Cancer Research
November 1, 2010 • Volume 70 • Number 21

Contents

BREAKING ADVANCES

8253  Highlights from Recent Cancer Literature

REVIEW

8255  Cancer Stem Cells in the Central Nervous System – A Critical Review
Lars Prestegarden and Per Øyvind Enger

8259  Functional MicroRNA Is Transferred between Glioma Cells
Mark Kataoksiw, Benjamin Buller, Xinli Wang, Thomas Rogers, and Michael Chopp

8264  Definition of Ubiquitination Modulator COP1 as a Novel Therapeutic Target in Human Hepatocellular Carcinoma
Yun-Han Lee, Jesper B. Andersen, Ho-Taek Song, Adam D. Judge, Daekwan Seo, Tsuyoshi Ishikawa, Jens U. Marquardt, Mitsuteru Kitade, Marjan E. Durkin, Chiara Raggi, Hyun Goo Woo, Elizabeth A. Conner, Itzhak Avital, Ian MacLachlan, Valentina M. Factor, and Snorri S. Thorgeirsson

8270  DLC1 Negatively Regulates Angiogenesis in a Paracrine Fashion
Yi-Ping Shih, Yi-Chun Liao, Yuan Lin, and Su Hao Lo

CLINICAL STUDIES

8276  Transcriptome Analysis Reveals that p53 and β-Catenin Alterations Occur in a Group of Aggressive Adrenocortical Cancers
Bruno Ragazzoni, Rossella Libé, Sébastien Gaujoux, Guillaume Assié, Amato Fratticci, Pierre Lanuary, Eric Clauer, Xavier Bertagna, Frédérique Tissier, Aurélien de Reyniès, and Jérôme Bertherat

8282  Transcriptional Activation by pRB and Its Coordination with SWI/SNF Recruitment
Stephen Flowers, George R. Beck, Jr., and Elizabeth Moran

8288  MicroRNA Expression and Clinical Outcomes in Patients Treated with Adjuvant Chemotherapy after Complete Resection of Non–Small Cell Lung Carcinoma
INTEGRATED SYSTEMS AND TECHNOLOGIES

8299 Integrated Microfluidic and Imaging Platform for a Kinase Activity Radioassay to Analyze Minute Patient Cancer Samples Cong Fang, Yanju Wang, Nam T. Vu, Wei-Yu Lin, Yao-Te Hsieh, Liudmilla Rubbi, Michael E. Phelps, Markus Müschen, Yong-Mi Kim, Arion F. Chatziioannou, Hsian-Rong Tseng, and Thomas G. Graeber

Précis: Rapid and sensitive pharmacodynamic assays that can handle very small patient samples are needed to assist the clinical development of targeted therapeutics.


Précis: Metabolic profiling of blood serum by NMR and mass spectroscopy can detect breast cancer relapse before it occurs, opening a window of opportunity for patients and oncologists to improve treatment.

PRCOS ENVIRONMENT AND IMMUNOLOGY

8319 Angiotensin-(1-7) Reduces Fibrosis in Orthotopic Breast Tumors Katherine L. Cook, Linda J. Metheny-Barlow, E. Ann Tallant, and Patricia E. Gallagher

Précis: An endogenous peptide hormone of the renin-angiotensin system reduces fibrosis in the tumor microenvironment, thereby decreasing proliferation of cancer-associated fibroblasts that contribute to malignant progression.

8329 Heparanase Enhances Local and Systemic Osteolysis in Multiple Myeloma by Upregulating the Expression and Secretion of RANKL Yang Yang, Yongsheng Ren, Vishnu C. Ramani, Li Nan, Larry J. Suva, and Ralph D. Sanderson

Précis: Study provides important mechanistic insights into the action of a key driver of bone metastasis.


Précis: Study describes refinements to active immunotherapy by adoptive T-cell transfer that can heighten effective antitumor T-cell responses in non-lymphodepleted hosts, prompting clinical investigations.

8347 Cdc42-Interacting Protein 4 Promotes Breast Cancer Cell Invasion and Formation of Invadopodia through Activation of N-WASp Christina S. Pichot, Constandina Arvanitis, Sean M. Hartig, Samuel A. Jensen, John Bechill, Saad Marzouk, Jindan Yu, Jeffrey A. Frost, and Seth J. Corey

Précis: Cell membrane remodeling proteins containing BAR domains are a functionally unique class of proteins being found to contribute to cell migration and invadopodia formation in invasive breast cancers.

