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Qing-Wen Xu, Wei Zhao, Yue Wang, Maureen A. Sartor, Dong-Mei Han, Jixin Deng, Bakesh Pommala, Jiang-Ying Yang, Qing-Yun Zhang, Guo-Qing Liao, Yi-Mei Qu, Lu Li, Fang-Fang Liu, Hong-Mei Zhao, Yan-Hui Yin, Wei-Feng Chen, Yu Zhang, and Xiao-Song Wang

Précis: This important paper reports an integrated technology to uncover the cancer-specific antigen genome as a reservoir for novel immunological and clinical targets.

6362
Evolutionary Approaches to Prolong Progression-Free Survival in Breast Cancer
Ariosto S. Silva, Yoonseok Kam, Zayar P. Khin, Susan E. Minton, Robert J. Gillies, and Robert A. Gatenby

Précis: This work challenges the paradigm of maximum tolerated dose for drug treatment in cancer by proposing a combination strategy to burden chemoresistant cells with a chronic futile efflux of noncytotoxic drugs, with only the minimal chemotherapy dose needed to block tumor growth.

MICROENVIRONMENT AND IMMUNOLOGY
6371
Neuropilin-1 Identifies a Subset of Bone Marrow Gr1+ Monocytes That Can Induce Tumor Vessel Normalization and Inhibit Tumor Growth
Alessandro Carrer, Silvia Moimas, Serena Zacchigna, Lucia Pattarini, Lorena Zentilin, Giulia Ruosi, Miguel Mano, Milena Sinigaglia, Federica Maitone, Guido Serini, Enrico Giraudo, Federico Buzzolino, and Mauro Giacca

Précis: Neuropilin-1 expressing monocytes (NEM) are able to stabilize the tumor vasculature, thereby improving tumor oxygenation and reducing tumor malignancy, invasiveness, and resistance to chemotherapy.
TWIST1 Is an ERK1/2 Effector That Promotes Invasion and Regulates MMP-1 Expression in Human Melanoma Cells

Michele B. Weiss, Ethan V. Abel, Melanie M. Mayberry, Kevin J. Basile, Adam C. Berger, and Andrew E. Aplin

Precis: Findings define the mechanism of action of a core regulator of EMT in tumor cell invasion through its action in a previously unrecognized signaling cascade that may have general implications in cancer.

p38 MAPK in Myeloma Cells Regulates Osteoclast and Osteoblast Activity and Induces Bone Destruction

Jin He, Zhiqiang Liu, Yuhuan Zheng, Jianfei Qian, Haiyan Li, Yong Lu, Jingda Xu, Bangxing Hong, Mingjun Zhang, Pei Lin, Zhen Cai, Robert Z. Orlowski, Larry W. Kwak, Qing Yi, and Jing Yang

Precis: Findings suggest that p38 MAPK inhibitors developed clinically should be repositioned to evaluate their use in treating osteolytic bone lesions in myeloma, with potentially broader implications to treat bone metastasis occurring in various cancers.

Polypliodization of Murine Mesenchymal Cells Is Associated with Suppression of the Long Noncoding RNA H19 and Reduced Tumorigenicity

Ofer Shoshani, Hassan Massalha, Nir Shani, Sivan Kagan, Orly Ravid, Shalom Madar, Luba Trakhtenbrot, Dena Leshkowitz, Gideon Rechavi, and Dov Zipori

Precis: Findings reveal a critical link between a noncoding RNA and the polyploid character and low tumorigenicity of mesenchymal stromal cells.

Loss of PPP2R2A Inhibits Homologous Recombination DNA Repair and Predicts Tumor Sensitivity to PARP Inhibition

Peter Kalev, Michal Simicek, Iria Vazquez, Sebastian Munck, Liping Chen, Thomas Soin, Natasha Danda, Wen Chen, and Anna Sablina

Precis: Findings suggest that downregulation of a PP2A family phosphatase in tumors may predict therapeutic responses to a promising new class of anticancer agents currently in clinical trials.

Genetically Mediated Nf1 Loss in Mice Promotes Diverse Radiation-Induced Tumors Modeling Second Malignant Neoplasms

Grace Choi, Brian Huang, Emile Pinarbas, Steve E. Braunstein, Andrew E. Horvai, Scott Kogan, Smita Bhatia, Bruce Faddgeon, and Jean L. Nakamura

Precis: A mouse model of second malignant neoplasms reveals that loss of the Nf1 gene drives genotoxin-induced tumorigensis in multiple tissue types. Concordant with this mouse model, genetically-mediated Nf1 loss also occurs in human second malignant neoplasms.

miR-23b Represses Proto-oncogene Src Kinase and Functions as Methylation-Silenced Tumor Suppressor with Diagnostic and Prognostic Significance in Prostate Cancer

Shahana Majid, Altaf A. Dar, Sharanjot Saini, Sumit Arora, Varahram Shabryari, Mohd Saif Zaman, Inik Chang, Soichiro Yamamura, Yuichiro Tanaka, Guoren Deng, and Rajvir Dahiya

Precis: This study documents the diagnostic, prognostic, and functional significance of microRNA-23b as a tumor suppressor gene in prostate cancer.

