

## BREAKING ADVANCES

- 5197 | **Highlights from Recent Cancer Literature**

## REVIEWS

- 5199 | **Potential for Targeting the Fibroblast Growth Factor Receptors in Breast Cancer**  
Nancy E. Hynes and Julien H. Dey
- 5203 | **A Need for Basic Research on Fluid-Based Early Detection Biomarkers**  
Katherine J. Martin, Marcia V. Fournier, G. Prem Veer Reddy, and Arthur B. Pardee

## PRIORITY REPORTS

- 5207 | **Distinct Genomic Alterations in Prostate Cancers in Chinese and Western Populations Suggest Alternative Pathways of Prostate Carcinogenesis**  
Xueying Mao, Yongwei Yu, Lara K. Boyd, Guoping Ren, Dongmei Lin, Tracy Chaplin, Sakunthala C. Kudahetti, Elzbieta Stankiewicz, Liyan Xue, Luis Beltran, Manu Gupta, R. Tim D. Oliver, Nick R. Lemoine, Daniel M. Berney, Bryan D. Young, and Yong-Jie Lu
- Précis:* Populational genetic differences in prostate cancer patients may accelerate the identification of causative factors and targeted therapeutics.
- 5213 | **Selective BRAF<sup>V600E</sup> Inhibition Enhances T-Cell Recognition of Melanoma without Affecting Lymphocyte Function**  
Andrea Boni, Alexandria P. Cogdill, Ping Dang, Durga Udayakumar, Ching-Ni Jenny Njauw, Callum M. Sloss, Cristina R. Ferrone, Keith T. Flaherty, Donald P. Lawrence, David E. Fisher, Hensin Tsao, and Jennifer A. Wargo
- Précis:* Selective inhibitors of oncogenic BRAF can blunt its ability to drive immune evasion and restore immunosurveillance without compromising T cell function, possibly helping inform optimal therapeutic applications of this provocative class of new agents.

- 5220 | **Dexamethasone Destabilizes Nmyc to Inhibit the Growth of Hedgehog-Associated Medulloblastoma**  
Vivi M. Heine, Markus Priller, Jason Ling, David H. Rowitch, and Ulrich Schüller

*Précis:* Findings establish mechanisms by which a growth inhibitory steroid can inhibit medulloblastoma, a common and aggressive pediatric tumor.

## CLINICAL STUDIES

- 5226 | **Pancreatic Cancers Epigenetically Silence *SIP1* and Hypomethylate and Overexpress *miR-200a/200b* in Association with Elevated Circulating *miR-200a* and *miR-200b* Levels**  
Ang Li, Noriyuki Omura, Seung-Mo Hong, Audrey Vincent, Kimberly Walter, Margaret Griffith, Michael Borges, and Michael Goggins

*Précis:* Findings suggest the possibility of a mechanism-based, serum-based diagnostic assay for detecting pancreatic cancer.

## MICROENVIRONMENT AND IMMUNOLOGY

- 5238 | **Breast Cancer Cells in Three-dimensional Culture Display an Enhanced Radioresponse after Coordinate Targeting of Integrin  $\alpha 5\beta 1$  and Fibronectin**  
Jin-Min Nam, Yasuhito Onodera, Mina J. Bissell, and Catherine C. Park
- Précis:* A strategy to target extracellular matrix deposited by cancer cells can selectively enhance the killing effects of radiation.

5249 **Interleukin-7 Permits Th1/Tc1 Maturation and Promotes *Ex vivo* Expansion of Cord Blood T Cells: A Critical Step toward Adoptive Immunotherapy after Cord Blood Transplantation**  
Craig C. Davis, Luciana C. Marti, Gregory D. Sempowski, Durairaj A. Jeyaraj, and Paul Szabolcs

*Précis:* Findings describe a novel method to generate an immunotherapy product from cord blood transplant grafts that can be frozen, thawed, and infused any time after transplant to boost immunity, helping to reduce the risk of infections, or can be further manipulated to elicit antileukemia activity.

5259 **Increased Immunogenicity of Tumor-Associated Antigen, Mucin 1, Engineered to Express  $\alpha$ -Gal Epitopes: A Novel Approach to Immunotherapy in Pancreatic Cancer**  
Takashi Deguchi, Masahiro Tanemura, Eiji Miyoshi, Hiroaki Nagano, Tomohiko Machida, Yoshiaki Ohmura, Shogo Kobayashi, Shigeru Marubashi, Hidetoshi Eguchi, Yutaka Takeda, Toshinori Ito, Masaki Mori, Yuichiro Doki, and Yoshiki Sawa

*Précis:* A straightforward peptid-based immunotherapy leveraged by an intriguing stimulatory approach, using  $\alpha$ -gal epitopes may help overcome immune suppressive barriers erected by cancers, increasing efficacy.

