REVIEW
3381 The Early Detection of Pancreatic Cancer: What Will It Take to Diagnose and Treat Curable Pancreatic Neoplasia?
Anne Marie Lennon, Christopher L. Wolfgang, Marcia Irene Canto, Alison P. Klein, Joseph M. Herman, Michael Goggins, Elliot K. Fishman, Itab Kamel, Matthew J. Weiss, Luis A. Diaz, Nickolas Papadopoulos, Kenneth W. Kinzler, Bert Vogelstein, and Ralph H. Hruban

PERSPECTIVE
3390 Enhancement of the T-cell Armamentarium as a Cell-Based Therapy for Prostate Cancer
W. Nathaniel Brennen, Charles G. Drake, and John T. Isaacs

MEETING REPORT
3396 Oncolytic Viruses Targeting Tumor Stem Cells
E. Antonio Chiocca, Donald Blair, and R. Allan Mufson

CLINICAL STUDIES
3399 Favorable Prognostic Impact in Loss of TP53 and PIK3CA Mutations after Neoadjuvant Chemotherapy in Breast Cancer
Yi-Zhou Jiang, Ke-Da Yu, Jing Bao, Wen-Ting Peng, and Zhi-Ming Shao

MICROENVIRONMENT AND IMMUNOLOGY
3408 Local and Systemic Protumorigenic Effects of Cancer-Associated Fibroblast-Derived GDF15
Francesca Bruzzese, Christina Hagglof, Alessandra Leone, Elin Sjoberg, Maria Serena Roca, Sara Killelram, Tobias Sjoblom, Peter Hammarsten, Lars Egevad, Anders Bergh, Arne Ostman, Alfredo Budillon, and Martin Augsten
Précis: This study demonstrates for the first time that cancer-associated fibroblasts can exert systemic effects on malignant cell growth beyond the local tumor microenvironment, with potential implications for controlling metastatic progression.

3418 LSECtin Expressed on Melanoma Cells Promotes Tumor Progression by Inhibiting Antitumor T-cell Responses
Feng Xu, Jing Liu, Di Liu, Biao Liu, Min Wang, Zhiyuan Hu, Xuemei Du, Li Tang, and Fuchu He
Précis: A T-cell-suppressive molecule studied solely in antigen-presenting cells to date is found to be expressed frequently in melanoma cells, engendering a novel mechanism of immune escape with implications for novel therapeutic strategies.

3429 Metalloprotease-Mediated Tumor Cell Shedding of B7-H6, the Ligand of the Natural Killer Cell–Activating Receptor NKp30
Eva Schlecker, Nathalie Fiegler, Annette Arnold, Peter Altevogt, Stefan Rose-John, Gerhard Moldenhauer, Antje Sucker, Annette Paschen, Elke Pogge von Strandmann, Sonja Teztor, and Adelheid Cerwenka
Précis: Blocking the ability of tumor cells to proteolytically shed a cell surface ligand recognized by natural killer immune cells can enhance the recognition and destruction of tumor cells, with implications for how to promote or sustain NK cell–based immunotherapies for cancer.

3441 Immunosuppressive Myeloid Cells Induced by Chemotherapy Attenuate Antitumor CD8+ T-Cell Responses through the PD-1–PD-L1 Axis
Zhi-Chun Ding, Xiaoyun Lu, Miao Yu, Henrique Lemos, Lei Huang, Phillip Chandler, Kebin Liu, Matthew Walters, Antoni Krasinfs, Matthias Mack, Bruce R. Blazar, Andrew L. Mellor, David H. Munn, and Gang Zhou
Précis: Chemotherapy may restrain its own efficacy by eliciting myeloid cells that have immnosuppressive activities, with implications for creating regimens of immunochemotherapy that tilt toward more effective, durable responses.
3454 Complement C5a Receptor Facilitates Cancer Metastasis by Altering T-Cell Responses in the Metastatic Niche
Surya Kumari Vadrevu, Navin K. Chintala, Sharad K. Sharma, Priya Sharma, Clayton Cleveland, Linley Riediger, Sasikanth Manne, David P. Fairlie, Wojciech Gorczyca, Othon Almanza, Magdalena Karbowniczek, and Maciej M. Markiewski
Précis: These findings offer a preclinical rationale to translate complement-based immunotherapies to the clinic as a strategy to prevent or reduce metastatic progression.

3466 Autologous T-cell Therapy for Cytomegalovirus as a Consolidative Treatment for Recurrent Glioblastoma
Andrea Schuessler, Corey Smith, Leone Beagley, Glen M. Boyle, Sweera Rehan, Katherine Matthews, Linda Jones, Tania Crough, Vijayendra Dasari, Kerenafalit Klein, Amy Smalley, Hamish Alexander, David G. Walker, and Rajiv Khanna
Précis: Early clinical findings for a CMV-based immunotherapy tested in aggressive brain tumors encourage further evaluation of the therapeutic efficacy of this platform technology.

MOLECULAR AND CELLULAR PATHOBIOLOGY
3477 NCOA1 Directly Targets M-CSF1 Expression to Promote Breast Cancer Metastasis
Li Qin, Ye-Lin Wu, Michael J. Toneff, Dabing Li, Lan Liao, Xiuhua Gao, Fiona T. Bane, Jean C.-Y. Tien, Yixiang Xu, Zhen Feng, Zhihui Yang, Yan Xu, Sarah M. Theissen, Yi Li, Leonie Young, and Jianming Xu
Précis: These results define a regulatory axis controlled by a nuclear coactivator implicated in breast cancer relapse, which acts to promote metastasis by recruiting macrophages that drive this process.

