## Highlights of This Issue 1345

### REVIEW

1347  The Role of Hypoxia and Exploitation of the Hypoxic Environment in Hematologic Malignancies  
Barbara Muz, Pilar de la Puente, Feda Azab, Micah Luderer, and Abdel Kareem Azab

### CELL CYCLE AND SENESCENCE

1355  Viral Oncogene Expression in the Stem/Progenitor Cell Compartment of the Mouse Intestine Induces Adenomatous Polyps  
Maria Teresa Sáenz Robles, Jean Leon Chong, Christopher Koivisto, Anthony Trimboli, Huayang Liu, Gustavo Leone, and James M. Pipas

### CELL DEATH AND SURVIVAL

1365  Selective Protection of Normal Cells during Chemotherapy by RY4 Peptides  
Xiao-Rong Wu, Lihua Liu, Zhi-Fu Zhang, Bing Zhang, Hongzhe Sun, Gerald L. Chan, and Na Li

1377  Involvement of Extracellular Vesicle Long Noncoding RNA (linc-VLDLR) in Tumor Cell Responses to Chemotherapy  
Kenji Takahashi, Irene K. Yan, Joseph Wood, Hiroaki Haga, and Tushar Patel

### CHROMATIN, GENE, AND RNA REGULATION

1388  EZH2 Represses Target Genes through H3K27-Dependent and H3K27-Independent Mechanisms in Hepatocellular Carcinoma  
Shu-Bin Gao, Qi-Fan Zheng, Bin Xu, Chang-Bao Pan, Kang-Li Li, Yue Zhao, Qi-Lin Zheng, Xiao Lin, Li-Xiang Xue, and Guang-Hui Jin

1398  Decreased Expression of Cystathionine β-Synthase Promotes Glioma Tumorigenesis  
Naoharu Takano, Yasmeen Sarfraz, Daniele M. Gilkes, Pallavi Chaturvedi, Lisha Xiang, Makoto Suematsu, David Zagg, and Gregg L. Semenza

### DNA DAMAGE AND REPAIR

1407  Hypoxia Provokes Base Excision Repair Changes and a Repair-Deficient, Mutator Phenotype in Colorectal Cancer Cells  
Norman Chan, Mohsin Ali, Gordon P. McCallum, Ramya Kumareswaran, Marianne Koritzinsky, Brady G. Wouters, Peter G. Wells, Steven Gallinger, and Robert G. Bristow

### GENOMICS

1416  CD44-Mediated Adhesion to Hyaluronic Acid Contributes to Mechanosensing and Invasive Motility  
Yushan Kim and Sanjay Kumar

1430  Tumor Cell–Derived MMP3 Orchestrates Rac1b and Tissue Alterations That Promote Pancreatic Adenocarcinoma  

### ONCOGENES AND TUMOR SUPPRESSORS

1440  Snail Cooperates with KrasG12D In Vivo to Increase Stem Cell Factor and Enhance Mast Cell Infiltration  
Lawrence M. Knab, Kazumi Ebine, Christina R. Chow, Sania S. Raza, Vaibhav Sahai, Akash P. Patel, Krishan Kumar, David J. Bentrem, Paul J. Grippo, and Hidayatullah G. Munshi

1449  Oncogenic Ras/ERK Signaling Activates CDCP1 to Promote Tumor Invasion and Metastasis  
Takamasa Uekata, Satoko Fuji, Yuri Miyazawa, Reika Iwakawa, Mako Narisawa-Saito, Katsuhiko Nakashima, Koji Tsuta, Hitoshi Tsuda, Tohru Kiyono, Jun Yokota, and Ryuichi Sakai

1460  Nonamplified FGFR1 Is a Growth Driver in Malignant Pleural Mesothelioma  
Lindsay A. Marek, Trista K. Hinz, Anne von Massenhausen, Kyle A. Olszewski, Emily K. Kleczko, Dina Boehm, Mary C. Weiser-Evans, Raphael A. Nemenoff, Hans Hoffmann, Arne Warth, Joseph M. Gozgit, Sven Perner, and Lynn E. Heasley
Differential Requirement for Src Family Tyrosine Kinases in the Initiation, Progression, and Metastasis of Prostate Cancer
Irwin H. Gelman, Jennifer Peresie, Kevin H. Eng, and Barbara A. Foster

Internalization by Multiple Endocytic Pathways and Lysosomal Processing Impact Maspin-Based Therapeutics
Thomas M. Bodenstine, Richard E. B. Seftor, Elisabeth A. Seftor, Zhila Khalkhali-Ellis, Nicole A. Samii, J. Cesar Monarrez, Grace S. Chandler, Philip A. Pemberton, and Mary J. C. Hendrix

The Lipid Kinase PI4KIIIβ Is Highly Expressed in Breast Tumors and Activates Akt in Cooperation with Rab11a
Anne A. Morrow, Mohsen Amir Alipour, Dave Bridges, Zemin Yao, Alan R. Saltiel, and Jonathan M. Lee

Targeting TBK1 Inhibits Migration and Resistance to MEK Inhibitors in Mutant NRAS Melanoma
Ha Linh Vu and Andrew E. Aplin

A Macrophage-Dominant PI3K Isoform Controls Hypoxia-Induced HIF1α and HIF2α Stability and Tumor Growth, Angiogenesis, and Metastasis
Shweta Joshi, Alok R. Singh, Muamera Zulcic, and Donald L. Durden

About the Cover
Pancreatic ductal adenocarcinoma (PDAC) is associated with a pronounced fibro-inflammatory stromal reaction that contributes to tumor progression. A critical step in invasion and metastasis is the epithelial-to-mesenchymal transition (EMT), which can be regulated by the Snail family of transcription factors. Overexpression of Snail and mutant Kras<sup>G12D</sup> in the pancreas of transgenic mice causes fibrosis. The cover image shows a pancreatic section from a 3-month-old Kras<sup>G12D/</sup>Snail mouse that was analyzed for fibrosis using trichrome staining (blue = fibrosis). Please see the article by Knab and colleagues (beginning on page 1440), which demonstrates that Snail also modulates inflammation in the mouse pancreas.