CONSISTENCY OF CHROMOSOMAL INSTABILITY WITH SURVIVAL OUTCOME IN DIFFERENT CANCERS

We aimed to determine whether the chromosome instability (CIN) score, defined as the number of chromosome instability foci in breast, colorectal, and lung cancer cells, is associated with survival outcome in different cancers.

Methods

We used the Cancer Genome Atlas Project (TCGA) dataset of 1,108 breast, 806 colorectal, and 1,024 lung cancer patients, with a median follow-up of 60 months. The CIN score was calculated as the number of chromosome instability foci per 10,000 cells. The association between the CIN score and survival was assessed using Kaplan-Meier and Cox regression analyses.

Results

In breast cancer, a higher CIN score was associated with worse survival (log-rank test, p = 0.01). In colorectal cancer, a higher CIN score was associated with better survival (log-rank test, p = 0.04). In lung cancer, a higher CIN score was associated with worse survival (log-rank test, p = 0.02).

Discussion

Our findings suggest that the chromosome instability (CIN) score is associated with survival outcome in different cancers, with a consistent pattern of association in breast and colorectal cancer and a contrasting pattern in lung cancer. These results highlight the importance of further research to understand the biological basis of these associations and to develop personalized treatment strategies.
Tumor-Evoked Regulatory B Cells Promote Breast Cancer Metastasis by Converting Resting CD4+ T Cells to T-Regulatory Cells

Precis: Findings indicate that tumor-evoked regulatory B cells are crucial for lung metastasis, acting to convert resting T cells to regulatory T cells that promote immune escape in the target tissue.

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

Precis: Findings reveal that addition of IL-21 to culture provides an extrinsic reprogramming signal to generate effective T-cell immunotherapy.

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

Precis: Rapidly growing interest in combined regimens of chemoimmunotherapy is based upon emerging evidence that the efficacy of certain chemotherapeutic agents relies upon coordinate immune stimulatory effects.

Anti-TIM3 Antibody Promotes T Cell IFN-γ-Mediated Antitumor Immunity and Suppresses Established Tumors

Precis: The first antibody targeting investigations for a little studied T-cell co-inhibitory receptor establish single agent activity and mechanism of action in multiple preclinical mouse models of cancer and primary carcinogenesis.
THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

3590

**Bel-2 Inhibits Nuclear Homologous Recombination by Localizing BRCA1 to the Endomembranes**
Corentin Laulier, Aurélie Barascu, Josée Guirouilh-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.

3603

**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 Ralli, 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.

3616

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

3625

**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.

3635

**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.

3649

**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.

3658

**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.

3669

**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.
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

Précis: A novel marker of epithelial stem cells is suggested that functionally contributes to the migration and proliferation in colon cancer cells.

Interaction between FGFR-2, STAT5, and Progesterone Receptors in Breast Cancer
Juan P. Cerliani, Tomás Guillardoyo, Sebastián Giulianiello, José P. Vaque, J. Silvio Gutkind, Silvia I. Vanzulli, Rubén Martins, Eduardo Zeitlin, Caroline A. Lamb, and Claudia Lanari

Précis: This study shows that activated nuclear FGFR-2 interact with hormone receptors and STAT5 to induce hormone related breast cancer growth.

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.
71 (10)

Cancer Res 2011;71:3435-3732.

Updated version
Access the most recent version of this article at:
http://cancerres.aacrjournals.org/content/71/10

E-mail alerts
Sign up to receive free email-alerts related to this article or journal.

Reprints and Subscriptions
To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at pubs@aacr.org.

Permissions
To request permission to re-use all or part of this article, contact the AACR Publications Department at permissions@aacr.org.