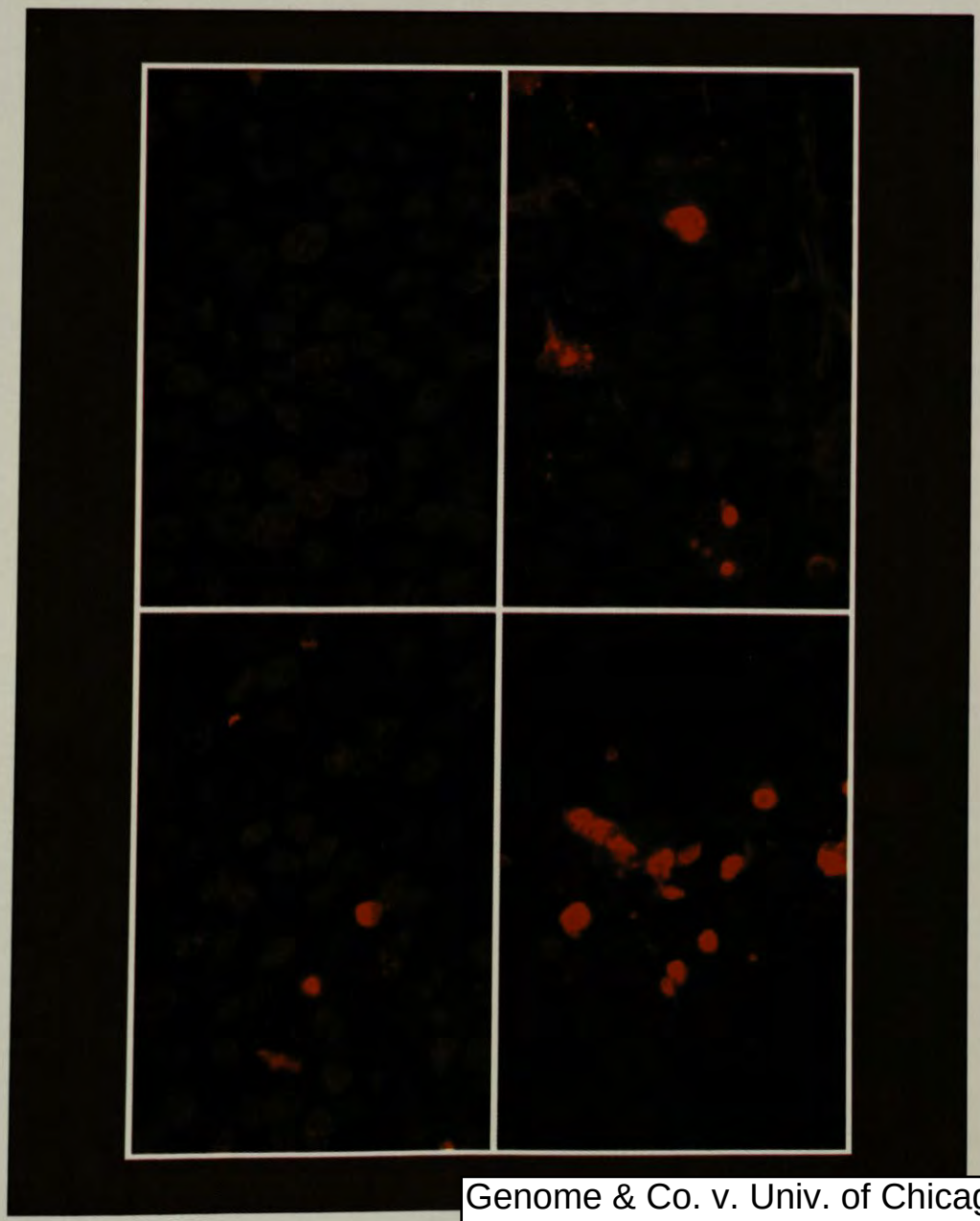
www.aacrjournals.org

AACR American Association for Cancer Research

May 15, 2008
Volume 14
Number 10
Pages 2895–3236

Clinical Cancer Research



Clinical Cancer Research

The Journal of Clinical and Translational Research

Clinical Cancer Research

The Journal of Clinical and Translational Research

Publishing Information

Clinical Cancer Research (ISSN 1078-0432) is published twice monthly, one volume per year, by the American Association for Cancer Research, Inc., 615 Chestnut Street, 17th Floor, Philadelphia, PA 19106-4404. Periodicals postage paid at Philadelphia, PA, and additional mailing offices. POSTMASTER: Send address changes to AACR Member Services department, 615 Chestnut Street, 17th Floor, Philadelphia, PA 19106-4404.

