Contents

Cancer Research
January 15, 2012 • Volume 72 • Number 2

BREAKING ADVANCES

377 Highlights from Recent Cancer Literature

REVIEWS

379 JNK-Induced Apoptosis, Compensatory Growth, and Cancer Stem Cells
Fei Chen

387 Metastasis-Associated Protein 1/Nucleosome Remodeling and Histone Deacetylase Complex in Cancer
Da-Qiang Li, Suresh B. Pakala, Sujit S. Nair, Jeyanthi Eswaran, and Rakesh Kumar

PRIORITY REPORTS

395 Stress-Regulated Transcription Factor ATF4 Promotes Neoplastic Transformation by Suppressing Expression of the INK4a/ARF Cell Senescence Factors
Michiko Horiguchi, Satoru Koyanagi, Akinori Okamoto, Satoshi O. Suzuki, Naoya Matsunaga, and Shigehiro Ohdo

397 Increased Survival of Glioblastoma Patients Who Respond to Antiangiogenic Therapy with Elevated Blood Perfusion
A. Gregory Sorensen, Kyrre E. Emblem, Pavlina Polaskova, Dominique Jennings, Heisoo Kim, Marek Ancukiewicz, Metyun Wang, Patrick Y. Wen, Percy Ivy, Tracy T. Batchelor, and Rakesh K. Jain

CLINICAL STUDIES

408 Genetic Variants in Oxidative Stress-Related Genes Predict Chemoresistance in Primary Breast Cancer: A Prospective Observational Study and Validation
Ke-Da Yu, A-Ji Huang, Lei Fan, Wen-Feng Li, and Zhi-Ming Shao

Précis: This study offers compelling evidence that genetic polymorphisms in oxidative stress-related genes in the host affect chemosensitivity, such that host gene status must be considered to optimize personalized chemotherapy beyond variations in simply the tumor cells themselves.

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420 Interleukin-10 Ablation Promotes Tumor Development, Growth, and Metastasis
Takashi Tanikawa, Cailin Moira Wilke, Ilona Kryczek, Grace Y. Chen, John Kao, Gabriel Núñez, and Weiping Zou

Précis: This study of cancer susceptibility and progression in mice lacking IL-10 challenges the generally held view that this immune inhibitory cytokine supports cancer, instead offering powerful evidence that endogenous IL-10 actually suppresses cancer by impeding the development of 2 key cellular mechanisms of immune escape.

430 Potent Induction of Tumor Immunity by Combining Tumor Cryoablation with Anti-CTLA-4 Therapy
Rebecca Waitz, Stephen B. Solomon, Elena N. Petre, Anne E. Trumble, Marcella Fassó, Larry Norton, and James P. Allison

Précis: One use of the recently approved immune activating drug ipilimumab may be to enhance the benefits of tumor cryoablation, a simple older treatment strategy being explored anew in breast and prostate cancers, where it might be very effectively combined with immunotherapy to enhance cure rates in patients with localized tumors.

MICROENVIRONMENT AND IMMUNOLOGY

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Platelet-Derived MHC Class I Confers a Pseudonormal Phenotype to Cancer Cells That Subverts the Antitumor Reactivity of Natural Killer Immune Cells
Theresa Placke, Melanie Orgel, Martin Schaller, Gundram Jung, Hans-Georg Rammensee, Hans-Georg Kopp, and Helmut Rainer Salih

Précis: This important paper elucidates a fascinating mechanism of immune escape from NK cells in which platelets function to shield cancer cells and promote their metastatic spread.

Chromogranin A Regulates Tumor Self-Seeding and Dissemination
Eleonora Dondossola, Luca Crippa, Barbara Colombo, Elisabetta Ferrero, and Angelo Corti

Précis: Findings define a role for a circulating regulator of multidirectional trafficking of tumor cells between tumors, blood, and normal tissues, with general implications for metastasis formation and tumor progression.

Tumor Suppressive MicroRNAs miR-34a/c Control Cancer Cell Expression of ULBP2, a Stress-Induced Ligand of the Natural Killer Cell Receptor NKG2D
Anja Heinemann, Fang Zhao, Sonali Pechlivanis, Jürgen Eberle, Alexander Steinel, Sven Diederichs, Dirk Schadendorf, and Annette Paschen

Précis: The perspective that tumor suppressor functions often manifest as immune responses against tumor cells is quickly widening with broader investigations in more valid immunocompetent models of cancer.

PREVENTION AND EPIDEMIOLOGY
Circulating Insulin-Like Growth Factors and IGF-Binding Proteins in PSA-Detected Prostate Cancer: The Large Case–Control Study ProtecT
Mari-Anne Rowlands, Jeff M.P. Holly, David Gunnell, Jenny Donovan, J. Athene Lane, Freddie Hamdy, David E. Neal, Steven Oliver, George Davey Smith, and Richard M. Martin

Précis: This large UK-based case–control study suggests potentially important associations of circulating IGF-II, IGFBP-2, and IGFBP-3 in prostate cancers that are detected by the PSA test.
Regulation of Matrix Metalloproteinase Genes by E2F Transcription Factors: Rb–Raf-1 Interaction as a Novel Target for Metastatic Disease
Jackie L. Johnson, Smitha Pillai, Danielle Pernazza, Saïd M. Sebti, Nicholas J. Lawrence, and Srikumar P. Chellappan

Précis: Matrix metalloproteases regulated by the Rb–E2F pathway may serve as its major connection to invasion and metastasis control, with implications for therapeutic intervention such as through targeting the Rb–Raf-1 interaction as illustrated in this study.

Androgen Deprivation Causes Epithelial–Mesenchymal Transition in the Prostate: Implications for Androgen-Deprivation Therapy
Yuting Sun, Bu-Er Wang, Kevin G. Leong, Peng Yue, Li Li, Suchit Jhunjhunwala, Darrell Chen, Kyounghee Seo, Zora Modrusan, Wei-Qiang Gao, Jeffrey Settleman, and Leisa Johnson

Précis: Findings argue that androgen-deprivation therapy, used widely in prostate cancer treatment, can trigger epithelial–mesenchymal transition, a foreboding event that may detract from the response to other treatments.

Hyaluronan Synthase HAS2 Promotes Tumor Progression in Bone by Stimulating the Interaction of Breast Cancer Stem–Like Cells with Macrophages and Stromal Cells

Précis: Findings define a mechanism used by cancer stem cells to produce an extracellular matrix glycosaminoglycan that may help seed a metastatic niche in foreign organ microenvironments, with major implications for antimetastatic therapy.

Correction: CD8⁺ T Cells Regulate Bone Tumor Burden Independent of Osteoclast Resorption
Epithelial–mesenchymal transition (EMT) is a key developmental process and has also been implicated in cancer metastasis and therapeutic resistance. The factors contributing to EMT in human cancers remain unclear. Sun and colleagues show that androgen deprivation can promote EMT in normal mouse prostate as well as in human prostate cancer, revealing a potentially important consequence of a standard of care treatment for prostate malignancies. This image corresponds to an immunofluorescence staining of E-cadherin (epithelial marker) and vimentin (mesenchymal marker) in postcastration (androgen-deprived) mouse prostate tissue. Cells that express both markers are likely to be undergoing EMT. Red, Vimentin; green, E-cadherin; blue, DAPI. For details, see the article by Sun and colleagues on page 527 of this issue.
72 (2)


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