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 Sánchez Robles, Jean Leon Chong, Christopher Koivisto, Anthony Trimble, 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, Li Hua 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 Yue, 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 Zagzag, 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, Bradly 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
Takamasu Uekata, Satoko Fuji, Yuri Miyazawa, Reika Iwakawa, Mako Narisawa-Saito, Katsuhiko Nakashima, Koji Tsuta, Hitoshi Tsuda, Toshiro 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, Diana Boehm, Mary C. Weiser-Evans, Raphael A. Nemenoff, Hans Hoffmann, Arne Warth, Joseph M. Gozgit, Sven Perner, and Lynn E. Heasley

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, Bradly 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
Takamasu Uekata, Satoko Fuji, Yuri Miyazawa, Reika Iwakawa, Mako Narisawa-Saito, Katsuhiko Nakashima, Koji Tsuta, Hitoshi Tsuda, Toshiro 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, Diana Boehm, Mary C. Weiser-Evans, Raphael A. Nemenoff, Hans Hoffmann, Arne Warth, Joseph M. Gozgit, Sven Perner, and Lynn E. Heasley
### Table of Contents

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>1470</td>
<td>Differential Requirement for Src Family Tyrosine Kinases in the Initiation, Progression, and Metastasis of Prostate Cancer</td>
<td>Irwin H. Gelman, Jennifer Peresie, Kevin H. Eng, and Barbara A. Foster</td>
</tr>
<tr>
<td>1480</td>
<td>Internalization by Multiple Endocytic Pathways and Lysosomal Processing Impact Maspin-Based Therapeutics</td>
<td>Thomas M. Bodenstine, Richard E. B. Setfor, Elisabeth A. Seftor, Zhila Khalkhali-Ellis, Nicole A. Samii, J. Cesar Monarrez, Grace S. Chandler, Philip A. Pemberton, and Mary J. C. Hendrix</td>
</tr>
<tr>
<td>1492</td>
<td>The Lipid Kinase PI4KIIIβ Is Highly Expressed in Breast Tumors and Activates Akt in Cooperation with Rab11a</td>
<td>Anne A. Morrow, Mohsen Amir Alipour, Dave Bridges, Zemin Yao, Alan R. Saltiel, and Jonathan M. Lee</td>
</tr>
<tr>
<td>1509</td>
<td>Targeting TBK1 Inhibits Migration and Resistance to MEK Inhibitors in Mutant NRAS Melanoma</td>
<td>Ha Linh Vu and Andrew E. Aplin</td>
</tr>
<tr>
<td>1520</td>
<td>A Macrophage-Dominant PI3K Isoform Controls Hypoxia-Induced HIF1α and HIF2α Stability and Tumor Growth, Angiogenesis, and Metastasis</td>
<td>Shweta Joshi, Alok R. Singh, Muamera Zulcic, and Donald L. Durden</td>
</tr>
</tbody>
</table>

**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 KrasG12D in the pancreas of transgenic mice causes fibrosis. The cover image shows a pancreatic section from a 3-month-old KrasG12D/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.