5270 **Angiopoietin-2 Regulates Gene Expression in TIE2-Expressing Monocytes and Augments Their Inherent Proangiogenic Functions**  
Seth B. Coffelt, Andrea O. Tal, Alexander Scholz, Michele De Palma, Sunil Patel, Carmen Urbich, Subhra K. Biswas, Craig Murdoch, Karl H. Plate, Yvonne Reiss, and Claire E. Lewis

*Précis:* Findings show that a tumor-derived cytokine, angiopoietin-2, stimulates the tumor-promoting functions of a subset of circulating monocytes that drive tumor angiogenesis.

5281 **Periostin, a Cell Adhesion Molecule, Facilitates Invasion in the Tumor Microenvironment and Annotates a Novel Tumor-Invasive Signature in Esophageal Cancer**  
Carmen Z. Michaylira, Gabrielle S. Wong, Charles G. Miller, Christie M. Gutierrez, Hiroshi Nakagawa, Rachel Hammond, Andres J. Klein-Szanto, Ju-Seog Lee, Sang Bae Kim, Meenhard Herlyn, J. Alan Diehl, Phyllis Gimotty, and Anil K. Rustgi

*Précis:* Findings illustrate the utility of organotypic cultures to discover invasion markers and other novel biological effectors in cancer.

5293 **Targeted Activation of RNA Helicase Retinoic Acid-Inducible Gene-1 Induces Proimmunogenic Apoptosis of Human Ovarian Cancer Cells**  
Kirsten Kübler, Nadine Gehrke, Soheila Riemann, Volker Böhnert, Thomas Zillinger, Evelyn Hartmann, Martin Pölcher, Christian Rudlowski, Walther Kuhn, Gunther Hartmann, and Winfried Barchet

*Précis:* Findings suggest that mimicking the conditions of viral infection in cancer promotes pro-immunogenic cell death, and may help to overcome barriers to effective immunotherapy.

## MOLECULAR AND CELLULAR PATHOBIOLOGY

5305 **The Phosphoinositide 3-Kinase Regulatory Subunit p85 $\alpha$  Can Exert Tumor Suppressor Properties through Negative Regulation of Growth Factor Signaling**  
Cullen M. Taniguchi, Jonathon Winnay, Tatsuya Kondo, Roderick T. Bronson, Alexander R. Guimaraes, José O. Alemán, Ji Luo, Gregory Stephanopoulos, Ralph Weissleder, Lewis C. Cantley, and C. Ronald Kahn

*Précis:* Genetic deficiency in a PI3K regulatory subunit elevates cancer incidence and progression establishing a functional role in tumor suppression.

5316 **HPV16 E2 Is an Immediate Early Marker of Viral Infection, Preceding E7 Expression in Precursor Structures of Cervical Carcinoma**  
Yuezhen Xue, Sophie Bellanger, Wenying Zhang, Diana Lim, Jeffrey Low, Declan Lunny, and Françoise Thierry

*Précis:* Staining of the HPV E2 protein in clinical samples may provide an easy route for early detection of HPV infection, helping to control carcinogenic progression.

5326 **Wnt Inhibitor Dickkopf-1 as a Target for Passive Cancer Immunotherapy**  
Nagato Sato, Takumi Yamabuki, Atsushi Takano, Junkichi Koinuma, Masato Aragaki, Ken Masuda, Nobuhisa Ishikawa, Nobuoki Kohno, Hiroyuki Ito, Masaki Miyamoto, Haruhiko Nakayama, Yohei Miyagi, Eiju Tsuchiya, Satoshi Kondo, Yusuke Nakamura, and Yataro Daigo

*Précis:* Functional evidence is offered for a novel biomarker and therapeutic target that may be relevant to many human cancers.

