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6140 KIT Oncogenic Mutations: Biologic Insights, Therapeutic Advances, and Future Directions
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Caroline H. Johnson, Mary E. Spilker, Laura Goetz, Scott N. Peterson, and Gary Siuzdak

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J. Jason Morton, Gregory Bird, Yosef Refaeli, and Antonio Jimeno

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Helene M. Langevin, Patricia Keely, Jun Mao, Lisa M. Hodges, Robert Schleip, Gary Deng, Boris Hinz, Melody A. Swartz, Beverley A. de Valois, Suzanna Zick, and Thomas Findley

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INTEGRATED SYSTEMS AND TECHNOLOGIES

6171 EpCAM-Regulated Transcription Exerts Influences on Nanomechanical Properties of Endometrial Cancer Cells That Promote Epithelial-to-Mesenchymal Transition
Ya-Ting Hsu, Pawel Osmulski, Yao Wang, Yi-Wen Huang, Lu Liu, Jianhua Ruan, Victor X. Jin, Nameer B. Kirma, Maria E. Gazynska, and Tim Hui-Ming Huang
Précis: This study advances understanding of how the biophysical properties of cancer cells must be altered to achieve an epithelial-mesenchyme transition in their status, a pivotal step in gaining invasive properties that can elude normal tissue barriers.

MICROENVIRONMENT AND IMMUNOLOGY

6183 BPTF Depletion Enhances T-cell–Mediated Antitumor Immunity
Kimberly Mayes, Suehyb G. Alkhaitib, Kristen Peterson, Aiman Alhazmi, Carolyn Song, Vivian Chan, Tana Blevins, Mark Roberts, Catherine I. Dumur, Xiang-Yang Wang, and Joseph W. Landry
Précis: The results of this study document a novel chromatin regulator, which, when inhibited, improves antitumor immunity.

6193 Nutritional Stress Induced by Tryptophan-Degrading Enzymes Results in ATF4-Dependent Reprogramming of the Amino Acid Transporter Profile in Tumor Cells
Elina Timosenko, Hemza Ghabbane, Jonathan D. Silk, Dawn Shepherd, Uzi Gileadi, Lauren J. Howson, Robert Laynes, Qi Zhao, Robert L. Strausberg, Lars R. Olsen, Stephen Taylor, Francesca M. Buffa, Richard Boyd, and Vincenzo Cerundolo
Précis: These findings reveal the mechanisms by which cancer cells but not T cells can compensate for tryptophan deprivation in a tumor microenvironment by upregulating the expression of amino acid transporters that mediate cellular tryptophan uptake.
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6205 Snail1-Dependent Activation of Cancer-Associated Fibroblast Controls Epithelial Tumor Cell Invasion and Metastasis
Lorena Alba-Castellón, Rubén Olivera-Salguero, Aida Mestre-Farrera, Raúl Peña, Mercedes Herrera, Félix Bonilla, J. Ignacio Casal, Josep Baulida, Cristina Peña, and Antonio García de Herreros
Précis: Eliminating Snail1 function in tumor stromal fibroblasts prevents the invasive capacity of epithelial tumor cells.

6218 Interleukin-30 Promotes Breast Cancer Growth and Progression
Laura Iezzi, Clara Natoli, and Emma Di Carlo
Précis: This study describes the breast cancer-promoting activity of endogenous IL30 in the tumor microenvironment, which promotes tumor cell proliferation, migration, and inflammatory characters associated with a metastatic program, with potential biomarker and therapeutic implications.

6220 Ccl22 Diverts T Regulatory Cells and Controls the Growth of Melanoma
Irina Aionldi, Claudia Cocco, Carlo Sorrentino, Domenico Angelucci, Serena Di Meo, Lamberto Manzoli, Silvia Esposito, Domenico Ribatti, Maria Bertolotto, Laura Iezzi, Clara Natoli, and Emma Di Carlo
Précis: This study describes the breast cancer-promoting activity of endogenous IL30 in the tumor microenvironment, which promotes tumor cell proliferation, migration, and inflammatory characters associated with a metastatic program, with potential biomarker and therapeutic implications.

6230 Thymic Stromal Chemokine TSLP Acts through Th2 Cytokine Production to Induce Cutaneous T-cell Lymphoma
Précis: A growth-reinforcing cycle reported in atopic dermatitis also functions in cutaneous T-cell lymphoma, not only inducing a Th2-dominant tumor environment but also stimulating tumor cell proliferation in this malignancy.