8357 Differential Effects of VEGFR-1 and VEGFR-2 Inhibition on Tumor Metastases Based on Host Organ Environment Yoon-Jin Lee, Daniel L. Karl, Ugwuji N. Maduekwe, Courtney Rothrock, Sandra Ryeom, Patricia A. D’Amore, and Sam S. Yoon

Précis: VEGF promotes tumor angiogenesis primarily through activation of VEGFR-2, but vascularization of liver metastases is dependent on VEGFR-1 activation.

8368 CD4+ T-Cell Help in the Tumor Milieu Is Required for Recruitment and Cytolytic Function of CD8+ T Lymphocytes Rinke Bos and Linda A. Sherman

Précis: Antitumor efficacy of tumor-specific CD8 T cells relies upon two T-cell helper functions that must be delivered within the tumor microenvironment.
Tumor-Reactive CD8⁺ Early Effector T Cells Identified at Tumor Site in Primary and Metastatic Melanoma
Andrea Anichini, Alessandra Molla, Claudia Veggetti, Ilaria Bersani, Roberta Zappasodi, Flavio Arienti, Fernando Ravagnani, Andrea Maurichi, Roberto Patuzzo, Mario Santinami, Hanspeter Pircher, Massimo Di Nicola, and Roberta Mortarini

Précis: Findings suggest development of early phases of antitumor immunity even in advanced cancers, with definition of an “early effector” subset of T cells that may be a useful tool to monitor immunity at the tumor site.

Antibodies to Merkel Cell Polyomavirus T Antigen Oncoproteins Reflect Tumor Burden in Merkel Cell Carcinoma Patients
Kelly G. Paulson, Joseph J. Carter, Lisa G. Johnson, Kevin W. Cuhill, Jayasri G. Iyer, David Schrama, Juergen C. Becker, Margaret M. Madeleine, Paul Nghiem, and Denise A. Galloway

Précis: Antibodies that are rare in population controls but common in Merkel cell carcinoma patients can be used to monitor the burden of disease in patients.
The Oncoprotein c-Ski Functions as a Direct Antagonist of the Transforming Growth Factor-β Type I Receptor
Nathalie Ferrand, Azeddine Atfi, and Céline Prunier

Précis: The concept that oncoproteins or tumor suppressor proteins are “cytosolic” or “nuclear” in function is increasingly untenable, with an increasing number found to exert distinct functions in different cellular compartments where they can be found.

RAP80 Acts Independently of BRCA1 in Repair of Topoisomerase II Poison-Induced DNA Damage
Junko Iijima, Zhihong Zeng, Shunichi Takeda, and Yoshihito Taniguchi

Précis: Findings define a critical function in the resistance of cancer to the widely employed DNA damaging anticancer agent etoposide.

BRAF Inactivation Drives Aneuploidy by Deregulating CRAF
Tamihiro Kamata, Jahan Hussain, Susan Giblett, Robert Hayward, Richard Marais, and Catrin Pritchard

Précis: Study defines a new function for the c-RAF kinase in supporting cancer development.

Transforming Properties of 8p11-12 Amplified Genes in Human Breast Cancer
Zeng-Quan Yang, Gang Liu, Aliccia Bollig-Fischer, Craig N. Giroux, and Stephen P. Ethier

Précis: Results offer new possible strategies to address the eventual acquisition of hormone independence in 8p11-12 amplified, estrogen receptor positive, luminal B type breast cancers, a significant clinical problem.

Evidence of an Adaptive Response Targeting DNA Nonhomologous End Joining and Its Transmission to Bystander Cells
Holger Klammer, Munira Kadhim, and George Iliakis

Précis: Study elucidates mechanisms underlying adaptive response and bystander effects in cells exposed to low doses of radiation, with the promise of improved strategies for radiation treatment of human tumors.

Overexpression of Transcription Factor Sp2 Inhibits Epidermal Differentiation and Increases Susceptibility to Wound- and Carcinogen-Induced Tumorigenesis
Tae-Hyung Kim, Shannon L. Chiera, Keith E. Linder, Carol S. Trempus, Robert C. Smart, and Jonathan M. Horowitz

Précis: Findings argue that overexpression of Sp transcription factor Sp2 occurring in a variety of human cancers is likely to have significant functional impact.

