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.

The Promise of MicroRNA Replacement Therapy

Andreas G. Bader, David Brown, and Matthew Winkler

The Sympathetic Nervous System Induces a Metastatic Switch in Primary Breast Cancer


Précis: Metastasis promoted by macrophages may be assisted by the sympathetic nervous system and thus blocked by drugs that antagonize adrenergic signaling.

Quantitative Imaging of Lymphatic Function with Liposomal Indocyanine Green

Steven T. Proulx, Paola Luciani, Stefanie Derzsi, Matthias Rinderknecht, Viviane Mumprecht, Jean-Christophe Leroux, and Michael Detmar

Précis: Quantitative noninvasive imaging of lymphatic flow will greatly assist the study of experimental cancer drugs being developed to target lymphatics, as well as the ability to image lymphedema and sentinel lymph nodes in cancer.

Loss of Osteoclasts Contributes to Development of Osteosarcoma Pulmonary Metastases

Liliana Endo-Munoz, Andrew Cumming, Danny Rickwood, Danielle Wilson, Claudia Cueva, Charlotte Ng, Geoffrey Strutton, A. Ian Cassady, Andreas Evdokiou, Scott Sommerville, Ian Dickinson, Alexander Guminski, and Nicholas A. Saunders

Précis: Findings suggest that osteoclast-preserving therapies may help prevent or delay metastatic development in osteosarcoma.

Visible Drug Delivery by Supramolecular Nanocarriers Directing to Single-Platformed Diagnosis and Therapy of Pancreatic Tumor Model

Sachiko Kaida, Horacio Cabral, Michiaki Kumagai, 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.
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.

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 Guaitieri, 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.

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, Muneh Inaba, Norimitsu Inoue, Susumu Ikehara, and Toshiro Inaba

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

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.

MOLECULAR AND CELLULAR PATHOBIOLOGY

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.

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.

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.

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.
BRCA1-Associated Epigenetic
Regulation of p73 Mediates an Effector
Pathway for Chemosensitivity in
Ovarian Carcinoma
Nageatte Ibrahim, Lei He, Chee-Onn Leong,
Deyin Xing, Beth Y. Karlan,
Elizabeth M. Swisher, Bo R. Rueda,
Sandra Orsulic, and Leif W. Ellisen

Précis: 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.

Cyclin-Dependent Kinase–Mediated
Phosphorylation Plays a Critical Role
in the Oncogenic Functions of PELP1
Binoj C. Nair, Sujit S. Nair, Dimple Chakravarty,
Rambabu Challa, Bramanandum Manavathi,
P. Renee Yew, Bakesh Kumar,
Rajeshwar Rao Tekmal, and Ratna K. Vadlamudi

Précis: Results define a key intersection between
cell cycle control and estrogen receptor
signaling that has implications for breast
cancer progression.

Oncogenic Wip1 Phosphatase Is
Inhibited by miR-16 in the DNA
Damage Signaling Pathway
Xinna Zhang, Guohui Wan,
Sizolwenkosi Mlotshwa, Vicki Vance,
Franklin G. Berger, Hexin Chen,
and Xiongbin Lu

Précis: Findings define a mechanism by which a
DNA damage-induced microRNA controls a
nodal regulator of DNA damage signaling.

Human Papillomavirus Seropositivity
Synergizes with MDM2 Variants to
Increase the Risk of Oral Squamous
Cell Carcinoma
Xingming Chen, Erich M. Sturgis, Dapeng Lei,
Kristina Dahlstrom, Qingyi Wei, and Guojun Li

Précis: Findings define a genetic marker
elevating susceptibility to HPV-associated oral
cancers, particularly in never smokers, never
drinkers, and oropharyngeal cancer patients.

