BREAKING ADVANCES

4911 Highlights from Recent Cancer Literature

CANCER RESEARCH 75TH ANNIVERSARY

COMMENTARIES

4913 Commentary on "Humanization of an Anti-VEGF Monoclonal Antibody for the Therapy of Solid Tumors and Other Disorders"
Napoleone Ferrara

4916 Commentary on "Proteasome Inhibitors: A Novel Class of Potent and Effective Antitumor Agents"
Kenneth D. Tew

REVIEW

4918 Somatic Engineering of Oncogenic Chromosomal Rearrangements: A Perspective
Danilo Maddalo and Andrea Ventura

PERSPECTIVE

4924 Challenging Roadblocks to Cancer Cure
Massimo Loda

INTEGRATED SYSTEMS AND TECHNOLOGIES

4931 Mathematical Modeling of Cancer Immunotherapy and Its Synergy with Radiotherapy
Raphael Serre, Sebastien Bengzkey, Laetitia Padovani, Christophe Meille, Nicolas Andre, Joseph Ciccolini, Fabrice Barlesi, Xavier Muracciole, and Dominique Barbolosi
Précis: This report presents a mathematical algorithm that can model the efficacy of any drug combination in silico before being implemented at bedside.

4941 A Simple PSA-Based Computational Approach Predicts the Timing of Cancer Relapse in Prostatectomized Patients
Ilaria Stura, Domenico Gabriele, and Caterina Guiot
Précis: The mathematical model presented in this report offers a tool to elaborate the follow-up of clinical data in a manner to predict prostate cancer recurrence.

4948 Integrated Classification of Prostate Cancer Reveals a Novel Luminal Subtype with Poor Outcome
Précis: A novel approach to subtyping human prostate cancer provides important diagnostic and prognostic information of potential clinical value at both early and late disease stages.

MICROENVIRONMENT AND IMMUNOLOGY

4959 BAFF and APRIL from Activin A–Treated Dendritic Cells Upregulate the Antitumor Efficacy of Dendritic Cells In Vivo
Michael R. Shurin, Yang Ma, Anton A. Keskinov, Ruijing Zhao, Anna Lokshin, Marianna Agassandian, and Galina V. Shurin
Précis: A cell fate-determining factor related to TGFβ exerts positive effects on tumor immunity and increases the antitumor potential of dendritic cell vaccines.

4970 Activation of the c-Met Pathway Mobilizes an Inflammatory Network in the Brain Microenvironment to Promote Brain Metastasis of Breast Cancer
Fei Xing, Yin Liu, Sambad Sharma, Kerui Wu, Michael D. Chan, Hui-Wen Lo, Richard L. Carpenter, Linda J. Melhem-Barlow, Xiaobo Zhou, Shadi A. Qasem, Boris Pasche, and Kounosuke Watabe
Précis: This potentially seminal study identifies c-Met as a master regulator of vascular elements in the brain metastatic niche, also identifying the available natural compound pterostilbene as a chemopreventive for brain metastasis, which can be studied immediately in the clinic.

4981 Syndecan-1 (CD138) Suppresses Apoptosis in Multiple Myeloma by Activating IGF1R Receptor: Prevention by SynstatinIGF1R Inhibits Tumor Growth
DeannaLee M. Beauvais, Oisun Jung, Yang Yang, Ralph D. Sanderson, and Alan C. Rapraeger
Précis: These results offer a preclinical proof of concept for exploration of an IGF1 receptor binding peptide as an experimental therapeutic to attack both tumor cells and the tumor vasculature in multiple myeloma.
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### MOLECULAR AND CELLULAR PATHOBIOLOGY

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### Summary

- **TMEM2** is a SOX4-regulated gene that mediates metastatic migration and invasion in breast cancer.
- Metabolic stress-induced phosphorylation of KAP1 Ser473 blocks mitochondrial fusion in breast cancer cells.
- Rebound effects caused by withdrawal of MET kinase inhibitor are quenched by a MET therapeutic antibody.
- RPL23 links oncogenic RAS signaling to p53-mediated tumor suppression.
- Activation of Wnt/β-catenin in Ewing sarcoma cells antagonizes EWS/ETS function and promotes phenotypic transition to more metastatic cell states.
- MEF2D transduces microenvironment stimuli to ZEB1 to promote epithelial–mesenchymal transition and metastasis in colorectal cancer.
- HTLV-1 viral factor HBZ induces CCR4 to promote T-cell migration and proliferation.
- Tyrosine phosphatase PTPRI/DEP-1 is an essential promoter of vascular permeability, angiogenesis, and tumor progression.
Cross-Cancer Genome-Wide Analysis of Lung, Ovary, Breast, Prostate, and Colorectal Cancer Reveals Novel Pleiotropic Associations

