Highlights from Recent Cancer Literature


Systemic DNA Damage Related to Cancer


Role for Stromal Heterogeneity in Prostate Tumorigenesis

Maria A. Kiskowski, Roger S. Jackson, Jheelam Banerjee, Xiaohong Li, Minchul Kang, Juan M. Iturregui, Omar E. Franco, Simon W. Hayward, and Neil A. Bhowmick

Précis: Heterogeneity of stromal TGF-β responsiveness supports cooperative intratumoral signaling and prostate adenocarcinoma progression.

Précis: This genetic bioinformatics study reports the development of a cancer model offering a unified perspective on the complex signaling and regulatory networks that comprise different human cancers.

Endoglin Regulates Cancer–Stromal Cell Interactions in Prostate Tumors

Diana Romero, Christine O’Neill, Aleksandra Terzic, Liangru Contois, Kira Young, Barbara A. Conley, Raymond C. Bergan, Peter C. Brooks, and Calvin P.H. Vary

Précis: Findings show how a TGF-β accessory receptor being explored as a therapeutic target acts to support the viability of cancer-associated fibroblasts in the tumor microenvironment, which are key drivers of angiogenesis and growth.

Expression of Id-1 Is Regulated by MCAM/MUC18: A Missing Link in Melanoma Progression

Maya Zigler, Gabriel J. Villares, Andrey S. Dobroff, Hua Wang, Li Huang, Russell B. Brauer, Takaafumi Kamiya, Vladislava O. Melnikova, Renduo Song, Ran Friedman, Rhoda M. Alani, and Menashe Bar-Eli

Précis: Mechanistic findings reveal how an important cell adhesion molecule melanoma regulates metastatic progression.
Tumor-Evoked Regulatory B Cells Promote Breast Cancer Metastasis by Converting Resting CD4⁺ T Cells to T-Regulatory Cells

Drawings of the text are not provided, but it can be inferred that the content of this section discusses the role of tumor-evoked regulatory B cells in promoting breast cancer metastasis through the conversion of resting CD4⁺ T cells to T-Regulatory cells.

Reprogramming CD19-Specific T Cells with IL-21 Signaling Can Improve Adoptive Immunotherapy of B-Lineage Malignancies

This section likely discusses the findings that addition of IL-21 to culture provides an extrinsic reprogramming signal to generate effective T-cell immunotherapy for B-lineage malignancies.

Unraveling Cancer Chemoimmunotherapy Mechanisms by Gene and Protein Expression Profiling of Responses to Cyclophosphamide

Further discussion of the mechanisms and responses to cyclophosphamide in cancer chemoimmunotherapy.

miR-125b Is Methylated and Functions as a Tumor Suppressor by Regulating the ETS1 Proto-oncogene in Human Invasive Breast Cancer

Studies on the role of miR-125b in breast cancer, highlighting its function as a tumor suppressor by regulating the ETS1 proto-oncogene.

Human Glioma Growth Is Controlled by MicroRNA-10b

Investigations on the oncogenic functions of microRNA-10b in glioma biology through in silico, in vitro, and in vivo approaches.

Increased Survival following Tumorigenesis in Ts65Dn Mice that Model Down Syndrome

Studies showing increased survival in Ts65Dn mice, a model for Down Syndrome, following tumorigenesis.

Evidence That Serum Levels of the Soluble Receptor for Advanced Glycation End Products Are Inversely Associated with Pancreatic Cancer Risk: A Prospective Study

Prospective study suggesting that soluble forms of the receptor for advanced glycation end-products might prevent pancreatic cancers thought to be driven by proinflammatory stimuli.
Bel-2 Inhibits Nuclear Homologous Recombination by Localizing BRCA1 to the Endomembranes
Corentin Laulier, Aurélie Barascu, Josée Guirouillé-Barbat, Gaëlle Pennarun, Catherine Le Chalony, François Chevalier, Gaëlle Palierne, Pascale Bertrand, Jean Marc Verbavatz, and Bernard S. Lopez

Précis: Findings suggest a new tumor suppressor function and new mode of regulation for BRCA1, with general implications for understanding the role of homologous recombination in the maintenance of genome stability.

Deciphering the Molecular Events Necessary for Synergistic Tumor Cell Apoptosis Mediated by the Histone Deacetylase Inhibitor Vorinostat and the BH3 Mimetic ABT-737
Adrian P. Wiegmans, Amber E. Alsop, Michael Bots, Leonie A. Cluse, Steven P. Williams, Kellie-Marie Banks, Rachael Balli, Clare L. Scott, Anna Frenzel, Andreas Villunger, and Ricky W. Johnstone

Précis: An extensive analysis of the basis for cancer cell death synergy between two important new classes of molecular targeted therapies stimulates interest in evaluation of their clinical combination.

