BREAKING ADVANCES

6399 Highlights from Recent Cancer Literature

REVIEWS

6401 MicroRNAs and Metastasis: Little RNAs Go a Long Way
Derek M. Dykxhoorn

6407 CD73: A Novel Target for Cancer Immunotherapy
Bin Zhang

PRIORITY REPORTS

6412 Type 1 Insulin-like Growth Factor Receptor Translocates to the Nucleus of Human Tumor Cells
Tamara Aleksic, Meenali M. Chitnis, Olga V. Perestenko, Shan Gao, Peter H. Thomas, Gareth D. Turner, Andrew S. Protheroe, Mark Howarth, and Valentine M. Macaulay

Précis: Findings provide new insight into the role of the IGF-1R in cancer, and may have implications for clinical use of IGF-1R inhibitors in cancer treatment.

6420 A Cancer Detection Platform Which Measures Telomerase Activity from Live Circulating Tumor Cells Captured on a Microfilter
Tong Xu, Bo Lu, Yu-Chong Tai, and Amir Goldkorn

Précis: Study describes a rapid, efficient, quantitative and versatile strategy with great promise for cancer detection by blood test, applicable to gauging therapeutic response and relapse of tumors.

INTEGRATED SYSTEMS AND TECHNOLOGIES

6427 Low-Field Magnetic Resonance Imaging to Visualize Chronic and Cycling Hypoxia in Tumor-Bearing Mice
Hironobu Yasui, Shingo Matsumoto, Nallathamby Devasahayam, Jeeva P. Munsinghe, Rajani Choudhuri, Keita Saito, Sankaran Subramanian, James B. Mitchell, and Murali C. Krishna

Précis: High resolution non-invasive methods for visualizing regions of tumor hypoxia could ease preclinical development of new principles to attack these regions, which are typically highly resistant to therapy.

6437 Glioblastoma-Specific Protein Interaction Network Identifies PP1A and CSK21 as Connecting Molecules between Cell Cycle-Associated Genes

Précis: This paper describes two novel molecules that connect cell cycle regulation which are perturbed in glioblastoma.

6448 In silico Estimates of Tissue Components in Surgical Samples Based on Expression Profiling Data
Yipeng Wang, Xiao-Qin Xia, Zhenyu Jia, Anne Sawyers, Huazhen Yao, Jessica Wang-Rodriquez, Dan Mercola, and Michael McClelland

Précis: Expression profiles identify deviant clinical samples that would otherwise adversely affect biomarker discovery.
The Histone Demethylase JMJD2B Is Regulated by Estrogen Receptor α and Hypoxia, and Is a Key Mediator of Estrogen Induced Growth
Jun Yang, Adrian M. Jubb, Luke Pike, Francesca M. Buffa, Helen Turley, Dilair Baban, Russell Leek, Kevin C. Gatter, Jiannis Ragoussis, and Adrian L. Harris

Précis: Findings provide a biological rationale to therapeutically target histone demethylases for breast cancer treatment.

Immunologic Consequences of Signal Transducers and Activators of Transcription 3 Activation in Human Squamous Cell Carcinoma
Emilia Albesiano, Meghan Davis, Alfred P. See, James E. Han, Michael Lim, Drew M. Pardoll, and Young Kim

Précis: Findings highlight the nodal role of STAT3 in activating immune evasion mechanisms erected by tumors, reinforcing interest in STAT3 targeting for cancer therapy.

Steroid Receptor Coactivator-3 Expression in Lung Cancer and Its Role in the Regulation of Cancer Cell Survival and Proliferation
Di Cai, David S. Shames, Maria Gabriela Raso, Yang Xie, Young H. Kim, Jonathan R. Pollack, Luc Girard, James P. Sullivan, Boming Gao, Michael Peyton, Meera Nanjundan, Lauren Byers, John Heymach, Gordon Mills, Adi F. Gazdar, and John D. Minna

Précis: A histone acetyltransferase and nuclear hormone receptor is implicated in lung cancer maintenance and resistance to EGFR inhibitors.

Interaction of TAp73 and Breast Cancer–Associated Gene 3 Enhances the Sensitivity of Cervical Cancer Cells in Response to Irradiation-Induced Apoptosis
Thomas Ho-Yin Leung and Hextan Yuen-Sheung Ngan

Précis: Findings define a mechanism through which transcriptionally active isoforms of the p53 homolog p73 promote cancer radiosensitivity.

Genome-Wide Identification of PAX3-FKHR Binding Sites in Rhabdomyosarcoma Reveals Candidate Target Genes Important for Development and Cancer
Liang Cao, Yunkai Yu, Sven Bilke, Robert L. Walker, Limia H. Mayeemuddin, David O. Azorsa, Fan Yang, Marbin Pineda, Lee J. Helman, and Paul S. Meltzer

Précis: Findings offer a framework to systematically evaluate targeted approaches to treatment of a common pediatric cancer.

