

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. Munasinghe, 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 PPIA and CSK21 as Connecting Molecules between Cell Cycle-Associated Genes**
Jayashree Ladha, Sainitin Donakonda, Shipra Agrawal, Balam Thota, Mallavarapu R. Srividya, Sambandam Sridevi, Arimappagan Arivazhagan, Kandavel Thennarasu, Anandh Balasubramaniam, Bangalore A. Chandramouli, Alangar Sattiyaranjandas Hegde, Paturu Kondaiah, Kumaravel Somasundaram, Vani Santosh, and Satyanarayana M.R. Rao
- 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-Rodriguez, Dan Mercola, and Michael McClelland
- Précis:* Expression profiles identify deviant clinical samples that would otherwise adversely affect biomarker discovery.

MICROENVIRONMENT AND IMMUNOLOGY

6456 **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.

6467 **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.

MOLECULAR AND CELLULAR PATHOBIOLOGY

6477 **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, Boning Gao, Michael Peyton, Meera Nanjundan, Lauren Byers, John Heymach, Gordon Mills, Adi F. Gazdar, Ignacio Wistuba, Thomas Kodadek, and John D. Minna

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

6486 **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.

6497 **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, Linnia H. Mayeenuddin, 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.

6509 **A KRAS-Variant in Ovarian Cancer Acts as a Genetic Marker of Cancer Risk**

Elena Ratner, Lingeng Lu, Marta Boeke, Rachel Barnett, Sunitha Nallur, Lena J. Chin, Cory Pelletier, Rachel Blitzblau, Renata Tassi, Trupti Paranjape, Pei Hui, Andrew K. Godwin, Herbert Yu, Harvey Risch, Thomas Rutherford, Peter Schwartz, Alessandro Santin, Ellen Matloff, Daniel Zelterman, Frank J. Slack, and Joanne B. Weidhaas

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

6516 **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.

PREVENTION AND EPIDEMIOLOGY

6527 **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, Neonila Szeszenia-Dabrowska, Dana Mates, Jan Gromiec, Ivana Holcatova, Maria Merino, Stephen Chanock, Wong-Ho Chow, and Nathaniel Rothman

Précis: Findings establish that renal cancer risk from exposure to a suspected carcinogen is particularly high in genetically susceptible individuals.

6537 **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.

6548 **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.

6556 **Antitumor Effect after Radiofrequency Ablation of Murine Hepatoma Is Augmented by an Active Variant of CC Chemokine Ligand 3/Macrophage Inflammatory Protein-1 α**

Noriho 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.

6566 **Targeting Wild-Type and Mutant p53 with Small Molecule CP-31398 Blocks the Growth of Rhabdomyosarcoma by Inducing Reactive Oxygen Species-Dependent Apoptosis**

Jianmin Xu, Laura Timares, Clay Heilpern, Zhiping Weng, Changzhao Li, Hui Xu, Joseph G. Pressey, Craig A. Elmetts, 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.

6577 **Mitochondrial Chaperone Trap1 and the Calcium Binding Protein Sorcin Interact and Protect Cells against Apoptosis Induced by Antifolates**

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.

6587 **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. Hawtin, Varsha Gandhi, and William Plunkett

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

TUMOR AND STEM CELL BIOLOGY

6598 **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.

6609 **Epigenetic Silencing of miR-137 Is an Early Event in Colorectal Carcinogenesis**

Francesc Balaguer, Alexander Link, Juan Jose Lozano, Miriam Cuatrecasas, Takeshi Nagasaka, C. Richard Boland, and Ajay Goel

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

6619 **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.

6629 **Dvl2 Promotes Intestinal Length and Neoplasia in the *Apc*^{Min} 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.

6639 **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.

6649 **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.

6659 **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.

6670 **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

6682 **Retraction: Spontaneous Human Adult Stem Cell Transformation**

Ricardo de la Fuente, Antonio Bernad, Javier Garcia-Castro, Maria C. Martin, and Juan C. Cigudosa

CORRECTIONS

6683 **Correction: Effective Immunotherapy against Murine Gliomas Using Type 1 Polarizing Dendritic Cells—Significant Roles of CXCL10**

6683 **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.

