BREAKING ADVANCES

3963  Highlights from Recent Cancer Literature

REVIEW

3965  Long Noncoding RNA and Cancer: A New Paradigm
      Arunoday Bhan, Milad Soleimani, and Subhrangsu S. Mandal

PRIORITY REPORT

3982  Epithelial-to-Mesenchymal Transition Contributes to Immunosuppression in Breast Carcinomas
      Anushka Dongre, Mohammad Rashidian, Ferenc Reinhardt, Aaron Bagnato, Zuzana Keckesova, Hidde L. Ploegh, and Robert A. Weinberg
      Précis: Immune cells and immunomodulatory markers protect local tumor cells from immune attack and can be potentially targeted to enhance the sensitivity of tumors to therapy.

MOLECULAR AND CELLULAR PATHOBIOLOGY

3990  SIRT3-Mediated Dimerization of IDH2 Directs Cancer Cell Metabolism and Tumor Growth
      Xianghui Zou, Yueming Zhu, Seong-Hoon Park, Guoxiang Liu, Joseph O’Brien, Haiyan Jiang, and David Gius
      Précis: These findings identify SIRT3 as a potential tumor suppressor that controls cancer cell metabolism and malignant progression.

4000  ArL13b Promotes Gastric Tumorigenesis by Regulating Smo Trafficking and Activation of the Hedgehog Signaling Pathway
      Jia Shao, Linlin Xu, Limin Chen, Qiqin Lu, Xinxeng Xie, Wei Shi, Huanling Xiong, Chao Shi, Yuan Huang, Jinghong Mei, Hai Ruo, Hua Lu, Nonghua Lu, and Shiwen Luo
      Précis: ArL13b plays crucial roles in Smo-mediated signal transduction, activation of the Hh pathway, and tumor growth of gastric cancer, which may be a potential novel molecule target for the development of anticancer therapy.

TUMOR AND STEM CELL BIOLOGY

4014  IGFBP7 Deletion Promotes Hepatocellular Carcinoma
      Précis: IGFBP7 acts as a tumor suppressor gene that suppresses liver cancer, both by directly inhibiting cancer cell growth and by stimulating an anti-tumor immune response, with therapeutic implications to improve liver cancer management.

4026  Autocrine BMP-4 Signaling Is a Therapeutic Target in Colorectal Cancer
      Yuichiro Yokoyama, Toshiaki Watanabe, Yusuke Tamura, Yoshinobu Hashizume, Kohei Miyazono, and Shogo Ehata
      Précis: A growth factor that is part of the TGFβ family is implicated in this study as a new target for the treatment of colorectal cancer.

4039  A Naturally Generated Decoy of the Prostate Apoptosis Response-4 Protein Overcomes Therapy Resistance in Tumors
      Nikhil Hebbar, Ravshan Burikhanov, Nidhi Shukla, Shirley Oiu, Yanning Zhao, Kojo S.J. Ellenitoba-Johnson, and Vivek M. Rangnekar
      Précis: PAF, a novel fragment of the tumor suppressor Par-4, may be harnessed to induce paracrine growth inhibition of heterogeneous tumors and overcome therapeutic resistance.

4051  ARHGAP18 Downregulation by miR-200b Suppresses Metastasis of Triple-Negative Breast Cancer by Enhancing Activation of RhoA
      Brock Humphries, Zhishan Wang, Yunfei Li, Jing-Ru Jhan, Yiguuo Jiang, and Chengfeng Yang
      Précis: Studies of a RhoGAP overexpressed in aggressive triple-negative breast cancers contradict the conventional view that RhoGAP family members function as tumor suppressors.
The Alkylating Chemotherapeutic Temozolomide

4102 Identification of New Tumor Suppressor Genes in Comprehensive Evaluation of Protein Coding Mononucleotide Microsatellites in Microsatellite-Unstable Colorectal Cancer

4078 Intestine-Specific Homeobox Gene ISX Integrates IL6 Signaling, Tryptophan Catabolism, and Immune Suppression

4102 β-Catenin Is a Candidate Therapeutic Target for Myeloid Neoplasms with del(5q)

Liping Li, Yue Sheng, Wenshu Li, Chao Hu, Nupur Mittal, Kaoru Tohyama, Amber Seba, You-Yang Zhao, Howard Ozer, Tongyu Zhu, and Zhijian Qian

Précis: These results suggest a strategy to eliminate leukemic stem cells, which drive a common chromosomally defined class of myeloid neoplasms, perhaps enabling an individualized treatment for this subset of leukemia patients.