Gordon Fehringer, Peter Kraft, Paul D. Pharoah, on behalf of Ovarian Cancer Association Consortium (OCAC); Rosalind A. Eeles, on behalf of The PRACTICAL Consortium; Nilanjan Chatterjee, Frederick R. Schumacher, Joelleen M. Schildkraut, Sara Lindström, Paul Brennan, Heike Bickelboller, Richard S. Houhston, Maria Teresa Landi, Neil Caporaso, Angela Risch, Ali Amin Al Olama, Sonja I. Berndt, Maria Jose Sanchez, Heli Nevanlinna, Petra H. Peeters, Julian Peto, Alfons Meindl, Bertram M. Peter Lichtner, Jianjun Liu, Eiliv Lund, Enes Makalic, Mattias Johansson, Rudolf Kaaks, Muhammad G. Kibriya, Albert Hofman, John L. Hopper, Astrid Irwanto, Nichola Johnson, Per Hall, Aditi Hazra, Rebecca Hein, Stuart Feinstein, and Mary Ann Jordan

Précis: This study identifies candidate prognostic markers for periampullary tumors, which arise in the vicinity of the ampulla of Vater, an enlargement of liver and pancreas ducts where they join and enter the small intestine, a class of cancers where genetic characterization has lagged.
TUMOR AND STEM CELL BIOLOGY

5143 Rapid Reprogramming of Primary Human Astrocytes into Potent Tumor-Initiating Cells with Defined Genetic Factors
Fang Li, Xinjian Liu, John H. Sampson, Darell D. Bigner, and Chuan-Yuan Li
Précis: This study describes a method to rapidly generate tumor-initiating cells from primary human astrocytes, potentially offering an important new tool for studies of glioma biology and therapeutics development.

5151 miR-214 and miR-148b Targeting Inhibits Dissemination of Melanoma and Breast Cancer
Francesca Orso, Lorena Quirico, Federico Virga, Elisa Penna, Daniela Dettori, Daniela Cimino, Roberto Coppo, Elena Grassi, Angela Rita Elia, Davide Busa, Silvia Deaglio, Maria Felice Brizzi, Michael B. Stadler, Paolo Provero, Michele Caselle, and Daniela Taverna
Précis: These findings define an antagonistic relationship of two microRNAs in determining the dissemination of cancer cells via tumor-endothelial cell interactions, with potential implications for therapeutic intervention.

5163 αvβ6 Integrin Promotes Castrate-Resistant Prostate Cancer through JNK1-Mediated Activation of Androgen Receptor
Huimin Lu, Tao Wang, Jing Li, Carmine Fedele, Qin Liu, Jianzhong Zhang, Zhong Jiang, Dhanpat Jain, Renato V. Iozzo, Sheila M. Violette, Paul H. Weinreb, Roger J. Davis, Daniel Gioeli, Thomas J. FitzGerald, Dario C. Altieri, and Lucia R. Languino
Précis: These results describe a novel pathway that promotes castrate-resistant prostate cancer initiated by PTEN deletion, with potential implications for treatment of this advanced stage disease.

5175 GON4L Drives Cancer Growth through a YY1–Androgen Receptor–CD24 Axis
Neeraj Agarwal, Garrett M. Dancik, Andrew Goodspeed, James C. Costello, Charles Owens, Jason E. Duex, and Dan Theodorescu
Précis: This work identifies a novel oncogene that drives cancer growth via the transcription factor YY1 and the androgen receptor, offering a new platform for biomarker and therapeutic opportunities.

CORRECTION

5186 Correction: Combining miR-10b–Targeted Nanotherapy with Low-Dose Doxorubicin Elicits Durable Regressions of Metastatic Breast Cancer

ABOUT THE COVER

Neurons require transport of ATP-producing mitochondria for survival. Antiproliferative concentrations of the anticancer drugs paclitaxel and ixabepilone that bind along microtubule lengths significantly inhibited anterograde transport of fluorescently labeled mitochondria in human neuroblastoma cells, whereas the microtubule end-binding drugs eribulin and vincristine inhibited transport only at significantly higher concentrations. The electron micrographic image shows a section of a control mouse sciatic nerve in which mitochondria were transported in the absence of drug (a control). Paclitaxel, but not eribulin, inhibited transport in mouse sciatic nerves. For details, see article by Smith and colleagues on page 5115.