





# Table of Contents

- 1241** Nkx2.8 Inhibits Epithelial–Mesenchymal Transition in Bladder Urothelial Carcinoma via Transcriptional Repression of *Twist1*  
Chunping Yu, Zhuowei Liu, Qihong Chen, Yonghong Li, Lijuan Jiang, Zhiling Zhang, and Fangjian Zhou  
*Significance:* These findings highlight a novel EMT signaling axis as a candidate target for therapeutic intervention in advanced urothelial carcinomas.
- 1253** Therapy-Educated Mesenchymal Stem Cells Enrich for Tumor-Initiating Cells  
Michael Timaner, Nitzan Letko-Khait, Ruslana Kotsifruk, Madeleine Benguigui, Ofra Beyar-Katz, Chen Rachman-Tzemah, Ziv Raviv, Tomer Bronshtein, Marcelle Machluf, and Yuval Shaked  
*Significance:* These results establish a mechanism by which mesenchyme stem cells in the tumor microenvironment promote chemoresistance, and they propose a novel drug delivery system to overcome this challenge.
- 1266** Deletion of the von Hippel-Lindau Gene in Hemangioblasts Causes Hemangioblastoma-like Lesions in Murine Retina  
Herui Wang, Matthew J. Shepard, Chao Zhang, Lijin Dong, Dyvon Walker, Liliana Guedez, Stanley Park, Yujuan Wang, Shida Chen, Ying Pang, Qi Zhang, Chun Gao, Wai T. Wong, Henry Wiley, Karel Pacak, Emily Y. Chew, Zhengping Zhuang, and Chi-Chao Chan  
*Significance:* This study describes a model that phenotypically recapitulates a form of retinal pathogenesis that is driven by genetic loss of the VHL tumor suppressor, providing a useful tool for its study and therapeutic intervention.
- 1275**  GADD45 $\beta$  Loss Ablates Innate Immunosuppression in Cancer  
Daniela Verzella, Jason Bennett, Mariafausta Fischietti, Anil K. Thotakura, Camilla Recordati, Fabio Pasqualini, Daria Capece, Davide Vecchiotti, Daniel D'Andrea, Barbara Di Francesco, Marcella De Maglie, Federica Begalli, Laura Tornatore, Salvatore Papa, Toby Lawrence, Stuart J. Forbes, Antonio Sica, Edoardo Alesse, Francesca Zazzeroni, and Guido Franzoso  
*Significance:* These findings define a myeloid-based immune checkpoint that restricts T-cell trafficking into tumors, with potentially important therapeutic implications to generally improve the efficacy of cancer immunotherapy.
- 1293** Inflammasome Adaptor ASC Suppresses Apoptosis of Gastric Cancer Cells by an IL18-Mediated Inflammation-Independent Mechanism  
Virginie Deswaerte, Paul Nguyen, Alison West, Alison F. Browning, Liang Yu, Saleela M. Ruwanpura, Jesse Balic, Thaleia Livis, Charlotte Girard, Adele Preaudet, Hiroko Oshima, Ka Yee Fung, Hazel Tye, Meri Najdovska, Matthias Ernst, Masanobu Oshima, Cem Gabay, Tracy Putoczki, and Brendan J. Jenkins  
*Significance:* Inflammasome activation that elevates IL18 helps drive gastric cancer by protecting cancer cells against apoptosis, with potential implications for new therapeutic strategies in this setting.
- 1308** Germinal Centers Determine the Prognostic Relevance of Tertiary Lymphoid Structures and Are Impaired by Corticosteroids in Lung Squamous Cell Carcinoma  
Karina Siliņa, Alex Soltermann, Farkhondeh Movahedian Attar, Ruben Casanova, Zina M. Uckelely, Helen Thut, Muriel Wandres, Sergejs Isajevs, Phil Cheng, Alessandra Curioni-Fontecedro, Periklis Foukas, Mitchell P. Levesque, Holger Moch, Aija Linē, and Maries van den Broek  
*Significance:* Corticosteroid treatment during chemotherapy negatively affects the development of tertiary lymphoid structures and abrogates their prognostic value in patients with lung cancer.
- 1321** Inactivation of Cancer-Associated-Fibroblasts Disrupts Oncogenic Signaling in Pancreatic Cancer Cells and Promotes Its Regression  
Patricia Daurer, Xianda Zhao, Vineet K. Gupta, Nikita Sharma, Kousik Kesh, Prisca Gnamlin, Vikas Dudeja, Selwyn M. Vickers, Sulagna Banerjee, and Ashok Saluja  
*Significance:* In an established mouse model of pancreatic cancer, administration of the promising experimental drug Mimmelide was found to actively deplete reactive stromal fibroblasts and to trigger tumor regression, with implications for stromal-based strategies to attack this disease.
- 1334**  Combined Mutation of *Apc*, *Kras*, and *Tgfb $\beta$ 2* Effectively Drives Metastasis of Intestinal Cancer  
Eri Sakai, Mizuho Nakayama, Hiroko Oshima, Yuta Kouyama, Atsushi Niida, Satoshi Fujii, Atsushi Ochiai, Keiichi I. Nakayama, Koshi Mimori, Yutaka Suzuki, Chang Pyo Hong, Chan-Young Ock, Seong-Jin Kim, and Masanobu Oshima  
*Significance:* These findings illuminate how key driver mutations in colon cancer cooperate to drive the development of metastatic disease, with potential implications for the development of suitable prevention strategies.

# Table of Contents

## TRANSLATIONAL SCIENCE

**1347** Statin-Induced Cancer Cell Death Can Be Mechanistically Uncoupled from Prenylation of RAS Family Proteins

Rosemary Yu, Joseph Longo, Jenna E. van Leeuwen, Peter J. Mullen, Wail Ba-Alawi, Benjamin Haibe-Kains, and Linda Z. Penn

*Significance:* The use of statins to target cancer cell EMT may be useful as a therapy to block cancer progression.

**1358** Brain-Mimetic 3D Culture Platforms Allow Investigation of Cooperative Effects of Extracellular Matrix Features on Therapeutic Resistance in Glioblastoma

Weikun Xiao, Rongyu Zhang, Alireza Sohrabi, Arshia Ehsanipour, Songping Sun, Jesse Liang, Christopher M. Walthers, Lisa Ta, David A. Nathanson, and Stephanie K. Seidlits

*Significance:* Three-dimensional culture scaffolds of glioblastoma provide a better physiological representation over current methods of patient-derived cell culture and xenograft models.

## CORRECTION

**1371** Correction: KLF6 Suppresses Metastasis of Clear Cell Renal Cell Carcinoma via Transcriptional Repression of E2F1

 AC icon indicates Author Choice

For more information please visit [www.aacrjournals.org](http://www.aacrjournals.org)

## ABOUT THE COVER

Tertiary lymphoid structures (TLS) develop in the human tumor microenvironment and correlate with prolonged survival. TLS are organized structures that resemble follicles of lymph nodes and contribute to local immune responses. Using immunofluorescence and quantitative pathology on human lung cancer and mouse lung samples, it was shown that TLS development followed sequential steps from simple lymphocytic aggregates to organized structures with lymphoid stromal cells and finally to mature TLS with a germinal center. Neoadjuvant chemotherapy and corticosteroid treatment significantly reduced the development of mature TLS, which was associated with poor outcome in patients with lung cancer. For details, see article by Siliņa and colleagues on page 1308.

