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Cancer Research

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Précis: *This study is the first to characterize rearrangement-driven expression of activated splice variants of the androgen receptor, which arise in advanced prostate cancer as a mechanism of resistance to the next generation of antiandrogen drugs*

490 **Macrophage Delivery of an Oncolytic Virus Abolishes Tumor Regrowth and Metastasis after Chemotherapy or Irradiation**
Munitta Muthana, Samuel Rodrigues, Yung-Yi Chen, Abigail Welford, Russell Hughes, Simon Tazzyman, Magnus Essand, Fiona Morrow, and Claire E. Lewis

Précis: *The use of tumor-homing macrophages to deliver an oncolytic virus may leverage favorable responses to chemotherapy in cancer, potentially identifying a niche to apply a technology that has yet to produce much clinical impact.*

496 **Disruption of Wild-Type IDH1 Suppresses D-2-Hydroxyglutarate Production in IDH1-Mutated Gliomas**
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Précis: *Findings provide insights into how an important oncometabolite is produced by a particularly deadly subset of gliomas, with implications for prognosis and therapy.*

502 **Pharmacological Inhibition of the Wnt Acyltransferase PORCN Prevents Growth of WNT-Driven Mammary Cancer**
Kyle David Proffitt, Babita Madan, Zhiyuan Ke, Vishal Pendharkar, Lijun Ding, May Ann Lee, Rami N. Hannoush, and David M. Virshup

Précis: *This study offers preclinical proof of concept for a safe and effective strategy to target the many types of tumors driven by a deregulated Wnt pathway.*

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508 **Proinflammatory Homeobox Gene, *ISX*, Regulates Tumor Growth and Survival in Hepatocellular Carcinoma**
Shih-Hsien Hsu, Li-Ting Wang, King-Teh Lee, Yao-Li Chen, Kwei-Yan Liu, Jau-Ling Suen, Chee-Yin Chai, and Shen-Nien Wang

Précis: *An intestinal homeodomain protein widely overexpressed in liver cancer may provide a key connection between long-term chronic inflammation and malignant development.*

INTEGRATED SYSTEMS AND TECHNOLOGIES

519 **Systems Analysis of BCL2 Protein Family Interactions Establishes a Model to Predict Responses to Chemotherapy**
Andreas U. Lindner, Caoimhín G. Concannon, Gerhardt J. Boukes, Mary D. Cannon, Fabien Llambi, Deborah Ryan, Karen Boland, Joan Kehoe, Deborah A. McNamara, Frank Murray, Elaine W. Kay, Suzanne Hector, Douglas R. Green, Heinrich J. Huber, and Jochen H.M. Prehn

Précis: *This study reports the development of a computational tool that can reliably predict colon cancer patient responses to chemotherapy and might also be useful for prognosis and patient stratification in the future.*

529 **Hyperpolarized ^{13}C-Pyruvate Magnetic Resonance Reveals Rapid Lactate Export in Metastatic Renal Cell Carcinomas**
Kayvan R. Keshari, Renuka Sriram, Bertram L. Koelsch, Mark Van Criekinge, David M. Wilson, John Kurhanewicz, and Zhen J. Wang

Précis: *This preclinical study offers proof of concept for a noninvasive characterization of dynamic cellular metabolism and transporter expression in cancer, with the potential to determine tumor aggressiveness and treatment responses.*

MICROENVIRONMENT AND IMMUNOLOGY

539 **VEGFA-VEGFR Pathway Blockade Inhibits Tumor-Induced Regulatory T-cell Proliferation in Colorectal Cancer**
Magali Terme, Simon Pernot, Elie Marcheteau, Federico Sandoval, Nadine Benhamouda, Orianne Colussi, Olivier Dubreuil, Antoine F. Carpentier, Eric Tartour, and Julien Taieb

Précis: *A central pathway of tumor angiogenesis also has a pivotal role in driving immune escape, illustrating a tight integration of pathways driving malignant progression.*

550 **Cell Surface Receptor FPR2 Promotes Antitumor Host Defense by Limiting M2 Polarization of Macrophages**
Ying Liu, Keqiang Chen, Chunyan Wang, Wanghua Gong, Teizo Yoshimura, Mingyong Liu, and Ji Ming Wang

Précis: *A G protein-coupled receptor implicated in airway inflammation responses supports immune surveillance by restraining macrophages to the tumor cell–killing M1 phenotype.*