- 5337 **Phosphorylation and Activation of Cell Division Cycle Associated 5 by Mitogen-Activated Protein Kinase Play a Crucial Role in Human Lung Carcinogenesis**  
Minh-Hue Nguyen, Junkichi Koinuma, Koji Ueda, Tomoo Ito, Eiju Tsuchiya, Yusuke Nakamura, and Yataro Daigo  
*Précis:* Findings offer a mechanistic rationale for a new approach for lung cancer treatment with small molecule inhibitors of the ERK kinase-substrate pathway that is aberrantly activated in lung cancer cells.
- 5348 **Altered Dynamics of Intestinal Cell Maturation in *Apc*<sup>1638N/+</sup> Mice**  
Donghai Wang, Rossanna C. Pezo, Georgia Corner, Cristina Sison, Martin L. Lesser, Shailesh M. Shenoy, John M. Mariadason, Robert H. Singer, and Leonard H. Augenlicht  
*Précis:* In situ imaging of transcription sites in single intestinal cells along villi reveal that key pathways of transcriptional control are far more dynamic than previously appreciated in maintaining tissue homeostasis and organization that are disrupted during tumorigenesis.
- 5358 **Taspase1 Functions as a Non-Oncogene Addiction Protease that Coordinates Cancer Cell Proliferation and Apoptosis**  
David Y. Chen, Han Liu, Shugaku Takeda, Ho-Chou Tu, Satoru Sasagawa, Brian A. Van Tine, Dongsi Lu, Emily H-Y. Cheng, and James J-D. Hsieh  
*Précis:* Findings rationalize therapeutic interest in developing inhibitors of a druggable protease that may have a selective role in supporting cancer cell proliferation and survival.
- 5368 **ADAM17 Regulates Epidermal Growth Factor Receptor Expression through the Activation of Notch1 in Non-Small Cell Lung Cancer**  
Anja Baumgart, Stefan Seidl, Petros Vlachou, Lars Michel, Nadya Mitova, Nicole Schatz, Katja Specht, Ina Koch, Tibor Schuster, Rebekka Grundler, Marcus Kremer, Falko Fend, Jens T. Siveke, Christian Peschel, Justus Duyster, and Tobias Dechow  
*Précis:* Findings define a novel molecular circuitry of Notch-dependent EGFR regulation in lung non-small cell lung cancer, highlighting novel targets for therapeutic attack.
- 5379 **High-Mobility Group A1 Proteins Regulate p53-Mediated Transcription of *Bcl-2* Gene**  
Francesco Esposito, Mara Tornincasa, Paolo Chieffi, Ivana De Martino, Giovanna Maria Pierantoni, and Alfredo Fusco  
*Précis:* Findings identify a potentially important, broad acting new mechanism of anti-apoptosis in cancer.
- 5389 **Poly(ADP-Ribose) Polymerase Is Hyperactivated in Homologous Recombination-Defective Cells**  
Ponnari Gottipati, Barbara Vischioni, Niklas Schultz, Joyce Solomons, Helen E. Bryant, Tatjana Djureinovic, Natalia Issaeva, Kate Sleeth, Ricky A. Sharma, and Thomas Helleday  
*Précis:* Mechanistic findings suggest insights into how PARP inhibitors kill BRCA1/2-defective cancer cells and how to identify tumors that are sensitive to this new class of experimental clinical therapeutics.
- 5399 **High Wnt Signaling Represses the Proapoptotic Proteoglycan *syndecan-2* in Osteosarcoma Cells**  
François-Xavier Dieudonné, Allison Marion, Eric Hay, Pierre Jacques Marie, and Dominique Modrowski  
*Précis:* Novel mechanistic insights into an important oncogenic pathway of Wnt signaling in osteosarcoma are revealed.
- 5409 **Confirmation of Linkage to and Localization of Familial Colon Cancer Risk Haplotype on Chromosome 9q22**  
Courtney Gray-McGuire, Kishore Guda, Indra Adrianto, Chee Paul Lin, Leanna Natale, John D. Potter, Polly Newcomb, Elizabeth M. Poole, Cornelia M. Ulrich, Noralane Lindor, Ellen L. Goode, Brooke L. Fridley, Robert Jenkins, Loic Le Marchand, Graham Casey, Robert Haile, John Hopper, Mark Jenkins, Joanne Young, Daniel Buchanan, Steve Gallinger, Mark Adams, Susan Lewis, Joseph Willis, Robert Elston, Sanford D. Markowitz, and Georgia L. Wiesner  
*Précis:* This linkage and association study confirms and markedly refines the position of a 9q susceptibility locus for familial colon neoplasia.

## PREVENTION AND EPIDEMIOLOGY

- 5419 **Colorectal Cancer Incidence Trends in the United States and United Kingdom: Evidence of Right- to Left-Sided Biological Gradients with Implications for Screening**  
Rafael Meza, Jihyouon Jeon, Andrew G. Renehan, and E. Georg Luebeck  
*Précis:* Biomathematical models of incidence trends in colorectal cancer argue for age, sex and site-directed approaches to population screening.