3489 G Protein–Coupled Receptor Kinase GRK5 Phosphorylates Moesin and Regulates Metastasis in Prostate Cancer
Prabir Kumar Chakraborty, Yushan Zhang, Alexandra S. Coomes, Wan-Ju Kim, Rachel Stupay, Lauren D. Lynch, Tamieka Atkinson, Jae I. Kim, Zhongzhen Nie, and Yehia Daaka
Précis: G protein–coupled receptors are readily druggable targets for which significant opportunities may exist in cancer therapy, as suggested by this study of the prometastatic contributions of GRK5 to prostate cancer.

3501 NADPH Oxidase NOX4 Supports Renal Tumorigenesis by Promoting the Expression and Nuclear Accumulation of HIF2α
Jennifer L. Gregg, Robert M. Turner II, Guimin Chang, Disha Joshi, Ye Zhan, Li Chen, and Jodi K. Maranchie
Précis: These findings offer direct evidence that NOX4 is critical for renal tumorigenesis and offer a preclinical rationale to target NOX4 for therapeutic management of renal cancer.

3512 Galectin-1 Drives Pancreatic Carcinogenesis through Stroma Remodeling and Hedgehog Signaling Activation
Neus Martínez-Bosch, Maite G. Fernández-Barrena, Mireia Moreno, Elena Ortiz-Zapater, Jessica Munne-Collado, Mar Iglesias, Sabine André, Hane-Joachim Gabius, Rosa F. Hwang, Françoise Poirier, Carolina Navas, Carmen Guerra, Martin E. Fernández-Zapico, and Pilar Navarro
Précis: These findings identify a lectin-like molecule in the tumor microenvironment in pancreatic cancer as a tractable target for therapy, with potential impact at several levels in both malignant and stromal cells.

PREVENTION AND EPIDEMIOLOGY
3525 No Causal Association Identified for Human Papillomavirus Infections in Lung Cancer
Précis: Although HPV DNA has been detected in some lung cancers, hinting at a causal connection like that in cervical cancer, the deeper analysis performed in this study does not encourage this hypothesis.
Targeting Mitochondrial Oxidative Metabolism in Melanoma Causes Metabolic Compensation through Glucose and Glutamine Utilization

Ji-Hong Lim, Chi Luo, Francisca Vazquez, and Pere Puigserver

Precis: Because cancer cells are as metabolically flexible as they are genetically malleable, therapeutic strategies to attack cancer cell metabolism need to address multiple pathways at once.

The RAD51-Stimulatory Compound RS-1 Can Exploit the RAD51 Overexpression That Exists in Cancer Cells and Tumors

Jennifer M. Mason, Hillary L. Logan, Brian Budke, Megan Wu, Michal Pawlowski, Ralph R. Weichselbaum, Alan P. Kozikowski, Douglas K. Bishop, and Philip P. Connell

Precis: This study describes a novel therapeutic strategy to turn the heightened DNA repair capabilities of cancer cells against themselves, offering a preclinical proof of concept for a generalized approach to treat many kinds of human cancer.

API5 Confers Tumoral Immune Escape through FGF2-Dependent Cell Survival Pathway

Kyung Hee Noh, Seok-Ho Kim, Jin Hee Kim, Kwon-Ho Song, Young-Ho Lee, Tae Heung Kang, Hee Dong Han, Anil K. Sood, Joanne Ng, Kwanghee Kim, Chung Hee Sonn, Vinay Kumar, Cassian Yee, Kyung-Mi Lee, and Tae Woo Kim

Precis: These findings identify a novel pathway of immune escape in tumors that could be targeted to potentiate the efficacy of cancer vaccines or T-cell immunotherapies in the clinic, with immediate implications for the design of immunchemotherapy combinations that could heighten antitumor efficacy.

Re-engineering Vesicular Stomatitis Virus to Abrogate Neurotoxicity, Circumvent Humoral Immunity, and Enhance Oncolytic Potency

Alexander Muik, Lawton J. Stubbert, Roza Z. Jahedi, Yvonne Geiß, Janine Kimpel, Catherine Dold, Reinhard Tober, Andreas Volk, Sabine Klein, Ursula Dietrich, Beta Yadollahi, Theresa Falls, Hrvoje Miletic, David Stojdl, John C. Bell, and Dorothee von Laer

Precis: As cancer treatment tools, oncolytic viruses have mostly fallen short of expectations, with only sparse evidence for clinical efficacy so far, but the engineered viral platform described here lacks several of the major drawbacks that have hampered clinical development.
Oxidative Stress Activates SIRT2 to Deacetylate and Stimulate Phosphoglycerate Mutase

Yanping Xu, Fulong Li, Lei Lv, Tingting Li, Xin Zhou, Chu-Xia Deng, Kun-Liang Guan, Qun-Ying Lei, and Yue Xiong

These results reveal a mechanism that maintains NADPH homeostasis in response to oxidative stress, not only easing cell proliferation in tumors but also licensing conditions for metabolic adaptation to otherwise growth-inhibitory conditions.