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PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells
Manuscript NO: 33302
Title: Next-generation sequencing traces human induced pluripotent stem cell lines clonally generated from heterogeneous cancer tissue
Reviewer's code: 02546300
Reviewer's country: Iran
Science editor: Fang-Fang Ji
Date sent for review: 2017-02-07
Date reviewed: 2017-02-19

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[Y] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[Y] Minor revision
[ ] Grade E: Poor		[Y] No	[ ] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

The manuscript is well written and easy to follow. But the aim of the study is not clearly indicated in the title and also in the manuscript. It is not known exactly for what purpose the cell lines were used for NGS. If the aim of authors was to characterize the obtained cell lines, then the authors had to first do karyotype analysis to establish a karyogram of the cell lines, then doing molecular analysis. If they were about to find new or relevant mutations to colon cancer, it is nonsense because they had to firstly prove that the cell lines are in fact cancer cell lines. Other important concern is even if the cell lines are established and proved, functional analysis should be done to prove the involvement of mutations in pathogenesis of cancer. NGS might reveals many mutations which have nothing to do with the disease.

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PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells
Manuscript NO: 33302
Title: Next-generation sequencing traces human induced pluripotent stem cell lines clonally generated from heterogeneous cancer tissue
Reviewer's code: 02446041
Reviewer's country: United States
Science editor: Fang-Fang Ji
Date sent for review: 2017-02-07
Date reviewed: 2017-02-28

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[Y] Grade A: Excellent	[Y] Grade A: Priority publishing	Google Search:	[Y] Accept
[ ] Grade B: Very good	[ ] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[ ] Minor revision
[ ] Grade E: Poor		[Y] No	[ ] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

Comment: The author produced Colon cancer tissue-derived iPSCs by retroviral gene transfer (OCT3/4 OCT3/4 , SOX2SOX2 , and KLF4 and characterized 10 iPSCs lines with NGS. It's of great interest to compare both at the genome level. Specific comment: Page 5: "Primary cells from cancer tissue were cultured for one day at approximately 5%–10% confluency and then incubated with the pantropic retrovirus vector solution (OCT3/4, KLF4, and SOX2) at 37 °C for further one day." What does it mean to have "Primary cells?" What's the nature of such Primary cells? Given the heterogeneity of tumor, Primary cells might be normal stroma cells, not cancer cells. "Thirteen non-synonymous SNVs were compared among the genotypes of the ten iPSC lines and both the tissues. A missense mutation in EIF2AK2, TTN, ULK4, MCC, FLT4, STK19, STK31, TRRAP, WNK1, PLK1orPIK3R5 of the respective iPSC lines was not identical to the genotypes of both the tissues. However, the genomes of all iPSC lines did not have mutations in ERBB2and MKNK2 that were the genotypes of the cancer tissues,

suggesting the preference of their starting cells without such mutations." These are not written with Standard English. Please re-write. E.g., what's "both tissues"? How could you "suggesting the preference of their starting cells without such mutations?" "It was expected that the genomes of the non-cancer tissues had genotypes identical to that of their germline whereas the genomes of the cancer tissues had somatic mutation. In detail, as the cancer tissues would consist of heterogeneous cell populations, their genomes must be heterogeneous genotypes. Meanwhile, it was also expected that the genome sequences of the respective iPSC linesplay a role as the tracer of their starting single cells from the cancer tissues. It was likely that the genomic mutations of each iPSC line originated from those of each single cell present within thecancer tissues." "Ten iPSC lines were clonally generated from primary cells of cancer tissues, and were subjected to next-generation sequencing. Genome mutations of iPSCs were different from genotypes of cancer tissues." Why is that? What's the driver mutation in iPSCs? Many sections are not written with Standard English, such as "In contrast, genomes of all iPSC lines did not have some mutations that were genotypes of cancer tissues," (core tip). All the figure legends should be written in a concise manner.