

## Author Point-to-Point Reply Letter to Reviewers

**Manuscript Title:** Novel Mechanism of drug resistance to proteasome inhibitors in multiple myeloma

**Manuscript Number:** WJSC 47564

We are very grateful to the editors and four outstanding reviewers for their thoughtful and enthusiastic review of our manuscript. We have rewritten some sentences and made editorial changes accordingly.

### Reviewer reports:

**Reviewer #1:** The m/s can be accepted for publication, after corrections of some grammar/typo errors, i.e., line 113: delete left parenthesis; line 163: delete comma.

**A:** We have checked the grammar and spelling through the manuscript. The corrections have been made accordingly.

**Reviewer #2:** I suggest inserting a table with all subgroups of Multiple Myeloma, based on their molecular and cytogenetic abnormalities with the different degree of resistance, and for each resistance pattern the actual therapeutic approach, rating the Level-of-Evidence (with references), and the potential therapeutic approaches, rating the Level-of-Evidence (with references).

**A:** According to the reviewer's suggestion, we have configured a new Table 1 to summarize the major molecular and cytogenetic abnormalities of multiple myeloma and their associated prognosis (Page 4). Corresponding references are cited. In general, subtypes with poor prognosis indicate high degree of drug resistance. However, the definite correlation between these subtype and resistance pattern has not been well studied in the literature.

**Reviewer #3:** The invited editorial is current and relevant. 1. Generic names such as melphalan, cyclophosphamide, doxorubicin etc should be rendered in lower case (p. 5 line 4) 2...unlike (p. 8 line 3) should be rendered 'unlikely'.

**A:** We have revised these words as suggested by the reviewer.