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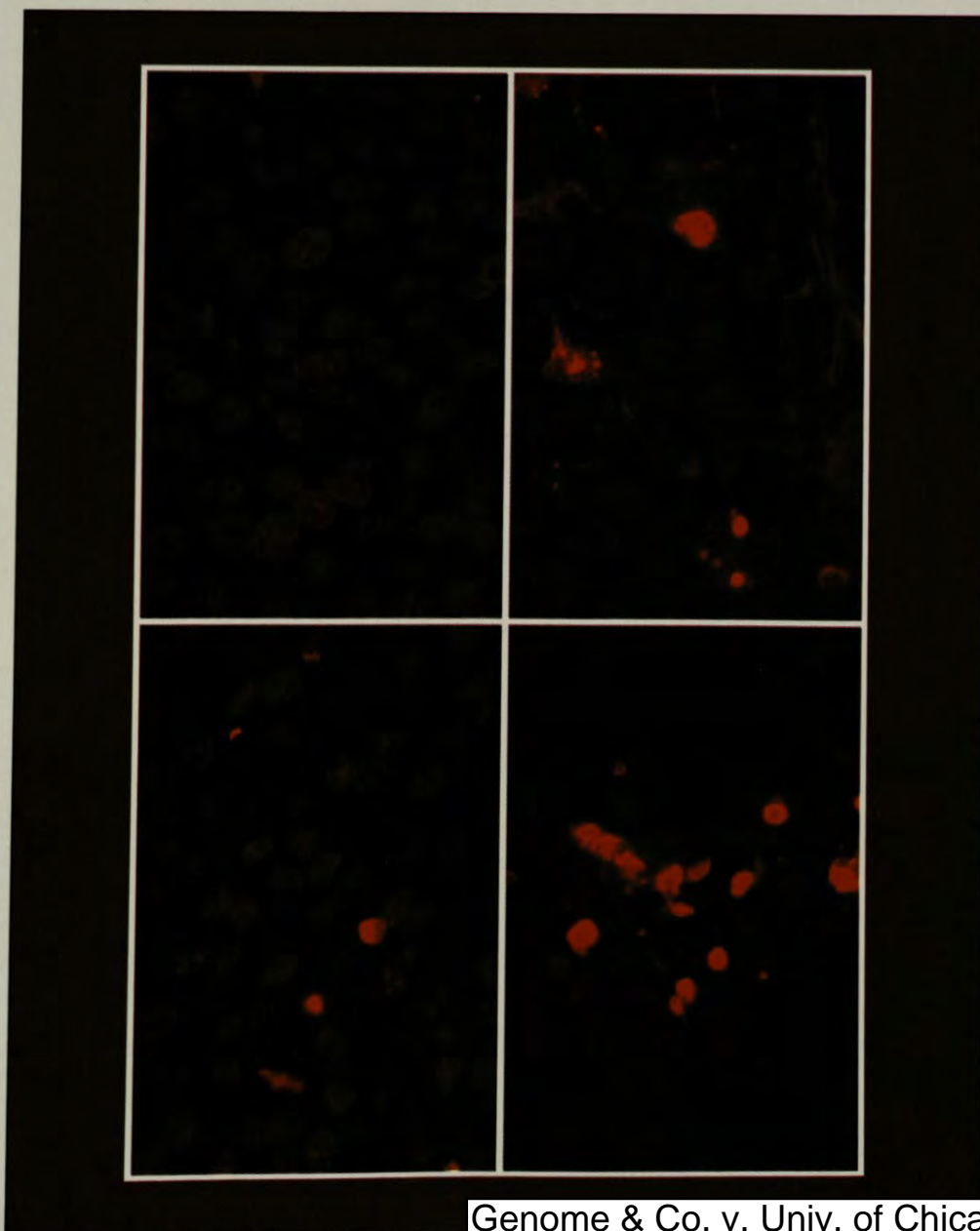
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Clinical Cancer Research

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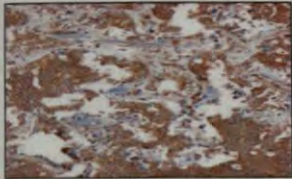
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Clinical Activity of GM-CSF and Thalidomide in Prostate Cancer

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.

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