Hippo Pathway Effector Yap Is an Ovarian Cancer Oncogene
Chad A. Hall, Runsheng Wang, Jianguo Miao, Esther Oliva, Xiaoyun Shen, Thomas Wheeler, Susan G. Hilsenbeck, Sandra Orsulic, and Scott Goode

Précis: Cumulative findings on the role of the Hippo pathway regulated transcription factor Yap in human ovarian cancer suggest a major role for this pathway in ovarian cancer progression.

Activation of Forkhead Box O Transcription Factors by Oncogenic BRAF Promotes p21<sup>181</sup>-Dependent Senescence
Peter L.J. de Keizer, Leisl M. Packer, Anna A. Szypowska, Paulien E. Riedl-Polderman, Niels J.F. van den Broek, Alain de Bruin, Tobias D. Dansen, Richard Marais, Arjan B. Brenkman, and Boudewijn M.T. Burgering

Précis: Study defines key mechanisms by which a central oncogenic driver in melanoma can trigger cell senescence, with implications for understanding the relationships between cancer and aging.

A Major Role of p95/611-CTF, a Carboxy-Terminal Fragment of HER2, in the Down-modulation of the Estrogen Receptor in HER2-Positive Breast Cancers
Josep Lluís Parra-Palau, Kim Pedersen, Vicente Peg, Maurizio Scailtriti, Pier Davide Angelini, Marta Escorihuela, Sandra Mancilla, Alexandra Sánchez Pla, Santiago Ramón y Cajal, José Baselga, and Joaquín Arribas

Précis: Discovery of a new mechanism of ER regulation mediated by HER2 fragments suggests a new strategy to improve patient responses to endocrine therapy in breast cancer.
**The miR-17-92 Cluster of MicroRNAs Confers Tumorigenicity by Inhibiting Oncogene-Induced Senescence**
Lixin Hong, Maoyi Lai, Michelle Chen, Changchuan Xie, Rong Liao, Young Jun Kang, Changchun Xiao, Wen-Yuan Hu, Jiahuai Han, and Peiqing Sun

**Précis:** Study defines a mechanistic basis to understand the pro-oncogenic role of an important microRNA gene cluster in cancer.

---

**Serum 25-Hydroxyvitamin D and Cancer Mortality in the NHANES III Study (1988–2006)**
D. Michel Freedman, Anne C. Looker, Christian C. Abnet, Martha S. Linet, and Barry I. Graubard

**Précis:** In this prospective study in NHANES III, overall cancer mortality risks were unrelated to baseline vitamin D status.

---

**Detection of Elevated Plasma Levels of Epidermal Growth Factor Receptor Before Breast Cancer Diagnosis among Hormone Therapy Users**
Sharon J. Pitteri, Lynn M. Amon, Tina Busald Buson, Yuzheng Zhang, Melissa M. Johnson, Alice Chin, Jacob Kennedy, Chee-Hong Wong, Qing Zhang, Hong Wang, Paul D. Lampe, Ross L. Prentice, Martin W. McIntosh, Samir M. Hanash, and Christopher I. Li

