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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 30133
Title: Dendritic cells engineered to secrete anti-Dc00502947 antibody augment cytotoxic T lymphocyte response against pancreatic cancer in vitro
Reviewer's code: 00502947
Reviewer's country: Australia
Science editor: Yuan Qi
Date sent for review: 2016-09-14 16:54
Date reviewed: 2016-10-12 20:03

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

COMMENTS TO AUTHORS

The authors present work on an interesting approach to enhance cytotoxic T cell responses against pancreatic cancer cells. The work appears to be novel. There are however several issues with this research and the manuscript. The English and scientific terminology throughout the manuscript needs major attention by the authors. The discussion tends to repeat what is in the Introduction. It is not clear whether the data presented are the mean+/-SD of triplicates of one experiment and this is representative of 3 experimental runs or the mean +/SD of three experiments. Please make this clear. In the statistics it should be made clear which post hoc test was used? I find the number of * in Fig 5 confusing. Can you draw lines across the columns and place the star(*) on these to indicating what is being compared as per Fig3? The western blots in Fig 2A is not acceptable some of these lanes look as if they come from different runs, lanes then cut and collected into the presented figur. You should show a blot which been used to run these together. Fig 4: It looks as if there is a mistake in Fig 4A. Have the Total RNA vs RNA tumour-antiDcR3 antibody been mixed up?

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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 30133
Title: Dendritic cells engineered to secrete anti-Dc03471272 antibody augment cytotoxic T lymphocyte response against pancreatic cancer in vitro
Reviewer's code: 03471272
Reviewer's country: Japan
Science editor: Yuan Qi
Date sent for review: 2016-09-14 16:54
Date reviewed: 2016-09-23 10:33

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	[ ] Minor revision
[ ] Grade E: Poor		[Y] No	[Y] Major revision
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		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

This manuscript has shown that dendritic cells engineered to secrete anti-DcR3 antibody can stimulate cytotoxic T lymphocyte responses against pancreatic cancer cells in vitro. It provided important contribution to development of immunotherapy for pancreatic cancers. The proposed method is convincing. However, the writing often lacks clarity and sharpness, and the Results and Discussion sections are poorly organized. The authors should remove ambiguities, repetition and confusion. In addition, there are some minor points that need to be addressed to make this manuscript suitable for publication: 1. It would be better to explain the underlying molecular mechanisms of weak antigenicity in pancreatic cancers. 2. The authors should explain how to obtain peripheral blood monocyte cells. 3. The authors should provide more detailed information about the pancreatic tumors and nonmalignant control tissues which they used for this study. 4. The manuscript would be improved if the authors confirm the effect of their method using dendritic cells obtained from several individuals. 5. The authors described "over 90% of the cultured primary tumor cells showed a DcR3-positive expression" in Figure 1A, but it seems unclear. 6. I suggest that the text

about previous studies be moved from the Discussion section to the Introduction section. 7. There are some typographical errors throughout the manuscript.

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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 30133
Title: Dendritic cells engineered to secrete anti-Dc00503118 antibody augment cytotoxic T lymphocyte response against pancreatic cancer in vitro
Reviewer's code: 00503118
Reviewer's country: United States
Science editor: Yuan Qi
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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	[ ] Minor revision
[ ] Grade E: Poor		[Y] No	[Y] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

The manuscript entitled "Dendritic cells engineered to secrete anti-DcR3 antibody augment cytotoxic T lymphocyte response against pancreatic cancer in vitro" by Chen et al. examines the effect of DC producing anti-DcR3 antibody on their ability to generate CTL response. Authors show that by engineering DC to produce anti-DcR3 antibodies they can augment superior CTL response. The reviewer`s concerns and comments are listed below: 1. Figure 1: DC are terminally differentiated cells, they do not proliferate, and short encounter with naive antigen specific T cells has been shown to be sufficient for optimum priming of CTL precursors. Authors claim that DC secreting anti-DcR3 antibody can generate superior anti-tumor T cell response. DcR3 has been previously shown to up-regulate of some co-stimulatory molecules but down-modulate others and modulate T cell response towards Th2 subtype (Hsu et al. Journal of Immunology, 2002). Therefore, they should include data showing co-stimulatory molecules and MHC class I and MHC class II molecules expression in DC with/without DcR3expression. 2. Figure 3: (a). There is minimal effect on cytotoxicity by anti-DcR3 producing DC in Fig. 3A. (b). Authors should show data on quantification

of CTL response generated, either by tetramer assay and/or by ELISPOT assay. (c). If authors claim of generating superior CTL response is true and it is minimal in quantitative terms, authors should re-stimulate primary CTL response generated under similar conditions as used for initial priming and see if they can generate superior antigen specific CTL response. Authors should also look for memory markers in such CTL. It has been shown that DcR3 can block apoptosis in Jurkat just like Fas-Fc antibody. Authors should make sure that the effect they are seeing in better cytolytic function is not because of blockade of AICD in CTL rather than better CTL response generation due to superior priming of CTL precursors by engineered DC. Authors should check AICD in CTL in presence and absence of engineered DC to rule that out. 3. Figure 4: Figure 4A labeling might not be correct as the data contradicts what is shown in Fig. 4B. 4. Figure 5: Authors show that CD8 T cells generated produce higher levels of IFN-gamma and CD4 produce higher levels of IL-4. Authors should include data showing complete cytokine production profile of CD4 T cells by including data showing IL-10, TGF-beta, IL-4 and IFN-gamma production in the same experiments. Dc3R has been shown to skew T cell response towards Th2 and Th2 biased CD4 T cells by producing IL-10 might inhibit CTL generation. Such data is essential to know engineered DC`s ability to generate superior CTL response in physiological scenario where CD4 and CD8 T cells are not separated.