Critical Reviews™ in Oncogenesis, 16(3-4), 141-142 (2011)

Preface: Special Issue on Yin Yang 1 and Oncogenesis

This special issue on Yin Yang (YY) 1 and Oncogenesis is of particular interest and relevance to the field of cancer, and it addresses the potential role of YY1 as an oncogene. Interestingly, since its discovery in 1991, more than a thousand published reports have described the pleiotropic activities and functions of YY1 in both normal and cancerous tissues. YY1 has been implicated in cell development and growth, differentiation, apoptosis, resistance to cytotoxic stimuli, and tumor metastasis and as a cancer prognostic and/or diagnostic biomarker. Ample evidence indicates the role of YY1 in cancer, with a few exceptions, and suggests its potential oncogenic role; however, the direct demonstration of YY1 as a de facto oncogene has not been documented as yet. This special issue by experienced contributors in the YY1 field provides an up-to-date overview of the many activities and functions of YY1 in cancer models at both the biochemical and molecular levels.

The role of YY1 as an oncogene has been addressed by many contributors. Dr. Atchison and his colleagues present an extensive overview and an up-to-date analysis of the current status of the YY1 field and emphasize the significant advances that have been made in deciphering the molecular mechanisms underlying YY1 activities and functions in cancer. They propose that YY1 may function as an oncogene indirectly via its multitude of biochemical and molecular effects. In an extensive complementary review, Zhang et al address the multiple roles that YY1 exerts through its DNA binding activity and recruitment of associated proteins, all of which participate in the complex mechanism of action mediated by YY1. These authors also discuss the controversy regarding the role of YY1 in some cancers, though they support the notion that YY1 may be considered as an oncogene. The reviews by Atchison et al and Zhang et al ought to be considered as key references for those involved in the YY1 field and those who are being introduced to this field, and they both present extensive lists of relevant publication references.

Drs. Thiaville and Kim discuss clearly how YY1 controls a large fraction of imprinted genes in mammals and that the exact expression levels of imprinted genes are critical for the survival of an organism. Thus, that there is no regulation of these imprinted genes plays an important role in the pathogenesis of many diseases including cancer. Drs. Bonavida and Baritaki describe the potential novel role of YY1 in the initiation and development of cancer metastasis. They provide evidence that YY1 participates in the epithelial to mesenchymal transition (EMT) in the metastatic cascade. Their review describes how YY1 is an intricate factor in the regulation of EMT via the dysregulated nuclear factor κB/Snail/YY1/Raf-kinase inhibitor protein/phosphatase and tensin homologue circuit that has been shown to regulate both EMT and drug resistance, and they suggest the potential role of YY1 as a target for therapeutic interventions. Zhu et al discuss how YY1 can function as a redox sensor and explain the molecular structure and conformational changes in YY1 that are induced by the cellular redox status. They also explore the therapeutic potential of targeting YY1 in cancer. Noteworthy is Dr. Klar's discussion of the less-known and less-studied YY1 homologue, YY2. He reviews the literature about YY2 and how YY2 shares many of the known activities of YY1 while also having its own unique features. Dr. Klar warns about the cross-reactivity observed among many commercially available antibodies directed against YY1 that also are cross-reactive with YY2. Thus, it is clear that several reported studies about YY1 have not considered the involvement of YY2 in their analyses, which can be a problem in the interpretations of the findings. Dr. Klar recommends paying attention to the interrelationship between YY1 and YY2. Nicholson et al review the literature about the current status of YY1 in various cancers and its prognostic significance. They discuss the controversies that have been reported regarding the association of YY1 with the progression of cancer. Clearly, because of the complex mechanisms of reaction of YY1 in any tumor tissue or histological type of cancer, one might expect to observe contradic-

0893-9675/11/$35.00

tory results; thus one needs to pay attention to the particular models used and their clinical validation for any conclusion. Dr. Bonavida and colleagues present new unpublished data on the expression of YY1 in various hematologic malignancies and YY1's potential role in pathogenesis, prognosis, and therapy. The studies presented deal with the expression of YY1 on representative hematologic malignancies including B non-Hodgkin lymphoma, AIDS-related lymphoma, multiple melanoma, and children's chronic lymphocytic leukemia.

Overall, the various contributions about YY1 in this volume reflect a global overview of the current status of YY1 as well as several projections made for future studies. The direct demonstration that YY1 is an oncogene must be determined unequivocally. Furthermore, the potential of targeting YY1 in the treatment of resistant/metastatic cancer is worth pursuing and validation is needed in preclinical animal models bearing tumor xenografts.

I wish to acknowledge the excellent reports by the various contributors of this volume. I also acknowledge the assistance of Daphne Liang, Melissa Cao, and Diana Hardy for their efforts in the preparation of this volume for publication.

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