

Editorial

It was with great pleasure that I agreed to be guest editor for this special issue of *Current Cancer Drug Targets*. The MDM2 oncogene is important for cancer initiation, progression and response to therapy, and new information about MDM2 is being uncovered every month. Since its discovery over thirteen years ago, MDM2 has become a widely-researched molecule, generating thousands of papers about its role in various stages of cancer. Although the p53-dependent pathways have been extensively investigated for many years, new information about the effects of this interaction continues to be revealed. More recently, the p53-independent activity of MDM2 has increasingly attracted more researchers. Because of the sheer amount of research detailing both the p53-dependent and -independent pathways, new reviews about MDM2 are both timely and important. I trust that you will find the reviews in this issue of *Current Cancer Drug Targets* to be as informative and thought provoking as I did. The topics addressed span the range of MDM2 research, from the historical perspective to the latest discoveries about splice variations, therapeutic targeting, and proteins interacting with MDM2.

Bond, Hu and Levine illustrate in great detail what has been discovered about the p53-dependent effects of MDM2, and the p53/MDM2 relationship. Although the existence of the auto-regulatory loop between MDM2 and p53 has been known for many years, new proteins depending on the interaction are still being discovered, and the complex relationship between p53 and MDM2 is finally becoming clear. Their review is an excellent introduction to the MDM2 field, from the viewpoint of the protein's earliest known function. On the other hand, the review by Zhang and Zhang discusses the many and diverse newly discovered p53-independent interactions of MDM2. These include a variety of proteins involved in signal transduction guiding the cell cycle and apoptosis, as well as other cellular processes. This article is sure to spark the interest of many readers, because MDM2 interacts with so many different proteins and is involved in nearly every important cellular pathway.

The review by Harris encompasses the most up-to-date information on the alternative splicing of MDM2. Not only does MDM2 interact with a large number of proteins, there also exist splice variants of the protein, which may have other interactions, or different effects on the same proteins. The article by Rayburn, Zhang, He and Wang addresses the clinical relevance of MDM2 expression. Even before it was known that MDM2 had any effects on proteins other than p53, MDM2 was known to be an indicator for worse prognosis in cancer patients. This review describes the effects of MDM2 expression in various human cancers, and addresses the role of MDM2 in various stages of cancer development and progression, as well as therapeutic intervention.

In this issue, three additional articles provide a comprehensive review on intervention approaches to inhibiting MDM2 functions. The review by Zhang, Wang and Agrawal provides a historic perspective and brief summary on antisense approaches