Submission of Manuscripts

Clinical Cancer Research publishes original articles describing clinical research on the cellular and molecular characterization, prevention, diagnosis, and therapy of human cancer. Its focus is on innovative clinical research and translational research that bridges the laboratory and the clinic. *Clinical Cancer Research* is especially interested in clinical trials evaluating new treatments for cancer; research on molecular abnormalities that predict incidence, response to therapy, and outcome; and laboratory studies of new drugs and biological agents that will lead to clinical trials in patients.

Online submission of new manuscripts is available at http://ccr.msubmit.net. Please refer to the Information for Authors link at http://clincancerres.aacrjournals.org before submitting a manuscript.

Subscription Information

Institutions and nonmember individuals, contact the AACR Subscription office. *For the US, Canada and Mexico*, AACR Subscription office, Turpin Distribution, 'The Bleachery', 143 West Street, New Milford, CT 06776; Phone: (860) 350-0041; Fax: (860) 350-0039; E-mail: turpinNA@turpin-distribution.com. *For other countries*, AACR Subscription Office, Turpin Distribution, Pegasus Drive, Stratton Business Park, Biggleswade, Belfordshire SGI8 8TQ, UK. Phone: (44) 1767-601-640; E-mail: custserv@turpin-distribution.com

Subscriptions to *Clinical Cancer Research* are available for $110 annually for members and $290 for individual nonmembers. Print subscription includes online access. Online-only access is available for $75 annually for members. *Clinical Cancer Research* is only available to institutions as a combined subscription with *Cancer Research*. The combined 2008 institutional subscription price of $1940 includes $725 for a subscription to *Clinical Cancer Research*. The standard institutional subscription allows access to authorized users at computers located in the subscribing library. For networked or remote institutional access, a site license is required. For institutional site license queries e-mail sitelicense@aacr.org. Claims for missing issues made within 90 days of the issue date will be honored while supplies last. Institutions and nonmember individuals, contact AACR Subscription office at the aforementioned address. AACR members should contact the AACR Member Services department at membership@aacr.org.

Single issue copies and copies of back stock of the journal may be ordered from AACR Subscription office at the aforementioned address as long as supplies permit. Prices are available on request. Orders outside the U.S. add $3.00/copy to offset postage costs.

Advertisements

Advertisement insertion orders and copy must be received one month prior to the date of issue in which the advertisement is to be published. The journal is mailed on approximately the 1st and 15th days of the month of issue. Inquiries about advertising should be directed to M. J. Mrvica Associates, Inc., 2 West Taunton Ave., Berlin, NJ 08009; Phone: (856) 768-9360; Fax: (856) 753-0064.

Copyright and Permissions

As a not-for-profit organization incorporated in the United States, AACR adheres to U.S. copyright law (PL 94-553), which became effective January 1, 1978. The law stipulates that copyright for works is vested in the author from the moment of creation and remains the property of the author until legally transferred. Authors who wish to publish articles and other material in AACR journals must formally transfer copyright to AACR. The copyright transfer form must be signed by all authors before AACR can proceed with publication. Appropriate forms for transfer of copyright will be requested from all authors after a manuscript has been deemed potentially acceptable.

Authors—complete the form available online at www.aacrsmartsubmit.org. The journal will not publish a paper unless the form is properly filled out and signed by all authors. Since the federal government does not recognize private copyright for work performed by its employees as part of their official duties, the journal will accept papers from government laboratories without copyright transfer, provided that the authors abide by the same provisions required of other authors and sign the appropriate section of our copyright transfer form.

