

## ESPS PEER REVIEW REPORT

**Name of journal:** World Journal of Stem Cells

**ESPS manuscript NO:** 13720

**Title:** Histone Modifications: Targeting Head and Neck Cancer Stem Cells

**Reviewer code:** 01236209

**Science editor:** Yue-Li Tian

**Date sent for review:** 2014-08-29 17:00

**Date reviewed:** 2014-09-01 18:06

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

This manuscript reviewed the recent progress in epigenetic regulation in HNSCC and CSC. The authors first introduced the background of HNSCC and CSC. And then the authors summarized the epigenetic regulations, including DNA methylation, histone acetylation and methylation, in HNSCC. Last, the authors described pharmacological inhibitors for epigenetic regulators, such as NFκB, HDAC and HAT, and their therapeutic application in HNSCC. The manuscript summarized a large amount of literatures. However, it seems to me the information is not well organized, especially the section of "2.0 - Epigenetics of head and neck cancer and its stem cells". I would suggest that this section can be reorganized into three part: basic concept of epigenetic regulation, epigenetic regulation in HNSCC, and targeting epigenetics for HNSCC treatment. And the last part can be combined with the section of "3.0 - Tumor histone modifications: Evidence for an epigenetic mechanism responsible for acquired tumor resistance to therapy". Minor comments: 1. The authors used "methylation" in the manuscript referring to "DNA methylation". For example, in the abstract, "In this review, we present and discuss current knowledge on epigenetic modifications of HNSCC and CSC response to methylation and histone modifications", and the subtitle "2.1 - Methylation in HNSCC". However, they also discussed histone methylation. Therefore, please specify "DNA methylation", instead of using the word "methylation". 2. Page 6, the authors wrote: "2) the subpopulation of tumor cells generate both cancer cells and normal cells". Is it correct? 3. Page 9, the definition of CpG islands ("With the exception of the normally methylated CpG dinucleotides in

the genome, there are CpG-rich islands (approximately 1 kilobase in length) that precede demethylated gene promoters in normal cells") is incorrect. CpG islands exist in the genomic DNA in both cancer and normal cells, and they are not necessary to be upstream of demethylated gene promoters. 4. Page 9, "p16, a cell cycle controller encoded by the CDKN2A gene, which plays a critical role in inducing cellular senescence in tumor cells and is downregulated via hypermethylation by histone deacetylases". Histone deacetylases cannot catalyze DNA methylation. Please revise the sentence. Similarly, Page 14, "we found that endothelial cell-secreted factors, but not fibroblast cell-secreted factors, are able to dynamically acetylate histones in tumor cells". Neither endothelial cell-secreted factors nor fibroblast cell-secreted factors can acetylate histones. 5. Page 10, line 3, there is a tyop "RASf1A". 6. Page 11, "Histone acetylation results in chromatin decondensation, promotion of transcription, and inhibition of DNA methylation, and it is often correlated with formation of heterochromatin." Should it be euchromatin, instead of heterochromatin? 7. Page 13, "we must consider analyzing both global DNA and histone methylation patterns of expression concurrently in the progression of cancer." Use "global DNA and histone methylation levels", instead of "global DNA and histone methylation patterns of expression".

## ESPS PEER REVIEW REPORT

**Name of journal:** World Journal of Stem Cells

**ESPS manuscript NO:** 13720

**Title:** Histone Modifications: Targeting Head and Neck Cancer Stem Cells

**Reviewer code:** 00504335

**Science editor:** Yue-Li Tian

**Date sent for review:** 2014-08-29 17:00

**Date reviewed:** 2014-09-02 18:28

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Existing	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

## COMMENTS TO AUTHORS

It is well written manuscript. However, there is too many various abbreviations and it is difficult to search back for them. Maybe, a list of abbrevoation at the begining of the manuscript should be useful.