A KRAS Variant in Ovarian Cancer Acts as a Genetic Marker of Cancer Risk

Précis: A genetic variation in the KRAS oncogene that disrupts a regulatory microRNA binding site increases the risk of developing ovarian cancer.

KRAB Zinc Finger Protein ZNF382 Is a Proapoptotic Tumor Suppressor That Represses Multiple Oncogenes and Is Commonly Silenced in Multiple Carcinomas
Yingduan Cheng, Hua Geng, Suk Hang Cheng, Pei Liang, Yan Bai, Jisheng Li, Gopesh Srivastava, Margaret H.L. Ng, Tatsuo Fukagawa, Xiushan Wu, Anthony T.C. Chan, and Qian Tao

Précis: Cancer epigenetic studies of a little studied zinc finger protein reveal it to be a tumor suppressor that is widely attenuated in cancer.

Occupational Trichloroethylene Exposure and Renal Carcinoma Risk: Evidence of Genetic Susceptibility by Reductive Metabolism Gene Variants
Lee E. Moore, Paolo Boffetta, Sara Karami, Paul Brennan, Patricia S. Stewart, Rayjean Hung, David Zaridze, Vsevolod Matveev, Vladimir Janout, Helena Kollarova, Vladimir Bencko, Marie Navratilova, Neolina Szeszenia-Dabrowska, Dana Mates, Jan Gromiec, Ivana Holcatova, Maria Merino, Stephen Chanock, and Nathaniel Rothman

Précis: Findings establish that renal cancer risk from exposure to a suspected carcinogen is particularly high in genetically susceptible individuals.
Anti–Placental Growth Factor Reduces Bone Metastasis by Blocking Tumor Cell Engraftment and Osteoclast Differentiation

Lieve Coenegrachts, Christa Maes, Sophie Torrekens, Riet Van Looveren, Massimiliano Mazzone, Theresa A. Guise, Roger Bouillon, Jean-Marie Stassen, Peter Carmeliet, and Geert Carmeliet

Précis: Preclinical findings indicate a key role for placental growth factor in promoting bone metastasis, suggesting an opportunity for antibody-based adjuvant therapy.

The Human WRN and BLM RecQ Helicases Differentially Regulate Cell Proliferation and Survival after Chemotherapeutic DNA Damage

Frances J. Mao, Julia M. Sidorova, Julia M. Lauper, Mary J. Emond, and Raymond J. Monnat

Précis: Study reveals how different RecQ DNA helicases modulate the response to distinct chemotherapeutic agents, and may have potential to serve as biomarkers of tumor-specific chemotherapeutic sensitivity.

Antitumor Effect after Radiofrequency Ablation of Murine Hepatoma Is Augmented by an Active Variant of CC Chemokine Ligand 3/Macrophage Inflammatory Protein-1α

Noriko Iida, Yasunari Nakamoto, Tomohisa Baba, Hidetoshi Nakagawa, Eishiro Mizukoshi, Makoto Naito, Naofumi Mukaida, and Shuichi Kaneko

Précis: Findings illustrate the potential of chemokine-based immunotherapy to cooperate with radioablative therapies in clinic.

Targeting Wild-Type and Mutant p53 with Small Molecule CP-31398 Blocks the Growth of Rhabdomyosarcoma by Inducing Reactive Oxygen Species–Dependent Apoptosis

Jinanm Xu, Laura Timares, Clay Heilpern, Zhiping Weng, Changzhao Li, Hui Xu, Joseph G. Pressey, Craig A. Elmets, Levy Kopelovich, and Mohammad Athar

Précis: A novel small molecule-based strategy to modulate p53 function exerts antitumor activity in a common and aggressive type of childhood soft tissue cancer.

Mitochondrial Chaperone Trap1 and the Calcium Binding Protein Sorcin Interact and Protect Cells against Apoptosis Induced by Antibiotic Agents

Matteo Landriscina, Gabriella Laudiero, Francesca Maddalena, Maria Rosaria Amoroso, Annamaria Piscazzi, Flora Cozzolino, Maria Monti, Corrado Garbi, Alberto Fersini, Piero Pucci, and Franca Esposito

Précis: A novel mechanism of apoptosis resistance is described that may contribute to chemoresistance in colorectal carcinoma cells.

Responses in Mantle Cell Lymphoma Cells to SNS-032 Depend on the Biological Context of Each Cell Line

Rong Chen, Sherri Chubb, Tiewei Cheng, Rachael E. Hauvin, Varsha Gandhi, and William Plunkett

Précis: Findings emphasize the challenges of applying targeted therapies to consistent effect in heterogeneous human tumors without full knowledge of their biological context.