**Précis:** Findings suggest a marker that may make it possible to predict the emergence of breast cancer, particularly among women treated with menopausal hormone therapy.
<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
<th>Précis</th>
</tr>
</thead>
<tbody>
<tr>
<td>8630</td>
<td><strong>DNA Damage Recognition via Activated ATM and p53 Pathway in Nonproliferating Human Prostate Tissue</strong></td>
<td>Sari Jäämaa, Taija M. af Hallström, Anna Sankila, Ville Rantanen, Hannu Koistinen, Ulf-Håkan Stenman, Zhewei Zhang, Zhengming Yang, Angelo M. De Marzo, Kimmo Taari, Mirja Ruutu, Leif C. Andersson, and Mariikki Laiho</td>
<td><strong>Précis:</strong> Human prostate tissue shows unexpected activation of DNA damage response signaling pathway markers implicating susceptibility of the luminal cells to DNA damage.</td>
</tr>
<tr>
<td>8642</td>
<td><strong>Heat Shock Protein 90 Inhibition Depletes LAT51 and LAT52, Two Regulators of the Mammalian Hippo Tumor Suppressor Pathway</strong></td>
<td>Catherine J. Huntoon, Monica D. Nye, Liyi Geng, Kevin L. Peterson, Karen S. Flatten, Paul Haluska, Scott H. Kaufmann, and Larry M. Karnitz</td>
<td><strong>Précis:</strong> Findings identify an important mechanism by which HSP90 inhibitors currently being tested in clinical trials may disable a tumor suppressor pathway and promote tumorigenesis.</td>
</tr>
<tr>
<td>8651</td>
<td><strong>FTY720 (Fingolimod) Sensitizes Prostate Cancer Cells to Radiotherapy by Inhibition of Sphingosine Kinase-1</strong></td>
<td>Dmitri Pchejetski, Torsten Bohler, Leyre Brizuela, Lysann Sauer, Nicolas Doumerc, Muriel Golzio, Vishal Salunke, Justin Teissié, Bernard Malavaud, Jonathan Waxman, and Olivier Cuvillier</td>
<td><strong>Précis:</strong> Radiosensitizing properties of a sphingolipid analogue FTY720 (Fingolimod) in clinical testing for multiple sclerosis offer a rationale for its application in prostate cancer treatment.</td>
</tr>
<tr>
<td>8662</td>
<td><strong>Cediranib/AZD2171 Inhibits Bone and Brain Metastasis in a Preclinical Model of Advanced Prostate Cancer</strong></td>
<td>Juan Juan Yin, Luhua Zhang, Jeera Munasinghe, R. Ilona Linnoila, and Kathleen Kelly</td>
<td><strong>Précis:</strong> Findings support the utility of applying antiangiogenic therapies to treat advanced cancer patients with metastasis.</td>
</tr>
<tr>
<td>8674</td>
<td><strong>F3-Targeted Cisplatin-Hydrogel Nanoparticles as an Effective Therapeutic That Targets Both Murine and Human Ovarian Tumor Endothelial Cells In vivo</strong></td>
<td>Ira Winer, Shouyan Wang, Youg-Eun Koo Lee, Wenzhe Fan, Yusong Gong, Daniela Burgos-Ojeda, Greg Spahlinger, R. Kopelman, and Ronald J. Buckanovich</td>
<td><strong>Précis:</strong> Ovarian cancers may be highly responsive to strategies that target the tumor vasculature, increasing interest in focusing on such strategies to improve therapeutic outcomes.</td>
</tr>
<tr>
<td>8684</td>
<td><strong>Telomerase Inhibition Potentiates the Effects of Genotoxic Agents in Breast and Colorectal Cancer Cells in a Cell Cycle–Specific Manner</strong></td>
<td>Raina A. Tamakawa, Helen B. Fleisig, and Judy M.Y. Wong</td>
<td><strong>Précis:</strong> Results suggest that the protective role of telomerase in cell cycle–restricted DNA damage repair can be exploited for combined anticancer chemotherapy.</td>
</tr>
<tr>
<td>8695</td>
<td><strong>γ-Tocotrienol Inhibits Pancreatic Tumors and Sensitizes Them to Gemcitabine Treatment by Modulating the Inflammatory Microenvironment</strong></td>
<td>Ajaikumar B. Kunnumakkara, Bokyung Sung, Jayaraj Ravindran, Parveswaran Diagaradjane, Amit Deorukhkar, Sanjit Dey, Cemile Koca, Vivek R. Yadav, Zhimin Tong, Juri G. Gelovani, Sushovan Guha, Sunil Krishnan, and Bharat B. Aggarwal</td>
<td><strong>Précis:</strong> Preclinical findings strongly encourage clinical evaluation of a novel derivative of vitamin E as an adjuvant treatment with standard of care chemotherapy in pancreatic cancer patients.</td>
</tr>
<tr>
<td>8706</td>
<td><strong>Targeted Radiosensitization of Cells Expressing Truncated DNA Polymerase β</strong></td>
<td>Sari Neijenhuis, Manon Verwijs-Janssen, Lenie J. van den Broek, Adrian C. Begg, and Conchita Vens</td>
<td><strong>Précis:</strong> This study demonstrates the feasibility of tumor-targeted radiosensitization in tumor cells exhibiting BER/SSBR deficiencies.</td>
</tr>
</tbody>
</table>
Loss of PTEN Expression by Blocking Nuclear Translocation of EGR1 in Gefitinib-Resistant Lung Cancer Cells Harboring Epidermal Growth Factor Receptor–Activating Mutations
Chizuko Yamamoto, Yuji Basaki, Akihiko Kawahara, Kazutaka Nakashima, Masayoshi Kage, Hiroto Izumi, Kimitoshi Kohno, Hidetaka Uramoto, Kosei Yasumoto, Michihiko Kuwano, and Mayumi Ono
Précis: Results reinforce the therapeutic importance of PTEN expression in treatment of lung adenocarcinoma with EGFR targeting drugs.