Systemic Delivery of Salmonella typhimurium Transformed with IDO shRNA Enhances Intratumoral Vector Colonization and Suppresses Tumor Growth

Céline A. Blache, Edwin R. Manuel, Teodora I. Kaltcheva, Andrea N. Wong, Joshua D.J. Ellenhorn, Bruce R. Blazar, and Don J. Diamond

Precis: IDO blockade can leverage hypoxia-targeting infections that recruit neutrophils with powerful tumor-killing capacity, further expanding the broad acting modifier effects of IDO on adaptive and innate mechanisms of immune escape in tumors.

Modulation of the ATPase and Transport Activities of Broad-Acting Multidrug Resistance Factor ABCC10 (MRP7)

Ekaterina V. Malofeeva, Natalya Domanitskaya, Mariya Gudima, and Elizabeth A. Hopper-Borge

Precis: Findings suggest that the approved multikinase inhibitor sorafenib may enhance chemotherapeutic efficacy of drugs that are effluxed by an important mediator of drug resistance in cancer cells.
6468 elf4E/4E-BP Ratio Predicts the Efficacy of mTOR Targeted Therapies
Tommy Alain, Masahiro Morita, Bruno D. Fonseca, Akiko Yanagiya, Nadeem Siddiqui, Mamatha Bhat, Domenick Zammit, Victoria Marcus, Peter Metrakos, Lucie-Anne Voyer, Valentina Gandin, Yi Liu, Ivan Topisirovic, and Nahum Sonenberg

Précis: This report establishes that a ratio of the translational regulatory factors elf4E and 4E-BP, rather than simply their individual levels or phosphorylation status, may serve as a generalized marker to predict the clinical therapeutic response to mTOR inhibitors in any cancer setting.

6477 Cyclin D1 Activity Regulates Autophagy and Senescence in the Mammary Epithelium
Nelson E. Brown, Rinath Jeselsohn, Teeru Bihani, Miaofen G. Hu, Parthena Foltopoulou, Charlotte Kupershaw, and Philip W. Hinds

Précis: Mammary epithelial cells expressing a kinase defective cyclin D1 survive due to an upregulation of autophagy, which if blocked, results in senescence.

6490 Obesity and Overfeeding Affecting Both Tumor and Systemic Metabolism Activates the Progesterone Receptor to Contribute to Postmenopausal Breast Cancer
Erin D. Giles, Elizabeth A. Wellberg, David P. Astling, Steven M. Anderson, Ann D. Thor, Sonali Jindal, Aik-Choon Tan, Pepper S. Schadin, and Paul S. MacLean

Précis: Striking findings may help explain why obese postmenopausal women have relatively increased risks of breast cancer.

6502 The CRTCl-NEDD9 Signaling Axis Mediates Lung Cancer Progression Caused by LKB1 Loss
Yan Feng, Ye Wang, Zuo Yun Wang, Zhaoyuan Fang, Fei Li, Yijun Gao, Hongyan Liu, Tian Xiao, Fuming Li, Yang Zhou, Qiwei Zhai, Xiaolong Liu, Yihua Sun, Nabeel Bardeesy, Kwok-kin Wong, Haiquan Chen, Zhi-qin Xiong, and Hongbin Ji

Précis: Results decipher the mechanism through which mutation of the tumor suppressor LKB1 in lung cancer leads to progression and metastasis, offering mechanistic insights into how to attack these processes.

6512 Host Immune Defense Peptide LL-37 Activates Caspase-Independent Apoptosis and Suppresses Colon Cancer

Précis: Findings suggest that a bacteriocidal factor secreted by macrophages, PMNs, and colonocytes contributes to colon cancer suppression by activating a novel pathway of apoptosis in colon cancer cells.

CORRECTION: The Kynurenine Pathway in Brain Tumor Pathogenesis

ABOUT THE COVER
Obesity increases the risk for breast cancer after menopause. Animal studies reveal that obesity and ovariectomy-induced overfeeding converge to promote progesterone receptor (PR)-positive mammary tumors as shown by high nuclear PR immunohistochemical staining. Elevated PR expression positively correlated with tumor expression of glycolytic and lipogenic enzymes, glucose uptake, and proliferation markers. A similar relationship between PR expression and metabolic capacity was observed in tumors from postmenopausal women. Metformin treatment during the window of weight gain following ovariectomy caused PR downregulation and tumor regression. For details, see article by Giles and colleagues on page 6490.