Ligand-Independent Toll-like
Receptor Signals Generated by
Ectopic Overexpression of MyD88
Generate Local and Systemic
Antitumor Immunity
Zachary C. Hartman, Takeyu Osada,
Oliver Glass, Xiao Y. Yang, Gang-Jun Lei,
H. Kim Lyerly, and Timothy M. Clay

Précis: Ectopic expression of a common
TLR adapter signaling protein can exert all
the benefits of TLR signaling to
antitumor immunity.

Differential Mechanisms of Acquired
Resistance to Insulin-like Growth
Factor-1 Receptor Antibody Therapy
or to a Small-Molecule Inhibitor,
BMS-754807, in a Human
Rhabdomyosarcoma Model
Fei Huang, Warren Hurlburt, Ann Greer,
Karen A. Reeves, Stephen Hillerman,
Han Chang, Joseph Fargnoli,
Friedrich Graf Finckenstein,
Marco M. Gottardis, and Joan M. Carboni

Précis: Study offers the first definition and
comparison of acquired resistance mechanisms
for IGF-1R targeted therapies.

Discovery and Canine Preclinical
Assessment of a Nontoxic
Procaspase-3–Activating Compound
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

Précis: Findings demonstrate that direct
activation of procaspase-3 by a small molecule
can be well tolerated and efficacious as an
anticancer strategy.
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<td>Crucial Roles for Protein Kinase C Isoforms in Tumor-Specific Killing by Apoptin</td>
<td>Jie Jiang, Daryl Cole, Nigel Westwood, Lee Macpherson, Farzin Farzaneh, Ghulam Mufti, Madhavshavattavassoli, and Joop Gäken</td>
<td>Precis: Mechanistic studies reveal the basis for a cancer-selective cell death pathway that might be exploited to improve the treatment of multiple myeloma.</td>
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<td>Rui Zhu, Jason Heaney, Joseph H. Nadeau, Sara Ali, and Angabin Matin</td>
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<td>Melissa K. Brunckhorst, Hui Wang, Rong Lu, and Qin Yu</td>
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<td>Chun-Peng Liao, Helty Adisetiyo, Mengmeng Liang, and Pradip Roy-Burman</td>
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<td>Coactivated Platelet-Derived Growth Factor Receptor α and Epidermal Growth Factor Receptor Are Potential Therapeutic Targets in Intimal Sarcoma</td>
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<td>In vivo Imaging of Tumor Transduced with Bimodal Lentiviral Vector Encoding Human Ferritin and Green Fluorescent Protein on a 1.5T Clinical Magnetic Resonance Scanner</td>
<td>Hoe Suk Kim, Hye Rim Cho, Seung Hong Choi, Ji Su Woo, and Woo Kyung Moon</td>
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A Specific Need for CRKL in p210BCR-ABL–Induced Transformation of Mouse Hematopoietic Progenitors
Ji-Heui Seo, Lisa J. Wood, Anupriya Agarwal, Thomas O’Hare, Collin R. Elsea, Ian J. Griswold, Michael W.N. Deininger, Akira Imamoto, and Brian J. Druker

Précis: Results reveal a previously undefined linkage in BCR-ABL effector signaling that is essential to drive transformation of hematopoietic progenitor cells.

Modifying Akt Signaling in B-Cell Chronic Lymphocytic Leukemia Cells
Sebastian W. Hofbauer, Josefina D. Piñón, Gabriele Brachtl, Lucia Haginger, Wei Wang, Karin Jöhrer, Ingeborg Tinhofer, Tanja Nicole Hartmann, and Richard Greil

Précis: A survival pathway in chronic lymphocytic leukemia responding to antigenic and stromal support might be targeted by disrupting an Akt pathway mediating this support.

ABOUT THE COVER
Chronic stress promotes adrenergic-dependent infiltration of macrophages into primary mammary tumors, leading to enhanced metastasis. In an immunofluorescence analysis, anti–α2-adrenergic receptor (green), anti-F4/80 (red), and nuclear counterstaining (blue) were used to visualize 66c14 mammary tumor cryosections from control and stressed mice. For details, see the article by Sloan and colleagues on page 7042 of this issue.