561 **CD40-Mediated Activation of Chronic Lymphocytic Leukemia Cells Promotes Their CD44-Dependent Adhesion to Hyaluronan and Restricts CCL21-Induced Motility**
Tamara Girbl, Elisabeth Hinterseer, Eva Melanie Grössinger, Daniela Asslaber, Karin Oberascher, Lukas Weiss, Cornelia Hauser-Kronberger, Daniel Neureiter, Hubert Kerschbaum, David Naor, Ronen Alon, Richard Greil, and Tanja Nicole Hartmann

Précis: *The evolution of a specific adhesion event in the lymph node microenvironment where a particular leukemia arises is found to be a critical event in determining the outgrowth of these cancers.*

571 **CXCR2 Expression in Tumor Cells is a Poor Prognostic Factor and Promotes Invasion and Metastasis in Lung Adenocarcinoma**
Pierre Saintigny, Erminia Massarelli, Steven Lin, Young-Ho Ahn, Yulong Chen, Sangeeta Goswami, Baruch Erez, Michael S. O'Reilly, Diane Liu, J. Jack Lee, Li Zhang, Yuan Ping, Carmen Behrens, Luisa M. Solis Soto, John V. Heymach, Edward S. Kim, Roy S. Herbst, Scott M. Lippman, Ignacio I. Wistuba, Waun Ki Hong, Jonathan M. Kurie, and Ja Seok Koo

Précis: *A logical strategy to treat smoking-associated lung cancers is suggested by the definition of a proinflammatory signaling axis that cooperates with Ras mutations commonly found in this disease.*

583 **Lysyl Oxidase Plays a Critical Role in Endothelial Cell Stimulation to Drive Tumor Angiogenesis**
Ann-Marie Baker, Demelza Bird, Jonathan C. Welti, Morgane Gourlaouen, Georgina Lang, Graeme I. Murray, Andrew R. Reynolds, Thomas R. Cox, and Janine T. Erler

Précis: *Findings point to a new general mechanism for restricting VEGF-driven tumor angiogenesis, with important clinical and therapeutic implications in a wide variety of solid tumor types.*

595 **High-Avidity T Cells Are Preferentially Tolerized in the Tumor Microenvironment**
Ziqiang Zhu, Vinod Singh, Stephanie K. Watkins, Vincenzo Bronte, Jennifer L. Shoe, Lionel Feigenbaum, and Arthur A. Hurwitz

Précis: *T cells that are designed to be more potent for antitumor activity appear to lose their ability to control tumor growth when they persist in the tumor, offering new insights into why T-cell immunotherapies may fail.*

605 **Durable Adoptive Immunotherapy for Leukemia Produced by Manipulation of Multiple Regulatory Pathways of CD8$^+$ T-Cell Tolerance**
Melissa M. Berrien-Elliott, Stephanie R. Jackson, Jennifer M. Meyer, Craig J. Rouskey, Thanh-Long M. Nguyen, Hideo Yagita, Philip D. Greenberg, Richard J. DiPaolo, and Ryan M. Teague

Précis: *Simultaneous inhibition of the CTLA4, PD1, and LAG3 pathways of T-cell tolerance can relieve immune escape in leukemia and empower durable responses to adoptively transferred tumor-reactive T cells.*

617 **CD103 or LFA-1 Engagement at the Immune Synapse between Cytotoxic T Cells and Tumor Cells Promotes Maturation and Regulates T-cell Effector Functions**
Katarzyna Franciszkiewicz, Audrey Le Floc'h, Marie Boutet, Isabelle Vergnon, Alain Schmitt, and Fathia Mami-Chouaib

Précis: *This study shows how integrins that regulate the strength of the interaction between tumor cells and tumor-reactive T cells can alter their killing efficiency.*

629 **Tissue Damage–Associated "Danger Signals" Influence T-cell Responses That Promote the Progression of Preneoplasia to Cancer**
Ying He, Jikun Zha, Yamin Wang, Wenhua Liu, Xuanming Yang, and Ping Yu

Précis: *Release of the tissue damage-associated molecule HMGB1 by budding prostate tumors exerts an early impact on immune escape and malignant progression.*

640 **Homing of Human B Cells to Lymphoid Organs and B-Cell Lymphoma Engraftment Are Controlled by Cell Adhesion Molecule JAM-C**
Carmen Doñate, Christiane Ody, Thomas McKee, Sylvie Ruault-Jungblut, Nicolas Fischer, Patricia Ropraz, Beat A. Imhof, and Thomas Matthes