6253 Trametinib Drives T-cell–Dependent Control of KRAS-Mutated Tumors by Inhibiting Pathological Myelopoiesis
Précis: This study reveals a new perspective on the antitumor activity of FDA-approved MEK inhibitors, revealing that they enhance protective immunity in vivo by influencing multiple cell types in divergent ways, acting overall to prevent the accumulation of immunosuppressive leukocytes in tumor beds.

6266 Agonistic CD40 mAb-Driven IL12 Reverses Resistance to Anti-PD1 in a T-cell–Rich Tumor
Shin Foong Ngio, Arabella Young, Stephen I. Blake, Geoffrey R. Hill, Hideo Yagita, Michele W.L. Teng, Alan J. Korman, and Mark J. Smyth
Précis: This study offers a proof-of-concept framework to systematically identify immune conditioning agents that can convert PD1hi T cells to PD1lo T cells, with clinical implications for the management of patients resistant to anti-PD1 immune checkpoint antibodies.

Molecular and Cellular Pathobiology

6278 Wnt Signaling Promotes Breast Cancer by Blocking ITCH-Mediated Degradation of YAP/TAZ Transcriptional Coactivator WPB2
Shen Kiat Lim, Ssu Yi Lu, Shin-ae Kang, Hock Jin Tan, Zilin Li, Zhen Ning-Adrian Woe, Yee Swee Guan, Vishnu Priyanka Reddy Chichili, J. Sivaraman, Thomas Putti, Aye Aye Thike, Puay Hoon Tan, Marius Sudol, David M. Virshup, Siew Wee Chan, Wanjun Hong, and Yoon Pin Lim
Précis: This study identifies how a new oncogene in breast cancer is normally suppressed to prevent aberrant growth but becomes activated to promote cancer, with potential implications to understand and therapeutically exploit a critical interface between the WNT and Hippo signaling pathways that drive this disease.

6290 MXN1 Is Oncogenically Upregulated in African-American Prostate Cancer
Li Zhang, Jianghua Wang, Yongquan Wang, Yiqun Zhang, Patricia Castro, Longjiang Shao, Arun Sreekumar, Nagireddy Putluri, Nilanjan Guha, Saligramma Deepak, Arunkumar Padmanaban, Chad J. Greighton, and Michael Ittmann
Précis: An oncogene regulated by androgen and AKT is activated in prostate cancers relatively more frequently in African-American men, potentially offering a novel therapeutic target to address the increased incidence of aggressive disease in this patient population.
THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

6331 Preclinical Efficacy of the Auristatin-Based Antibody–Drug Conjugate BAY 1187982 for the Treatment of FGFR2–Positive Solid Tumors
Anette Sommer, Charlotte Kopitz, Christoph A. Schatz, Carl F. Nissing, Christoph Mahler, Hans-Georg Lerchen, Beatrix Stelte-Ludwig, Stefanie Hammer, Simone Geven, Joachim Schuhmacher, Manuela Braun, Ruprecht Zierer, Sabine Wittener-Rump, Axel Harrenga, Frank Ditmer, Frank Reetz, Heiner Apeler, Rolf Jautelat, Hung Huynh, Karl Ziegelbauer, and Bertolt Kreft
Précis: These findings offer a novel strategy to target ALDH activity, a functional marker in cancer stem-like cells, which in combination with platinum-based therapies are shown to have efficacious effects in ovarian cancer.

6340 RK-33 Radiosensitizes Prostate Cancer Cells by Blocking the RNA Helicase DDX3
Min Xie, Farhad Vesuna, Saritha Tantravedi, Guus M. Bol, Marise R. Heerma van Voss, Katriana Nugent, Reem Malek, Kathleen Gabrielson, Paul J. van Diest, Phuoc T. Tran, and Venu Raman
Précis: These findings offer preclinical proof of concept for a candidate small-molecule therapy that can increase the efficacy of radiotherapy without increasing apparent side effects.

6351 Ovarian Cancer Chemoresistance Relies on the Stem Cell Reprogramming Factor PBX1
Jin-Gyoun Jung, Je-Ming Shih, Joon Tae Park, Emily Gerry, Tae Ho Kim, Ayse Ayhan, Karen Handschuh, Ben Davidson, Amanda N. Fader, Licia Selleri, and Tian-Li Wang
Précis: These findings offer a mechanistic rationale to target the PBX1/STAT3 axis in ovarian cancers to defeat a key mechanism of chemoresistance, which emerges in nearly every patient after first-line treatment.

