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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
Manuscript NO: 36512
Title: Antifibrogenic effects of vitamin D derivatives on mouse pancreatic stellate cells
Reviewer's code: 00037961
Reviewer's country: United States
Science editor: Ya-Juan Ma
Date sent for review: 2017-10-10
Date reviewed: 2017-10-11
Review time: 1 Day

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[Y] Accept
[Y] Grade B: Very good	[Y] 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

This study compares the molecular effects of three different D-vitamins, vitamin D2, vitamin D3 and calcipotriol, in vitro in pancreatic stellate cells (PSCs) isolated from mouse pancreas. Fully activated cells were exposed to D-vitamins and were visualized for vitamin A containing lipid droplets by oil-red staining. Alpha-smooth muscle actin (α-SMA), a marker of PSC activation, was monitored by immunofluorescence and immunoblot analysis. Rate of DNA synthesis was quantified by (BrdU) incorporation assays. Real-time PCR was employed to monitor gene expression, and protein levels of interleukin-6 (IL-6) were measured by ELISA. Uptake of proline was determined using 18F-proline. Results show that sustained culture of originally quiescent PSCs induced cell proliferation, loss of lipid droplets and exhibition of stress fibers, indicating cell activation. All three D-vitamins diminished significantly expression of α-SMA and increased the storage of lipids. No such effects were observed when D vitamins were

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added to fully-activated cells, while incorporation of BrdU remained unaffected under both experimental conditions. Treatment of re-cultured PSCs with D vitamins was associated with lower expression of IL-6 and increased expression of the vitamin D receptor gene. There was no effect of D-vitamins on the expression of transforming growth factor-β1 and collagen type 1 (chain α1). The lowest uptake of proline, a main component of collagen, was observed in calcipotriol-treated PSCs. The authors conclude that the three D-vitamins inhibit, with similar efficiencies, activation of PSCs in vitro, but cannot reverse the phenotype once the cells are fully activated. Comment: This is an interesting study which shows that vitamin D exerts distinct effects on quiescent and activated PSCs in vitro. In quiescent PSCs, vitamin D prevents the exhibition of a myofibroblastic phenotype. In fully activated cells, vitamin D fails to induce a complete reversal of the myofibroblastic phenotype, but still exerts antifibrotic effects on PSCs by inhibiting uptake of proline and expression of interleukin-6. Three vitamin D derivatives, vitamin D2, vitamin D3 and calcipotriol,displayed very similar biological effects. The findings encourage a further evaluation of vitamin D effects in pancreatic cancer and chronic pancreatitis which are characteristic features of pancreatic fibrosis. Minor comments: Please reconcile the nonsignificance of the data of calcipotriol in Fig.6. A statement in this regard will be helpful to the readers. Also please provide a statement of what methodological differences contrasted the antiproliferative effects of vitamin D3 on a published report on murine PSC's? Finally the author's statement of recognizing the follow-up studies in animal models to evaluate the antifibrotic effects of vitmin D in vivo will be of great interest for future studies.

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Name of journal: World Journal of Gastroenterology
Manuscript NO: 36512
Title: Antifibrogenic effects of vitamin D derivatives on mouse pancreatic stellate cells
Reviewer's code: 01558248
Reviewer's country: Taiwan
Science editor: Ya-Juan Ma
Date sent for review: 2017-10-10
Date reviewed: 2017-10-18
Review time: 7 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
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[ ] Grade E: Poor		[Y] No	[ ] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

1.p4, Two decades ago, pancreatic stellate cells (PSCs) were..-->"Two decades ago" corrected in the end of this sentence. 2.p4. ..great detail (reviewed in[1])--> detail reported by xxx [1] 3.p5, Although they displayed slightly different molecular effects, the general efficiency of the three vitamin D derivatives was similar. --> This was results of your study or from reference? 4.p11,..reduced DNA synthesis rather slightly (data not shown). -->data not shown, how to prove? or you can neglect this points. the next "...too low for reproducible results (data not shown) 5. The section of Discussion--> need to add more discussion according to the points in the results in a different paragraph. 6.p13, .. In this regard, the applicability of 18F-proline as a molecular probe for positron emission tomography (PET) might be of particular interest. --> What you mean or you can delete this sentence because not related your manuscript. 7.p15, The section "Comment" not a normal format in a manuscript and delete it.