Précis: *Findings suggest an important new therapeutic target that may have general applications in the treatment of a variety of types of human lymphoma.*

652 **Expression of CD137 on Hodgkin and Reed–Sternberg Cells Inhibits T-cell Activation by Eliminating CD137 Ligand Expression**
Weng Tong Ho, Wan Lu Pang, Siew Meng Chong, Antonio Castella, Suhail Al-Salam, Teng Ee Tan, Mei Chung Moh, Liang Kai Koh, Shu Uin Gan, Cheong Kin Cheng, and Herbert Schwarz

Précis: *Findings show how Hodgkin lymphomas escape immune control, with implications for leveraging more effective immunotherapy to treat this disease.*

662 **Twist1 Induces CCL2 and Recruits Macrophages to Promote Angiogenesis**
Janine M. Low-Marchelli, Veronica C. Ardi, Edward A. Vizcarra, Nico van Rooijen, James P. Quigley, and Jing Yang

Précis: *Findings show how a gene implicated in EMT and metastasis also promotes angiogenesis by recruiting macrophages into the tumor microenvironment.*

672 **Myeloid-Derived Suppressor Cells Function as Novel Osteoclast Progenitors Enhancing Bone Loss in Breast Cancer**
Anandi Sawant, Jessy Deshane, Joel Jules, Carnella M. Lee, Brittney A. Harris, Xu Feng, and Selvarangan Ponnazhagan

Précis: *Seminal findings define a novel crucial role for myeloid-derived suppressor cells in driving bone metastasis, with implications for how to block this deadly aspect of many cancers including breast cancer.*

683 **RANKL Expression, Function, and Therapeutic Targeting in Multiple Myeloma and Chronic Lymphocytic Leukemia**
Benjamin Joachim Schmiedel, Carolin Andrea Scheible, Tina Nuebling, Hans-Georg Kopp, Stefan Wirths, Miyuki Azuma, Pascal Schneider, Gundram Jung, Ludger Grosse-Hovest, and Helmut Rainer Salih

Précis: *Findings establish an immunotherapeutic means to neutralize the detrimental function of RANKL while potently stimulating the antitumor properties of NK cells against malignant hematopoietic cells.*

MOLECULAR AND CELLULAR PATHOBIOLOGY

695 **MYC Acts via the PTEN Tumor Suppressor to Elicit Autoregulation and Genome-Wide Gene Repression by Activation of the Ezh2 Methyltransferase**
Mandeep Kaur and Michael D. Cole

Précis: *Results reveal a new model for MYC-mediated gene repression, which is linked to the PTEN tumor suppressor, possibly explaining the long-standing question of why MYC autoregulation is lost in cancers.*

706 **Nitric Oxide–Dependent Downregulation of *BRCA1* Expression Promotes Genetic Instability**
Vasily A. Yakovlev

Précis: *This study offers an incisive new perspective on the complex role of reactive nitrogen species in cancer, revealing that they promote genetic instability not directly but indirectly by shifting DNA repair from high-fidelity to error-prone mechanisms.*

716 **Identification of an Aurora Kinase Inhibitor Specific for the Aurora B Isoform**
Hua Xie, Mee-Hyun Lee, Feng Zhu, Kanamata Reddy, Cong Peng, Yan Li, Do Young Lim, Dong Joon Kim, Xiang Li, Soouk Kang, Haitao Li, Weiya Ma, Ronald A. Lubet, Jian Ding, Ann M. Bode, and Zigang Dong

Précis: *Although a variety of Aurora kinase inhibitors have been described, with some now in clinical trials, this is the first study to identify an inhibitor specific for the Aurora B isoform that appears to exert special features in cancer.*

725 ***SMAD2*, *SMAD3* and *SMAD4* Mutations in Colorectal Cancer**
Nicholas I. Fleming, Robert N. Jorissen, Dmitri Mouradov, Michael Christie, Anuratha Sakthianandeswaren, Michelle Palmieri, Fiona Day, Shan Li, Cary Tsui, Lara Lipton, Jayesh Desai, Ian T. Jones, Stephen McLaughlin, Robyn L. Ward, Nicholas J. Hawkins, Andrew R. Ruszkiewicz, James Moore, Hong-Jian Zhu, John M. Mariadason, Antony W. Burgess, Dana Busam, Qi Zhao, Robert L. Strausberg, Peter Gibbs, and Oliver M. Sieber