5430 **Interaction between Adiponectin and Leptin Influences the Risk of Colorectal Adenoma**  
Taiki Yamaji, Motoki Iwasaki, Shizuka Sasazuki, and Shoichiro Tsugane

*Précis: Findings offer the first epidemiological evidence for the role of two important adipokines in the early stage of colorectal tumorigenesis, distinct from their involvement in insulin resistance.*

5465 **Synthetic Lethality through Combined Notch–Epidermal Growth Factor Receptor Pathway Inhibition in Basal-Like Breast Cancer**  
Yiyu Dong, Aimin Li, Jianbo Wang, Jason D. Weber, and Loren S. Michel

*Précis: Preclinical findings define and establish the rationale for combining Notch and EGFR inhibition as a combinatorial therapy to treat aggressive basal-like breast cancers that are difficult to manage clinically.*

5475 **FOXO1A Is a Target for HER2-Overexpressing Breast Tumors**  
Yanyuan Wu, Xiyang Shang, Marianna Sarkissyan, Dennis Slamon, and Jaydutt V. Vadgama

*Précis: Findings define a potentially important mechanism by which HER2-overexpressing breast cancers become resistant to the anti-HER2 therapeutic agent trastuzumab (Herceptin).*

5486 **High Levels of Nrf2 Determine Chemoresistance in Type II Endometrial Cancer**  
Tao Jiang, Ning Chen, Fei Zhao, Xiao-Jun Wang, Beihua Kong, Wenxin Zheng, and Donna D. Zhang

*Précis: Findings rationalize a broadly applicable approach to increase the efficacy of chemotherapeutic drugs and to combat chemoresistance.*

5438 **Essential Requirement for PP2A Inhibition by the Oncogenic Receptor c-KIT Suggests PP2A Reactivation as a Strategy to Treat c-KIT<sup>+</sup> Cancers**  
Kathryn G. Roberts, Amanda M. Smith, Fiona McDougall, Helen Carpenter, Martin Horan, Paolo Neviani, Jason A. Powell, Daniel Thomas, Mark A. Guthridge, Danilo Perrotti, Alistair T.R. Sim, Leonie K. Ashman, and Nicole M. Verrills

*Précis: Findings suggest activation of an anti-oncogenic protein phosphatase as a strategy to treat drug-resistant cancers driven by the c-KIT oncogene.*

5448 **Halogenated Benzimidazole Carboxamides Target Integrin  $\alpha_4\beta_1$  on T-Cell and B-Cell Lymphomas**  
Richard D. Carpenter, Arutselvan Natarajan, Edmond Y. Lau, Mirela Andrei, Danielle M. Solano, Felice C. Lightstone, Sally J. DeNardo, Kit S. Lam, and Mark J. Kurth

*Précis: Novel molecular tools are described to improve structural understanding of an integrin target that may be useful to broadly attack lymphomas.*

5497 **Development of Human Single-Chain Antibodies to the Transferrin Receptor that Effectively Antagonize the Growth of Leukemias and Lymphomas**  
Ronan Crépin, Anne-Laure Goenaga, Betsy Jullienne, Houcine Bougherara, Christine Legay, Karim Benihoud, James D. Marks, and Marie-Alix Poul

*Précis: Findings describe a new type of fully human antibody that is effective for immunotherapy of iron-dependent tumors.*

5457 **PTEN Loss Compromises Homologous Recombination Repair in Astrocytes: Implications for Glioblastoma Therapy with Temozolomide or Poly(ADP-Ribose) Polymerase Inhibitors**  
Brian McEllin, Cristel V. Camacho, Bipasha Mukherjee, Brandon Hahm, Nozomi Tomimatsu, Robert M. Bachoo, and Sandeep Burma

*Précis: Findings establish a mechanistic rationale to treat PTEN-deficient tumors with PARP inhibitors presently in clinical development, possibly expanding the scope of their application beyond merely BRCA1/2-deficient tumors.*

5507 **The Phosphoinositide 3-Kinase Inhibitor PI-103 Downregulates Choline Kinase  $\alpha$  Leading to Phosphocholine and Total Choline Decrease Detected by Magnetic Resonance Spectroscopy**  
Nada M.S. Al-Saffar, L. Elizabeth Jackson, Florence I. Raynaud, Paul A. Clarke, Ana Ramírez de Molina, Juan C. Lacal, Paul Workman, and Martin O. Leach

