1447 | **Highlights from Recent Cancer Literature**

1449 | **Everolimus in Advanced Pancreatic Neuroendocrine Tumors: The Clinical Experience**
James C. Yao, Alexandrina T. Phan, Valentine Jehl, Gaurav Shah, and Funda Meric-Bernstam

1453 | **Chromothripsis and Focal Copy Number Alterations Determine Poor Outcome in Malignant Melanoma**
Daniela Hirsch, Ralf Kemmerling, Sean Davis, Jordi Camps, Paul S. Meltzer, Thomas Ried, and Heiko van der Kuip

**PREVIOUS REPORTS**

1457 | **Cisplatin Hypersensitivity of Testicular Germ Cell Tumors Is Determined by High Constitutive Noxa Levels Mediated by Oct-4**
Matthias Gutekunst, Thomas Mueller, Andrea Weilbacher, Michael A. Dengler, Jens Bedke, Stephan Kruck, Moshe Oren, Walter E. Aulitzky, and Heiko van der Kuip

1462 | **Choline Metabolism in a Murine Glioma Model Using Magnetic Resonance Spectroscopy and $^{11}$C-Choline Positron Emission Tomography**

1470 | **Acute and Fractionated Irradiation Differentially Modulate Glioma Stem Cell Division Kinetics**
Xuefeng Gao, J. Tyson McDonald, Lynn Hlatky, and Heiko Enderling

**MICROENVIRONMENT AND IMMUNOLOGY**

1481 | **The Planar Cell Polarity Pathway Drives Pathogenesis of Chronic Lymphocytic Leukemia by the Regulation of B-Lymphocyte Migration**
Markéta Kaucká, Karla Plevová, Šárka Pavlová, Pavlína Janovská, Archana Mishra, Jan Verner, Jiřina Procházková, Pavel Krejčí, Jana Kotasová, Petra Ovesná, Boris Tichý, Yvona Brychtová, Michael Doube, Alois Kozubík, Jiří Mayer, Šárka Pospíšilová, and Vítězslav Bryja

1489 | **Autoantibody Signatures Involving Glycolysis and Splicesome Proteins Precede a Diagnosis of Breast Cancer among Postmenopausal Women**
Jon J. Ladd, Timothy Chao, Melissa M. Johnson, Ji Qiu, Alice Chin, Rebecca Israel, Sharon J. Pitteri, Jianning Mao, Mei Wu, Lynn M. Amon, Martin McIntosh, Christopher Li, Ross Prentice, Nora Disis, and Samir Hanash

1492 | **The Delicate Balance among Three Types of T Cells in Concurrent Regulation of Tumor Immunity**

**INTEGRATED SYSTEMS AND TECHNOLOGIES**

1495 | **Multimodal Elucidation of Choline Metabolism in a Murine Glioma Model Using Magnetic Resonance Spectroscopy and $^{11}$C-Choline Positron Emission Tomography**

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1509 | **Delicate Balance among Three Types of T Cells in Concurrent Regulation of Tumor Immunity**

**INTEGRATED SYSTEMS AND TECHNOLOGIES**

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**MICROENVIRONMENT AND IMMUNOLOGY**

1515 | **The Delicate Balance among Three Types of T Cells in Concurrent Regulation of Tumor Immunity**

**INTEGRATED SYSTEMS AND TECHNOLOGIES**

1520 | **Multimodal Elucidation of Choline Metabolism in a Murine Glioma Model Using Magnetic Resonance Spectroscopy and $^{11}$C-Choline Positron Emission Tomography**

**MICROENVIRONMENT AND IMMUNOLOGY**

1525 | **The Delicate Balance among Three Types of T Cells in Concurrent Regulation of Tumor Immunity**
Acidity Generated by the Tumor Microenvironment Drives Local Invasion

Preciso: Striking findings show that tumor invasion into adjacent normal tissues proceeds in the direction of low pH and that simply lowering the acidity of adjacent tissues in vivo by administering sodium bicarbonate is sufficient to block invasion.

Interstitial Flow in a 3D Microenvironment Increases Glioma Invasion by a CXCR4-Dependent Mechanism
Jennifer M. Munson, Ravi V. Bellamkonda, and Melody A. Swartz

Preciso: Strategies to alter interstitial flow patterns in brain tumors may combat invasive dissemination and therapeutic failures occurring in this disease.

Localized Immunotherapy via Liposome-Anchored Anti-CD137 + IL-2 Prevents Lethal Toxicity and Elicits Local and Systemic Antitumor Immunity
Brandon Kwong, S. Annie Gai, Jamal Elkhader, K. Dane Wittrup, and Darrell J. Irvine

Preciso: A nanoparticle-based platform for intratumoral delivery of potent immunotherapeutic agents enables antitumor immunity while avoiding systemic toxicities.