Précis: *Through a combined analysis of SMAD gene mutations in colorectal cancer, this article shows a common pathogenic mechanism and a new way to understand how SMAD mutations compromise the TGF-β pathway.*

736 **Epigenetic Regulation by Z-DNA Silencer Function Controls Cancer-Associated ADAM-12 Expression in Breast Cancer: Cross-talk between MeCP2 and NF1 Transcription Factor Family**
Bimal K. Ray, Srijita Dhar, Carolyn Henry, Alexander Rich, and Alpana Ray

Précis: *Findings highlight a novel epigenetic regulatory process involving Z-DNA and several epigenetic factors that contribute to overexpression of breast cancer–associated genes.*

745 **Bcl3 Selectively Promotes Metastasis of ERBB2-Driven Mammary Tumors**
Alison Wakefield, Jitka Soukupova, Amelie Montagne, Jill Ranger, Rhiannon French, William J. Muller, and Richard W. E. Clarkson

Précis: *The study reveals that the oncogene Bcl3 is critical for breast cancer metastasis by controlling tumor cell motility.*

756 **miR-186 Downregulation Correlates with Poor Survival in Lung Adenocarcinoma Where It Interferes with Cell-Cycle Regulation**
Junchao Cai, Jueheng Wu, Huizhong Zhang, Lishan Fang, Yongbo Huang, Yi Yang, Xun Zhu, Rong Li, and Mengfeng Li

Précis: *Results define a tumor suppressor function for a microRNA that blocks cell-cycle progression by directly targeting the pivotal cell-cycle regulators cyclin D1, CDK2, and CDK6.*

PREVENTION AND EPIDEMIOLOGY

767 **Common Single-Nucleotide Polymorphisms in the Estrogen Receptor β Promoter Are Associated with Colorectal Cancer Survival in Postmenopausal Women**
Michael N. Passarelli, Amanda I. Phipps, John D. Potter, Karen W. Makar, Anna E. Coghill, Karen J. Wernli, Emily White, Andrew T. Chan, Carolyn M. Hutter, Ulrike Peters, and Polly A. Newcomb

Précis: *Estrogen receptor β is suspected to play a role in colorectal cancer progression by modifying pathways that influence malignant invasion and metastasis.*

THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

776 **Combination Therapy Targeting the Chk1 and Wee1 Kinases Shows Therapeutic Efficacy in Neuroblastoma**
Mike R. Russell, Kirill Levin, JulieAnn Rader, Lili Belcastro, Yimei Li, Daniel Martinez, Bruce Pawel, Stuart D. Shumway, John M. Maris, and Kristina A. Cole

Précis: *Findings offer preclinical proof of concept that inhibitors of a key mitotic regulator can be highly efficacious for treating neuroblastoma, one of the most aggressive pediatric tumors.*

785 **DNA Damage–Specific Control of Cell Death by Cryptochrome in p53-Mutant Ras–Transformed Cells**
Jin Hyup Lee, Shobhan Gaddameedhi, Nuri Ozturk, Rui Ye, and Aziz Sancar

Précis: *Findings show how different regulators of the circadian clock affect distinct pathways of intrinsic apoptosis in malignant cells.*

792 **Histone Deacetylase Inhibitor AR-42 Differentially Affects Cell-cycle Transit in Meningeal and Meningioma Cells, Potently Inhibiting *NF2*-Deficient Meningioma Growth**
Sarah S. Burns, Elena M. Akhmametyeva, Janet L. Oblinger, Matthew L. Bush, Jie Huang, Volker Senner, Ching-Shih Chen, Abraham Jacob, D. Bradley Welling, and Long-Sheng Chang

Précis: *Preclinical investigations establish the potential utility of a pan-HDAC inhibitor in treatment of meningioma, a type of brain tumor.*

804 ***De Novo* Design of a Tumor-Penetrating Peptide**
Luca Alberici, Lise Roth, Kazuki N. Sugahara, Lilach Agemy, Venkata R. Kotamraju, Tambet Teesalu, Claudio Bordignon, Catia Traversari, Gian-Paolo Rizzardi, and Erkki Ruoslahti

Précis: *Nanotherapies incorporating effective tumor-penetrating peptides may improve drug delivery to tumor vessels and into the extravascular tumor tissue.*