Epigenetic Silencing of MicroRNA-203 Dysregulates ABL1 Expression and Drives Helicobacter-Associated Gastric Lymphomagenesis
Vanessa J. Craig, Sergio B. Cogliatti, Hubert Rehrauer, Thomas Wiendisch, and Anne Müller

Précis: Progression of H. pylori-associated gastritis to gastric MALT lymphoma is epigenetically regulated by promoter methylation of a microRNA that regulates the ABL oncogene.

Following Cytochrome c Release, Autophagy Is Inhibited during Chemotherapy-Induced Apoptosis by Caspase 8–Mediated Cleavage of Beclin 1
Hua Li, Peng Wang, Quanhong Sun, Wen-Xing Ding, Xiao-Ming Yin, Robert W. Sobol, Donna B. Stolz, Jian Yu, and Lin Zhang

Précis: This study provides direct evidence that cleavage of Beclin 1 by caspases functions as a critical switch for turning off autophagy for effective killing of cancer cells.

The Dual EGFR/HER2 Inhibitor Lapatinib Synergistically Enhances the Antitumor Activity of the Histone Deacetylase Inhibitor Panobinostat in Colorectal Cancer Models
Melissa J. LaBonte, Peter M. Wilson, Will Fazzone, Jared Russell, Stan G. Louie, Anthony El-Khoueiry, Heinz-Josef Lenz, and Robert D. Ladner

Précis: Findings provide a preclinical rationale to combine HDAC inhibitors with EGFR and HER2-targeted therapies in clinical trials seeking to improve colorectal cancer treatment.

Contribution of Abcc10 (Mrp7) to In Vivo Paclitaxel Resistance as Assessed in Abcc10−/− Mice

Précis: This is the first study to define an ATP-binding transporter other than P-glycoprotein that mediates cytotoxic sensitivity to taxanes.

STAT3 Mediates Resistance to MEK Inhibitor through MicroRNA miR-17
Bingbing Dai, Jieru Meng, Michael Peyton, Luc Girard, William G. Bornmann, Lin Ji, John D. Minna, Bingliang Fang, and Jack A. Roth

Précis: This study suggests strategies to overcome resistance to MEK kinase inhibitors which are presently being evaluated in clinical trials.

Differential Expression of S6K2 Dictates Tissue-Specific Requirement for S6K1 in Mediating Aberrant mTORC1 Signaling and Tumorigenesis
Caterina Nardella, Andrea Lunardi, Giuseppe Fedele, John G. Clohessy, Andrea Alimonti, Sara C. Kozma, George Thomas, Massimo Loda, and Pier Paolo Pandolfi

Précis: Findings suggest clinical evaluation of S6 kinase inhibitors in a subset of adrenal gland tumors lacking the tumor suppressor PTEN.
**TUMOR AND STEM CELL BIOLOGY**

**Effects of Carbon Ion Beam on Putative Colon Cancer Stem Cells and Its Comparison with X-rays**

Xing Cui, Kazuhiro Oonishi, Hirohiko Tsujii, Takeshi Yasuda, Yoshitaka Matsumoto, Yoshiya Furusawa, Makoto Akashi, Tadashi Kamada, and Ryuichi Okayasu

**Précis:** This is the first study to show that carbon ion beam therapy may have advantages over photon beam therapy in targeting cancer stem-like cells for destruction.

**ΔNp63 Versatilely Regulates a Broad NF-κB Gene Program and Promotes Squamous Epithelial Proliferation, Migration, and Inflammation**

Xinping Yang, Hai Lu, Bin Yan, Rose-Anne Romano, Yansong Bian, Jay Friedman, Praveen Duggal, Clint Allen, Ryan Chuang, Reza Ehsanian, Han Si, Satrajit Sinha, Carter Van Waes, and Zhong Chen

**Précis:** Mechanistic findings reveal how the interaction of two key epidermal regulatory transcription factors orchestrate inflammatory changes characteristic of injury and malignant transformation.

**Does the Hepatitis B Antigen HBx Promote the Appearance of Liver Cancer Stem Cells?**

Alla Arzumanyan, Tiffany Friedman, Irene O.L. Ng, Marcia M. Clayton, Zhaorui Lian, and Mark A. Feitelson

**Précis:** This work establishes a link between chronic HBV infection and liver cancer by showing that the virus oncoprotein, HBx, promotes the appearance of "stemness" markers.

**PHLDA1 Expression Marks the Putative Epithelial Stem Cells and Contributes to Intestinal Tumorigenesis**


**Correction:** Oncogenic Synergism between ErbB1, Nucleolin, and Mutant Ras

**ABOUT THE COVER**

Breast cancer induces the generation of regulatory B cells (tBregs) from resting B cells. As a result, tBregs convert T cells into Tregs which infiltrate CCL17/CCL22-expressing lungs to protect metastasizing cancer cells from NK cells. For details, see the article by Olkhanud and colleagues on page 3505 of this issue.