*Précis: Findings describe a noninvasive method to monitor the pharmacodynamics of PI3K inhibitors that are currently in early stage clinical trials.*

## THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

5518 **RG7204 (PLX4032), a Selective BRAF<sup>V600E</sup> Inhibitor, Displays Potent Antitumor Activity in Preclinical Melanoma Models**

Hong Yang, Brian Higgins, Kenneth Kolinsky, Kathryn Packman, Zenaida Go, Raman Iyer, Stanley Kolis, Sylvia Zhao, Richard Lee, Joseph F. Grippo, Kathleen Schostack, Mary Ellen Simcox, David Heimbrook, Gideon Bollag, and Fei Su

*Précis: Striking first report of the preclinical efficacy of a mutant Raf kinase-specific inhibitor augurs promise for its ongoing clinical development.*

5567 **Extracellular Protease ADAMTS9 Suppresses Esophageal and Nasopharyngeal Carcinoma Tumor Formation by Inhibiting Angiogenesis**

Paulisally Hau Yi Lo, Hong Lok Lung, Arthur Kwok Leung Cheung, Suneel S. Apte, Kwok Wah Chan, Fung Mei Kwong, Josephine Mun Yee Ko, Yue Cheng, Simon Law, Gopesh Srivastava, Eugene R. Zabarovsky, Sai Wah Tsao, Johnny Cheuk On Tang, Eric J. Stanbridge, and Maria Li Lung

*Précis: Tumor suppressive effects of an extracellular protease implicated in aerodigestive cancers are mediated by anti-angiogenic effects.*

5577 **Frequent Attenuation of the WWOX Tumor Suppressor in Osteosarcoma Is Associated with Increased Tumorigenicity and Aberrant RUNX2 Expression**

Kyle C. Kurek, Sara Del Mare, Zaidoun Salah, Suhaib Abdeen, Hussain Sadiq, Suk-hee Lee, Eugenio Gaudio, Nicola Zanesi, Kevin B. Jones, Barry DeYoung, Gail Amir, Mark Gebhardt, Matthew Warman, Gary S. Stein, Janet L. Stein, Jane B. Lian, and Rami I. Aqeilan

*Précis: Findings establish the pathobiological significance of a suspected tumor suppressor in human osteosarcoma, a very aggressive bone cancer, with potential prognostic and therapeutic implications.*

## TUMOR AND STEM CELL BIOLOGY

5528 **The Polycomb Group Protein Bmi-1 Is Essential for the Growth of Multiple Myeloma Cells**

Zainab Jagani, Dmitri Wiederschain, Alice Loo, Dan He, Rebecca Mosher, Paul Fordjour, John Monahan, Michael Morrissey, Yung-Mae Yao, Christoph Lengauer, Markus Warmuth, William R. Sellers, and Marion Dorsch

*Précis: An oncogenic Polycomb group protein found to be a critical driver in multiple myelomas, one of the most deadly blood cancers.*

5539 **Effects of Ionizing Radiation on Self-Renewal and Pluripotency of Human Embryonic Stem Cells**

Kitchener D. Wilson, Ning Sun, Mei Huang, Wendy Y. Zhang, Andrew S. Lee, Zongjin Li, Shan X. Wang, and Joseph C. Wu

*Précis: Human embryonic stem cells maintain their tumorigenic potential even after significant ionizing radiation exposures.*

5549 **A Mouse Model of Melanoma Driven by Oncogenic KRAS**

Carla Milagre, Nathalie Dhomen, Felipe C. Geyer, Robert Hayward, Maryou Lambros, Jorge S. Reis-Filho, and Richard Marais

*Précis: Mouse model findings offer evidence that KRAS activation may be a founder event in melanoma.*

5558 **Shedding of RANKL by Tumor-Associated MT1-MMP Activates Src-Dependent Prostate Cancer Cell Migration**

Aaron L. Sabbota, Hyeong-Reh Choi Kim, Xiaoning Zhe, Rafael Fridman, R. Daniel Bonfil, and Michael L. Cher

*Précis: Findings establish a mechanism of prostate cancer cell invasion that is enhanced by a protease-directed autocrine loop amenable to therapeutic attack.*

5587 **Compensatory Upregulation of Tyrosine Kinase Etk/BMX in Response to Androgen Deprivation Promotes Castration-Resistant Growth of Prostate Cancer Cells**