813 **Polo-like Kinase 1: A Potential Therapeutic Option in Combination with Conventional Chemotherapy for the Management of Patients with Triple-Negative Breast Cancer**
Virginie Maire, Fariba Némati, Marion Richardson, Anne Vincent-Salomon, Bruno Tesson, Guillem Rigaill, Eléonore Gravier, Bérengère Marty-Prouvost, Leanne De Koning, Guillaume Lang, David Gentien, Aurélie Dumont, Emmanuel Barillot, Elisabetta Marangoni, Didier Decaudin, Sergio Roman-Roman, Alain Pierré, Francisco Cruzalegui, Stéphane Depil, Gordon C. Tucker, and Thierry Dubois

Précis: *This study suggests a promising therapeutic target for chemotherapy combination treatment of patients with triple-negative breast cancers, which tend to be more aggressive and less treatable than other types of breast cancer.*

824 **Dual Targeting of EGFR and HER3 with MEHD7945A Overcomes Acquired Resistance to EGFR Inhibitors and Radiation**
Shyhmin Huang, Chunrong Li, Eric A. Armstrong, Chimera R. Peet, Jarob Saker, Lukas C. Amler, Mark X. Sliwkowski, and Paul M. Harari

Précis: *By anticipating a common resistance mechanism to EGFR inhibitors, a new agent that can overcome HER3 signaling as well as target the EGFR has great potential to address a current therapeutic barrier in the field.*

834 **Resistance to Irreversible EGF Receptor Tyrosine Kinase Inhibitors through a Multistep Mechanism Involving the IGF1R Pathway**
Alexis B. Cortot, Claire E. Repellin, Takeshi Shimamura, Marzia Capelletti, Kreshnik Zejnullahu, Dalia Ercan, James G. Christensen, Kwok-Kin Wong, Nathanael S. Gray, and Pasi A. Jänne

Précis: *Prophylactic blockade of known mechanisms of drug resistance before they can emerge will be critical for generating more effective strategies of targeted combination therapy.*

844 **MDA-9/Syntenin and IGFBP-2 Promote Angiogenesis in Human Melanoma**
Swadesh K. Das, Sujit K. Bhutia, Belal Azab, Timothy P. Kegelman, Leyla Peachy, Prasanna K. Santhekadur, Santanu Dasgupta, Rupesh Dash, Paul Dent, Steven Grant, Luni Emdad, Maurizio Pellecchia, Devanand Sarkar, and Paul B. Fisher

Précis: *This work highlights novel targets to reverse the production of new blood vessels by tumors.*

855 **Real-time *In Vivo* Molecular Detection of Primary Tumors and Metastases with Ratiometric Activatable Cell-Penetrating Peptides**
Elamprakash N. Savariar, Csilla N. Felsen, Nadia Nashi, Tao Jiang, Lesley G. Ellies, Paul Steinbach, Roger Y. Tsien, and Quyen T. Nguyen

Précis: *Improved methods to detect tumors and metastases in preclinical models are needed for longitudinal animal studies and are vital to move the field beyond increasingly irrelevant cell culture models of cancer.*

865 **Specific Elimination of $CD133^+$ Tumor Cells with Targeted Oncolytic Measles Virus**
Patricia Bach, Tobias Abel, Christopher Hoffmann, Zoltan Gal, Gundula Braun, Iris Voelker, Claudia R. Ball, Ian C.D. Johnston, Ulrich M. Lauer, Christel Herold-Mende, Michael D. Mühlebach, Hanno Glimm, and Christian J. Buchholz

Précis: *Preclinical studies show how to improve the efficacy of oncolytic viruses by targeting them to CD133+ stem cells in multiple orthotopic and xenograft mouse models of cancer.*

875 **Targeting Folate Receptors to Treat Invasive Urinary Bladder Cancer**
Deepika Dhawan, José A. Ramos-Vara, James F. Naughton, Liang Cheng, Philip S. Low, Ryan Rothenbuhler, Christopher P. Leamon, Nikki Parker, Patrick J. Klein, Iontcho R. Vlahov, Joseph A. Reddy, Michael Koch, Linda Murphy, Lindsey M. Fourez, Jane C. Stewart, and Deborah W. Knapp

Précis: *This preclinical phamacologic study shows how folate receptors on bladder cancer cells can be exploited to specifically target therapies and elicit regressions in a highly relevant canine model of invasive disease.*