To read the complete version of AACR's Copyright and Permissions Policy, please visit http://www.aacr.org/home/scientists/publications-of-the-aacr/copyright-and-permissions-policy.aspx. This policy includes further information on authors' rights of usage, permission requests from third parties, free access to AACR journals, funding agency requirements, and the National Institutes of Health Public Access Policy.

Clinical Cancer Research is abstracted and/or indexed in *Chemical Abstracts, Current Contents/Clinical Medicine, and Index Medicus/MEDLINE.*

Clinical Cancer Research

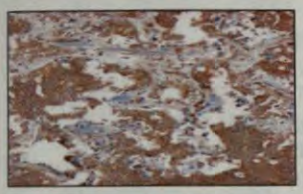
Highlights

Selected Articles from This Issue

May 15, 2008

Clinical Activity of GM-CSF and Thalidomide in Prostrate Cancer

Garcia *et al.* _____ Page 3052



Granulocyte macrophage colony-stimulating factor (GM-CSF) and the immunomodulatory agent thalidomide have clinical activity in advanced prostate cancer. To determine the biological and clinical effects of this combination before to radical prostatectomy, Garcia and coworkers conducted a phase II study. They found that the combination was safe and did not impact on the perioperative morbidity of radical prostatectomy. Although pathologic responses were not observed, most patients achieved a reduction in prostate-specific antigen. Further, they found that the administration of GM-CSF and thalidomide induces the infiltration of dendritic cells and T cells into tumor tissue, showing that the clinical activity of GM-CSF and thalidomide in prostate cancer is immune mediated.

RRM1 Polymorphisms Predict Gemcitabine Response

Kim *et al.* _____ Page 3083

Gemcitabine-treated patients with high tumoral expression of ribonucleotide reductase M1 (RRM1) generally have poor prognosis, due to a decreased efficacy of gemcitabine therapy. Two polymorphisms in the promoter sequence of *RRM1* have been previously shown to regulate *RRM1* expression. Here, Kim and colleagues investigated whether these polymorphisms are correlated with the efficacy of gemcitabine-based chemotherapy in lung cancer patients. They detected significant differences in response rates to gemcitabine according to the allelotypes of the *RRM1* promoter sequence. These polymorphisms, which can be determined using germline DNA, may be useful as predictive markers of gemcitabine-based therapy.

Managing Hypertension Induced by VEGF Signaling Inhibitors

Curwen *et al.* _____ Page 3124

Hypertension is frequently encountered when inhibitors of vascular endothelial growth factor (VEGF) signaling are administered to cancer patients. Here, Curwen and colleagues report on a preclinical examination of hypertension induced by a VEGF signaling inhibitor, cediranib, in rats. They found that moderate blood pressure increases induced by cediranib were managed by coadministration of an angiotensin-converting enzyme inhibitor. A calcium antagonist was required, however, to reverse more severe hypertensive responses. Importantly, coadministration of the calcium antagonist did not affect the antitumor activity of cediranib. These data indicate that hypertension is a consequence of inhibiting physiologic VEGF signaling and show that it can be controlled with appropriately selected antihypertensive medication.

Interaction of Imatinib with Human Organic Ion Carriers

Hu *et al.* _____ Page 3141

The activity of imatinib in leukemia has recently been linked to the organic cation transporter 1 (OCT1) gene *SLC22A1*. To further understand mechanisms involved in the drug's cellular entry, Hu and colleagues characterized the interaction of imatinib with 15 transporters in amphibian and mammalian models. They found that imatinib could be transported by various ABC transporters and by OATP1A2, but not by OCT1. An expression microarray, however, showed that *SLC22A1* provides a composite surrogate for the expression of multiple transporters relevant to imatinib. Given that it is highly expressed in the intestine, gliomas, and leukemia cells, these findings suggest that OATP1A2 may play a key role in imatinib pharmacokinetics and pharmacodynamics.

Clinical Cancer Research

Contents

May 15, 2008
Vol 14, No 10

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.