Bojie Dai, Hege Chen, Shengjie Guo, Xi Yang, Douglas E. Linn, Feng Sun, Wei Li, Zhiyong Guo, Kexin Xu, Oekyung Kim, Xiangtian Kong, Jonathan Melamed, Shaopeng Qiu, Hegang Chen, and Yun Qiu

*Précis: Findings identify a compensatory mechanism activated in prostate after androgen ablation, apparently contributing to androgen resistance.*

5597 **Inhibition of the Sodium-Potassium-Chloride Cotransporter Isoform-1 Reduces Glioma Invasion**

Brian R. Haas and Harald Sontheimer

*Précis: Findings rationalize an immediate opportunity to reposition a drug presently used for non-cancer indications as a treatment for primary brain tumors.*

5607 **Exchange Protein Directly Activated by Cyclic AMP Increases Melanoma Cell Migration by a Ca<sup>2+</sup>-Dependent Mechanism**

Erdene Baljinnyam, Mariana S. De Lorenzo, Lai-Hua Xie, Mizuka Iwatsubo, Suzie Chen, James S. Goydos, Martha C. Nowycky, and Kousaku Iwatsubo

*Précis:* A novel mechanism is described for invasive migration of melanoma cells, suggesting new routes to attack metastatic disease.

5618 **Atoh1 Inhibits Neuronal Differentiation and Collaborates with Gli1 to Generate Medulloblastoma-Initiating Cells**

Olivier Ayrault, Haotian Zhao, Frederique Zindy, Chunxu Qu, Charles J. Sherr, and Martine F. Roussel

*Précis:* Findings define two transcription factors that are sufficient to transform a neuronal progenitor into a tumor-initiating cell in the common childhood brain tumor medulloblastoma.

5628 **Alternatively Spliced RAGEv1 Inhibits Tumorigenesis through Suppression of JNK Signaling**

Anastasia Z. Kalea, Fiona See, Evis Harja, Maria Arriero, Ann Marie Schmidt, and Barry I. Hudson

*Précis:* Findings define a mechanism through which a novel theranostic biomarker in cancer may be used to suppress malignant disease.

## CORRECTIONS

5639 **Correction: Intratumoral Delivery and Suppression of Prostate Tumor Growth by Attenuated *Salmonella enterica* serovar *typhimurium* Carrying Plasmid-Based Small Interfering RNAs**

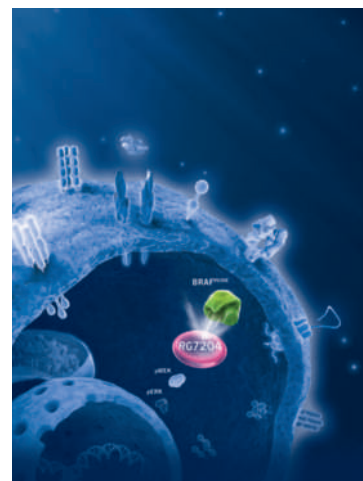
5639 **Correction: ΔNp63α Repression of the *Notch1* Gene Supports the Proliferative Capacity of Normal Human Keratinocytes and Cervical Cancer Cells**

5639 **Correction: C-Propeptides of Procollagens Iα1 and II that Differentially Accumulate in Enchondromas versus Chondrosarcomas Regulate Tumor Cell Survival and Migration**

5640 **Corrections: 2009 San Antonio Breast Cancer Symposium Abstracts**

## ABOUT THE COVER

RG7204 (PLX4032) is a small molecule inhibitor that selectively blocks the activity of oncogenic BRAF<sup>V600E</sup> kinase. The BRAF<sup>V600E</sup> mutation is common in several human cancers, with especially high prevalence in melanoma. In the present study, Yang and colleagues describe the effect of RG7204 on tumor cells. RG7204 suppresses ERK activation and cellular proliferation in tumor cells with BRAF<sup>V600E</sup> but not in cells expressing only wild-type BRAF. Significantly, RG7204 treatment caused partial or complete tumor regressions and improved survival of animals bearing BRAF<sup>V600E</sup> tumors, demonstrating potent antitumor activity. These preclinical efficacy data generated in several melanoma xenograft models have foreshadowed the clinical results observed in a multi-center Phase I trial that has been enriched with metastatic melanoma patients testing positive for the BRAF<sup>V600E</sup> mutation. For details, see the article by Yang and colleagues on page 5518 of this issue.



# Cancer Research

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