885 **Hypomethylating Therapy in an Aggressive Stroma-Rich Model of Pancreatic Carcinoma**
Reena Shakya, Tamas Gonda, Michael Quante, Martha Salas, Samuel Kim, Jenna Brooks, Steffen Hirsch, Justine Davies, Angelica Cullo, Kenneth Olive, Timothy C. Wang, Matthias Szabolcs, Benjamin Tycko, and Thomas Ludwig

Précis: *The prototypical demethylating drug 5-aza-dC exhibits strong single-agent activity in an aggressive mouse model of pancreatic cancer characterized by an abundant stroma that resembles human tumors, with the drug efficacy reflecting effects on both the stromal and the malignant epithelial compartments of the tumor.*

897 **Therapeutic Effects of Deleting Cancer-Associated Fibroblasts in Cholangiocarcinoma**
Joachim C. Mertens, Christian D. Fingas, John D. Christensen, Rory L. Smoot, Steven F. Bronk, Nathan W. Werneburg, Michael P. Gustafson, Allan B. Dietz, Lewis R. Roberts, Alphonse E. Sirica, and Gregory J. Gores

Précis: *Preclinical observations suggest that the Bax mimetic drug navitoclax may be useful for triggering apoptosis of cancer-associated fibroblasts in the tumor microenvironment as a generalized strategy to attack solid tumors that rely on these cells.*

TUMOR AND STEM CELL BIOLOGY

908 **Glutathione-Deficient Mice have Increased Sensitivity to Transplacental Benzo[a]pyrene-Induced Premature Ovarian Failure and Ovarian Tumorigenesis**
Jinhwan Lim, Gregory W. Lawson, Brooke N. Nakamura, Laura Ortiz, Jin A. Hur, Terrance J. Kavanagh, and Ulrike Luderer

Précis: *Provocative findings suggest insights into the etiology of ovarian cancers initiated in pregnant women by polycyclic aromatic hydrocarbons found in tobacco smoke, air pollution, and grilled foods.*

918 **RNA Trafficking by Acute Myelogenous Leukemia Exosomes**
Jianya Huan, Noah I. Hornick, Matthew J. Shurtleff, Amy M. Skinner, Natalya A. Goloviznina, Charles T. Roberts Jr, and Peter Kurre

Précis: *Cancer cells appear to subvert their microenvironment in part by secreting exosomes that transfer cancer-promoting proteins and RNAs into stromal cells.*

930 **Convergence of the ZMIZ1 and NOTCH1 Pathways at C-MYC in Acute T Lymphoblastic Leukemias**
Lesley A. Rakowski, Derek D. Garagiola, Choi M. Li, Margaret Decker, Sarah Caruso, Morgan Jones, Rork Kuick, Tomasz Cierpicki, Ivan Maillard, and Mark Y. Chiang

Précis: *A novel oncogene that cooperates with NOTCH1 to drive C-MYC expression is critical to license the emergence of diverse solid and liquid tumors by NOTCH1.*

942 **Definition of Molecular Determinants of Prostate Cancer Cell Bone Extravasation**
Steven R. Barthel, Danielle L. Hays, Erika M. Yazawa, Matthew Opperman, Kempland C. Walley, Leonardo Nimrichter, Monica M. Burdick, Bryan M. Gillard, Michael T. Moser, Klaus Pantel, Barbara A. Foster, Kenneth J. Pienta, and Charles J. Dimitroff

Précis: *This study offers the first comprehensive mechanism of how metastatic cancer cells traverse the vascular endothelium.*

953 **Chromosome Instability Modulated by *BMI1–AURKA* Signaling Drives Progression in Head and Neck Cancer**
Chun-Hung Chou, Neng-Kai Yang, Ting-Yun Liu, Shyh-Kuan Tai, Dennis Shin-Shian Hsu, Ya-Wei Chen, Yann-Jang Chen, Cheng-Chi Chang, Cheng-Hwai Tzeng, and Muh-Hwa Yang

Précis: *This important study reveals a mechanistic link between cancer progression and chromosomal instability, and it provides a rationale for clinical evaluation of Aurora kinase inhibitors to treat a type of cancer with a rapidly rising incidence.*