Histone Methyltransferase MLL1 Regulates MDR1 Transcription and Chemoresistance
Hairong Huo, Pellegrino G. Magro, E. Christy Pietsch, Brijesh B. Patel, and Kathleen W. Scotto
Précis: Findings suggest an approach to attack drug resistance in acute lymphoblastic leukemias and other cancers where oncogenic activations of MLL1 occur.

Basal and Treatment-Induced Activation of AKT Mediates Resistance to Cell Death by AZD6244 (ARRY-142886) in Braf-Mutant Human Cutaneous Melanoma Cells
Y.N. Vashisht Gopal, Wanleng Deng, Scott E. Woodman, Kakajan Komurov, Prahlad Ram, Paul D. Smith, and Michael A. Davies
Précis: Findings offer a rationale for combining an MEK inhibitor with a PI3K-AKT pathway inhibitor to improve the treatment of malignant melanomas with a Braf mutation.

Tumor Cell Kill by c-MYC Depletion: Role of MYC-Regulated Genes that Control DNA Double-Strand Break Repair
Kaisa R. Luoto, Alice X. Meng, Amanda R. Wasylshen, Helen Zhao, Carla L. Coackley, Linda Z. Penn, and Robert G. Bristow
Précis: Findings suggest that anti-MYC agents may prevent genetic instability but may not be useful for radiosensitization or chemosensitization of cancer cells.

Phosphorylation of RalB Is Important for Bladder Cancer Cell Growth and Metastasis
Hong Wang, Charles Owens, Nidhi Chandra, Mark R. Conaway, David L. Brautigan, and Dan Theodorescu
Précis: Mechanistic findings suggest specific tactics to blunt Ral GTpase signaling that could offer an effective approach to treat metastatic bladder cancer.

TUMOR AND STEM CELL BIOLOGY

Synthetic Lethality Screens Reveal RPS6 and MST1R as Modifiers of Insulin-like Growth Factor–1 Receptor Inhibitor Activity in Childhood Sarcomas
Précis: Probing of the IGF-1 receptor axis in childhood sarcomas reveals resistance mechanisms through activation of alternative tyrosine kinases.

BRCA1-IRIS Overexpression Promotes Cisplatin Resistance in Ovarian Cancer Cells
Kerri L. Chock, Jamie M.S. Allison, Yoshiko Shimizu, and Wael M. ElShamy
Précis: Mechanistic study suggests novel strategies to defeat therapeutic resistance in ovarian cancer, which persists as a top priority to improve clinical treatment of this disease.

PML-RARα and Dnmt3a1 Cooperate in vivo to Promote Acute Promyelocytic Leukemia
Précis: Findings argue that levels of a DNA methyltransferase are rate limiting for progression of acute promyelocytic leukemias.

Alternative Cyclin D1 Splice Forms Differentially Regulate the DNA Damage Response
Zhiping Li, Xuanmao Jiao, Chenguang Wang, L. Andrew Shirley, Hany Elsaleh, Olav Dahl, Min Wang, Evi Soutoglou, Erik S. Knudsen, and Richard G. Pestell
Précis: Expression of splice isoform cyclin D1a increases the DNA damage response as compared with cyclin D1b.

Nuclear Receptor COUP-TFI Controls Pancreatic Islet Tumor Angiogenesis by Regulating Vascular Endothelial Growth Factor/Vascular Endothelial Growth Factor Receptor-2 Signaling
Jun Qin, Xinpu Chen, Li-yuan Yu-Lee, Ming-Jer Tsai, and Sophia Y. Tsai
Précis: Findings reveal a master transcriptional regulator of VEGF signaling in endothelial cells that is crucial to support tumor angiogenesis.
8822 | EGFR Promotes Lung Tumorigenesis by Activating miR-7 through a Ras/ERK/Myc Pathway That Targets the Ets2 Transcriptional Repressor ERF
Yu-Ting Chou, Hua-Heng Lin, Ying-Chang Lien, Yuan-Hung Wang, Chun-Fu Hong, Yu-Rung Kao, Sheng-Chieh Lin, Ying-Che Chang, Shu-Yu Lin, Shu-Jen Chen, Hua-Chien Chen, Shauh-Der Yeh, and Cheng-Wen Wu

**Précis:** Findings identify the microRNA miR-7 as a modulator of EGFR-mediated oncogenesis with important potential applications as a theranostic target in lung cancer.