Id-1 Is a Key Transcriptional Regulator of Glioblastoma Aggressiveness and a Novel Therapeutic Target

Preciso: A factor associated previously with angiogenesis support is found to control the aggressiveness and self-renewal potential of glioblastoma, the most common and deadly primary adult brain tumor.

FoxA1 Specifies Unique Androgen and Glucocorticoid Receptor Binding Events in Prostate Cancer Cells
Biswayoyoti Sahu, Marko Laakso, Paivi Pihlajamaa, Kristian Ovaska, Ievgenii Sininilnikov, Sampsa Hautaniemi, and Olli A. Jänne

Preciso: The findings of this study raise questions about the precise specificity of accepted androgen receptor pathways in castration-resistant prostate tumors under androgen-deprived states.

ALX1 Induces Snail Expression to Promote Epithelial-to-Mesenchymal Transition and Invasion of Ovarian Cancer Cells
Hong Yuan, Hiroaki Kajiyama, Satoko Ito, Nobuhisa Yoshikawa, Toshinori Hyodo, Eri Asano, Hitoshi Hasegawa, Masao Maeda, Kiyofumi Shibata, Mihinari Hamaguchi, Fumitaka Kikkawa, and Takeshi Senga

Preciso: A homeobox transcription factor implicated in mesenchymal differentiation and craniofacial development upregulates the EMT regulator Snail to drive invasion and metastasis.

Epigenetic Regulator Smchd1 Functions as a Tumor Suppressor

Preciso: Results identify a chromatin modifier that may act through the same pathways as MLL chimeric proteins in driving a variety of hematopoietic cancers.

Prospective Analysis of Body Mass Index, Physical Activity, and Colorectal Cancer Risk Associated with β-Catenin (CTNNB1) Status
Tepppei Morikawa, Aya Kuchiba, Paul Lochhead, Reiho Nishihara, Mai Yamauchi, Yu Imamura, Xiaoyun Liao, Zhi Rong Qian, Kimmie Ng, Andrew T. Chan, Jeffrey A. Meyerhardt, Edward Giovannucci, Charles S. Fuchs, and Shuji Ogino

Preciso: Obesity and low physical activity associate with increased risk of colorectal cancers that do not involve β-catenin, the chief target of the WNT pathway, but not risk of β-catenin-positive colorectal cancers, which may be more aggressive.
THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

1611

Imatinib Radiosensitizes Bladder Cancer by Targeting Homologous Recombination
Boling Qiao, Martin Kerr, Blaz Groselj, Mark T.W. Teo, Margaret A. Knowles, Robert G. Bristow, Roger M. Phillips, and Anne E. Kiltie

Précis: The tyrosine kinase inhibitor Gleevec may have additional uses to radiosensitize tumors that are defective in non-homologous end joining (NHEJ), with the potential to greatly expand clinical applications of this agent.

1621

Targeting XRCC1 Deficiency in Breast Cancer for Personalized Therapy
Rebeka Sultana, Tarek Abdel-Fatah, Rachel Abbotts, Claire Hawkes, Nada Albarakati, Claire Seedhouse, Graham Ball, Stephen Chan, Emad A. Rakha, Ian O. Ellis, and Srinivasan Madhusudan

Précis: Findings suggest how XRCC1 deficiency in breast cancer can inform choice of targeted chemotherapies for treatment, based on the synthetic lethality that can be achieved with the inhibition of particular mechanisms of DNA double-strand break repair.

ABOUT THE COVER

Intravital image of tumor growth within a dorsal window chamber. HCT116/GFP-expressing tumors were grown within a dorsal window chamber, where its growth was monitored over time. Images were captured following excitation with an Argon laser at 488 nm and emission was collected with a 498–538 nm bandpass filter using an Olympus FV1000 multiphoton microscope. Tumor at day 14 was pseudo-colored red in order to superimpose the tumor image on day 4 (green). Growth was quantified along radial lines from the centroid of the day 4 tumor and compared with registered images of the peritumoral pH to correlate growth and invasion to acidity. For details, see article by Estrella and colleagues on page 1524.

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HER2 Drives Luminal Breast Cancer Stem Cells in the Absence of HER2 Amplification: Implications for Efficacy of Adjuvant Trastuzumab

Précis: HER2 selectively regulates the cancer stem cell population in luminal breast cancers, perhaps explaining the clinical benefits of adjuvant trastuzumab therapy in tumors where the HER2 gene is not amplified.