, Jun Amano, Zenzo Isogai, Shumpei Niida, Kayoko Oguri, Minoru Okayama, John A. McDonald, Koji Kimata, Shun'ichiro Taniguchi, and Naoki Itano

Précis: Stromal hyaluronan serves as a microenvironmental signal for recruitment of tumor-associated macrophages, which are key cells involved in tumor neovascularization.

7084

Dacarbazine Treatment before Peptide Vaccination Enlarges T-Cell Repertoire Diversity of Melan-A–Specific, Tumor-Reactive CTL in Melanoma Patients
Belinda Palermo, Duilia Del Bello, Alessandra Sottini, Federico Serana, Claudia Ghidini, Novella Gualtieri, Virginia Ferraresi, Caterina Catricalà, Filippo Belardelli, Enrico Proietti, Pier Giorgio Natali, Luisa Imberti, and Paola Nisticò

Précis: Clinical findings support the concept that the use of chemotherapy before a cancer vaccine can promote renewal of tumor-reactive T cells and extend survival.

7093

IFNγ Markedly Cooperates with Intratumoral Dendritic Cell Vaccine in Dog Tumor Models
Kai Mito, Kikuya Sugiura, Kana Ueda, Takako Hori, Takashi Akazawa, Jyoji Yamate, Hiroshi Nakagawa, Shingo Hatoya, Muneo Inaba, Norimitsu Inoue, Susumu Ikehara, and Toshio Inaba

Précis: Findings suggest a mechanism through which caveolin-1 can mediate antimetastatic effects in melanoma.

7102

Chemotherapy-Induced Genotoxic Stress Promotes Sensitivity to Natural Killer Cell Cytotoxicity by Enabling Missing-Self Recognition
Jason H. Fine, Peter Chen, Aruz Mesci, David S.J. Allan, Stephan Gasser, David H. Raulet, and James R. Carlyle

Précis: Genotoxic and cell-stressing chemicals sensitize tumor cells to MHC-independent missing-self recognition by NK cells.
### THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

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<td>Nagatte Ibrahim, Lei He, Chee-Ann Leong, Deyin Xing, Beth Y. Karlman, Elizabeth M. Swisher, Bo R. Rueda, Sandra Orsulic, and Leif W. Ellisen</td>
<td>Results define a regulatory mechanism that supports contributions of the p53-related protein p73 as a key mediator of the response to platinum chemotherapy in certain ovarian carcinomas.</td>
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<td><strong>Human Papillomavirus Seropositivity Synergizes with MDM2 Variants to Increase the Risk of Oral Squamous Cell Carcinoma</strong></td>
<td>Xingming Chen, Erich M. Sturgis, Dapeng Lei, Kristina Dahlstrom, Qingyi Wei, and Guojun Li</td>
<td>Précis: Findings define a genetic marker elevating susceptibility to HPV-associated oral cancers, particularly in never smokers, never drinkers, and oropharyngeal cancer patients.</td>
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<td>Binoj C. Nair, Sujit S. Nair, Dimple Chakravarty, Rumbabu Challia, Bramanandum Manavathi, P. Renee Yew, Bakesh Kumar, Rajeshwar Rao Tekmal, and Ratna K. Vadlamudi</td>
<td>Précis: Results define a key intersection between cell cycle control and estrogen receptor signaling that has implications for breast cancer progression.</td>
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<td>Zachary C. Hartman, Takuya Osada, Oliver Glass, Xiao Y. Yang, Gang-jun Lei, H. Kim Lyerly, and Timothy M. Clay</td>
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<td>Quinn P. Peterson, Danny C. Hsu, Chris J. Novotny, Diana C. West, Dewey Kim, Joanna M. Schmit, Levent Dirikolu, Paul J. Hergenrother, and Timothy M. Fan</td>
<td>Précis: Findings demonstrate that direct activation of procaspase-3 by a small molecule can be well tolerated and efficacious as an anticancer strategy.</td>
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### PREVENTION AND EPIDEMIOLOGY

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<td><strong>Relationship between Radiation Exposure and Risk of Second Primary Cancers among Atomic Bomb Survivors</strong></td>
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Crucial Roles for Protein Kinase C Isoforms in Tumor-Specific Killing by Apoptin
Jie Jiang, Daryl Cole, Nigel Westwood, Lee Macpherson, Farzin Farzaneh, Ghulam Mufti, Mahvash Tavassoli, and Joop Gäken
Précis: Mechanistic studies reveal the basis for a cancer-selective cell death pathway that might be exploited to improve the treatment of multiple myeloma.

Colorectal Tumors Are Effectively Eradicated by Combined Inhibition of β-Catenin, KRAS, and the Oncogenic Transcription Factor ITF2
Luca Mologni, Hafedh Dekhil, Monica Ceccon, Stefania Purgante, Cathy Lan, Loredana Cleris, Vera Magistrini, Franca Formelli, and Carlo B. Gambacorti-Passerini
Précis: Findings offer preclinical proof of concept for a highly effective combinatorial therapy for colorectal tumors which targets three key oncoproteins.

Deficiency of Splicing Factor 1 Suppresses the Occurrence of Testicular Germ Cell Tumors
Rui Zhu, Jason Heaney, Joseph H. Nadeau, Sara Ali, and Angabin Matin
Précis: Findings strengthen the emerging evidence that alterations in RNA splicing occurring widely in cancer cells functionally contributes to malignant development.

Using the Transcription Factor Inhibitor of DNA Binding 1 to Selectively Target Endothelial Progenitor Cells Offers Novel Strategies to Inhibit Tumor Angiogenesis and Growth
Précis: Findings establish a strategy to follow and target bone marrow–derived endothelial progenitor cells that are vital for tumor angiogenesis.
ABOUT THE COVER

Chronic stress promotes adrenergic-dependent infiltration of macrophages into primary mammary tumors, leading to enhanced metastasis. In an immunofluorescence analysis, anti-β2-adrenergic receptor (green), anti-F4/80 (red), and nuclear counterstaining (blue) were used to visualize 66cl4 mammary tumor cryosections from control and stressed mice. For details, see the article by Sloan and colleagues on page 7042 of this issue.