BREAKING ADVANCES

617 Highlights from Recent Cancer Literature

REVIEWS

619 Emerging Links between E2F Control and Mitochondrial Function
Elizaveta V. Benevolenskaya and Maxim V. Frolov

624 GOLPH3 Links the Golgi, DNA Damage, and Cancer
Matthew D. Buschman, Juliati Rahajeng, and Seth J. Field

PRIORITY REPORT

628 A Unique Subset of Epithelial Ovarian Cancers with Platinum Sensitivity and PARP Inhibitor Resistance
Raphael Ceccaldi, Kevin W. O’Connor, Kent W. Mouw, Adam Y. Li, Ursula A. Matulonis, Alan D. D’Andrea, and Panagiotis A. Konstantinopoulos

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

635 Accelerated Tumor Progression in Mice Lacking the ATP Receptor P2X7
Elena Adinolfi, Marina Capece, Alessia Franceschini, Simonetta Falzoni, Anna L. Giuliani, Alessandra Rotondo, Alba C. Sarti, Massimo Bonora, Susanne Syberg, Domenica Cortigiano, Paolo Finton, Niklas R. Jorgensen, Luigi Abelli, Laura Emionite, Lizzia Raffaghello, Vito Pistoia, and Francesco Di Virgilio

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.

645 Prostaglandin E2 Inhibits p53 in Human Breast Adipose Stromal Cells: A Novel Mechanism for the Regulation of Aromatase in Obesity and Breast Cancer
Xiuyi Wang, Maria M. Docanto, Hiromichi Sasaki, Kathleen Cunningham Foundation Consortium for Research into Familial Breast Cancer, Camden Lo, Evan R. Simpson, and Kristy A. Brown

Précis: These results show that in addition to its conventional roles in cell-cycle arrest and apoptosis, p53 may also prevent mammary gland hyperplasia and dysplasia by inhibiting expression of aromatase in breast adipose stromal cells.

656 β-Catenin Promotes Regulatory T-cell Responses in Tumors by Inducing Vitamin A Metabolism in Dendritic Cells
Yuan Hong, Indumathi Manoharan, Amol Suryawanshi, Tanmay Majumdar, Melinda L. Angus-Hill, Pandelakis A. Koni, Balaji Manicasamy, Andrew L. Mellor, David H. Munn, and Santhakumar Manicasamy

Précis: In this seminal study, yet another fundamental oncogenic pathway is linked to immune escape, a fundamental driver of malignant conversion that is coordinated with tumor growth, offering new opportunities to reposition cancer cell-centric therapeutic drugs in trials in which they may be more properly conceptualized as immunotherapeutic agents.

656 Genetic Mutation of p53 and Suppression of the miR-17~92 Cluster Are Synthetic Lethal in Non-Small Cell Lung Cancer due to Upregulation of Vitamin D Signaling

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.
Stem Cell Transplantation ReversesChemotherapy-Induced Cognitive Dysfunction
Munjal M. Acharya, Vahan Mattirosian,
Nicole N. Chmielewski, Nevine Hanna,
Katherine K. Tran, Alicia C. Liao, Lori-Ann Christie,
Vipan K. Paulhar, and Charles L. Limoli

Precis: 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.

elF4E 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. Schwertzfeiger,
Alexey O. Benyumov, I. Carlos Manivel, Shunan Li,
Anja-Katrin Bielinsky, Douglas Yee, Peter B. Bitterman,
and Vitaly A. Polunovsky

Precis: 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.

Interaction between p53 Mutation and a Somatic HDMX Biomarker Better Defines Metastatic Potential in Breast Cancer
Anna M. Grawenda, Elen K. Møller, Suzanne Lam,
Emmanouela Repapi, Amina F.A.S. Teunisse,
Grethe I.G. Alnase, Anne-Lise Børresen-Dale,
Vessela N. Kristensen, Colin R. Goding,
Aart G. Jochemsen, Hege Edvardsen, and
Gareth L. Bond

Precis: 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.

HOXB7 Promotes Malignant Progression by Activating the TGFβ Signaling Pathway
Shou Liu, Rideook Jin, Yvonne Hui, Jie Fu, Chunfa Jie,
Sheng Feng, David Reisman, Qian Wang, Daping Fan,
Saraswati Sukumar, and Hexin Chen

Precis: 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.

Reprogramming of the ERα and ERβ Target Gene Landscape Triggers Tamoxifen Resistance in Breast Cancer
Verena Theves, Ronald Simon, Petra Schroeter,
Magdalena Schlötzer, Tobias Anzeneder,
Reinhard Buttmér, Vladimir Benes, Guido Sauter,
Barbara Bubwinkel, Robert J. Nicholson,
Hans-Peter Sinn, Andreas Schneeweiß,
Ulrich Deuschle, Marc Zapatka, Stefanie Heck, and
Peter Lichter

Precis: These findings suggest that activation of the estrogen-related receptor ERβ 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.

BRCA2-Deficient Sarcomatoid Mammary Tumors Exhibit Multidrug Resistance
Janneke E. Jaspers, Wendy Sol, Ariena Kersbergen,
Andreas Schlücker, Charlotte Guyader, Guotai Xu,
Lodewyk Wessels, Piet Borst, Jos Jonkers, and
Sven Rottenberg

Precis: 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.

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

Precis: 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.

Epigenetic Silencing of miR-490-3p Reactivates the Chromatin Remodeler SMARCD1 to Promote Helicobacter pylori–Induced Gastric Carcinogenesis
Jing Shen, Zhangang Xiao, William K.K. Wu,
Maggie H. Wang, Ka F. To, Yangchao Chen,
Weiqin Yang, May S.M. Li, Vivian Y. Shin,
Joanna H. Tong, Wei Kang, Lin Zhang, Minxing Li,
Lin Wang, Lan Lu, Ruby L.Y. Chan, Sunny H. Wong,
Jun Yu, Matthew T.V. Chan, Francis K.L. Chan,

Precis: 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, Toshiro 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

Cep63 Recruits Cdk1 to the Centrosome—Letter
Mohammad Alsara, Harald Löffler, Anne Fechter, Jiri Bartek, and Alwin Kramer

CORRECTION

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.