4127 Monitoring the Vascular Response and Resistance to Sunitinib in Renal Cell Carcinoma In Vivo with Susceptibility Contrast MRI

Simon P. Robinson, Jessica K.R. Boult, Naveen S. Vasudev, and Andrew R. Reynolds

Précis: This study illustrates how a noninvasive magnetic resonance imaging method can track vascular phenotypes, which correspond with therapeutic responses produced by an antiangiogenic drug in kidney tumors.

MICROENVIRONMENT AND IMMUNOLOGY

4135 Enhanced Therapeutic Efficacy and Memory of Tumor-Specific CD8 T Cells by Ex Vivo PI3K-δ Inhibition

Rasha Abu Eid, Shamim Ahmad, Yuan Lin, Mason Webb, Zuzana Berzong, Rajesh Shrimali, Takumi Kumai, Sudha Ananth, Paulo C. Rodriguez, Esteban Celis, John Janik, Mikayel Mkrtichyan, and Samir N. Khleif

Précis: These findings highlight clinical implications for PI3K-δ inhibition in CD8 T cells, which appear to enhance the efficacy of adoptive cell transfer therapies and vaccine-based immunotherapies.

4146 Immune Checkpoint Blockade, Immunogenic Chemotherapy or IFN-α Blockade Boost the Local and Abscopal Effects of Oncolytic Virotherapy

Laetitia Fend, Takahiro Yamazaki, Christelle Remy, Catherine Fahrner, Murielle Gantzer, Virginie Nourtier, Xavier Prvéille, Eric Quéméneur, Oliver Kepp, Julien Adam, Aurélien Marabelle, Jonathan M. Pitt, Guido Kroemer, and Laurence Zitvogel

Précis: These findings suggest how to optimize the effects of oncolytic vaccinia viruses used to treat cancer, using methods to improve the efficacy of immune cells infiltrating local and distant tumors.

4158 An Immunosuppressive Dendritic Cell Subset Accumulates at Secondary Sites and Promotes Metastasis in Pancreatic Cancer


Précis: An immunosuppressive DC population can be targeted in multiple ways to stimulate tumor immunity and prevent disease progression in PDAC.
INTEGRATED SYSTEMS AND TECHNOLOGIES

3D Mathematical Modeling of Glioblastoma Suggests That Transdifferentiated Vascular Endothelial Cells Mediate Resistance to Current Standard-of-Care Therapy
Huaming Yan, Mónica Romero-López, Lesly I. Benítez, Kaijun Di, Hermann B. Frieboes, Christopher C.W. Hughes, Daniela A. Bota, and John S. Lowengrub
Précis: These striking findings suggest that using combinatorial therapies to target transdifferentiated vascular endothelial cells present in glioblastomas could eradicate these deadly brain tumors without recurrence.

Competition between DNA Methylation, Nucleotide Synthesis, and Antioxidation in Cancer versus Normal Tissues
Sha Cao, Xiwen Zhu, Chi Zhang, Hong Qian, Heinz-Bernd Schuttler, Jianping Gong, and Ying Xu
Précis: Reduced global DNA methylation levels in cancer cells versus normal cells are regulated by competition for key metabolites, whose shifting levels may serve as potential prognostic markers for cancer.

PREVENTION AND EPIDEMIOLOGY

Risk of Second Malignancies in Solid Organ Transplant Recipients Who Develop Keratinocyte Cancers
Rachel D. Zamoiski, Elizabeth Yanik, Todd M. Gibson, Elizabeth K. Cahoon, Margaret M. Madeleine, Charles F. Lynch, Sally Gustafson, Marc T. Goodman, Melissa Skeans, Ajay K. Israni, Eric A. Engels, and Lindsay M. Morton
Précis: Second cancer risks after keratinocyte cancers in solid organ transplant recipients differ somewhat from the general population, providing insight into the immunosuppressive roots of squamous cell carcinogenesis.

CORRECTION

Correction: Noninvasive In Vivo Imaging and Biologic Characterization of Thyroid Tumors by ImmunoPET Targeting of Galectin-3

ABOUT THE COVER

Mesenchymal carcinoma cells recruit immunosuppressive Tregs and M2 macrophages to the tumor microenvironment relative to their epithelial counterparts, which recruit cytotoxic CD8⁺ T cells instead. In carcinomas that are comprised of heterogeneous mixtures of both epithelial and mesenchymal cells, minority subpopulations of immunosuppressive mesenchymal carcinoma cells are able to protect the entire tumor, including its epithelial cells, from immune attack. Immunofluorescence analysis of mixed tumor sections revealed that mesenchymal (green) and epithelial (white) carcinoma cells segregate to distinct sectors of the tumor. F480⁺ macrophages (red) are interspersed only among the mesenchymal cells of the tumor, while only a few scattered macrophages are found at the periphery of epithelial sectors within the same tumor. For details, see article by Dongre and colleagues on page 3982.