6362 Histone H3K27 Trimethylation Modulates Ovarian Cancer Chemoresistance Relies on the Stem Cell Reprogramming Factor PBX1
Rentian Wu, Qian Nie, Erin E. Tapper, Calvin R. Jerde, Garrett S. Dunlap, Shikshya Shrestha, Tarig A. Elraiyah, Steven M. Offer, and Robert B. Diasio
Précis: These findings suggest new biomarkers with potential clinical utility to identify patients who could benefit most from aggressive adjuvant chemotherapy.

6374 Integrative Genomic Analysis Identifies the Core Transcriptional Hallmarks of Human Hepatocellular Carcinoma
Coraille Allain, Gaëlle Angenard, Bruno Clément, and Cédric Coulouarn
Précis: These findings establish a rationale to pursue high-throughput meta-analysis of liver cancer patient specimens to develop and target common and subtype-specific cancer networks.

TUMOR AND STEM CELL BIOLOGY

6382 Impaired Planar Germ Cell Division in the Testis, Caused by Dissociation of RHAMM from the Spindle, Results in Hypofertility and Seminoma
Hualihao Li, Lucien Frappart, Jürgen Moll, Anne Winkler, Torsten Kroll, Jana Hamann, Iris Kufferath, Marco Groth, Stefan Taudien, Moritz Schütte, Marie-Laure Yaspo, Heike Heuer, Bodo M.H. Lange, Matthias Platzer, Kurt Zatloukal, Peter Herzlich, and Aspasia Ploubidou
Précis: These findings identify the spindle-associated protein RHAMM as an intrinsic regulator of male germ cell fate and as a gatekeeper preventing initiation of testicular germ cell tumors.
6396  EGFL6 Regulates the Asymmetric Division, Maintenance, and Metastasis of ALDH+ Ovarian Cancer Cells
Shoumei Bai, Patrick Ingram, Yu-Chih Chen, Ning Deng, Alex Pearson, Yashar S. Niknafs, Patrick O’Hayer, Yun Wang, Zhong-Yin Zhang, Elisa Boscolo, Joyce Bischoff, Euisik Yoon, and Ronald J. Buckanovich
Précis: These results offer preclinical proof of concept for a compelling new therapeutic target to improve the management of ovarian cancer.

6410  TG2 and NF-κB Signaling Coordinates the Survival of Mantle Cell Lymphoma Cells via IL6-Mediated Autophagy
Han Zhang, Zheng Chen, Roberto N. Miranda, L. Jeffrey Medeiros, and Nami McCarty
Précis: These results illuminate a novel interconnected network of signaling and autophagy pathways in a clinically problematic form of non-Hodgkin lymphoma, the disruption of which may offer an effective therapeutic strategy.

6424  Ablation of miR-10b Suppresses Oncogene-Induced Mammary Tumorigenesis and Metastasis and Reactivates Tumor-Suppressive Pathways
Jongchan Kim, Ashley N. Siverly, Dahu Chen, Min Wang, Yuan Yuan, Yumeng Wang, Hyemin Lee, Jinsong Zhang, William J. Muller, Han Liang, Boyi Gan, Xianbin Yang, Yutong Sun, M. James You, and Li Ma
Précis: These results establish the critical function of an oncomiR that drives metastasis, termed a metastamiR, and define the set of critical tumor suppressor mechanisms it overcomes to drive breast cancer progression.

CORRECTION
6436  Correction: miR-29b Mediates NF-κB Signaling in KRAS-Induced Non–Small Cell Lung Cancers

ABOUT THE COVER
Upregulation of the stem cell reprogramming factor PBX1 mediates resistance to platinum-based chemotherapy in ovarian cancer. Using an in vitro dual-color competition assay, PBX1-positive cells were labeled green and PBX1-negative cells were labeled red. It was found that PBX1-positive cells escaped the cytotoxic effects from a platinum-based agent, carboplatin, much more efficiently than did PBX1-negative cells, as demonstrated by an increased green to red ratio at several days following carboplatin treatment. For details, see article by Jung and colleagues on page 6351.
Cancer Research

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