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**Précis:** These findings offer major new insight into how the p53 family member p73 promotes the pathogenesis of highly malignant cancers, with implications for how to eradicate tumor-initiating cells and overcome drug resistance.

### CLINICAL STUDIES
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Jill A. Ohar, Mitchell Cheung, Jacqueline Talarchek, Suzanne E. Howard, Timothy D. Howard, Mary Hesdorffer, Hongzhuan Peng, Frank J. Rauscher, and Joseph R. Testa

**Précis:** BAP1 genetic testing may help identify individuals from families with a history of mesothelioma who are at higher risk of developing this cancer, but also with greater chances at long-term survival, an unusual pattern.

### INTEGRATED SYSTEMS AND TECHNOLOGIES
216  Transcriptome Analysis of Recurrently Deregulated Genes across Multiple Cancers Identifies New Pan-Cancer Biomarkers  
Bogumil Kaczkowski, Yuji Tanaka, Hideya Kawaji, Albin Sandelin, Robin Andersson, Masayoshi Itoh, Timo Lassmann, the FANTOM5 consortium, Yoshihide Hayashizaki, Piero Carninci, and Alistair R.R. Forrest

**Précis:** This genome-wide expression profiling approach identified new perspectives on DNA repetitive elements, often activated during cancer progression, as candidate biomarkers with pan-cancer potential.

### MICROENVIRONMENT AND IMMUNOLOGY
227  Control of PD-L1 Expression by Oncogenic Activation of the AKT–mTOR Pathway in Non–Small Cell Lung Cancer  
Kristin J. Lastwika, Willie Wilson III, Qing Kay Li, Jeffrey Norris, Haiying Xu, Sharon R. Ghazarian, Hiroshi Kitagawa, Shigeru Kawahata, Janis M. Taube, Sheng Yao, Linda N. Liu, Joell J. Gillis, and Phillip A. Dennis

**Précis:** This study contributes to the rapidly accumulating evidence that oncogene signaling drives immune escape, implying that anti-oncogenic therapeutic strategies may be useful primarily for leveraging immunochemotherapy combinations.
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Grethen K. Hubbard, Laura N. Mutton, May Khalili, Ryan P. McMullin, Jessica L. Hicks, Daniella Bianchi-Frias, Lucas A. Horn, Ibrahim Kulac, Michael S. Mouharek, Peter S. Nelson, Srinivasan Veynasaubramanian, Angelo M. De Marzo, and Charles J. Biebering

Précis: The mouse model described can recapitulate key histopathologic and molecular features of human prostate cancer, including development of genomic instability and overt metastases to lymph nodes, liver, and lung.

293 HBXIP and LSD1 Scaffolded by IncRNA Hotair Mediate Transcriptional Activation by c-Myc
Yinghui Li, Zhen Wang, Hui Shi, Hang Li, Lei L. Li, Runping Fang, Xiaoli Cai, Bowen Liu, Xiaodong Zhang, and Lihong Ye

Précis: This seminal study defines an oncogenic RNA/protein complex that serves as an effector for c-Myc in activating transcription of its target genes, illuminating long-standing questions concerning how c-Myc drives carcinogenesis.

305 EPHA2 Blockade Overcomes Acquired Resistance to EGFR Kinase Inhibitors in Lung Cancer
Katherine R. Amato, Shan Wang, Li Tan, Andrew K. Hastings, Wenchang Song, Christine M. Lovly, Catherine B. Meador, Fei Ye, Pengcheng Lu, Justin M. Balko, Daniel C. Colvin, Justin M. Cates, William Pao, Nathanael S. Gray, and Jin Chen

Précis: Targeting a cell surface receptor kinase involved in cell-cell interactions appears to mitigate an important pathway of drug resistance in preclinical models of lung cancer, with immediate impact on clinical testing of the discovery.

319 Gender-Specific Molecular and Clinical Features Underlie Malignant Pleural Mesothelioma

PREVENTION AND EPIDEMIOLOGY

370 Skin Cancer Risk Is Modified by KIR/HLA Interactions That Influence the Activation of Natural Killer Immune Cells
Karina A. Vinetresky, Margaret R. Karagas, Brock C. Christensen, Jacquelyn K. Kuriger-Laber, Ann E. Perry, Craig A. Storm, and Heather H. Nelson
Précis: These findings reveal associations between hematocyte-based cancers and activating signals for natural killer immune cells, demonstrating a role for natural killer cell tumor immunity in controlling the most common types of skin cancer.

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377 Characterization of a c-Rel Inhibitor That Mediates Anticancer Properties in Hematologic Malignancies by Blocking NF-kB–Controlled Oxidative Stress Responses
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Précis: These results provide mechanistic insight and preclinical proof of concept for a novel small molecule to treat human lymphoid malignancies, with additional application in recipients of allogeneic bone marrow transplants to ameliorate graft-versus-host disease, a major clinical challenge.

390 Maximizing the Efficacy of MAPK-Targeted Treatment in PTENLOF/BRAMUT Melanoma through PI3K and IGF1R Inhibition
Précis: These findings reveal that the efficacy of MAPK inhibitors for the treatment of PTEN-deficient and BRAF mutant melanoma can be significantly improved by incorporating pharmacological strategies that also inhibit PI3K and IGF1R signaling.
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**TUMOR AND STEM CELL BIOLOGY**

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Interactions between Adipocytes and Breast Cancer Cells Stimulate Cytokine Production and Drive Src/Sox2/miR-302b–Mediated Malignant Progression


Précis: This study identifies feed-forward signaling loops triggered by adipocyte-cancer cell interactions, driving inflammation and malignant growth and offering new therapeutic strategies to target breast cancers associated with obesity.

Correction: A Modeling Approach to Explain Mutually Exclusive and Co-Occurring Genetic Alterations in Bladder Tumorigenesis

Correction

Overall structure of a survivin dimer with deeply buried dimerization core residues shown by their molecular surface in gray and noncore residues shown by sticks in green. Qi and colleagues show that the deeply buried dimerization core residues in undruggable oncogenic dimeric proteins can be targeted using computational approaches for drug discovery to destroy these proteins. Specifically, a lead small-molecule inhibitor LQZ-7F targeting the dimerization core residues of survivin was discovered that induced proteasome-dependent survivin degradation, mitotic arrest, apoptosis, and blocked the growth of human xenograft tumors. For details, see article by Qi and colleagues on page 453.