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## From the editor

Since the success of the bcr-abl inhibitor imatinib in treating chronic myelogenous leukemia, it has been suggested that the era of cytotoxic agents is coming to a close, superceded by the era of targeted therapies. Indeed, it has long been the dream of medical oncologists that a single “magic bullet” could be found that would reverse the malignant phenotype precisely because it interfered with the underlying molecular mechanism of oncogenesis. Furthermore, targeted agents are touted as being less toxic than conventional chemotherapy.

This issue of *CCR Focus* strives to show that cytotoxic agents cannot be counted out in the war against cancer. Although the notion of individualized cancer therapy is attractive, we are still left with a projection that more than half a million Americans will die of cancer in 2008. This issue of *CCR Focus* brings together six articles underscoring the development of new cytotoxic agents in clinical oncology. With an outstanding overview by guest editor Beverly Teicher that familiarizes us with the mechanisms of action, the articles collectively argue that cytotoxics are still very much a vital part of drug development. Lee and Swain discuss a new class of microtubule stabilizing agents, the epothilones. Bennouna and colleagues introduce the *Clinical Cancer Research* audience to vinflunine, a new vinca alkaloid that may surpass vinorelbine in efficacy and safety. Choy and colleagues provides us with the development status of satraplatin, an oral platinum agent. Gautschi and coworkers show how agents inhibiting aurora kinase may be considered both cytotoxic and targeted therapy. Finally, Orlowski and Kuhn bring new light to the mechanisms underlying the activity of proteasome inhibitors such as bortezomib.

Indeed, given that the molecular target is known for all of the agents discussed in this issue of *CCR Focus*, we can now consider a new paradigm: Inhibiting a target will result in cytotoxicity if the drug’s target is critical to maintaining the malignant phenotype. These examples show that there is no clear distinction between a cytotoxic agent and a targeted therapy. Thus, epidermal growth factor receptor is a cytotoxic target if mutated or overexpressed and critical to sustaining cancer cell growth, but not when its expression is incidental to the cancer cell.

In the past, we identified anticancer agents because they killed cancer cells. Consequently, the original cytotoxic target was DNA and cell division was critical for efficacy. Today we attempt to find critical targets through molecular studies. This has resulted in more specific drugs and at times more dissappointment. But the new paradigm will better inform our search. Good anticancer agents will be those that inhibit critical targets. In this issue of *CCR Focus*, we hope to inform those interested but not expert in cancer drug development and to encourage those already working in the field.

Susan E. Bates, M.D.  
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*CCR Focus*

# Clinical Cancer Research

## From the Editor

Susan E. Bates

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