

Article information: <http://dx.doi.org/10.21037/tau-20-1339>

Review Comment

This article provides a reasonable overview of the clinical aspects of epigenetics in prostate cancer therapy. There are a few issues that need attention.

Comment 1: Sometimes the text becomes very colloquial and seems to be aimed at medical student level with poor grammar eg “epigenetics is way that cells can modify their gene programs without altering the genetic code itself”. Similar examples are throughout the text in particular in the first few pages.

RESPONSE: Thank you for pointing this out. We have revised the manuscript throughout and checked grammar.

Comment 2: there are some inaccuracies on the clinical components on page 2 eg (1) decipher, oncotype, etc are all genomic based not protein. (2) the term “relapse after local therapy” is too vague – minor PSA relapse would not be treated with docetaxel.

RESPONSE: We have reviewed and consolidated the clinical section, removing this part.

Comment 3: The article would benefit from subheadings eg under the “role of epigenetics in localized/advanced prostate cancer” there could be subheadings describing each type of modification.

RESPONSE: We agree and have inserted subheadings describing different types of epigenetic modifications in the manuscript.

Comment 4: the section on the role of epigenetics in localised disease seems to swing from pre-clinical to clinical applications erratically – the text should proceed sequentially from theory, to pre-clinical to clinical.

RESPONSE: Thank you- we have re-ordered this section as suggested.

Comment 5: Pg 5 – the authors state that AR activity is related to HDAC dysregulation but then don't elaborate.

RESPONSE: We elaborated on the interaction between AR activity and HDACs (page 5, lines 157-163).

Comment 6: Pg 5 – KDM4C is not explained/ clarified.

RESPONSE: We added more on the role of the lysine-specific demethylase KDM4C (page 6, lines 167-176).

Comment 7: Pg 5 – “reprogrammed to hijack regulatory elements implicated in prostate gland development” – this needs to be explained to the reader.

RESPONSE: We reworded this and elaborated in the revised manuscript (page 6, lines 186-189)

Comment 8: Pg 10 – “with low AR activity had longer rPFS then those who without”- something is very unclear here...

RESPONSE: We clarified this sentence in the manuscript (page 13, lines 421-423).

Comment 9: pg 11 – “a lethal cancer network” - jargon, please replace with scientific wording.

RESPONSE: We removed this.

Comment 10: The authors should mention BRD4 in disease pathogenesis and therapeutics.

RESPONSE: We added the role of BRD4 (page 9, lines 284-295).

Comment 11: Overall the authors need to concentrate to focus on text relevant to the title of the paper “Clinical Implications” – this suggests that the focus should be on prognostic epigenetic biomarkers, predictive epigenetic biomarkers or clinical tractable targets and the results of trials not on a superficial overview of the entire field.

RESPONSE: Thank you. We revised the manuscript throughout to be more succinct.