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## Breaking Advances

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## Reviews

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## Priority Report

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<td>A Unique Subset of Epithelial Ovarian Cancers with Platinum Sensitivity and PARP Inhibitor Resistance</td>
<td>Raphael Ceccaldi, Kevin W. O’Connor, Kent W. Mouw, Adam Y. Li, Ursula A. Matulonis, Alan D. D’Andrea, and Panagiotis A. Konstantinopoulos</td>
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**Précis:** These findings reveal a mechanism of platinum sensitivity that alters sensitivity to PARP inhibitors in a discordant manner, with potential implications for trials of this new class of drugs in ovarian cancer.

## Microenvironment and Immunology

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<td>Accelerated Tumor Progression in Mice Lacking the ATP Receptor P2X7</td>
<td>Elena Adinolfi, Marina Cepece, Alessia Franceschini, Simonetta Falzoni, Anna L. Giuliani, Alessandra Rontondo, Alba C. Sarti, Massimo Bonora, Susanne Syberg, Domenica Corgliano, Paolo Pinton, Niklas R. Jorgensen, Luigi Abelli, Laura Emionite, Lizza Raffaghello, Vito Pistoia, and Francesco Di Virgilio</td>
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**Précis:** These provocative genetic results challenge the notion that inflammation solely promotes tumor growth by showing how deletion of an important proinflammatory receptor, the P2X/ATP receptor, can impair antitumor responses and promote malignant progression.

## Molecular and Cellular Pathobiology

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**Précis:** These genetic findings suggest that vitamin D receptor agonists may be highly efficacious in p53 mutant lung cancers, a possibility with immediate implications for clinical evaluation.
676 Stem Cell Transplantation Reverses Chemotherapy-Induced Cognitive Dysfunction
Précis: Cancer survivors suffer from impaired cognition due to chemotherapy, a condition informally referred to as "chemobrain," but this very common side effect in cancer survivors has been little studied as an unmet medical need.

687 eIF4E Threshold Levels Differ in Governing Normal and Neoplastic Expansion of Mammary Stem and Luminal Progenitor Cells
Svetlana Avdulov, Jeremy Herrera, Karen Smith, Mark Peterson, Jose R. Gomez-Garcia, Thomas C. Beadnell, Kathryn L. Schwertfeger, Alexey O. Benyumov, J. Carlos Manivel, Shunan Li, Anja-Katrin Bielinsky, Douglas Yee, Peter B. Bitterman, and Vitaly A. Polunovsky
Précis: eIF4E overexpression, which occurs widely in cancer, appears to enable cells to evade DNA damage checkpoints, a feature that is associated with threshold levels but not changes in RNA cap-binding capabilities as might have been suspected.

698 Interaction between p53 Mutation and a Somatic HDMX Biomarker Better Defines Metastatic Potential in Breast Cancer
Précis: This study develops a simple paired biomarker for the p53 pathway in breast cancer, rendering it more clinically useful for predicting metastatic progression and patient prognosis.

709 HOXB7 Promotes Malignant Progression by Activating the TGFβ Signaling Pathway
Shou Liu, Rideok Jin, Yvonne Hui, Jie Fu, Chunfa Jie, Sheng Feng, David Reisman, Qian Wang, Daping Fan, Saraswati Sukumaru, and Hexin Chen
Précis: These findings reveal a mechanism that is required not only to promote cancer cell invasion and migration, but also to recruit and activate immunosuppressive tumor-associated macrophages in the tumor microenvironment.

720 Reprogramming of the ERβx and ERα Target Gene Landscape Triggers Tamoxifen Resistance in Breast Cancer
Précis: These findings suggest that activation of the estrogen-related receptor ERβx promotes resistance to antiendocrine therapy in breast cancer and provide a rationale to explore this receptor as a drug target for mitigating the endocrine-resistant phenotype in patients.

732 BRCA2-Deficient Sarcomatoid Mammary Tumors Exhibit Multidrug Resistance
Janneke E. Jaspers, Wendy Sol, Ariena Kersbergen, Andreas Schlicker, Charlotte Gayader, Guotai Xu, Lodewyk Wessels, Piet Borst, Jos Jonkers, and Sven Rottenberg
Précis: Epithelial-to-mesenchymal transition in murine tumors is associated with an acquisition of multidrug resistance due to increased expression of genes encoding drug efflux transporters.

THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

742 ERK5 Is a Critical Mediator of Inflammation-Driven Cancer
Katherine G. Finegan, Diana Perez-Madrigal, James R. Hitchin, Clare C. Davies, Allan M. Jordan, and Cathy Tournier
Précis: These findings highlight a kinase that fosters chronic inflammation in the setting of carcinogenesis, a key issue in understanding how an inflamed microenvironment supports cancer progression.

754 Epigenetic Silencing of miR-490-3p Reactivates the Chromatin Remodeler SMARCD1 to Promote Helicobacter pylori-Induced Gastric Carcinogenesis
Précis: This study shows how miRNA misregulation of a member of the SWI/SNF chromatin remodeling family contributes to the development of infection-associated stomach cancers.
Suppressing TGFβ Signaling in Regenerating Epithelia in an Inflammatory Microenvironment Is Sufficient to Cause Invasive Intestinal Cancer

Hiroko Oshima, Mizuho Nakayama, Tae-Su Han, Kuniko Naoi, Xiaoli Ju, Yusuke Maeda, Sylvie Robine, Kiichiro Tsuchiya, Toshio Sato, Hiroshi Sato, Makoto Mark Taketo, and Masanobu Oshima

Précis: These provocative results show how invasive colon cancers can develop simply as a result of chronic inflammation that engenders evolution of immune escape, alongside epithelial cell regeneration that seeks to restore colonic tissue in the face of ongoing inflammation.

LETTER TO THE EDITOR

777 Cep63 Recruits Cdk1 to the Centrosome—Letter
Mohammad Alsara, Harald Löfler, Anne Fechter, Jiri Bartek, and Alwin Krämer

CORRECTION

779 Correction: AIMP3 Haploinsufficiency Disrupts Oncogene-Induced p53 Activation and Genomic Stability

ABOUT THE COVER

Human neural stem cell (hNSC) transplantation reverses chemotherapy-induced cognitive dysfunction through a mechanism involving the preservation of host neuronal morphology. The image shows Golgi-Cox impregnated neurons in the hippocampus of rats treated with chronic cyclophosphamide and engrafted with hNSCs. Disruptions to overall granule and CA1 pyramidal cell neuronal architecture caused by cyclophosphamide were ameliorated in the brains of rats receiving hNSC transplantation when analyzed 2 months posttransplantation. For further details, see article by Acharya and colleagues on page 676.