967 **DKK2 Mediates Osteolysis, Invasiveness, and Metastatic Spread in Ewing Sarcoma**
Kristina Hauer, Julia Calzada-Wack, Katja Steiger, Thomas G.P. Grunewald, Daniel Baumhoer, Stephanie Plehm, Thorsten Buch, Olivia Prazeres da Costa, Irene Esposito, Stefan Burdach, and Günther H.S. Richter

Précis: *A family of antagonists of the Wnt pathway drives bone invasion and osteolysis in Ewing sarcoma, an aggressive pediatric malignancy, with implications for understanding bone invasion more generally.*

978 **Novel Oncogene–Induced Metastatic Prostate Cancer Cell Lines Define Human Prostate Cancer Progression Signatures**
Xiaoming Ju, Adam Ertel, Mathew C. Casimiro, Zuoren Yu, Hui Meng, Peter A. McCue, Rhonda Walters, Paolo Fortina, Michael P. Lisanti, and Richard G. Pestell

Précis: *Murine prostate cancer cell lines that can metastasize in immunocompetent hosts accurately reflect the genomic and transcriptomic changes that occur in human prostate cancer and provide an improved set of tools for the field to test new therapies.*

990 **Loss of miR-204 Expression Enhances Glioma Migration and Stem Cell-like Phenotype**
Zhe Ying, Yun Li, Jueheng Wu, Xun Zhu, Yi Yang, Han Tian, Wei Li, Bo Hu, Shi-Yuan Cheng, and Mengfeng Li

Précis: *Findings define a microRNA that controls the development of stem cell–like phenotypes and cell motility in malignant brain cancer cells, with possible implications in cancer stem cell–like functions generally.*

1000 **Dual Functions of the Homeoprotein DLX4 in Modulating Responsiveness of Tumor Cells to Topoisomerase II-Targeting Drugs**
Bon Q. Trinh, Song Yi Ko, Nicolas Barengo, Shiaw-Yih Lin, and Honami Naora

Précis: *This provocative study may explain why some tumors respond poorly to drugs that target topoisomerase II despite expressing high levels of this chromatin maintenance factor.*

1011 **Novel Mechanism of Apoptosis Resistance in Cancer Mediated by Extracellular PAR-4**
Ravshan Burikhanov, Tripti Shrestha-Bhattarai, Shirley Qiu, Nidhi Shukla, Nikhil Hebbar, Subodh M. Lele, Craig Horbinski, and Vivek M. Rangnekar

Précis: *Provocative findings offer new insights into how NF-κB regulates ER stress and extrinsic apoptosis signaling in cancer cells, with implications for cross-talk with pro-inflammatory signaling in cancer cells.*

1020 **ΔNp63α-Mediated Activation of Bone Morphogenetic Protein Signaling Governs Stem Cell Activity and Plasticity in Normal and Malignant Mammary Epithelial Cells**
Amanda L. Balboni, Justine A. Hutchinson, Andrew J. DeCastro, Pratima Cherukuri, Karen Liby, Michael B. Sporn, Gary N. Schwartz, Wendy A. Wells, Lorenzo F. Sempere, Paul B. Yu, and James DiRenzo

Précis: *Disrupting BMP signaling selectively inhibits a subset of tumor cells possessing stem-like capacity, with implications for general strategies to prevent cancer recurrence.*

LETTERS TO THE EDITOR

1031 **Fibroblast-Derived CCL2 Induces Cancer Stem Cells—Letter**
Gurcan Gunaydin, Yusuf Dolen, and S. Altug Kesikli

1032 **Fibroblast-Derived CCL2 Induces Cancer Stem Cells—Response**
Akihiro Tsuyada and Shizhen Emily Wang

RETRACTION

1034 **Retraction: Initial Analyses of Colon Cancer–Specific Antigen (CCSA)-3 and CCSA-4 as Colorectal Cancer–Associated Serum Markers**

ABOUT THE COVER

Twist1 is a key inducer of epithelial-mesenchymal transition during tumor metastasis and is upregulated in aggressive human cancers. A new role for Twist1 in tumor progression was uncovered, showing that Twist1 is capable of stimulating angiogenesis via CCL2 production and subsequent recruitment of macrophages from the tumor stroma. Using a Matrigel plug assay, the images show that mouse mammary tumor cells endogenously expressing high levels of Twist1 stimulated a strong angiogenic response, seen as red blood vessels in the isolated plugs. When Twist1 expression was suppressed in these cells, the angiogenic response was diminished. For details, see the article by Low-Marchelli and colleagues on page 662.