Reviewer’s report

**Title:** Small Interfering RNA Targeting Mcl-1 Enhances Proteasome Inhibitor-Induced Apoptosis in Solid Malignant Tumors

**Version:** 1  **Date:** 31 August 2011

**Reviewer:** Shehla SP Pervin

**Reviewer’s report:**

The authors convincingly demonstrate that the levels of Mcl-1 remains up regulated and stabilized in a number of human cancer cell lines treated with a number of proteosome inhibitors like Bortezomib, MG 132 and ALLN. They also show that down regulation of Mcl-1 along with proteosome inhibitors enhances anticancer effect. The work is extensive, well done and has important clinical implications. I have a few minor concerns: 1) The authors have extensively used human colon cancer cell lines, one lung and an ovarian cancer cell line. It will be good to use one or two breast cancer cell lines also, because most of them are resistant to proteosome inhibitors and knowing the status of Mcl-1 in these cells will advance the field. 2) A reference for the concentrations of CHX used should be included in the text. 3) Difference between relative cell viability between control siRNA+MG132 and Mcl-1siRNA+MG132 is small. Cell viability with only MG132 should be added. The authors should comment on this in the discussion. 4) In fig 6A, showing increased Annexin V levels, which is an early indicator of early membrane flippling, does not suggest the cells undergo apoptosis. The western blots in fig 6C show small amount of cleaved caspase-9 and 3. To convincingly show that apoptosis is induced in MG132+ Mcl-1 siRNA cells, caspase-3 assay using fluorometric substrate should be done. 5) In fig 3B, where relative levels of Mcl-1 fall with DMSO, CHX should be added. 6) A few blots reprobed with other anti apoptotic proteins should also be included.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

NO TO ALL