Metastasis-Associated Protein 1 Short Form Stimulates Wnt1 Pathway in Mammary Epithelial and Cancer Cells

Rakesh Kumar, Seetharaman Balasenthil, Suresh B. Pakala, Suresh K. Rayala, Aysegul A. Sahin, and Kazufumi Ohshiro

Précis: An important metastasis driver acts as an upstream regulator of Wnt signaling.

Epigenetic Silencing of miR-137 Is an Early Event in Colorectal Carcinogenesis

Francesca Balaguier, Alexander Link, Juan Jose Lozano, Miriam Cuatrecasas, Takeshi Nagasaki, C. Richard Boland, and Ajay Goel

Précis: Findings identify a tumor suppressive microRNA with potential applications as a disease biomarker in colorectal cancer.

Bcl9/Bcl9l Are Critical for Wnt-Mediated Regulation of Stem Cell Traits in Colon Epithelium and Adenocarcinomas

Jürgen Deka, Norbert Wiedermann, Pascale Anderle, Fabienne Murphy-Seiler, Jennyfer Bultinck, Sven Eyckerman, Jean-Christophe Stehle, Sylvie André, Nathalie Vilain, Olav Zilian, Sylvie Robine, Mauro Delorenzi, Konrad Basler, and Michel Aguet

Précis: A Wnt effector homologous to a developmental segment polarity gene in flies specifically mediates EMT and stem cell properties controlled by Wnt in cancer.
Dvl2 Promotes Intestinal Length and Neoplasia in the ApcMin Mouse Model for Colorectal Cancer
Ciara Metcalfe, Ashraf E.K. Ibrahim, Michael Graeb, Marc de la Roche, Thomas Schwarz-Romond, Marc Fiedler, Douglas J. Winton, Anthony Corfield, and Mariann Bienz
Précis: A potential positive modifier of colorectal cancer may act to coordinately promote beta-catenin and mTOR signaling.

Presence of a Putative Tumor-Initiating Progenitor Cell Population Predicts Poor Prognosis in Smokers with Non–Small Cell Lung Cancer
Aik T. Ooi, Vei Mah, Derek W. Nickerson, Jennifer L. Gilbert, Vi Luan Ha, Ahmed E. Hegab, Steve Horvath, Mohammad Alavi, Erin L. Maresh, David Chia, Adam C. Gower, Marc E. Lenburg, Avrum Spira, Luisa M. Solis, Ignacio I. Wistuba, Tonya C. Walser, William D. Wallace, Steven M. Dubinett, Lee Goodglick, and Brigitte N. Gomperts
Précis: A reparative progenitor airway epithelial cell that undergoes dysregulated repair in precancerous lesions is associated with poor prognosis in lung cancer.

Metastasis-Associated Protein 1 and Its Short Form Variant Stimulates Wnt1 Transcription through Promoting Its Derepression from Six3 Corepressor
Rakesh Kumar, Seetharaman Balasenthil, Bramanandam Manavathi, Suresh K. Rayala, and Suresh B. Pakala
Précis: Findings define the transcriptional mechanism through which an important metastatic driver regulates Wnt expression.

Intratumoral Localization of Aromatase and Interaction between Stromal and Parenchymal Cells in the Non–Small Cell Lung Carcinoma Microenvironment
Yasuhiro Miki, Takashi Suzuki, Keiko Abe, Satoshi Suzuki, Hiromichi Niikawa, Shinya Iida, Shuko Hata, Jun-ichi Akahira, Kazushige Mori, Dean B. Evans, Takashi Kondo, Hisafumi Yamada-Okabe, and Hironobu Sasano
Précis: Findings reveal regulation of aromatase expression in the lung carcinoma microenvironment that contributes to carcinogenesis.

Akt3-Mediated Resistance to Apoptosis in B-RAF–Targeted Melanoma Cells
Yongping Shao and Andrew E. Aplin
Précis: Resistance mechanisms that arise to B-RAF inhibitors need to be elucidated to optimize the clinical application of this class of experimental agents.

Retraction: Spontaneous Human Adult Stem Cell Transformation
Ricardo de la Fuente, Antonio Bernad, Javier Garcia-Castro, Maria C. Martin, and Juan C. Cigudosa

Correction: Effective Immunotherapy against Murine Gliomas Using Type I Polarizing Dendritic Cells—Significant Roles of CXCL10

Correction: Cell Surface Tetraspanin Tspan8 Contributes to Molecular Pathways of Exosome-Induced Endothelial Cell Activation
ABOUT THE COVER

Representative images from an immunohistochemical analysis of Six3 (upper panels) and β-catenin (lower panels) in virgin mammary glands from 12-week-old wild-type and MTA1/MTA1s –/– mice. Genetic depletion of MTA1/MTA1s leads to increased expression of Six3, a corepressor of Wnt1 transcription, and consequently, to downregulation of β-catenin in mammary glands. For details, see the article by Kumar and colleagues on page 6649 of this issue.