8832 | Characterization of a Candidate Tumor Suppressor Gene Uroplakin 1A in Esophageal Squamous Cell Carcinoma
Kar Lok Kong, Dora L. Kwong, Li Fu, Tim Hon Man Chan, Leilei Chen, Haibo Liu, Yan Li, Ying-Hui Zhu, Jiong Bi, Yan-Ru Qin, Simon Ying Kit Law, and Xin-Yuan Guan

**Précis:** A tetraspanin cell surface receptor represents an important new theranostic marker in esophageal cancer, a deadly disease with a rising incidence in developed countries.

8842 | In vivo Imaging of Inflammation- and Tumor-Induced Lymph Node Lymphangiogenesis by Immuno–Positron Emission Tomography
Viviane Mumprecht, Michael Honer, Benjamin Vigl, Steven T. Proulx, Eveline Trachsel, Manuela Kaspar, Nadja E. Banziger-Tobler, Roger Schibli, Dario Neri, and Michael Detmar

**Précis:** Proof-of-concept for a strategy of noninvasive imaging of lymph node lymphangiogenesis could permit early detection of metastasis in cancer patients.

8852 | Prognostic and Therapeutic Implications of Distinct Kinase Expression Patterns in Different Subtypes of Breast Cancer
Giampaolo Bianchini, Takayuki Iwamoto, Yuan Qi, Charles Coutant, Christine Y. Shiang, Baulang Wang, Libero Santarpia, Vicente Valero, Gabriel N. Hortobagyi, W. Fraser Symmans, Luca Gianni, and Lajos Pusztai

**Précis:** Study findings indicate that kinases regulating mitosis and immune functions convey distinct prognostic information that varies by clinical subtypes, suggesting strategies to combine kinase inhibitors for therapeutic benefit.

8863 | Maternal Embryonic Leucine Zipper Kinase is Upregulated and Required in Mammary Tumor-Initiating Cells In vivo
Lionel W. Hebbard, Jochen Maurer, Amber Miller, Jacqueline Lesperance, John Hassell, Robert G. Oshima, and Alexey V. Terskikh

**Précis:** Results offer preclinical proof-of-concept for targeting a little-studied kinase as a therapeutic strategy to destroy breast cancer–initiating cells.

8874 | Tumorigenic and Metastatic Activity of Human Thyroid Cancer Stem Cells
Matilde Todaro, Flora Iovino, Vincenzo Ettore, Patrizia Cammarreri, Guido Gambara, Virginia Espina, Gaspare Golotta, Francesco Dieli, Silvia Giordano, Ruggero De Maria, and Giorgio Stassi

**Précis:** Aldehyde dehydrogenase overexpression identifies thyroid cancer stem cells that could promote the development of novel approaches for thyroid malignancy.

8886 | Ionizing Radiation Activates the Nrf2 Antioxidant Response

**Précis:** A delayed adaptive mechanism of radioprotection is described that might be manipulated to mitigate complications of radiotherapy in normal tissues which arise late after radiation exposure.

8896 | Protein Tyrosine Phosphatase Receptor Type H9253 Is a Functional Tumor Suppressor Gene Specifically Downregulated in Chronic Myeloid Leukemia
Marco Della Peruta, Giovanni Martinelli, Elisabetta Moretti, Davide Pintani, Marzia Vezzalini, Andrea Mafficini, Tiziana Grafone, Ilaria Iacobucci, Simona Soverini, Marco Murineddu, Fabrizio Vinante, Cristina Tecchio, Giovanna Piras, Attilio Gabbas, Maria Monne, and Claudio Sori

**Précis:** Findings identify a novel clinically relevant tumor suppressor gene in chronic myelogenous leukemia.
<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>8907</td>
<td>Enhanced Genetic Instability and Dasatinib Sensitivity in Mammary Tumor Cells Lacking NEDD9</td>
<td>Mahendra K. Singh, Eugene Izumchenko, Andres J. Klein-Szanto, Brian L. Egleston, Marina Wolfson, and Erica A. Golemis</td>
</tr>
</tbody>
</table>

**Précis:** Although Nedd9 overexpression may act as a driver and biomarker for tumor aggressiveness, genetic deficiency in Nedd9 in mice selects for development of hyperaggressive mammary tumors.

