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# PEER-REVIEW REPORT

**Name of journal:** World Journal of Clinical Oncology

**Manuscript NO:** 59442

**Title:** Tumor-Specific Lytic Path 'Hyperploid Progression-Mediated Death': Resolving Side Effects Through Targeting RB/p53-mutant

**Reviewer's code:** 03245122
**Position:** Editorial Board
**Academic degree:** MD
**Professional title:** Professor
**Reviewer's Country/Territory:** China
**Author's Country/Territory:** United States
**Manuscript submission date:** 2020-09-11
**Reviewer chosen by:** Ya-Juan Ma
**Reviewer accepted review:** 2020-09-16 07:08
**Reviewer performed review:** 2020-09-19 12:27
**Review time:** 3 Days and 5 Hours

| | |
|---|---|
| **Scientific quality** | [ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good<br>[ ] Grade D: Fair [ ] Grade E: Do not publish |
| **Language quality** | [ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing<br>[ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection |
| **Conclusion** | [ ] Accept (High priority) [ ] Accept (General priority)<br>[ ] Minor revision [Y] Major revision [ ] Rejection |
| **Re-review** | [Y] Yes [ ] No |
| **Peer-reviewer statements** | Peer-Review: [Y] Anonymous [ ] Onymous<br>Conflicts-of-Interest: [ ] Yes [Y] No |

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**SPECIFIC COMMENTS TO AUTHORS**

This manuscript describes that clarification of Tumor-Specific Lytic Path might cast light on resolving the side effects of cytotoxic drugs of cancer therapy by targeting RB/p53-mutant. Firstly, the authors summarized the current status of chemoprevention and chemotherapy for various of cancers including colon cancer, lung cancer, breast cancer and head/neck cancer, introducing the mainline drugs used nowadays. Then the unresolved issue of side effect for the related drugs was discussed, including the chemoprevention and chemotherapy drugs. These issues limited the dose escalation and prolongation during treatment, impeding the cure of cancer. After that, the authors pointed out that the anti-tumor mechanism of cytotoxic drugs may be different from the mechanism underlying their side effects. Taking Taxol as an example, the authors explained how the lytic path would provide a mechanistic framework for developing cytotoxic drugs devoid of side effects by conferring tumor specificity at the genetic level. The topic is very interesting. The manuscript well-written and clearly described. But some points of view in the article need to be further supported by more discussion with relevant published evidence and/or other data to make the review more integrated and substantial. Specific Comments 1. Considering the authors pointed out that side effect was one of the most important obstacle against cytotoxic drug application in cancer cure, more reference need to be reviewed in section 5 of this manuscript. about the current research on developing cytotoxic drugs based on RB or p53 genetic mutants to avoid side effects. 2.The author considered the TSLP 'hyperploid progression mediated death (HPMD)' as tumor specific pathway and took Taxol induced chromosomal aneuploidy as an example. Recently, depletion of microtubule-associated protein ATIP3 (AT2 receptor-interacting protein 3) was approved to induce aneuploidy and sensitizes breast cancer cells to taxanes. As always,

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combination therapy plays important role in reducing side effect and improve therapy efficacy, therefore this part should be included in the manuscript to make the discussion stronger. 3. The references cited in this manuscript are rather old. I understand that the author integrated some of his own works in this manuscript , and of course they are really important and great work, however, as a review, more updated information need to be included.