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>8917</td>
<td>Gprc5a Deletion Enhances the Transformed Phenotype in Normal and Malignant Lung Epithelial Cells by Eliciting Persistent Stat3 Signaling Induced by Autocrine Leukemia Inhibitory Factor</td>
<td>Yulong Chen, Jiong Deng, Junya Fujimoto, Humam Kadara, Taoyan Men, Dafna Lotan, and Reuben Lotan</td>
</tr>
</tbody>
</table>

**Précis:** Findings reveal a mechanistic basis for understanding the tumor suppressor function of a G protein-coupled receptor expressed in normal lung epithelial cells.

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>8927</td>
<td>Tissue-Specific Pathways for Estrogen Regulation of Ovarian Cancer Growth and Metastasis</td>
<td>Monique A. Spillman, Nicole G. Manning, Wendy W. Dye, Carol A. Sartorius, Miriam D. Post, Joshua Chuck Harrell, Britta M. Jacobsen, and Kathryn B. Horwitz</td>
</tr>
</tbody>
</table>

**Précis:** Estrogen regulates unique genes in ovarian cancers that promote lymph node metastasis.

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>8937</td>
<td>Tuberous Sclerosis Complex 1: An Epithelial Tumor Suppressor Essential to Prevent Spontaneous Prostate Cancer in Aged Mice</td>
<td>Raleigh D. Kladney, Robert D. Cardiff, David J. Kwiatkowski, Gary G. Chiang, Jason D. Weber, Jeffrey M. Arbeit, and Zhi Hong Lu</td>
</tr>
</tbody>
</table>

**Précis:** Findings suggest that maintaining control of the nodal growth regulatory mTOR complexes during aging is crucial to prevent prostate cancer, the most common cancer in men.

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
</table>

**Précis:** Plasminogen activators and their receptors are well known to be involved in cancer cell migration and invasion, but this is the first study to show that they also induce cancer stem cell-like properties.

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>8959</td>
<td>Overexpression of the Protein Tyrosine Phosphatase PRL-2 Correlates with Breast Tumor Formation and Progression</td>
<td>Serge Hardy, Nau Nau Wong, William J. Muller, Morag Park, and Michel L. Tremblay</td>
</tr>
</tbody>
</table>

**Précis:** Evidence garnered from clinical specimens and mouse models defines an important new driver of breast cancer invasion and metastasis.

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>8968</td>
<td>Correction: Colorectal Tumors Are Effectively Eradicated by Combined Inhibition of β-Catenin, KRAS, and the Oncogenic Transcription Factor ITF2</td>
<td></td>
</tr>
<tr>
<td>8969</td>
<td>Correction: Activation of Murine Double Minute 2 by Akt in Mammary Epithelium Delays Mammary Involution and Accelerates Mammary Tumorigenesis</td>
<td></td>
</tr>
</tbody>
</table>
ABOUT THE COVER

9L gliosarcoma cells expressing cel-miR-67 transfer cel-miR-67 to naïve 9L cells. Coculture of cel-miR-67–expressing 9L cells with those that expressed a luciferase reporter containing a complementary sequence to cel-miR-67 results in suppression of luciferase protein expression in the acceptor cells. This image reveals colocalization of cel-miR-67 (dark dots, in situ hybridization signal) with eGFP in 9L cells that do not express cel-miR-67. These findings indicate that glioma cells can transfer functional miRNA from one cell to another. Thus, miRNA serves as an intercellular signaling molecule in glioma. For details, see the article by Katakowski and colleagues on page 8259 of this issue.
Cancer Research

70 (21)

Cancer Res 2010;70:8253-8969.

Updated version
Access the most recent version of this article at:
http://cancerres.aacrjournals.org/content/70/21

E-mail alerts
Sign up to receive free email-alerts related to this article or journal.

Reprints and Subscriptions
To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at pubs@aacr.org.

Permissions
To request permission to re-use all or part of this article, contact the AACR Publications Department at permissions@aacr.org.